id #128000

Effect of testosterone treatment on leucocyte telomere length in men at high risk for type 2 diabetes mellitus.

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Aims

Lower testosterone concentrations in older men are associated with poorer health outcomes, but underlying mechanisms, including possible links to the ageing process, remain unclear. We tested the hypothesis that testosterone treatment modulates leucocyte telomere length, a postulated marker of biological ageing, in overweight men with elevated blood glucose concentrations.

Methods

This was a pre-specified secondary analysis of Testosterone for the Prevention of Type 2 Diabetes Mellitus (T4DM), a randomised, placebo-controlled trial in 50-74-year-old men with waist circumference ≥95 cm and impaired glucose tolerance or newly diagnosed type 2 diabetes mellitus. Men received intramuscular testosterone undecanoate (1000 mg) every three months, or placebo, for two years with a background lifestyle program. Whole blood samples were collected at baseline and two years, and stored frozen at -80ºC until retrieval for extraction of DNA and measurement of telomere length. Leucocyte telomere length was assayed by multiplex quantitative polymerase chain reaction and expressed as relative telomere length (rTL), a ratio of telomeric DNA to β-globin, a single-copy control gene (T/S ratio).

Results

Participants were 60±6 years-old (mean±SD), 38% had BMI 30-34.99 kg/m^2 and 44% ≥35 kg/m^2. Mean rTL at baseline was 1.63±0.27 in testosterone-treated men (N=375) and 1.61±0.28 in placebo-treated men (N=345). At two years, mean rTL were 1.61±0.28 and 1.58±0.29, respectively. Change in rTL after 2 years treatment was -0.02±0.15 in testosterone-treated, and -0.03±0.12 in placebo-treated men. Adjusting for baseline values there was no effect of testosterone treatment on rTL at two years (mean difference 0.01 [95% CI, -0.01 to 0.03], *P*=0.24). Results were similar for rTL change at two years from baseline.

Conclusion

These rTL results in overweight middle-aged to older men do not support the hypothesis that testosterone modulates biological ageing. Larger studies with longer treatment durations might provide further information.

id #127745

Long-term effects of bariatric surgery on lifestyle behaviours

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Obesity carries significant health risks. Although bariatric surgery is an effective treatment for severe obesity, its long-term effects on diet, appetite and physical activity remain unclear[1-3].

This prospective study followed 57 adults over 36 months following Roux-en-Y gastric bypass (RYGB, n=7), sleeve gastrectomy (SG, n=21), laparoscopic adjustable gastric banding (LAGB, n=11) and dietary intervention (Diet, n=18). Dietary intake was recorded using 3-day food diaries, appetite measured via visual analogue scales and physical activity quantified by validated questionnaires covering light (<3.0 METs), moderate (3.0–6.0 METs), and vigorous (>6.0 METs) exercise. Within-group changes were analysed using Wilcoxon signed-rank tests.

At 36 months, SG and RYGB groups showed sustained weight loss (-30.6 kg and -28.5 kg, p<0.02), respectively, whereas LAGB induced early weight loss (-12.6 kg at 6 months, p<0.01) followed by partial regain. Diet lost weight initially (-2.7 kg at 12 months, p<0.01) returning to baseline by 24 months.

Energy intake decreased sharply after surgery in SG (-68%) and RYGB (-64%) at 1 month (p<0.01), with sustained reductions (36-40%) at 36 months. However, fat intake declined significantly in SG (35% to 28%) and RYGB (34.5% to 25.0%), while protein intake

increased in both (up to 25.5% and 32.0%, respectively) for 3 months only, with no sustained difference after 12 months. RYGB showed reduced carbohydrate intake and increased calcium intake (up to 1428.0 mg) at 3 years. LAGB did not change macronutrient intake beyond 12 months.

Physical activity increased significantly in RYGB (light: +165min/day; moderate: +112.5min/day at 36 months) and up to 24 months in SG. Appetite suppression persisted up to 24 months after RYGB and 36 months after SG ($p<0.01$).

SG and RYGB improved weight, intake, and appetite, with RYGB showing the greatest physical activity gain. LAGB showed less durable effects, highlighting the need for ongoing nutritional and behavioural support.

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id #128513

Replacing protein with carbohydrate or fat in infancy is associated with lower body weight in early childhood

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Abstract

High intakes of total protein and animal-sourced protein in infancy have been identified as risk factors for childhood obesity (1). However, it remains unclear whether reducing protein intake in infancy through isocaloric replacement with fat or carbohydrate influences body weight development. Thus, this study examined the association of substituting protein with fat or carbohydrate intake, and the substitution of protein subtypes at 9 months of age with body weight outcomes at 5 years of age. Data of 345 children from the Melbourne InFANT Program (2) who completed the 9-month and 5-year follow-ups were analysed. Dietary intake at 9 months was collected using three 24-hour recalls. Body mass index (BMI) z-score was measured at 9 months and 5 years of age. Multivariable linear and logistic regression models with adjustment for potential confounders examined the associations between macronutrient and protein subtype substitutions at 9 months and changes in BMI z-score or overweight status at 5 years. Substitution of 5%E or 100kJ protein intake with carbohydrate intake at age 9 months was associated with a 0.16-unit (95% CI: -0.29, -0.02) or 0.10-unit (95% CI: -0.18, -0.02) decrease in BMI z-score at 5 years of age. Similarly, replacing 5%E or 100kJ of protein intake with fat intake was associated with a 0.14-unit (95% CI: -0.27, -0.004) or 0.10-unit (95% CI: -0.18, -0.01) decrease in BMI z-score. No evidence of associations was found between substitution of protein with fat or carbohydrate intake and overweight status ($P>0.05$). Replacement of animal protein with plant or dairy protein was also not significantly associated with BMI z-score or overweight status. The present study supports the need to discourage excessive protein intake during infancy. This information will be valuable for informing the refinement of macronutrient intake recommendations during infancy and infant feeding guidelines.

id #129537

Inhibin deficiency promotes adiposity in female mice

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Ovarian inhibins, members of the transforming growth factor – beta superfamily, are classically known for their abilities to constrain follicle stimulating hormone (FSH) production at the pituitary. Roles for inhibins beyond the pituitary are poorly understood owing to knockout models developing pathological increases in activins, triggering gonadal tumour growth and lethal body wasting. We recently generated InhaR233A/R233A mice which produce bioinactive inhibin, but importantly, do not display pathological increases in circulating activin concentrations. Adult female InhaR233A/R233A mice display a 2-3 fold elevation in serum FSH concentrations and a consequent enhancement in ovulation rates. Interestingly, compared to wildtype controls, female InhaR233A/R233A mice display exacerbated body weight increase in response to high fat diet feeding, independent of food intake. Increased body mass was attributed to hypertrophy of white adipocytes and associated with changes in cellular lipolysis. Further investigations have studied the actions of unopposed activin signalling on adipose tissue and the contributions of sex hormones to the phenotype. We report the first evidence to suggest that loss of inhibin function may alter adiposity specifically in females. Significantly, these findings may suggest that inhibin withdrawal associated with ovarian inactivation in women may contribute to adiposity.

id #128258

Beyond the Scale: Perspectives on Comprehensive Obesity Management in a Tertiary Multidisciplinary Service

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"After the intensive phase, I would have liked a meeting twice a week. Once a fortnight, but twice a week. Just so that you can have that extra group, encouragement while you're going through step down"

"If you didn't lose weight, everyone was still very supportive. They would ask you 'oh what's been happening?'. So straight into finding reasons and help. Yeah, which was good. You need that as well, reflecting back"

This study explores the lived experiences of individuals participating in the Tertiary Obesity Multidisciplinary Service, with a focus on the perceived value and impact of the support received beyond weight loss outcomes.

A qualitative approach was employed to examine patient experiences within the Tertiary Obesity Multidisciplinary Service (TOMS), which delivers integrated care through a group-based intervention for individuals with complex obesity. Thirteen participants took part in semi-structured interviews, which were transcribed and analysed in NVivo using Braun and Clarke's (2006) theoretical thematic analysis framework.

While participants initially engaged with TOMS for chronic disease management and surgical preparation, they reported that the most valued aspects of the program were the supportive structures, multidisciplinary team involvement, peer support, and external accountability. The program's individualised and tailored care facilitated meaningful behaviour change, improved food literacy, and led to the development of sustainable healthy habits. Participants reported challenges in the stepdown phase due to reduced frequency of contact, which led to feelings of isolation and a loss of momentum. Participants suggested extended support and longer follow-up would be beneficial for long-term behaviour change and highlighted the importance of emotional and social support and motivation. Overall, participants described feeling happier, more energetic, and socially connected.

Findings suggest that multidisciplinary group programs like TOMS offer significant benefits beyond weight loss, particularly in promoting behavioural change and providing psychosocial support. These insights underscore the importance of incorporating patient perspectives into program design and highlight the value of integrated, person-centered care in managing complex obesity.

id #129539

Lipid lowering therapy in children and adolescents: who, when and what?

Andrew Martin[1]

1. Perth Children's Hospital, Nedlands, WA, Australia

The presentation will commence with a brief overview of lipid screening in childhood and recognition of lipid profiles.

The focus will then be on the role of lipid lowering therapy for children and adolescents, to prevent cardiovascular disease in later life. The monogenic disorders familial hypercholesterolaemia (FH) and familial chylomicronaemia syndrome (FCS) will serve as models to understand the approach to managing severe hypercholesterolaemia and severe hypertriglyceridaemia in childhood.

Current and emerging pharmacological therapies to reduce total and low-density lipoprotein-cholesterol (LDL-C) and triglycerides (TG) will be discussed.

The presentation will end by considering the options for children and young people with obesity and abnormal lipid profiles.

id #130565

Calcium shapes metabolic control of epigenetic reprogramming following fertilization to impact offspring health

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Calcium (Ca^{2+}) signals initiate embryo development at fertilization and are frequently disrupted in human assisted reproduction, which is associated with metabolic abnormalities in children. In mice, excess or inadequate Ca^{2+} signals at fertilization impair embryo development and alter adult metabolism, but the mechanisms are unknown. In this lecture, I will describe our work showing that excess Ca^{2+} signaling in one-cell mouse embryos alters the production of epimetabolites required for nuclear reprogramming and zygotic genome activation (ZGA). Mechanistically, excess Ca^{2+} increases pyruvate dehydrogenase activity, increasing acetyl-CoA production and decreasing lactate and presumably lactyl-CoA availability. These changes disrupt epigenetic marks including H3K27ac and H3K18la, impair ZGA by reducing RNA polymerase I activity, and compromise preimplantation embryo development. Exogenous lactyl-CoA rescues H3K18la, ZGA, and embryo development. These studies demonstrate that Ca^{2+} dynamics drive metabolic regulation of epigenetic reprogramming at fertilization, resulting in long-term offspring metabolic abnormalities.

id #128264

The new zinc-based contraceptive: advances in mechanism and delivery

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In response to urgent calls for more non-hormonal contraceptive options our team has tested a zinc-containing intrauterine hydrogel, to address the need for long-acting reversible protection from pregnancy. Our preliminary work has shown that zinc alone provides 100% contraceptive efficacy and reversibility in rats by causing zygote arrest. To determine the effective dose, mouse embryos were exposed to zinc and copper across a range of concentrations *in vitro* from embryonic day 1. Only the highest concentration of copper significantly decreased blastocyst development (69%), whilst zinc significantly inhibited embryo development in a dose dependant manner for all treatments. The highest concentration of zinc resulted in a 97% decrease in embryo development. However, mid to late

2-cell embryos treated with the same high concentration showed no significant difference in blastocyst development compared to the control. This further defines the window of effectiveness to between the zygote and the very early 2-cell stage. Unlike copper treated embryos, embryos treated with low concentrations of zinc also exhibited a significantly decreased rate of attachment to cultured human endometrial cells compared to controls. This finding suggests the possibility that a zinc contraceptive acts via a dual MOA, impacting the adhesive capacity of the embryo before implantation. Further we have demonstrated that zinc can be loaded into a hydrogel-type matrix, then gradually released into artificial uterine fluid (AUF) over an extended period. We loaded the matrix with zinc and submerged it in AUF at 37°C for 19 days. Zinc was successfully integrated into the matrix with no compromise to stability and released zinc into AUF without matrix degradation. This establishes the potential of a new delivery system, greatly improving the insertion procedure of an IUD and minimising pain. Our non-hormonal contraceptive device has the potential to transform family planning, addressing the key limitations of current methods.

id #128521

Spatial profiling identifies novel biomarkers in aggressive pituitary neuroendocrine tumours

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Aims

Aggressive and metastatic pituitary neuroendocrine tumours (PitNETs) are associated with significant morbidity and mortality and progress despite treatment with standard therapies. This study aimed to investigate the spatially defined gene expression of aggressive and metastatic PitNETs to identify prognostic and therapeutic biomarkers.

Methods

Aggressive and non-aggressive Pit-1, SF-1, T-Pit, and co-expressing Pit-1 and SF-1 pituitary neuroendocrine tumours were analysed using Nanostring GeoMx Digital Spatial Profiling. Tissue sections were stained with Pan-cytokeratin (PanCK), CD45, CD68 and the nuclear stain SYTO13. Regions of interest (ROIs) were selected to represent tumour areas with and without immune cell infiltrate. Gene expression was assessed using the GeoMx Human Whole Transcriptome Atlas. Samples were sequenced on a NextSeq 2000 and data processed with the GeoMx DSP software. Two normal pituitary samples were included and 33 pituitary tumours samples including aggressive Pit-1 (n=6), non-aggressive Pit-1 (n=6), aggressive SF1 (n=1), non-aggressive SF1 (n=5), non-aggressive SF1/Pit1 (n=6), aggressive T-Pit (n=3) and non-aggressive T-Pit (n=6).

Results

Aggressive PitNETs had reduced expression of tumours suppressor genes (*DIRAS, DAPK1, KNDC1, COX7A1, NEBL* and *KANK1*), and increased expression of oncogenes and immune-related genes (*SLC38A2, ANXA1, TGFBR2, HLADQA1 and STAT6*) compared to non-aggressive PitNETs. The differential gene expression of aggressive versus non-aggressive PitNETs varied within tumours in ROIs with increased compared to reduced immune cell infiltrate. Whilst a subset of genes were consistently upregulated (*GCH1, KPNA2* and *RNF157I*) and downregulated (*SEZ6L2, DZIP3, PODXL2, CTNND1*) in both aggressive lactotroph Pit1 and T-Pit PitNETs, the majority of differentially expressed genes were unique to each PitNET type. This suggests that although some molecular mechanisms are shared, the biology of aggressive behaviour differs between PitNET types.

Conclusions

PitNETs exhibit molecular intratumoural heterogeneity and distinct molecular profiles between tumour types. Differential gene expression between aggressive and non-aggressive PitNETs may present novel prognostic biomarkers and therapeutic targets.

id #128524

Enhanced neonatal viability in equine cloning using bone marrow-derived mesenchymal stem cells as nuclear donors

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Incomplete nuclear reprogramming remains a major limitation in somatic cell nuclear transfer (SCNT), often due to persistent epigenetic marks such as aberrant DNA methylation patterns that impair gene expression and compromise embryonic viability. In this context, highly plastic cells such as mesenchymal stem cells (MSCs) have emerged as promising nuclear donor candidates for improving cloning outcomes in horses [1]. This study compared the efficacy of bone marrow-derived mesenchymal stem cells (BM-MSCs) and adult dermal fibroblasts (ADF) as nuclear donors in equine SCNT. Embryonic development in vitro and reproductive success in vivo were evaluated. A total of 1,138 equine oocytes were collected via ovum pick-up (OPU) [2] over 60 sessions (703 for BM-MSCs; 435 for ADF). Day 7 blastocysts were produced by conventional SCNT procedures [2] and transferred individually to

recipient mares at Day 4 post-ovulation (96 for BM-MSCs; 42 for ADF). No significant differences were observed in the blastocyst formation rates (BM-MSCs: 33.65% vs ADF: 28.55%), Day 14 pregnancy rates (BM-MSCs: 55.21% [53/96] vs ADF: 57.14% [24/42]) or subsequent foaling rates (BM-MSCs: 41.50% vs ADF: 50.00%). Remarkably, 100% (22/22) of the foals from BM-MSC-derived embryos were born normal and healthy, whereas 75% (9/12) of those from ADF-derived embryos were viable ($P<0.05$). Furthermore, several surviving foals from the ADF group exhibited neonatal abnormalities, including minor limb deformities and umbilical enlargement, which required veterinary intervention. In conclusion, the use of BM-MSCs as nuclear donors resulted in better foaling outcomes and fewer postnatal complications, supporting their application as the preferred alternative to somatic fibroblasts in equine SCNT programs.

1. [1] Olivera R, Moro LN, Jordan R, Pallarols N, Guglielminetti A, Luzzani C, Miriuka SG, Vichera G. Bone marrow mesenchymal stem cells as nuclear donors improve viability and health of cloned horses. Stem Cells Cloning 2018; 11: 13-22. [2] Cortez JV, Hardwicke K, Cuervo-Arango J, Grupen CG. Cloning horses by somatic cell nuclear transfer: Effects of oocyte source on development to foaling. Theriogenology 2023; 203: 99-108.

id #128272

MicroRNA and CA-125 profiling in vaginal swab-derived extracellular vesicles for ovarian cancer diagnostics

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2. University of Otago, Wellington

Ovarian cancer (OC) has one of the poorest survival rates of gynaecological malignancies, due to absence of effective screening tools and reliable biomarkers for early detection. However, extracellular vesicle-encapsulated microRNAs (miRNAs) have recently emerged as promising biomarker candidates. While small EVs of exosomal size (30–150 nm) have been isolated from cervicovaginal secretions in endometriosis [1], their use in OC diagnostics remains unexplored. This study investigates whether EVs can be isolated from vaginal swabs collected from OC patients and whether these EVs contain candidate early OC-associated miRNAs previously identified by our group [2].

Matched serum and vaginal swab samples were collected from patients across varying OC stages (n=18). Swab samples were collected into 1mL 1xPBS pH 7.4 supplemented with 25 mM trehalose and HEPES, cleared via differential centrifugation and applied to a qEV1 Gen2 35 nm size exclusion column (Izon Science) to isolate EVs. EVs were characterised using established protocols according to MISEV2024 guidelines. Expression of identified candidate early OC-associated miRNAs (miR-200a/b/c-3p, miR-375-3p and miR-42) were assessed in serum and swab-derived EVs using qPCR. CA-125 concentration, in whole and EV-associated serum in parallel with vaginal-swab derived-EVs, was quantified via ELISA (Human CA125 DuoSet ELISA, R&D Systems) from matched patient samples. Diagnostic potential was assessed using receiver operating characteristic (ROC) curve analysis, comparing miRNA markers and EV CA-125 with conventional CA-125 serum levels.

Preliminary data suggests comparable CA-125 concentrations between whole serum and serum derived-EVs, with the expectation this translates to vaginal swab derived-EVs. Future analyses will identify EV-derived candidate biomarker miRNA expression and the success of vaginal-swab EV characterisation.

This is one of the first studies to assess feasibility of vaginal swab-derived EVs as a non-invasive biospecimen for OC biomarker discovery. Our findings will highlight the translational potential of vaginal EVs in developing novel early detection strategies for ovarian cancer.

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id #130577

Pathways in germline cyst breakdown and primordial follicle formation

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The ovary is the first organ to age, culminating in a life stage known as menopause. This event not only marks the end of fertility, but it also launches drastic fluctuations in systemic health that then accelerates aging of other organs. Remarkably, the timeline for ovarian aging is destined before birth in the form of the ovarian reserve, which is defined by the number of primordial follicles. Formation of too few or early demise of primordial follicles hastens ovarian aging leading to early menopause and premature ovarian insufficiency. The development of the ovarian reserve occurs during fetal development in mammals and across animal phyla. Initially, oocytes exist in clusters called germline cysts. At midgestation in humans, and late in gestation and shortly after birth in mice, germline cyst breakdown occurs, which includes a massive transfer of cytoplasmic cargo, including organelles such as Golgi, from donor oocytes to neighboring oocytes via intercellular bridges. Donor oocytes die while acceptor oocytes grow and become surrounded by pre-granulosa cells to form primordial follicles. Previously, we discovered that expression of two Iroquois family homeobox transcription factors, IRX3 and IRX5, direct oocyte—pre-granulosa cell interactions critical to establishing robust primordial follicles that are

equipped to transition into mature follicles with healthy oocytes. Additional studies have uncovered that IRX3/5 interact with cytoskeletal components to compartmentalize the oocyte cytoplasm. Further, live imaging studies exposed oocyte membrane and cytoplasmic infrastructure that highlight dynamic movement and interactions between neighboring oocytes and between oocyte and pregranulosa cells. Take together, these discoveries expose an early view of the innerworkings of oocyte machinery and cell-cell interactions that culminate in formation of nascent primordial follicles and establishes the ovarian reserve.

id #130833

Soma-germline communication in control of the sperm epigenome

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It is increasingly apparent that ancestral environmental conditions can affect phenotypes of future generations. In particular, a great deal of evidence indicates that parental exposure to stressors – ranging from social defeat to suboptimal diets to various environmental toxins – can all have significant effects on metabolism and behavior in children. In rodents, we and others have shown that *paternal* exposures can affect phenotypes in offspring, and there is some support for male germline effects in human epidemiological studies as well. The mechanistic basis by which paternal experiences are transmitted to the next generation remains unclear. A burgeoning literature has documented a wide variety of exposure effects on the sperm epigenome, with diets, stress, and various toxins reported to alter sperm RNAs, DNA modifications, and genome packaging. Our ongoing research seeks to address the unanswered question of how paternal experiences control the molecular contents of sperm. Answering this question is essential if we hope to understand why some exposures impact offspring traits, while others do not. In other words, we seek to define the tissues responsible for “choosing” environmental conditions – presumably those with predictive value regarding future environments – about which to inform offspring. Dietary and other exposures could impact the sperm epigenome via a wide range of mechanisms, from direct signaling in the developing germline through complex webs of inter- tissue signaling systems that link paternal sensing of environmental conditions to altered molecular contents of mature spermatozoa. I will discuss our latest efforts to develop systems for rigorous analysis of tissues responsible for controlling the sperm epigenome, and to explore signaling pathways in reproductive tissues that drive molecular changes in sperm in response to more naturalistic exposure paradigms.

id #130578

Reproductive Genetics on Demand: Inducible in vivo models provide clinically relevant platforms to uncover mechanisms of infertility and reproductive disorders.

Evdokia Dimitriadis[1]

1. The University of Melbourne, Melbourne, VIC, Australia

Successful implantation and pregnancy rely on highly dynamic remodeling of the uterus and coordinated signaling with the embryo. Failures in these processes are a leading cause of infertility, yet conventional genetic models have limited ability to reflect human disease. Most alter gene expression from conception, whereas in women, molecular disruptions often arise later in reproductive life. I present a novel **inducible, tissue-specific genetic model** that we developed to enable precise temporal control of gene expression in the uterus with applications in other reproductive tissues including placenta. This approach preserves normal embryonic development while allowing functional interrogation of key pathways during the peri-implantation window and beyond. Unlike traditional knockout strategies, this system can be applied broadly to investigate any gene in reproductive tissues, offering a versatile platform to uncover mechanisms of infertility, implantation failure, and pregnancy complications. This innovation represents a powerful step toward more realistic modeling of human reproductive disorders and accelerates discovery of potential therapeutic targets.

id #130834

Subdermal estradiol implant therapy in gender affirming hormone therapy regimens

Brendan Nolan[1]

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Presentation abstract coming soon.

id #130579

The Influence of Early Moderate Prenatal Alcohol Exposure and Maternal Diet on Offspring DNA Methylation: A Cross-Species Study

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Alcohol consumption during pregnancy can impact genome regulation in developing offspring, but research findings have been inconsistent. Our study utilized a murine model of short-term, moderate prenatal alcohol exposure (PAE) that mimics typical patterns

of alcohol use in human pregnancies. We found that even early moderate PAE was enough to cause site-specific DNA methylation changes in newborn pups, though it didn't alter behavioral outcomes in adult mice.

Using whole-genome bisulfite sequencing on neonatal brain and liver tissue, we observed a stochastic and mostly tissue-specific effect on DNA methylation. Some of these effects might even originate as early as gastrulation. Replication studies in human cohorts with Fetal Alcohol Spectrum Disorder (FASD) suggested that some of these effects were metastable in genes associated with disease-relevant traits, including intelligence, facial morphology, educational attainment, autism, and schizophrenia.A key finding from our murine model was that a maternal diet high in folate and choline protected against some of the damaging effects of early moderate PAE on DNA methylation.

These results show that early moderate alcohol exposure can affect fetal genome regulation even without visible phenotypic changes and highlight the potential of maternal dietary interventions as a preventative strategy. While our findings require cautious interpretation due to the study's small sample size and potential confounders, they support the idea that alcohol-induced epigenetic disruption may be partly due to interference with one-carbon metabolism.

id #130835

Implementation of Evidence-based Interventions for Childhood Obesity

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Childhood obesity remains a critical public health issue in the United States, with recent estimates indicating a continuous rise in prevalence such that 1 in 5 children are affected by obesity and 1 in 3 by overweight. In 2023, the American Academy of Pediatrics (AAP) released its first clinical practice guidelines for the evaluation and treatment of children and adolescents with obesity. As one of the guideline's co-authors, Dr. Sharifi will delve into the AAP guidelines, illuminating key recommendations and the barriers to translating these guidelines into practice. The discussion will explore the principles of implementation science to evaluate and overcome these barriers, focusing on systematic approaches to enhance the adoption of the guidelines.

Dr. Sharifi will present findings from her team's multi-site trials, which investigate the implementation of evidence-based interventions for childhood obesity. This includes both intensive health behavior and lifestyle treatments endorsed by the CDC and the promotion of guideline adoption in pediatric primary care through the use of electronic health record-based clinical decision support tools. The presentation will highlight successful strategies from these trials, such as formative evaluations and user-centered designs that tailor interventions to diverse contexts. Additionally, the presentation will cover mixed methods evaluations with hybrid trial designs, examining both effectiveness and implementation outcomes such as reach and costs.

Through these efforts, the aim is to bridge the gap between guideline recommendations and their adoption into routine care delivery, thereby promoting equitable access to effective childhood obesity interventions.

Attendees are invited to gain insights into the latest US clinical guidelines for pediatric obesity, implementation research methods, practical solutions for primary care settings, and collaborative efforts to enhance the health and well-being of children through evidence-based obesity management.

id #130836

Addressing adverse pregnancy outcomes across the continuum

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One in 5 pregnancies experiences an adverse outcome, the most devastating of which is stillbirth. Current approaches to reducing stillbirth focus on preventative care at the end of pregnancy. While gains are being made in reducing the rates of term stillbirth, these approaches fail to target the 85% of stillbirths that occur in the preterm period and completely ignore pregnancy loss that occurs before 20 weeks. Stillbirth is also not a condition, but rather the result of a number of conditions and the product of a broader interplay of individual, biological, structural, cultural and social factors. The underlying aetiologies of stillbirth, miscarriage, preterm birth, fetal growth restriction and preeclampsia overlap and are generally attributed to placental dysfunction; the origins of that poor placental function are not fully understood. The endometrial environment into which the embryo implants and the placenta develop is fundamental to establishing the trajectory of pregnancy, yet our understanding of the endometrium's role has been hampered by the inability to study it non-invasively. The study of menstrual fluid and menstruation has the potential to overcome this bottleneck, opening up new avenues to better understand and prevent adverse pregnancy outcomes across the continuum.

id #128279

Cafeteria diet exposure, not propensity for weight gain, impacts composition of the gut microbiota of rats: a within laboratory meta-analysis of 12 studies

Margaret J Morris[1], **Shyam Bhagavata Srinivasan** [1], **Michael D Kendig**[1, 2], **Kyoko Hasebe**[1], **Nadeem O Kaakoush**[1], **Sarah-Jane Leigh**[1]

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2. School of Life Sciences, University of Technology, Sydney, NSW, Australia

Aims: Preclinical studies have implicated gut microbiome composition in body weight control, but translatability of finding to humans remains uncertain, due to methodological differences in assessing relationships between diet induced obesity and microbiota. We performed an internal meta-analysis to determine whether inter-individual microbiota differences contribute to individual differences in diet-induced obesity proneness, defined by relative weight gain in response to a high-fat, high-sugar 'cafeteria' diet.

Methods: We collated faecal microbiome data from 12 studies using our validated model of diet-induced obesity (total 208 male and 74 female Sprague-Dawley rats fed chow (control) or cafeteria diet, study length from 3.5 to 13 weeks) and determined whether gut microbiota alpha diversity and composition differed between obese-prone and obese-resistant rats, upper and lower tertiles, based on percentage weight gain.

Results: We found consistent effects of cafeteria diet exposure on the gut microbiota, with marked changes in overall composition, and reduced gut microbial richness, Shannon's diversity index and gut microbial evenness. Furthermore, specific microbial genera previously associated with obesity, such as *Bacteroides* and *Blautia*, were enriched by cafeteria diet. Critically, alpha diversity measures and gut microbiota composition did not differ between obese-prone and obese-resistant rats in either diet group.

Conclusions: In rats, microbiota composition is substantially altered by cafeteria diet, but these changes are unrelated to resultant degree of weight gain. Our work suggests that microbiota-targeted interventions are unlikely to reduce diet-induced weight gain or adiposity.

id #130839

Liver-derived extracellular vesicles improve whole-body glycaemic control via inter-organ communication

Matthew Watt[1]

1. Monash University, Clayton, VIC, Australia

Small extracellular vesicles (EVs) are emerging as crucial mediators of inter-tissue communication. In this presentation, we will describe our recent work which demonstrates that liver-derived EVs play a pivotal role in acute regulation of whole-body glycaemic control in mice. We observed that hyperglycaemia triggers increased secretion of liver EVs into the circulation. These EVs enhance glucose effectiveness and insulin secretion through direct signalling to skeletal muscle and pancreas, respectively. Notably, this acute blood glucose lowering effect is preserved in both healthy and obese mice with metabolic-dysfunction associated liver disease (MASLD), despite significant remodelling of the liver-derived EV proteome in obesity. The efficacy of this mechanism was further validated using liver EVs from humans with and without progressive MASLD, suggesting a broad functional conservation of liver EV signalling across species and potential therapeutic applications. Our findings unveil a novel endocrine signalling pathway whereby liver EVs act on peripheral tissues to restore euglycaemia in the postprandial state, offering new insights into metabolic regulation and potential avenues for treating metabolic disorders.

id #130840

Harnessing the power of hepatokines for therapeutic gain

Matthew Watt[1]

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Obesity is a key risk factor for metabolic-dysfunction associated liver disease (MASLD) and type 2 diabetes. This presentation explores the intricate relationship between these conditions, focusing on the role of hepatokines, which are proteins secreted by the liver. Recent evidence suggests that dysregulated hepatokine secretion from fatty, inflamed livers may contribute to metabolic dysfunction in other tissues. Mass spectrometry proteomics studies have revealed the extensive number of hepatokines and their alterations in obesity and MASLD, and subsequent and subsequent studies using metabolic tracers have advanced our understanding of endocrine regulation in health and disease. This research has also identified potential targets for diagnostics and therapies. The talk will examine the biology of hepatokine secretion in health and disease, proposing that whilst hepatokine concentrations are often insufficient to counteract the lipid and inflammatory burden in obesity and MASLD, understanding these alterations could lead to novel therapeutic approaches. We will explore the potential of reintroducing specific hepatokines at pharmacological doses as a strategy to exploit this natural biology for treating metabolic disorders.

id #128281

From Crisis to Coordination: Impact of a Structured Obesity Treatment Program on Health Service Utilisation

Andrea Cawte[1, 2], **William Beningfield**[1, 3], **Helen D'Emden**[1, 2], **Caitlin Merz**[1, 4], **Scott Ruddell**[1, 5], **Matthew Seymour**[1, 6], **Keren Singh**[1], **Gemma Woodruff**[1, 4], **Abby Yu**[1, 4], **Robin Hay**[1, 2], **Helen MacLaughlin**[1, 2, 7]

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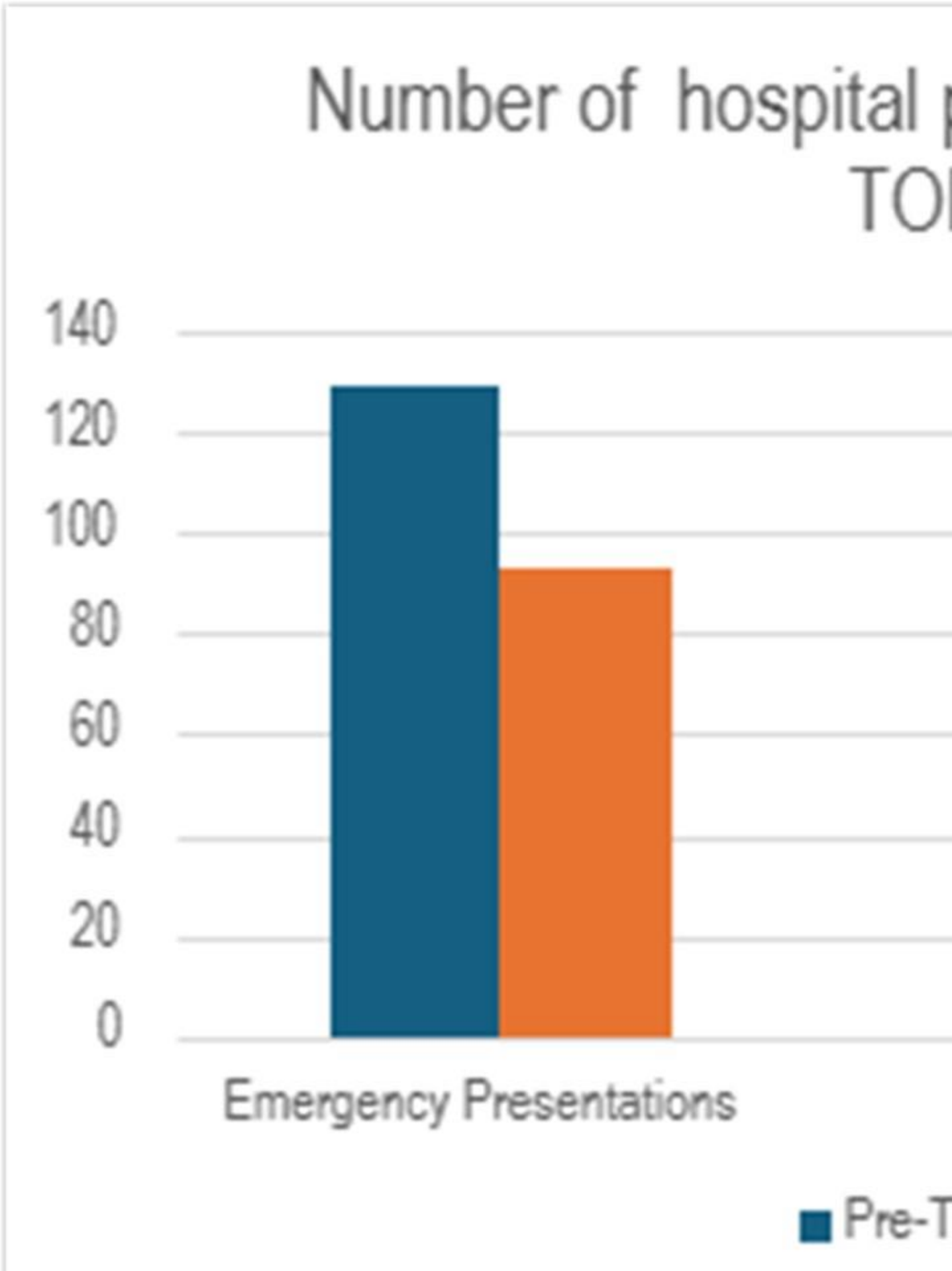
Number of hospital
TO
140
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Emergency Presentations
Pre-T

Evaluating a 12-month, three-phase, rapid weight-loss and weight stabilisation, multidisciplinary service (TOMS) for efficiencies of care for patients living with complex obesity.

Participants commencing in the TOMS program from January 2021 to May 2023 had tertiary healthcare occasions of service (OOS) recorded for the 12-month period prior to, and 12-month period post program completion. OOS included emergency presentations, admissions, bed days and outpatient appointments. For these outcome measures, incidence ratios (IR) were calculated pre and post TOMS. Counts of emergency and outpatient care for specific conditions and allied health specialties were compared using McNemar's test.

A total of 119 patients commenced TOMS during the study period; median BMI 46.4kg/m2 (40.5-54.8kg/m^2). Emergency presentations reduced by 28% (IR=0.72) from 129 to 93 post-TOMS. Of these, total respiratory presentations (including asthma) reduced by 20.7% (95%CI 12.2, 29.2) and asthma presentations reduced by 29.7% (95%CI 21.8, 37.7). Inpatient admissions decreased from 125 to 109 post-TOMS, a 13% reduction (IR 0.87), total bed days decreased by 25% (IR 0.75) from 484 to 366 after TOMS. Total outpatient appointments of 1759 pre- and 1248 post-TOMS, decreased by 28% (IR 0.72), including a 35.9% (95%CI 33.9-37.9%) decrease in diabetes appointments. Dietetics, pharmacy and physiotherapy appointments reduced by 28.8% (95%CI 26.6, 30.9), 35.0% (95%CI 33.0, 37.0) and 31.7% (95%CI 29.6, 33.8) respectively post-TOMS. Psychology appointments increased by 34.6% (95%CI 32.7, 36.5) and surgical outpatient appointments increased by 35.2% (95%CI 33.4, 37.2) post TOMS.

TOMS participation was associated with reduced overall healthcare utilisation, with greater use of psychology and surgical appointments post-TOMS indicating improved access to care in these areas. Future research could calculate the health economic benefits of TOMS.

id #128282

Hip and Vertebral Fractures in Young Adults Presenting to a Large Tertiary Health Service

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	Hip Fractures (86)
Risk factors for bone loss	**MTF 57 (66.3%)**
Malnutrition	13 (22.8%)
Epilepsy/seizure	9 (15.8%)
Liver cirrhosis	5 (8.8%)
Type 1 Diabetes Mellitus	4 (7.0%)
Type 2 Diabetes Mellitus	4 (7.0%)
Limb Weakness	4 (7.0%)
CKD V – Dialysis	3 (5.3%)
Thyroid disorder	2 (3.5%)
Cancer	1 (1.8%)
Glucocorticoids	3 (5.3%)
Antiepileptics	7 (12.3%)
Antidepressants	9 (15.8%
Opioids	4 (7.0%)
Benzodiazepines	3 (3.5%)
Current Smoker	21 (36.8%)
EtOH Excess	17 (29.8%)

Minimal-trauma fractures (MTF) in Young Adults (YA; aged 18–50 years) are uncommon. The associated frailty and long-term impact are under-recognised (1,2). This study characterises YAs presenting with hip and/or vertebral fractures to a tertiary health-network.

YAs presenting with MTF or high-energy fractures (HEF) of the hip or vertebrae to Western Health between January 2016 to December 2023 were identified using ICD-10AM codes. Data including patient demographics, injury-mechanism, comorbidities, medication exposures, bone densitometry results, metabolic bone clinic attendance and osteoporosis therapy were extracted from electronic medical records to be analysed.

86 YAs with hip fractures and 277 with vertebral fractures were eligible for inclusion. MTF predominated (66.3%, 57/86) in YAs with hip fractures (mean age 40.6±7.4, 61.4% males) while only 19.9% (55/277) of vertebral fractures (mean age 38.6±9.1 years, 47.3% males) were MTF. Both hip (77.2%, 44/57) and vertebral (74.5%, 41/55) MTFs had a high prevalence of comorbidites and medication exposures increasing risk for bone loss (Table 1). There were no documented risk factors in 58.6% (17/29) of hip and 70.7% (157/222) of vertebral HEF YAs. Only 29.8% (17/57) of hip MTF YAs and 18.2% (10/55) vertebral MTF YAs had bone densitometry performed, with 58.8% (10/17) and 60% (6/10) demonstrating low bone mass, respectively. There were 11 deaths (9.8% 11/112; 4 hip, 7 vertebral); all occurred in YAs with MTF.

This is the first Australian study to document vertebral MTFs prevalence in YAs and their comorbidities and the second Australian study (3) to highlight the high prevalence of hip MTF in a comorbid population of YAs. This group of YAs with MTF had a high mortality rate, not observed in YAs with HEF. Further research is needed to determine the relationship between MTF and mortality, methods to predict fracture risk in comorbid YAs, and the impact of secondary prevention measures.

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id #125725

Maternal protein intake during pregnancy and obesity risk in mothers and offspring: a prospective cohort study

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Aims: To understand the relationship between maternal dietary macronutrient composition and obesity outcomes in mothers and offspring.

Methods: We analyzed 66,360 singleton pregnancies from the Danish National Birth Cohort, with dietary intake assessed at gestational week 25. Outcomes included maternal postpartum weight retention (PPWR) at 6 and 18 months and offspring's birth weight, risks of small for gestational age (SGA) and large for gestational age (LGA), body mass index (BMI) z-scores, and overweight/obesity (OWOB) risk at ages 7, 11, and 14 y. Mixture models with response surface visualization examined interactive macronutrient associations, and mixed restricted cubic splines assessed potential nonlinear relationships between maternal protein intake and obesity outcomes.

Results: Mean maternal macronutrient intakes were 15.2% protein-energy, 30.2% fat-energy, and 54.1% carbohydrate-energy. Response surfaces revealed that maternal lower protein intake (%), diluted by higher fat and/or carbohydrate, was associated with *higher* maternal PPWR at 6 and 18 months, and *lower* birth weight and BMI z-scores in offspring at ages 7, 11, and 14 y. Mixed restricted cubic splines indicated nonlinear associations between maternal %protein intake and SGA risk (nonlinear P=0.003) and LGA (nonlinear P=0.04), with a threshold around 15% protein; below this, SGA risk increased whereas LGA risk decreased. Linear associations were observed for risks of substantial PPWR (PPWR >5 kg) and childhood OWOB risk (nonlinear P>0.05). Each 5% higher protein intake during pregnancy was related to a lower risk of substantial PPWR at 6 months (OR: 0.90; 95%-CI:0.85-0.95) and 18 months (OR:0.88; 0.82, 0.94) but higher risks of OWOB at ages 7 y (1.07; 1.01, 1.15) and 11 y (1.11; 95%-CI:1.03-1.18), with no association at 14 y (OR:1.02; 95%-CI:0.95-1.10).

Conclusions: Higher maternal protein intake during pregnancy was associated with lower PPWR and SGA risk but higher LGA and childhood OWOB risks, suggesting divergent effects on maternal and offspring obesity outcomes.

id #132126

Novel diagnostics and therapies to improve pregnancy outcomes

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Introduction

Pregnancy and birth are among the most dangerous days in your life. Stillbirth tragically ends 3 million pregnancies globally every year whilst fetal asphyxia inflicted by labour is a leading cause of neonatal seizures, cerebral palsy and death. Pregnancy can also be detrimental to the mother and multisystem organ injury can result from preeclampsia, with delivery, often at preterm gestations, being the only treatment.

We are developing a wearable device and software diagnostics to better monitor the fetus during pregnancy. Furthermore, we have identified a possible medical treatment for preeclampsia, metformin and examining possible treatments for fetal growth restriction.

Methods

With a team of electronic engineers we have used flexible electronics and artificial intelligence to develop a wearable fetal monitoring device. Using machine learning and deep learning we have developed an algorithm that accurately detects fetal asphyxia in labour. We identified metformin as a possible treatment for preeclampsia in laboratory assays and colleagues in south Africa performed a randomised control trial evaluating its potential as a treatment for preterm preeclampsia.

Results

We have developed a wearable sensor and wireless, portable hardware that is smaller and lighter than a smart phone that could be worn by patients in hospital and opens the possibility of a virtual hospital.

Utilising CTGs from labour, we have developed an algorithm that detects fetal asphyxia with a sensitivity of 90% compared to clinicians at 36% at a match specificity of 80% and validated this model on 2 datasets – an Australian dataset and an international dataset.

We have shown metformin reduces antiangiogenic markers of preeclampsia in laboratory assays and colleagues in South Africa conducted a randomised controlled trial enrolling 180 women with preterm preeclampsia demonstrated metformin prolonged pregnancy by 7 days ($p = 0.056$).

Conclusion

We are developing wearable fetal monitoring technology and software to better detect fetal asphyxia. We are also developing treatments for preeclampsia.

id #129310

Disrupting Polymerase Gamma Exonuclease in Adipose Tissue Protects Mice from Obesity and Related Complications

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5. School of Biomedical Sciences, University of New South Wales, Sydney, NSW

The risk of obesity-related complications such as diabetes, MASLD, cardiovascular disease and metabolic syndrome increases with mitochondrial dysfunction. Models of mitochondrial dysfunction such as polymerase gamma (PolG) mutator mice show lipodystrophy with lipotoxicity, despite reduced adiposity (Ross et al., 2025; Trifunovic et al., 2004). As the sole mitochondrial DNA (mtDNA) polymerase, PolG replicates, proofreads and repairs mtDNA. PolG mutation in PolG mutator mice impairs mtDNA maintenance, allowing mutations and deletions to accumulate. Subsequent mitochondrial dysfunction disturbs adipose metabolism, highlighting the necessity of mtDNA integrity. However, it is unknown whether adipose dysfunction in whole-body mitochondrial disorders mainly arises from mtDNA mutations in adipose tissue, or secondary to mutations of non-adipose tissues. Aiming to resolve this, we generated an adipose-specific exonuclease-deficient PolG mutator (PolG-AdipoQ) mouse model.

Here, we demonstrate that PolG-AdipoQ mice were resistant to weight gain with reduced fat mass and preserved lean mass compared to wildtype C57BL/6J mice when aged to 2 years. Moreover, PolG-AdipoQ mice fed a high fat diet (HFD) diet were resistant to adipocyte hypertrophy. Obesity resistance was likely due to increased energy expenditure from adipose browning, as Ucp1 was upregulated in PolG-AdipoQ mice. These mice also displayed elevated gene expression of Gdf15 and Fgf21 – mitokines of the mitochondrial integrated stress response – and were likely responsible for the enhanced thermogenesis. PolG-AdipoQ mice on HFD were also resistant to glucose intolerance, with increased physical activity and energy expenditure compared to wildtype mice. Lipidomic analyses further showed reduced triglyceride accumulation in the livers of PolG-AdipoQ mice fed HFD for 17 weeks. These results indicate that exonuclease-deficient PolG in adipose tissue protects against obesity and its metabolic complications. In conclusion, our findings suggest that mild mitochondrial stress in adipocytes may hormetically condition mitochondria and/or increase energy expenditure, preventing obesity in mice

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id #131871

Mitochondrial lipids permit hepatocyte mitophagy and suppress MASH

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Metabolic dysfunction-associated steatohepatitis (MASH) is a lipid-driven mitochondrial disease, arising from simple steatotic livers and often associated with excess body weight. However, the key lipid changes that drive the disease progression remain poorly characterized. Here, we identified a significant depletion of sphingosine 1-phosphate (S1P), a bioactive sphingolipid, in human MASH, compared to normal and simple steatotic livers. This was attributed to reduced expression of its biosynthetic enzyme sphingosine kinase 2 (SphK2) in both human and mouse MASH. Hepatocyte-specific ablation of Sphk2 reduced hepatic S1P levels, impaired hepatocyte mitophagy and exacerbated MASH pathology in mice. Mechanistically, mitochondrial S1P bound prohibitin 2 at F212, a modification we term S1Pylation, which was essential for recruiting LC3 and inducing PINK1 to sustain protective mitophagy in hepatocytes. Targeted supplementation of mitochondrial S1P in hepatocytes effectively preserved hepatocyte mitophagy and prevented MASH progression in high-fat, high-cholesterol diet-induced obese mice. Collectively, these findings reveal mitochondrial S1P as a critical lipid suppressor of MASH.

id #130591

Identifying Eating Disorders in Individuals with Obesity: Prevalence and Practical Screening Approaches

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id #131874

The Mitochondrial Interactosome can Regulate Mitochondrial Function in the Heart Through Interactions with the Cytoskeleton

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2. Victor Chang Cardiac Research Institute, Darlinghurst, NSW, Australia

Aim: Mitochondrial dysfunction is considered to drive the development of inherited cardiomyopathies. The mitochondrial interactosome is a supercomplex formed by ATP synthase, adenine nucleotide translocase (ANT) and voltage dependent anion channel (VDAC)-tubulin that regulate energy metabolism. Previously we proposed that VDAC modulates mitochondrial function through a structural-functional association between the L-type calcium channel, the cytoskeleton and mitochondria. However the molecular mechanism linking the cytoskeleton and the mitochondrial interactosome is unknown.

Method: Cardiomyocytes were isolated from wild-type mice and mitochondrial membrane potential was measured as changes in JC-1 fluorescence following activation of the L-type calcium channel by the dihydropyridine agonist BayK(-). We targeted VDAC with a VDAC peptide, inhibited the adenine nucleotide translocase with bongkrekic acid or atractyloside and inhibited the ATP synthase with oligomycin. Experiments were performed in the presence or absence of 5μM latrunculin-A or 1μM colchicine to depolymerise F-actin filaments or microtubules respectively.

Results: An increase in JC-1 fluorescence occurred upon application of 10μM BayK(-) (15.73 ± 1.57%, n=16) which was attenuated when preincubated with latrunculin-A or colchicine. Application of 10μM VDAC peptide, 10μM bongkrekic acid, 10μM atractyloside or 20μM oligomycin mimicked the increase in ψ_m induced by BayK(-). Preincubation of the myocytes with colchicine attenuated the increase in JC-1 upon addition of oligomycin and atractyloside but preincubation with latrunculin-A did not significantly alter the increase in JC-1 with oligomycin.

Conclusion: We propose that the L-type calcium channel associates with the mitochondrial interactosome via microtubules to regulate mitochondrial energetics on a beat-to-beat basis in the heart and that disturbances in these interactions can contribute to cardiomyopathies.

id #127778

Thyroid autoimmunity and preeclampsia risk: new insights from a rat model

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Thyroid autoimmunity (TAI) commonly affects women of reproductive age and increases risk of miscarriage and preterm birth. Some studies have reported associations with gestational hypertension and other vascular diseases (1-2), but no study has investigated the cardiovascular impacts of TAI during pregnancy in an animal model.

To induce TAI, female SD rats were immunised with porcine thyroglobulin in adjuvant and provided sodium iodide in drinking water (n=9). Controls received normal water and injections of adjuvant only (n=10, 'ADJ') or PBS (n=9, 'PBS'). Rats were time-mated thereafter and blood pressure assessed by tail-cuff on gestational day (GD) 9-10 and GD19. Rats were killed on GD20 and tissues collected. 3-4 rats/group underwent echocardiography prior.

Systolic blood pressure in pregnancy was unaffected by TAI or ADJ, but decreased with advancing gestation (-8%, $p_{(Time)}$=0.006). Maternal heart weight and left ventricular systolic function was unchanged. Litter size and fetal viability was unaffected. However, whole placental weight increased in TAI rats compared to ADJ (+14%, p=0.003) and PBS (+15%, p=0.004) rats, while placental efficiency was reduced (-12% vs. ADJ, p=0.02; -13% vs. PBS, p=0.009). Placental length was greater, but only compared to PBS rats (+9%, p=0.003). Dissected placental junctional zone weight increased (+24% vs. ADJ, p=0.009; +24% vs. PBS, p=0.008). Labyrinth zone weight appeared greater but only reached statistical significance when compared to PBS rats (+12% vs. PBS, p=0.03; TAI vs. ADJ, p=0.056). No changes occurred to fetal body weight, crown-rump length, or brain-to-body and brain-to-liver weight ratios.

Thyroid autoimmunity increased placental weight and reduced placental efficiency, despite no evidence of maternal hypertension or cardiac dysfunction. These placental changes are likely compensatory to prevent deficits in fetal growth, but may cause poor long-term outcomes in offspring. Other preeclampsia-like changes including proteinuria and a high uterine artery resistance index may still be present and are being investigated.

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id #128034

Key partner perspectives on adapting a healthy lifestyle program for children and young people in Boorloo/Perth, Western Australia

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Accessible, family-based, and multi-disciplinary lifestyle and behavioural interventions are urgently needed to address the increase in childhood obesity;[1,2] however, adopting and adapting such evidence-based programs is challenging and rarely implemented successfully.[3]

After extensive consultation with key healthcare partners and community groups, an equitable healthy lifestyle program from Aotearoa/New Zealand is being scaled out to pilot in East Boorloo/Perth.[4,5] The program targets groups disproportionately affected and includes home-based weight-related health assessments, and 6 months of weekly community-based group education sessions.[5]

The aim of this qualitative study was to determine the barriers and enablers for successful program implementation in Perth, and the outcome measures that would demonstrate program success, based on the perspectives of health organisation leaders, interested healthcare professionals, referrers, and community support personnel.

A workshop with 22 key partners was conducted in March 2024, and an open-ended survey with 26 additional participants was conducted from September-October 2024. Workshop audio was transcribed verbatim and data were analysed using Framework Analysis[6] incorporating the Consolidated Framework for Implementation Research (CFIR).[7,8]

Identified enablers of implementation included 1) Program design, 2) Leadership support, 3) Experienced implementation team, and 4) Urgent need for such a program. Identified barriers for implementation included 1) Constrained resources, 2) Compatibility with current health system structure, 3) Program suitability for different population groups, and 4) Engaging priority cohorts. The broader CFIR constructs will also be presented.

Identified outcome measures included participant (recruitment/retention, primary and secondary outcomes, experience, health knowledge), service (equity, health service capability, and others), and implementation outcomes (acceptability, sustainability, service integration and others).[9]

The identified perceived determinants have guided program development, and the agreed outcome measures have informed data collection and program evaluation. Engagement with key partners prior to adapting evidence-based innovations is vital to ensure place-based considerations are accounted for and implementation success is optimised.

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id #131875

Designing therapy that targets the L-type calcium channel to reduce cardiovascular morbidity and mortality

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Cardiovascular disease is the world's no. 1 killer responsible for premature death and disability affecting all stages of life. Sudden cardiac death accounts for approximately half of all heart disease related deaths and structural heart disease such as familial hypertrophic cardiomyopathy is the leading cause of death in people under the age of 30. Hypertrophic cardiomyopathy (HCM) is an autosomal dominant genetic heart disease that affects approximately1:500 of the general population. Pathogenic features include ventricular hypertrophy, myocardial fibrosis, and diastolic dysfunction. At the level of the myocyte there is cytoskeletal disarray, hypercontractility and altered mitochondrial function. Mitochondrial dysfunction is considered to be a key driver in HCM pathology. The recently FDA approved cardiac myosin small molecule inhibitor mavacamten has demonstrated effective improvement in symptoms associated with severe outflow tract obstruction. Calcium channel antagonists are prescribed for the treatment of the symptoms of hypertrophic cardiomyopathy and the prevention of arrhythmias. However, there is no treatment that prevents the hypertrophy. Identifying therapeutic strategies to prevent the development of HCM is a significant clinical need. We previously demonstrated that the L-type Ca^{2+} channel plays a role in the development of HCM facilitated by a structural-functional communication between the channel and mitochondria involving the auxiliary beta subunit. We have designed peptides that interfere with the binding of the auxiliary β_2 subunit to the α_{1C} subunit causing immobilisation of the β_2 subunit and decreasing mitochondrial metabolic activity. The peptides significantly improve contractility and prevent the development of the hypertrophy in murine models of HCM, providing evidence for an effective and safe first in class preventative therapy.

id #131876

Emerging Insights Into the Role of Brown Adipose Tissue in β-cell Function and Glucose Homeostasis

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Background: Pancreatic β-cells maintain glucose homeostasis by coordinating communication among organs and integrating nutritional and neural cues to regulate insulin secretion. Brown adipose tissue (BAT) is well known for regulating systemic metabolism and protecting against obesity through UCP1-mediated thermogenesis. However, whether BAT influences pancreatic β-cell function and glucose homeostasis has not been fully established.

Methods: Male UCP1KO mice and wild-type littermates were studied under chow diet conditions. Metabolic phenotyping was conducted, including glucose and insulin tolerance tests (GTT/ITT) and fasting insulin levels during GTT. β-cell function was assessed by glucose-stimulated insulin secretion (GSIS) from isolated islets. Immunofluorescence staining was performed on brain and

pancreatic sections to assess tyrosine hydroxylase (TH) expression in the brainstem locus coeruleus (LC) and TH-positive sympathetic innervation of pancreatic islets.

Results: UCP1KO mice displayed impaired glucose tolerance but unchanged insulin tolerance. This impaired glucose tolerance was due to insufficient insulin secretion during GTT. Isolated islets from UCP1KO mice showed no change in GSIS. Strikingly, TH-positive neurons were activated in the LC in the brainstem, and TH expression was also found increased in the pancreatic sections of UCP1KO mice, indicating increased SNS activation of β-cells, leading to decreased insulin secretion. However, this SNS induced impaired GTT was diminished under thermoneutral conditions. UCP1KO mice showed no difference in GTT at thermoneutrality, indicating the role of SNS in modulating glucose homeostasis.

Conclusions: Absence of UCP1 mimics dysfunctional BAT, which leads to impaired β-cell insulin secretion and glucose tolerance, at least in part through enhanced sympathetic drive from LC TH neurons to pancreatic islets. These findings provide emerging insights into a BAT–brain–islet axis that integrates neural pathways to regulate glucose homeostasis.

id #131877

An ad libitum-fed diet that matches the beneficial lifespan effects of caloric restriction but acts via opposite effects on the energy-splicing axis

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Caloric restriction (CR) with fasting extends lifespan but is difficult to maintain in humans. Here we compared conventional CR (20%; 18% protein, 67% carbohydrate, 15% fat; fed at 3pm) with periods of fasting to an *ad libitum*-fed low-protein, high-carbohydrate (LPHC) diet diluted 25% with non-digestible fiber (6% protein, 79% carbohydrate, 15% fat) and control fed mice (18% protein, 67% carbohydrate, 15% fat). Due to the cellulose, LPHC mice had an increase in food intake, but an overall decrease in energy intake (~15% CR) compared to controls. Both dietary approaches similarly enhanced longevity and metabolic health (e.g. adiposity, glucose tolerance, fatty liver) relative to controls. Proteomic analysis of liver tissue revealed that CR alone increased proteins associated with energy and mitochondrial pathway. By contrast LPHC diet reduced these pathways but increased abundance of proteins associated with RNA metabolism and spliceosome pathways. These results for LPHC support the “energy-splicing resilience” axis theory of aging. Our results suggest that *ad libitum*-fed diets can be designed to replicate, and potentially enhance, the geroprotective benefits of CR, albeit via different mechanisms, potentially offering a more sustainable dietary approach to longevity extension.

id #128037

An Implementation Research Logic Model for a kids’ healthy lifestyle program in Boorloo/Perth, WA: determinants, implementation strategies and outcome measures

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National and international recommendations to combat the inequitable increase in childhood obesity include multicomponent lifestyle education programs.[1,2] Scale-out of evidence-based interventions is notoriously difficult,[3] and such programs should be developed in partnership with community and groups disproportionately affected, including the Aboriginal community.[1,4]

An adaptation of an equitable healthy lifestyle program from Aotearoa/New Zealand is being piloted in East Boorloo/Perth, which includes weight-related health assessments, and 6 months of weekly community-based group education sessions on nutrition, physical activity and wellbeing.[5,6]

The aim of this implementation study was to consolidate and present the perspectives of Aboriginal community representatives, key partners (including health organisation leaders), and consumers of the pilot program into an Implementation Research Logic Model to enhance the rigor and reproducibility of the program scale-out.[7]

Data were gathered through a range of methods: a workshop with 29 attendees (28 Elders) from various Aboriginal community groups (April 2024); a workshop with 22 key partners (March 2024); an open-ended survey with 26 additional key partners (September-October 2024); and two focus groups with total 13 program consumers (May 2025). Audio was transcribed verbatim and data analysed using Framework Analysis[8] incorporating the Consolidated Framework for Implementation Research.[9,10]

Various participant perspectives were obtained including cultural and place-based considerations. Commonly identified implementation facilitators included program design, safe and respectful environment, and urgent demand for the program. Commonly identified barriers included constrained resources, program location, and busy lifestyle of program clients.

Identified determinants for successful local program implementation and outcome measures that would demonstrate program success will be presented in the Implementation Research Logic Model alongside implementation strategies and their expected mechanisms of effect.

The use of the Implementation Research Logic Model will help to visualise the link between key elements of the adapted program as well as guiding implementation of similar future programs.

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id #130599

Endocrine Nursing academic pathway-a career in endocrine nursing

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Content isn't available at the time of publishing.

id #128552

Circulating lipocalin-2 across the adult lifespan

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Lipocalin-2 (LCN2), a hormone produced by adipocytes, osteoblasts and renal tubular cells, is implicated in age-related diseases, including cardio-metabolic disease. To understand the role LCN2 may play in pathological states, we first need to elucidate the

relationship between circulating LCN2 with indices of cardio-metabolic health during “normal” ageing. This study examined the relationship between serum levels of LCN2, age and cardio-metabolic measures across the adult lifespan in males and females.

We conducted a pooled cohort analysis including 124 community-dwelling males (n = 52) and females (n = 72) (age 20 - 87 years, median BMI 25.92 (23.04, 29.81) kg/m^2). Serum LCN2 was analysed using a two-step chemiluminescent microparticle monoclonal immunoassay. The relationship between LCN2 and age was evaluated by linear regression and cubic spline. Simple linear regressions were performed to investigate the relationship between LCN2 and the following variables: BMI, VO_{2peak}, serum glucose, body composition (dual-energy X-ray absorptiometry). For every 1 year increase in age, LCN2 levels were 0.26 mg/L higher (p = 0.007, 95% CI [0.07, 0.45]). Each 1 unit increase in BMI (kg/m^2) was associated with 0.88 mg/L higher LCN2 levels (p = 0.027, [0.10, 1.66]) and each 1 unit increase in VO_{2peak} (mL/kg/min) was associated with 0.38 mg/L lower LCN2 (p = 0.003, [-0.63, -0.13]).There was no significant relationship between LCN2 and sex, glucose levels or body composition (all p > 0.05).

LCN2 increased linearly across the adult lifespan while it decreased as fitness level increased. Future research should build on these findings to determine whether LCN2 can be used as a biomarker for chronic disease and if exercise can mitigate age-related disease associated with LCN2 changes.

id #130600

Adult Growth Hormone Deficiency -Nurse Practitioner Led Service

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id #130601

Why, Who, What and how do I get an Endocrine Nurse in my hospital? – day in the life of an Endocrine Nurse

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I am an Endocrine Nurse.

What do you do? I didn’t know that role existed!, I need an Endocrine Nurse at my hospital!!....

You often hear these statements form nurses, medical staff and other disciplines when I mention my role. There are so few Endocrine Nurses in Victoria (and Australia), it sometimes feels like a secret society.

Endocrine Nursing – Is about hormones, blood tests, education…everything Endocrine but diabetes, but in some cases…also diabetes!

There is no University degree, tafe course or manual to follow – My role particularly, was a learn on the job situation, an independent role building the clinic, managing dynamic testing procedures, educating staff and patients and also assisting in the collection of data for research publications.

So, what happens, in the daily life of an Endocrine Nurse at a major Public Hospital in Melbourne?, and how can I fund one at my hospital? ….Come and find out!

id #130602

prolactinomas - medical vs surgical management

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Content isn't available at the time of publishing.

id #130603

Management of Osteoporosis in the context of current treatment options

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2. Fiona Stanley, Perth, WA, Australia

Osteoporosis treatments have become more complex with the introduction of 1st and 2nd line osteoanabolic treatment options and the need for consolidation or transitional therapies. This presentation will review the basic pathophysiology of osteoporosis, how anti-resorptive and osteoanabolic agents work and how to calculate absolute fracture risk using risk estimation in order to stratify patients to lifestyle treatment, antiresorptive treatment or osteoanabolic therapy.

id #127020

Practical approach to the medical management of Cushing's Syndrome

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Cushing's Syndrome is one of the most intricate and complex of endocrine disorders. The process includes confirming hypercortisolemia, conducting differential diagnosis and localisation, implementing definitive treatments, addressing the need for further treatments, managing complications caused by excessive cortisol, and ensuring life-long follow-up: the disease imposes a significant burden.

This year marks a significant development in Australia with the inclusion of osilodrostat, a steroidogenesis inhibitor, in the PBS for the medical treatment of Cushing's Syndrome. Previously, the medical management of Cushing's Syndrome was restricted to a limited number of agents considered suitable only for short-term or bridging therapy before more definitive treatments such as surgery or radiotherapy. Their use was limited by factors such as cost, tolerance, and efficacy. The introduction of an efficacious steroidogenesis inhibitor that can be used long-term has established new treatment pathways, allowing for the control of hypercortisolemia at any stage of the management protocol, including primary therapy, secondary therapy, long-term therapy, and emergency therapy. This medication results in rapid lowering of cortisol levels, which necessitates management of glucocorticoid withdrawal syndrome (GWS) and potential cortisol deficiency. Effective management of these conditions requires patient engagement, education, and support, where endocrine nurses and endocrinologists play a crucial role.

id #130604

Paediatric Obesity

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Childhood obesity is a critical and growing public health concern in Australia and New Zealand, with significant long-term physical, psychological, and social consequences. Early and ongoing support by health care providers skilled in working with families and children is critical to effectively address childhood obesity. I will focus on strategies you can use in your everyday practice to help you engage meaningfully with families affected by obesity achieving better health outcomes. I will also discuss the positive health impact seen with early intervention. Finally I will review the latest evidence for treatments such as specialized diets, GLP-1RA's and weight loss surgery.

id #128557

Novel approach using tuneable matrices for 3D bioprinting early-pregnancy placental organoid models

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Single cell-derived organoids enable the study of organ-like structures that recapitulate native tissue characteristics. However, many early-pregnancy organoid models are limited by their reliance on animal-derived matrices which are highly variable and cannot be tuned to mimic human *in vivo* tissue. Emerging high-throughput bioprinting technologies can precisely deposit cells within tuneable, biologically-relevant hydrogels, enhancing translational potential. Here, we characterise bioprinted placental organoids, generated using first-trimester trophoblasts (ACH-3Ps) together with human umbilical vein endothelial cells (HUVECs), or trophoblast stem cells (TSCs).

The RASTRUM drop-on-demand bioprinter was used to print the CT29 TSC line or ACH-3P with HUVECs in a polyethylene glycol (PEG)-based matrix. Matrix selection compared a 'blank' matrix without adhesion peptides to a 'rich' matrix containing fibronectin, laminin, collagen IV and hyaluronic acid. Matrices tested were all ~1.1kPa to mimic the stiffness of the decidua basalis where placental invasion takes place. In parallel, cells were manually Matrigel-embedded for comparison. Organoid growth was quantified over 12 days using an Incucyte imaging system. Organoids were immunolabelled *in situ* for E-cadherin, SDC1 and HLA-G and imaged using a Leica Stellaris confocal fluorescence microscope.

Bioprinted TSCs readily formed organoids, though they were significantly smaller than TSC organoids in Matrigel ($p<0.001$), which is less stiff. Both bioprinted and Matrigel-embedded organoids could differentiate into syncytiotrophoblast organoids ($SDC1^+$ and β-hCG^+) and extravillous trophoblast organoids ($HLA\text{-}G^+$) under predefined medium. The 'rich' matrix significantly increased organoid number ($p<0.0001$) and size ($p<0.05$-0.001) compared to either subtype alone in the 'blank'. Matrix selection for co-cultured ACH-3P and HUVEC organoids also favoured a rich matrix.

This trophoblast organoid model is an innovative, high-throughput approach that is tuneable to reflect the placental microenvironment. ACH-3Ps grew comfortably in 1.1kPa PEG-based matrix whereas TSCs seem to require a "richer" and softer environment, given they arise from the early blastocyst stage and invade the softer endometrium.

id #127790

Comparing food addiction phenotypes in animal models of obesity and binge eating

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Background: Excessive consumption of high-fat, high-sugar foods is implicated in the pathogenesis of obesity, binge-eating disorder and 'food addiction', estimated to affect one in five young Australians. Food addiction comprises a range of harmful eating behaviours derived from aspects of substance use disorder, including escalation of intake over time, high motivation for food reward, and compulsive consumption that continues despite adverse consequences. However, the relative prevalence of food addiction behaviours in obesity versus binge eating remains unclear. This study tested measures of escalation, motivation and compulsion for a high-fat high-sugar food in animal models of diet-induced obesity and binge-eating.

Method: Over a seven-week diet intervention, three groups of young adult female Sprague-Dawley rats (*n* = 12) were fed chow and water only (Control) or chow and water supplemented with continuous or restricted (1h/day, 3x/wk) access to sweetened condensed milk (SCM). Addiction-like behaviour was quantified by assessing (1) escalation of SCM intake over time; (2) motivation for SCM in progressive ratio tests; and (3) compulsive intake of SCM when adulterated with quinine and during a modified novelty-suppressed feeding test.

Results: Across the diet intervention, percent weight gain was greater in the Continuous group than the Control group, with intermediate weight gain in the Restricted group. Only the Restricted group exhibited 'binge-like' escalation of SCM intake and compulsive consumption of SCM in both the quinine adulteration test and the novelty suppressed feeding test, relative to Continuous and Control groups. However, motivation for SCM did not differ between groups, as assessed by progressive ratio breakpoints.

Conclusions: A preclinical model of binge eating (Restricted group) more closely recapitulated the phenotype of food addiction than diet-induced obesity (Continuous group). Despite the absence of changes in motivation for SCM, the pattern of access to high-fat, high-sugar foods appears the key predictor of addiction-like behaviour.

id #121647

Healthy or misleading? A study of food outlets categorised as 'healthy' on an Australian delivery platform

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Aims: Online food delivery platforms play an increasing role in our food environments and shaping dietary choices, yet little is known about whether these platforms validly categorise and promote healthy food outlets. This study aimed to quantify the healthiness of food outlets classified as 'healthy' on the Uber Eats platform in Victoria, Australia.

Methods: We conducted a web scrape of the Uber Eats Australia platform between November 2022 and January 2023. Data (including outlet name, category, and location) were extracted using an automated Python script. Outlets classified by the platform as 'healthy' were reclassified using the DIGIASSESS index (1), a validated food environment scoring tool developed for online food delivery platforms. A combination of automated and manual classification was used. Descriptive statistics were used to determine the proportion of each outlet type and overall healthiness.

Results: From the web scrape, 12,938 unique food outlets were identified, of which 1,408 were categorised as 'healthy' by the platform. Classifying the healthiness of these outlets using the DIGIASSESS index, we found that most were classified as "less healthy" (n=1,123, 79.7%) or "unhealthy" (n=180, 12.8%). Only a small proportion of outlets were classified as "healthy" (n=106, 7.5%). The most common outlet types within the 'healthy' category were "Independent – Takeaway" (n=166, 11.8%), "Independent – Cereal-Based Café Meals" (n=136, 9.7%), and "Service Station Convenience Stores" (n=104, 7.4%), all classified as "less healthy."

Conclusions: The Uber Eats' 'healthy' category does not accurately represent nutritional evidence of the healthiness of food outlets, potentially misleading consumers and hindering informed decision-making. Clearer, scientifically-informed, standardised criteria for categorising food outlets on online delivery platforms are needed to improve transparency, prevent misinformation, and support public health goals.

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id #128303

Gaining Strength While Losing Weight: Functional Improvements During a Very Low Energy Diet

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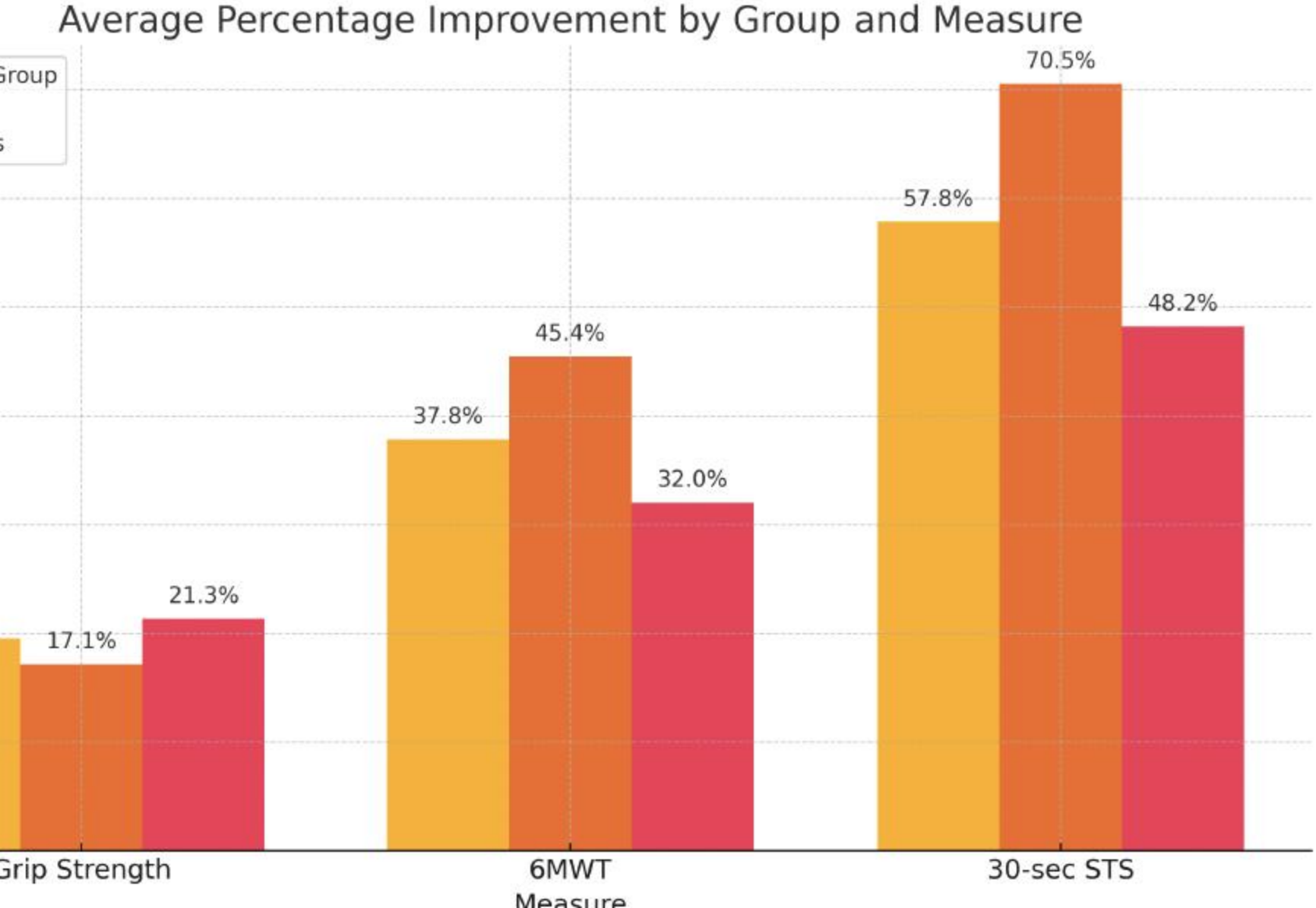
Very Low Energy Diets (VLEDs) are commonly used in tertiary obesity care to achieve rapid weight loss. However, there are concerns around the potential for muscle mass loss and reduced functional capacity. This study aimed to determine whether individuals undertaking a 12-week VLED could improve strength and endurance when supported by a physiotherapist-led exercise program within a multidisciplinary team (MDT) framework.

Forty-four participants (mean baseline BMI = 45.4 kg/m²) from the Tertiary Obesity Multidisciplinary Service (TOMS) at the Royal Brisbane and Women's Hospital were reviewed during the 2024–2025 period. Participants completed a 12-week VLED alongside a structured exercise program, which included weekly one-hour physiotherapy-led strength classes using gym equipment, therabands, and free weights. A home exercise prescription of two days of cardiovascular activity and three days of strength training was also provided. Functional outcomes were assessed at baseline and week 12 using grip strength (kg/f), the 6-minute walk test (6MWT, metres), and 30-second sit-to-stand (STS, repetitions). Body weight and BMI were recorded pre- and post-intervention.

Participants lost an average of 12.6 kg (SD 4.3, $p<0.001$) and a mean BMI reduction of 4.5 kg/m². Grip strength improved from 32.1 kg to 37.8 kg (mean difference +5.7 kg, $p<0.001$), exceeding the ≥5 kg threshold for clinical significance. The 6MWT distance increased from 385.8m to 494.1m (mean difference +108.3 m, $p<0.001$), well above the ≥50m threshold for significance. STS repetitions rose from 11.7 to 16.9 (mean difference +5.2 reps, $p<0.001$), exceeding the ≥2 rep threshold.

Despite rapid weight loss, participants demonstrated clinically and statistically significant gains in functional capacity. These findings support incorporating physiotherapy-led resistance training into VLED programs to enhance outcomes and preserve strength during weight loss.


Average Percentage Improvement by Group and Measure
Group
s
17.1%
21.3%
37.8%
45.4%
32.0%
57.8%
70.5%
48.2%
Grip Strength
6MWT
30-sec STS
Measure

id #128559

Generation of marsupial induced pluripotent stem cells with features of totipotency

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Australian marsupial populations are in significant decline. While traditional conservation approaches (e.g., habitat protection and breeding programs) have proven useful, next-generation technologies—such as genetic modification to enhance population fitness—are required to stem continuing losses. This study generated induced pluripotent stem cells (iPSCs) from the fat-tailed dunnart to provide critical starting material for such technologies. Pluripotency of the iPSCs was validated using transcriptomic and epigenomic analyses, embryoid body formation, differentiation into primordial germ cell-like cells (PGCLCs), and injection into mouse embryos.

Dunnart iPSCs strongly activated transcriptomic and epigenomic networks associated with pluripotency in other species; however, unique patterns of activation and inhibition were also observed. The dunnart iPSCs readily formed embryoid bodies expressing markers associated with differentiation into all three germ layers, as well as extraembryonic lineages. Furthermore, injection of dunnart iPSCs into mouse morulae or blastocysts demonstrated their capacity to contribute to both the inner cell mass and the trophoblast lineage. Applying established methods for differentiating mouse or human iPSCs into PGCLCs resulted in the robust induction of a similar PGCLC transcriptional network in dunnart iPSCs.

Altogether, this research has established reliable methods for generating dunnart iPSCs that exhibit characteristics of totipotency and a functional capacity to contribute to early embryonic development in vitro. However, validation in longer-term mouse or dunnart embryo cultures and further molecular analysis is essential for definitive classification. Genome-wide analysis of pluripotency gene activation and inhibition revealed a unique pattern, potentially reflecting a marsupial-specific pluripotency network currently under investigation. Fully elucidating this network will provide valuable insight into the most effective applications of marsupial iPSCs in next-generation conservation technologies such as de-extinction and programmed genetic fitness.

id #129073

Weight loss and resting energy expenditure during intermittent versus continuous energy restriction in women with obesity (the MATADOR2 Study)

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Background/Objectives: Our proof-of-concept study in men with obesity showed that interspersing 2-week blocks of energy balance (EB) after every 2 weeks of energy restriction (ER) improved weight loss over continuous ER. However, we did not examine resting energy expenditure (REE) during these 2-week EB blocks. The second **M**inimising **A**daptive **T**hermogenesis **A**nd **D**eactivating **O**besity **R**ebound study (MATADOR2) study investigated: [1] if 2-week EB blocks ameliorate reductions in REE commonly seen during ER; and [2] if, as previously shown in men, intermittent ER improves weight loss over continuous ER in women with obesity.

Participants/Methods: Fifty-three women with obesity were randomised to 12 weeks of either: [1] continuous (CON), or [2] intermittent (INT) ER completed as 6×2-week blocks of ER alternating with 5×2-week blocks of energy balance (22 weeks total). Fifty-two participants completed a 4-week baseline phase (CON: N=24, 41±7y, 96.9±12.4kg, 35.4±3.8 $kg \cdot m^{-2}$; INT: N=28, 40±7y, 98.9±11.8kg, 35.7±3.5 $kg \cdot m^{-2}$). During ER, energy intake was equivalent to 65% of weight maintenance requirements in both groups. Body weight, fat mass (FM), fat-free mass (FFM), and resting energy expenditure (REE) were measured throughout the study.

Results: For the N=18 INT and N=17 CON who completed the 12-week energy restriction intervention and 4-week post-intervention energy balance, weight loss was greater for INT (10.4±4.1 *vs* 8.5±1.8 kg; P=0.02). Weight change during the 5´2-week INT energy balance blocks was minimal (-0.2±0.2 kg). Despite larger weight loss in INT, absolute REE did not differ between groups after 12 weeks of energy restriction (INT: -568±489 *vs* CON: -606±428 kJ/d; P=0.2), nor after adjusting for changes in body composition (P>0.05). REE was partially restored in the INT group after each 2-week EB block by, on average, 166 ± 259 kJ/d (P=0.01).

Conclusions: Interrupting ER with energy balance 'rest periods' may reduce compensatory metabolic responses and, in turn, improve weight loss efficiency.

id #128818

Tirzepatide treatment and achieving weight reduction >5%, SBP reduction >5 mmHg and non-HDL cholesterol reduction >10%: A post hoc analysis from the SURMOUNT-1 3-year trial

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5. Liverpool Hospital, Sydney, NSW, Australia

Aims: This post-hoc analysis evaluated the proportion of participants who met the combined goal of weight reduction >5%, systolic blood pressure (SBP) reduction >5 mmHg and non-HDL cholesterol reduction >10% from baseline to Week-176 in SURMOUNT-1 3-year trial.

Methods: There were 568 participants with obesity and prediabetes who completed treatment with tirzepatide (n=454) or placebo (n=114) at Week-176 and had measures for all three outcomes (weight, blood pressure and lipids) or had any of the three measurements not meeting the threshold. Baseline characteristics were compared using ANOVA model for continuous data and Chi-square test for categorical data.

Results: Total 145 (25.5%) participants met the combined goal at Week-176. Participants meeting vs. not meeting the combined goal had higher mean SBP (130.0 vs. 124.4 mmHg), total cholesterol (203.6 vs. 186.1 mg/dL), non-HDL cholesterol (155.4 vs. 138.2 mg/dL), LDL cholesterol (123.0 vs, 108.7 mg/dL), and triglycerides (175.2 vs. 148.8 mg/dL) at baseline. Significantly more tirzepatide-treated participants (n=139, 30.6%) met the combined goal vs. placebo (n=6, 5.3%), p<0.0001. Moreover, 94.2% (n=131) TZP participants who met the combined goal also had an HbA1c <5.7%, 41.0% (n=57) had a BMI ≤27 kg/m^2 and 28.8% (n=40) had a WHtR <0.53. Of the six placebo participants who met the combined goal, all had HbA1c < 5.7%, 1 had a BMI ≤27 kg/m^2 and 1 had a WHtR of <0.53.

Conclusion: Significantly more participants treated with tirzepatide as compared with placebo achieved a combined clinical goal of weight reduction >5%, SBP reduction >5 mmHg and non-HDL cholesterol reduction >10% vs. placebo. Most of the tirzepatide participants meeting the combined goal also achieved normoglycemia, over 1 in 3 participants met the BMI goal, and 1 in 4 met the WHtR goal, suggesting central adiposity reduction. Outcomes trials are ongoing to further evaluate the cardiometabolic impact of tirzepatide.

id #130612

Incretin-based anti-obesity therapy: can we preserve muscle mass while losing fat?

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New anti-obesity medications based on gut-derived nutrient-stimulated hormones (incretins) induce substantial weight loss in randomised trials, enhanced by combining actions on multiple receptors. Semaglutide (a glucagon-like peptide-1 receptor agonist, GLP-1ra), tirzepatide (GLP-1 and GIP receptor dual agonist) and retatrutide (GLP-1, GIP, and glucagon-receptor triple agonist), induce up to ~15-24% weight loss in adults with overweight and obesity, with improvement in cardiovascular risk factors. However, these agents also cause rapid and significant loss of lean mass (~6 kg, ~10%), comparable to a decade or more of ageing. Maintaining muscle mass and function as humans age is crucial to avoiding sarcopenia and frailty, which are strongly linked to morbidity and mortality. In a two-year randomised controlled trial (RCT) of men with central adiposity and dysglycemia, testosterone treatment on a background of lifestyle intervention increased muscle mass (~0.4 kg) and reduced fat (~4.6 kg). However, in a 12-week 2x2 factorial RCT, exercise training outperformed testosterone treatment. Studies indicate that supervised resistance exercise training interventions with duration over 10 weeks can elicit increases in lean mass (~3 kg) and strength (~25%) in men and women. After a low-calorie diet, combining aerobic exercise with liraglutide improved weight loss maintenance compared to either alone. Retaining lean mass during incretin therapy could potentially blunt body weight (and fat) re-gain on cessation of weight loss pharmacotherapy. In overweight/obese adults with type 2 diabetes, 48-weeks treatment with bimagrumab, a monoclonal antibody targeting the myostatin signalling pathway, increased muscle mass (~1.7 kg, 3.6%), and reduced fat (~7.5 kg, 20%). Bimagrumab also has been trialled in conjunction with semaglutide and tirzepatide. Pending further results and availability of potential new therapies, tailored resistance exercise training should be recommended as an adjunct to incretin therapy, to optimise changes in body composition by preserving lean mass while achieving fat loss.

id #127543

Parent-focused behavioural interventions for the prevention of early childhood obesity: results of the TOPCHILD systematic review and individual participant data meta-analysis

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4. University of Sydney, Camperdown, NSW, Australia

Childhood obesity is a major global health issue. We aimed to evaluate the effectiveness of parent-focused behavioural obesity prevention interventions on child body mass index (BMI) z-score at age 24±6 months and weight-related behavioural outcomes.

We conducted an individual participant data (IPD) meta-analysis. We systematically searched databases and trial registers for randomised controlled trials comparing parent-focused behavioural obesity prevention interventions commencing before 12 months of age with usual care, no intervention or attention control. Investigators of eligible trials were invited to join the TOPCHILD Collaboration and share their IPD. Screening, data checking, re-coding, integrity, risk of bias and GRADE assessments were conducted in duplicate. The primary outcome was BMI z-score at age 24±6 months. Key secondary outcomes included obesity-related behaviours covering diet, feeding, physical activity, sleep and parenting. We conducted intention-to-treat two-stage random effects meta-analysis to determine effects overall and for pre-specified subgroups.

We included 31 trials with IPD from 28,825 children. Behavioural interventions had no effect on BMI z-score at age 24±6 months (17 trials, 6505 participants, mean difference [MD] -0.01; 95% confidence interval [CI] -0.08 to 0.05, high certainty, Fig 1, Table 1). This result was robust across individual-level subgroups (e.g. socioeconomic position, parental weight status, maternal age, Table 2) and trial-level subgroups (e.g. mode of intervention delivery, dose, setting, country), as well as sensitivity analysis accounting for different analysis methods, missing data, risk of bias and integrity. Interventions had no effect on key secondary outcomes, except for a small reduction in screen time at age 24±6 months (Table 1).

This large IPD meta-analysis of 31 trials found no effect of parent-focused early behavioural interventions on child BMI z-score at age 24±6 months. This supports the need for a multi-level approach within a broader systems framework to address the complex social and environmental determinants of childhood obesity.

Meta-analysis - BMI z-score at age 24 ± 6 m

Study	Mea
Australia (Campbell et al 2013)	1 (
Australia (Campbell et al 2016)	1 (
Australia (Daniels et al 2013)	0.
Australia (Wen et al 2012)	0.5
Australia (Wen et al 2022) A	0.
Australia (Wen et al 2022) B	1 (
Italy (Morandi et al 2019)	0.
Netherlands (Karssen et al 2021)	0.6
New Zealand (Taylor et al 2017a) A	0.
New Zealand (Taylor et al 2017a) B	0.7
New Zealand (Taylor et al 2017a) C	0.7
New Zealand (Taylor et al 2017b)	0.
Norway (Helle et al 2019)	0.4
Norway (Øverby et al 2017)	0 (
Norway (Røed et al 2021)	0.
Sweden (Döring et al 2016)	0.6
UK (Bryant et al 2021)	1.1
USA (Messito et al 2020)	1 (

Table 1. Primary and key secondary out

SD = standard deviation, CI = confidence

Outcome	N trials	N participants	Int me or
Primary outcome			
BMI z-score at age 24 ±6 months	17	6505	0.7
Key secondary outcomes			
Duration of exclusive breastfeeding assessed at 6 ±2 months	5	1653	12.
Vegetables consumed per day at age 24 ±6 months	12	4656	11 (92
Average screen time per day at age 24 ±6 months	7	2652	62.
Self-reported physical activity per day at age	1	314	25

Table 2. Subgroup analyses by individual-level charact
body mass index z-score at age 24±6 months

CI = confidence interval, BMI = body mass index

Continuous individual-level subgroups		
Covariate	**Number of studies**	**Numb partici**
Birthweight	16	6222
Gestational age at birth	7	3751
Maternal / birthing parent weight status	15	6048
Weighted standardised household income	6	2301
Categorical individual-level subgroups		
Covariate	**Number of studies**	**Numb partici**
Any formal childcare attendance at 0-12 months	4	1335
No		
Yes		
Any formal childcare attendance at 12-24 months	4	1025
No		
Yes		
Partner status	13	4714
In a partnership (married, de facto, living with partner)		

id #128568

Co-designing recommendations for sexual and reproductive health education alongside Australia's youth

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2. Women's Health Research Program, Hunter Medical Research Institute, New Lambton, NSW, Australia

3. The Research Centre, Family Planning Australia, Newington, Australia

4. Sexual and Reproductive Health Advisory Group, University of Newcastle, Australia

5. Maternity and Gynaecology, John Hunter Hospital, Newcastle, Australia

Poor reproductive health literacy is associated with poor sexual health and reproductive outcomes. Comprehensive sexuality education is recommended globally as an effective intervention, with evidence demonstrating reduced sexually transmitted infections and improved understanding of preventable infertility. Despite attempts to implement comprehensive sexuality education in Australia, the relevance and delivery vary among students, leading to inconsistent information retention and understanding. Simultaneously, Australia sustains alarmingly high rates of sexually transmitted infections in young people and an adult population with increasing reliance on assisted reproductive technologies. Accordingly, it is crucial to engage with end-users of education curricula to reduce the disparities observed in understanding and the resulting negative health manifestations.

Utilising focus groups, this project aimed to investigate the thoughts and perceptions of Australian adolescents aged 15-18 regarding their sexual health education. A key addition of this study was the collaborative work with a Youth Advisory Group, consisting of four tertiary students aged 20-23 years old. The role of the study's Youth Advisory Group was to review the focus group data alongside UNESCO's *International Technical Guidance for Sexuality Education* and the current Australian curriculum, to guide recommendations for strengthening Australian sexuality education.

The recommendations co-designed with the Advisory Group, considered a range of evidence together with their lived experience, to inform specific guidance for improving sexual and reproductive health education. Recommendations addressed issues including *the taboo of reproduction and sex within sexuality education, minimal understanding of what affects fertility, and implementing more inclusive reproductive content*.

Ultimately, collaborating with young people in guiding recommendations for reproductive education resulted in consumer-driven suggestions, contextualised to Australia's youth, for more relevant, engaging content. This study highlights opportunities for educators and stakeholders to adopt similar approaches for better engagement with their students, to support their reproductive health literacy and subsequent health outcomes.

id #128313

Losing Weight, Gaining Control: Diabetes Management Through TOMS

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5. Psychology Department, Royal Brisbane and Womens Hospital, Brisbane, Queensland, Australia

6. Endocrinology Department , Royal Brisbane and Womens Hospital, Brisbane, Queensland, Australia

7. School of Exercise and Nutrition Sciences, Queensland University of Technology, Brisbane, QLD , Australia

To evaluate the effectiveness of the Tertiary Obesity Multidisciplinary Service (TOMS)—a 12-month comprehensive weight-loss program involving physiotherapy, pharmacy, psychology, endocrinology, and dietetics—in improving glycemic control and reducing medication burden among individuals living with diabetes.

Participants with diabetes who commenced the TOMS program between January 2021 and June 2024 were included. Glycated haemoglobin (HbA1c) levels were collected at baseline, three, six and 12 months. Medication use, including insulin and sulfonylureas, was tracked throughout the program from documentation in the electronic medical record, with particular focus on adjustments during the intensive phase of the Very Low Energy Diet (VLED). Weight was tracked as a secondary outcome, collected at the same time.

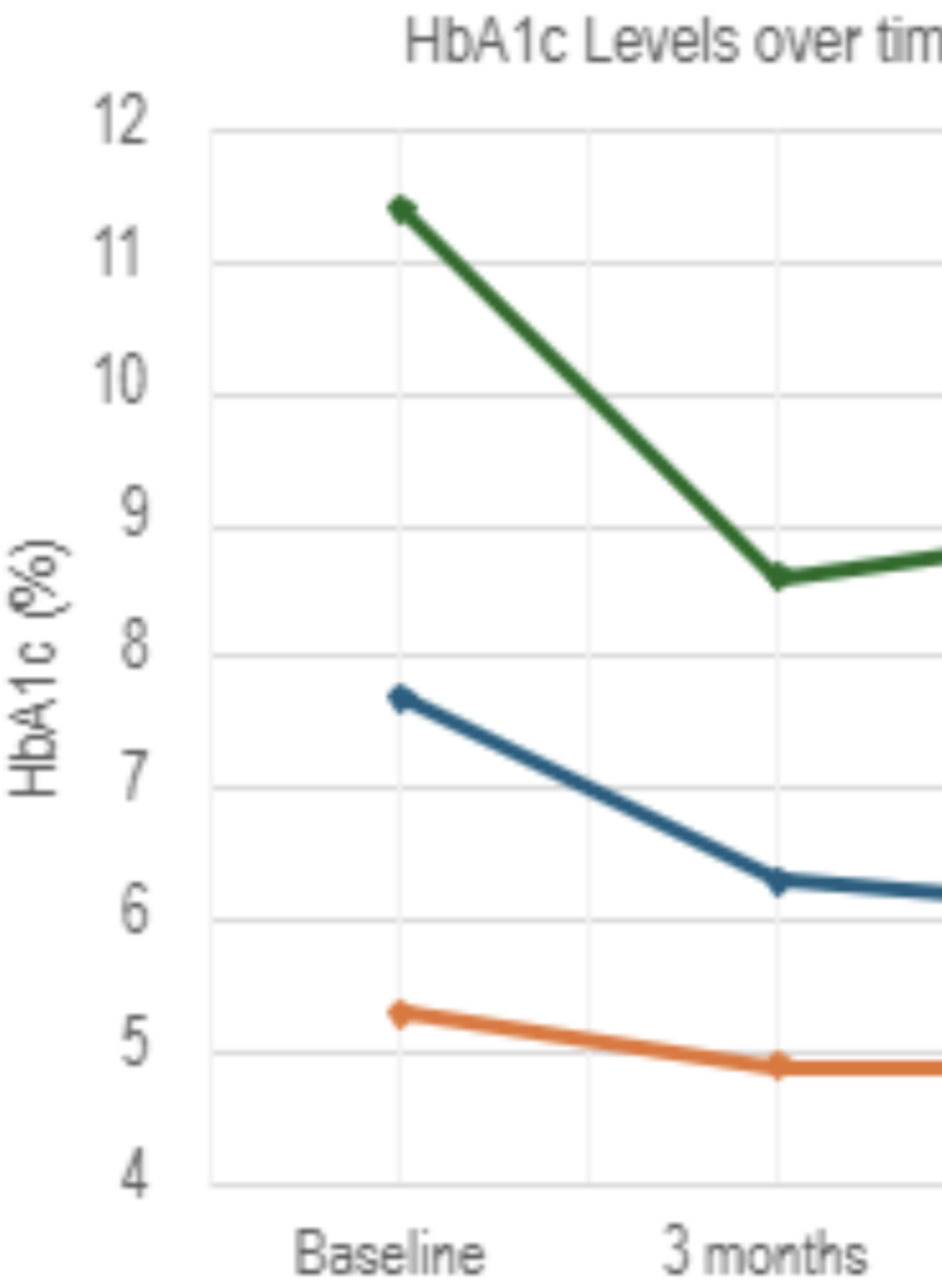
Of the 73 participants included, 47% (n=34) were on insulin or sulfonylureas at baseline, with 11% on both. During the intensive phase, 89 insulin adjustments were recorded: 70% of participants reduced their insulin dosage, and 17% ceased insulin entirely. Additionally, 64% of participants discontinued sulfonylureas.

HbA1c levels showed significant improvement over time. Mean HbA1c decreased from 7.7% at baseline (n=71) to 6.4% at 3 months (n=63), 6.4% at 6 months (n=49), and 6.5% at 12 months (n=27). All reductions were statistically significant ($p < 0.05$), indicating sustained glycemic improvements.

All participants had a baseline BMI >35kg/m2 (mean = 147kg), with mean decrease in weight of 12.2% from baseline to 12 months.

The TOMS program demonstrates that integrated, multidisciplinary obesity care can lead to meaningful improvements in glycemic control, weight and a substantial reduction in diabetes medication burden. These findings highlight the value of coordinated care in managing complex obesity and enhancing metabolic

health.


HbA1c Levels over tim
12
11
10
9
8
7
6
5
4
HbA1c (%)
Baseline
3 months

id #128569

Improving access: a point of care test for fetal growth restriction

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Fetal growth restriction (FGR) reflects placental dysfunction and incurs a 10+ fold increased risk of stillbirth. Current practice (fundal height with selective ultrasound) only identifies 14.5-22% of babies <3rd centile (1-2). We previously reported low maternal circulating serine peptidase inhibitor Kunitz type-1 (SPINT1) as associated with low birthweight (3). Here, we developed a novel, point-of-care test (POCT) for SPINT1, and measured circulating levels at 36 weeks' gestation to examine its performance as a screening test for FGR.

To develop the SPINT1 POCT, we utilized lanthanide-doped up-conversion nanoparticles (UCNP) bioconjugated with our SPINT1 detector antibody (UCNP-SPD). Our SPINT1 capture antibody was printed on a nitrocellulose membrane and assembled into test strips. Human plasma was diluted in running buffer, mixed with UCNP-SPD, and 50 µL of mixture added to the sample pad. The signal was read after 10 min using a strip reader equipped with a 980 nm laser. SPINT1 levels were quantified by generating a standard curve of known SPINT1 concentrations.

A case cohort of 36 week plasma samples was selected from a prospective population study in Melbourne. This included 30 cases who later delivered an infant with FGR (birthweight <3rd centile) and 111 randomly selected controls without FGR. Samples were run blinded, in triplicate.

Median SPINT1 level was 49.4 ng/ml (IQR 34.7-68.3 ng/mL) among 111 without FGR (the representative cohort). Median SPINT1 in those who later delivered with FGR was significantly lower ($p = 1.56 \times 10^{-5}$) at 30.9 ng/mL (IQR 21.4- 46.5 ng/mL). The area under the receiver operator curve (AUC) was 0.76 and the detection was 43.3% (sensitivity) at 90% specificity.

Our SPINT1 point-of-care test identifies pregnancies at risk of FGR better than current clinical care. It could be integrated into prenatal clinics as a screening test to better identify pregnancies with placental insufficiency and at 10-fold increased risk of stillbirth.

id #126012

Starting and Sustaining a Career in Science

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For this session, I have been asked to share a broad overview of my journey as a researcher, including key challenges and turning points, highlighting tips and suggestions, and future directions.

id #128572

Fetal growth restriction induces dynamic, sex-specific changes to molecular signatures in the placenta-heart axis of the near-term sheep

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Background

The interconnected relationship between placenta and heart is critical for establishing lifelong cardiovascular health. Intriguingly, sex differences in the placenta-heart axis in response to pregnancy complications are known; male placentae have impaired adaptability and reserve capacity compared with females, which may exacerbate heart development perturbations. Despite this, the underlying mechanisms that contribute to these responses remain unclear. Therefore, the current study aimed to characterise sex-specific molecular adaptations in the placenta-heart axis of the near-term sheep model of fetal growth restriction (FGR).

Methods

Left ventricle (LV) and placenta tissue was collected from control and FGR fetuses (n=4/sex/group) at 140d gestation (term=150d) and global gene expression was profiled using RNA-seq. Differential gene expression analysis was performed using the DESeq2 package (genes with adjusted $P<0.05$, $|\log2 \text{ fold change}| \geq 1$ were considered to be differentially regulated), and pre-ranked gene set enrichment analysis (GSEA) was performed to determine highly represented biological pathways.

Results

Female FGR placentae had enriched immune signalling (i.e. IFNα and IFNγ response; Inflammatory response) and vascular remodelling capability (i.e. Epithelial mesenchymal transition (EMT); complement; coagulation) when compared with male FGR placentae. In the LV, males increased mitochondrial activity (i.e. oxidative phosphorylation) but reduced immune and cytokine signalling (i.e. IL6/JAK/STAT3 signalling; TNFα via NFκB), growth signalling (i.e. TGFβ signalling, PI3K/AKT/MTOR signalling), structural remodelling (i.e. EMT; apical junction), and metabolism/transport (i.e. Heme metabolism; protein secretion), when compared with females.

Conclusion

These findings indicate that in response to FGR, males are more susceptible to adverse cardiovascular outcomes due to impaired molecular plasticity within the placenta-heart axis. The observed increase in cardiac oxidative phosphorylation in males suggests metabolic overcompensation that is not supported by sufficient structural adaptations in the heart or placenta. Ongoing studies aim to identify upstream regulators driving these observed sex differences in molecular responses to FGR.

id #128573

Adrenal Targeted Nano-biotechnology: Novel Gene Therapy for Adrenal Diseases

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Publish consent withheld

id #129341

Non-hormonal male contraception using a combination of adrenergic and purinergic receptor antagonists

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According to the United Nations, there are over 200 million pregnancies around the world each year and 121 million of these are unintended. While present contraceptive methods are effective, there is clearly a need to develop additional methods of contraception for males, a market which is clearly lacking. Therapeutic targets for male contraception are associated with numerous problems due to their focus on disrupting spermatogenesis or hormonal mechanisms to produce dysfunctional sperm. We have described a mechanism for male contraception that is both non-hormonal and non-spermatogenic. This biological strategy has been validated via the dual genetic deletion of α1A-adrenergic receptors and P2X1-purinergic receptors in male mice thereby blocking sympathetically mediated sperm transport through the vas deferens during the emission phase of ejaculation. This modification produced 100% infertility without effects on sexual behaviour or function. Sperm taken from the cauda epididymides of double knockout mice were microscopically normal and motile. Furthermore, double knockout sperm were capable of producing normal offspring following intracytoplasmic sperm injection into wild type ova and implantation of the fertilized eggs into foster mothers. Blood pressure and baroreflex function was reduced in double knockout mice but no more than single knockout of α1A-adrenergic receptors alone. These results suggest that this autonomic method of male contraception appears free from major physiological and behavioural side effects. In addition, they provide conclusive proof of concept that pharmacological antagonism of the P2X1-purinergic receptor and α1A-adrenergic receptor provides a safe and effective therapeutic target for a non-hormonal, readily reversible male contraceptive. Synthetic medicinal chemistry approaches to discover a suitable P2X1-purinergic receptor antagonist to use in combination with tamsulosin for this purpose has so far proved unsuccessful. However, our recent determination of the first cryo-EM structure for the P2X1 receptor will hopefully provide better chemical starting points for a successful synthetic medicinal chemistry program.

id #131903

Female endocrine, reproductive, metabolic health - the neglected burgeoning public health crisis

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id #125760

Post-treatment renin status and cardiovascular, renal and mortality outcomes in medically treated primary aldosteronism: a systematic review and meta-analysis

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Renin suppression persists in many patients with primary aldosteronism (PA) despite targeted medical treatment, which may indicate suboptimal mineralocorticoid receptor blockade. Hence renin is a suggested biomarker for medication titration in the Primary Aldosteronism Medical Treatment Outcome (PAMO) criteria. This study systematically reviewed the evidence on the association between post-treatment renin status and cardiovascular, renal, and mortality outcomes in medically treated patients with PA.

A systematic search of MEDLINE, Embase, CENTRAL and Web of Science was conducted on May 5th, 2025. Studies that investigated the association between post-treatment renin and clinical outcomes among medically treated patients with PA were included. The primary outcomes were the incidence of cardiovascular events, renal events, and mortality. Risk-of-bias was assessed using the QUIPS tool. Random-effects models were employed to estimate pooled hazard ratios (HRs) with 95% confidence intervals (CIs). Certainty-of-evidence was rated using the GRADE framework.

Twenty-four studies involving 6621 patients with PA on mineralocorticoid receptor antagonists were included. Most studies used plasm renin activity with a cut-off of 1.0 ng/mL/h to classify post-treatment renin as suppressed or unsuppressed. A meta-analysis demonstrated that unsuppressed post-treatment renin was associated with a lower risk of cardiovascular events with ≥5 years follow-up (pooled HR 0.33 [95%CI, 0.19–0.57], I^2=0%, three studies, 756 patients; moderate certainty). No significant association was found with renal events (pooled HR 0.95 [95%CI, 0.51–1.77], two studies, I^2=0%, very low certainty). One study reported a lower risk of mortality in patients with unsuppressed vs. suppressed post-treatment renin (HR 0.29 [95%CI, 0.09–0.98], 201 patients; moderate certainty).

In conclusion, unsuppressed renin following targeted medical therapy for PA is associated with a reduced risk of cardiovascular events, suggesting that normalisation of renin should serve as a therapeutic target. Prospective studies are warranted to confirm that medication titration to normalise renin improves clinical outcomes.

id #128577

Longitudinal anthropometric and metabolic outcomes of a specialist multidisciplinary childhood and adolescent obesity service

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Background

Healthy Weight Service (HWS) is WA's tertiary paediatric multidisciplinary obesity service. Similar approaches have been associated with improved weight status, but understanding of predictors of efficacy is incomplete.

Aims

To determine (1) changes in weight status with intervention; (2) the impact of age, sex, socio-economic disadvantage, baseline weight status and the COVID-19 pandemic; (3) observed changes in secondary outcomes related to obesity and its complications.

Methods

Using service databases, children aged 2-16 ≥ two weight/height measurements between 2016-2022 were included. Primary outcome was BMIz-score (2022 extended CDC). Secondary measurements included Body fat percentage, Blood pressure *z* scores for age, sex and height, HbA1c Fasting glucose, OGTT (glucose, Insulin), C-peptide, lipids, liver and renal function. Predictors included age, sex, Baseline BMiz-score, socioeconomic status (SEIFA) with confounders (treatment duration). Statistical analysis: multiple linear regression and multivariate imputation by chained equations.

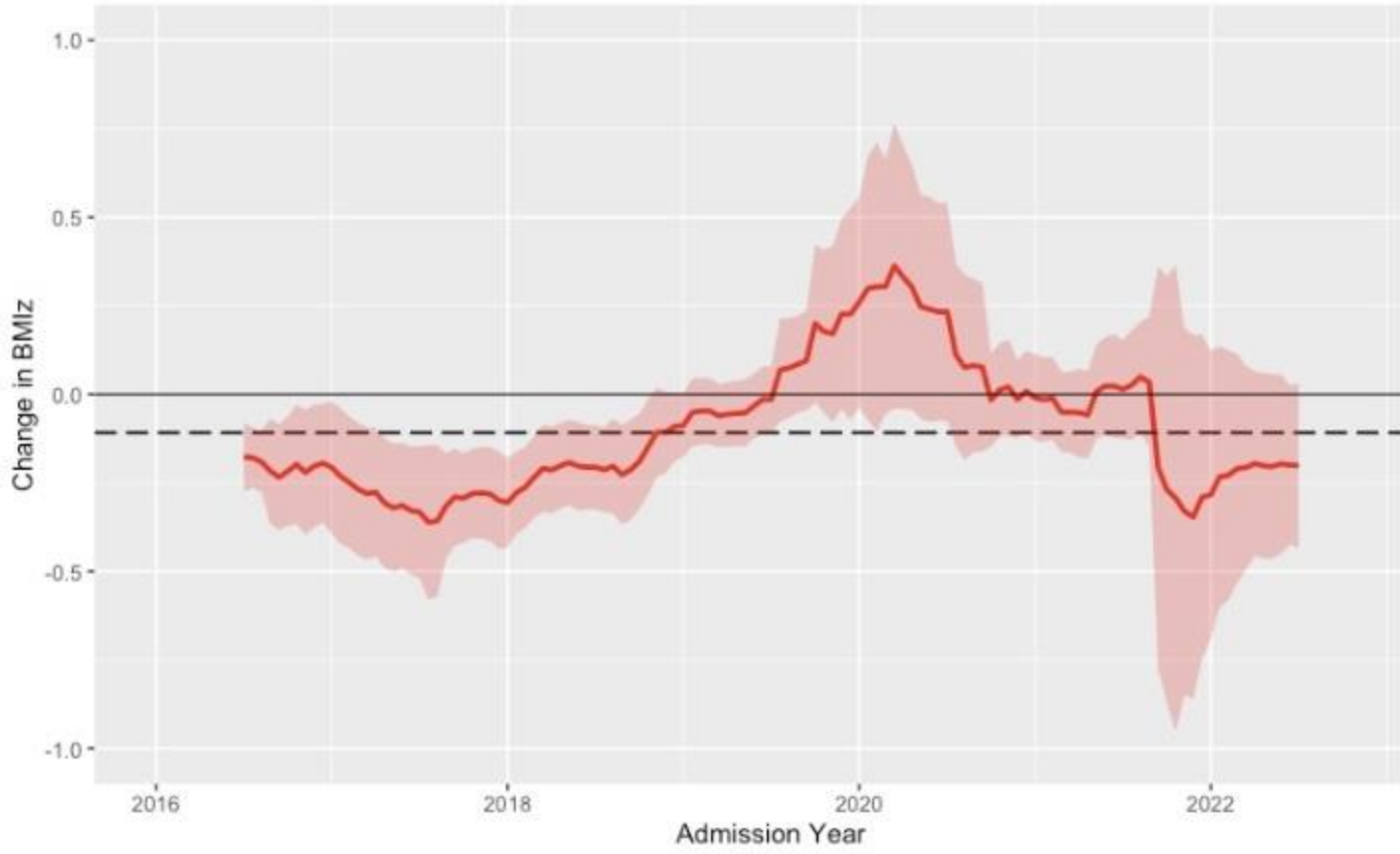
Results

At baseline, 90% of patients (n=464) met CDC-defined severe obesity. The preschool (aged 2-5), child (aged 6-12) and adolescent (aged 13-16) subgroups comprised 25%, 49% and 26% respectively.

Change in BMIz of -0.19 (95% CI -0.26, -0.13, $p < 0.001$, $N = 464$) was observed. Multiple linear regression showed younger age and higher baseline BMIz were independently associated with larger reductions in BMIz.

Analysis stratified by age subgroup found admission in 2020 was associated with a worse outcome in the child sub-group (coefficient $B = 0.36$, 95% CI 0.16, 0.56, $p < 0.001$, $n = 227$) (Figure)

Figure 1 Moving 1-year average of change in BMIz in the ch
subgroup with shaded 95% confidence intervals. The dashe
represents the subgroup average over the whole period



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Among the secondary outcomes, a significant change was observed in creatinine and ALP.

Conclusions

Significant improvements in weight status as measured by BMIz were observed particularly in younger patients with the most severe obesity. Patients aged 6-12 admitted in 2020 had worse weight status outcomes, suggesting a negative impact of the early COVID-19 pandemic on weight status outcomes in this age group.

id #129089

Association Between Dietary Patterns and Fat-Free Mass: A Systematic Review.

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Background: The influence of diverse dietary patterns on fat-free mass (FFM) in people with overweight or obesity, beyond individual dietary components, remains underexplored.

Aim: To synthesise evidence from observational studies on the association between various dietary patterns and FFM in adults from general populations with overweight or obesity.

Methods: We systematically searched Embase, Medline, Web of Science, and Google Scholar for observational studies published in English (-June 2024). Pooled effect estimates were calculated using the standardised mean difference (SMD) with 95% confidence

intervals (95%CIs) in random-effects meta-analyses. Subgroup analyses and heterogeneity statistics (I^2, Q, and τ^2) were also employed.

Results: From 3,381 initial records, 47 studies were included in the systematic review and 20 in the meta-analysis. Healthy dietary patterns showed no overall significant association with combined measures of FFM (-0.14[-0.36,-0.08]; I^2=78.7%, τ^2=0.07, Q=40.73, p<0.001). However, FFM measured in kilograms showed a significant negative association (-0.23[-0.38,-0.09]; I^2=41.1%, τ^2=0.01, Q=8.03, p=0.15), particularly in advanced economies. Neutral dietary patterns also showed no significant association (-0.31[-0.67, 0.04]; I^2=99.5%, τ^2=0.52 Q=518.72, p<0.001), though FFM percentage showed a negative association (-1.40[-2.59,-0.20]; I^2=99.4%, τ^2=0.42, Q=339.94, p<0.001). Notably, protein intake within neutral patterns showed a significant negative association with FFM (-0.54[-1.07,-0.01]; I^2=96.2%, τ^2=0.26, Q=137.29, p<0.001) and in advanced economies. Unhealthy dietary patterns had no overall significant association with FFM (0.08[0.18,0.34]; I^2=88.2%, τ^2=0.09, Q=50.56, p<0.001), but a significant negative association was observed in studies that included both working-age (18–64) and older adults (>65) (-0.09[-0.17,-0.01]; I^2=0.0%; τ^2=0.00, Q=2.20, p=0.53). High heterogeneity was observed across many analyses.

Conclusion: The relationship between dietary patterns and FFM in people with overweight or obesity is complex. While overall associations were often non-significant, specific healthy dietary patterns and, interestingly, higher protein intake showed some negative associations with FFM in certain subgroups. Unhealthy patterns generally lacked significant associations. Further research is needed to understand these relationships and the sources of heterogeneity.

id #128579

The Thermosensitive Kinase CLK3 Is Essential for Spermatogenesis and a Likely Driver of Heat-Induced Male Infertility.

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Male infertility affects approximately 1 in 20 men in the Western world and is the sole cause in one-third of couples undergoing assisted reproductive technologies. Approximately 75% of men present with low sperm count, poor motility and morphology, together with high levels of sperm DNA damage—factors closely linked to embryo loss. Testicular hyperthermia is a key contributor, as clinical studies show scrotal cooling improves semen quality in 66% of infertile men, with 44% achieving natural conception within a year despite five years of prior unsuccessful attempts.

Although the requirement for cooler testicular temperature has been known for over a century, the molecular basis for this sensitivity remains unresolved. Our research investigates thermally sensitive CDC-like kinases (CLKs), maximally active at 33°C but sharply inhibited by a 1°C rise—mirroring spermatogenesis sensitivity. In mammals, four CLK paralogues exist (CLK1–4). Mice lacking CLK1 or CLK2 remain fertile. As such, we developed transgenic models, including a Drosophila DOA knockdown and mouse $Clk3^{-/-}$ and $Clk4^{-/-}$ lines. While Clk4 deletion had no impact, loss of DOA or CLK3 caused male-specific infertility with hallmark features of heat stress including low sperm count, impaired motility, and elevated DNA damage. Females remain fertile and otherwise the animals are healthy.

We propose testicular temperature directly regulates CLK3 activity. Supporting this, hyperthermia causes a loss of piRNA by ~50%. piRNA are essential for spermatogenesis and transposable element (TE) repression. Notably, Heat stress, DOA knockdown, and CLK3 deletion all led to TE activation. As unregulated TE activity causes DNA damage, instability, and epigenetic disruption, we suggest CLK3 acts as a thermal sensor safeguarding germ cell genome integrity via piRNA-mediated TE suppression. These findings provide a mechanistic explanation for heat-induced male infertility and identifies CLK3 as a novel regulator of testicular temperature sensitivity.

id #127046

Local government perspectives on restricting unhealthy food advertising: A qualitative study

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Introduction: The World Health Organization states there is unequivocal evidence that food marketing influences food preferences and eating habits. This study aimed to investigate local government perspectives on restricting unhealthy food advertising on local government-owned infrastructure.

Methods: This qualitative study utilised individual and small-group interviews with representatives from LGs and other public health organisations across WA. Data were collected between June and October 2024 using semi-structured discussion guides. Purposive sampling ensured participants represented diverse LGs based on socio-economic status, geographic location, and annual revenue. A general inductive approach was used to analyse data.

Results: Thirty-four stakeholders from 15 LGs participated in the study. The main themes were: (1) policy understanding and interest; (2) policy development and approval; and (3) policy implementation and enforcement. Several barriers and enablers affecting policy development, adoption, and implementation were identified, influencing LG capacity, interest, and readiness. LGs with a clear commitment to protecting public health placed greater priority on developing a policy but identified the need for consistent definitions (e.g. unhealthy food) and frameworks (e.g. monitoring compliance of advertising agencies) to support them in this endeavour.

Conclusion: This study highlighted the need for additional support for LGs to adopt effective policies restricting unhealthy food advertising. Recommendations included offering targeted training for LG officers to build capacity in policy implementation and fostering partnerships with public health organisations to provide cohesive support and resources. Tools to simplify the process of consistently and accurately identifying foods that require advertising restrictions are important. Addressing these factors can significantly strengthen future policy efforts to reduce unhealth food advertising on government-owned infrastructure.

id #128582

Counting your oocytes before they hatch: Early-life ovarian reserve does not influence lifetime fertility.

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Within the ovary, there is a vast oversupply of oocytes, where 99.9% of the ovarian reserve (OR) is destined for atresia. This seemingly wasteful system raises the question; why are there so many oocytes in the ovary? Until now, OR quantification has been limited to a single-end-of-life measurement and unable to address this long-standing question. Currently, primordial follicle counts require removal of ovary tissue but we have developed a method to quantify OR in live 25-day-old mice for the first time. Thus, we aimed to determine if the number of primordial follicles in the ovary at 25d influenced lifetime reproductive output. In *Figla-Cre*$^{Tg/0}$-*tdTomato*$^{fl/0b}$ mice, which express fluorescent tdTomato in oocytes, the primordial follicles can be visualised through the surface of the ovary. This allowed us to surgically externalise and image the ovaries of 27 mice for OR quantification. Once the mice recovered from surgery, they were entered into a fertility trial until 13 months of age. OR was again quantified at this timepoint to examine rate of OR loss during reproductive decline. We monitored the pup production, inter-litter interval, and age at last litter across life to generate a comprehensive fertility dataset. Surprisingly, early-life OR was not associated with any of the fertility metrics. We are currently quantifying the end-of-life OR to be compared to the early-life OR. We will determine if the rank order of OR size in young females is preserved across life, as it has never been experimentally shown that early life OR determines when the ovarian reserve is depleted. Thus far, we have been able to show that a large OR early in life does not guarantee a prolonged reproductive lifespan, and for the first time, this technique has made it possible to quantify the OR at multiple ages in the same animal.

id #128583

Towards *in vitro* sperm capacitation and IVF for the fat-tailed dunnart (*Sminthopsis crassicaudata*).

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Since colonisation, Australia has witnessed widespread and devastating biodiversity losses and currently possesses the highest rate of mammalian extinctions globally. Marsupials are disproportionally impacted compared to other groups and remain particularly vulnerable to environmental threats. Over the past decade, assisted reproductive technologies (ARTs), including in vitro fertilisation (IVF), have been recognised as promising tools for conservation. However, progress in ART for Australian marsupials has been limited, and IVF protocols are yet to be established.

In this study, we used the fat-tailed dunnart (*Sminthopsis crassicaudata)* as a laboratory-based model to establish protocols for inducing and assessing sperm capacitation, a critical step towards achieving IVF. Epididymal spermatozoa were collected from adult dunnarts via swim-out and incubated in one of nine capacitation media. Sperm motility, longevity, and capacitation-related morphological changes were monitored. We adapted and optimised quantitative assays for motility, morphology, tyrosine phosphorylation, and the acrosome reaction for dunnart sperm.

Preliminary results indicated that a newly developed culture medium supports sustained progressive motility and morphological changes associated with capacitation in dunnart sperm under defined incubation conditions. The medium outperformed a standard comparative formulation, maintaining a significantly higher motility over a two hour period. By four hours, although overall motility declined in both media, the majority of motile sperm in the novel formulation exhibited morphological features consistent with capacitation. Further analyses are underway to expand replicates and quantify key capacitation-associated parameters across additional formulations.

These findings show that a high proportion of dunnart motility can be supported in simple media, and further challenges the notion that marsupial sperm requires complex media conditions to undergo capacitation. This work advances our understanding of marsupial sperm biology, and lays essential groundwork for optimisation of IVF protocols in marsupials, with the ultimate goal of developing next-generation conservation tools for threatened species.

id #126024

All in the Family: Lessons Learned from In Vitro Embryo Production in Horses, Donkeys, Mules and Zebras

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In vitro embryo production in equids has traditionally focused on horses, but recent advances are expanding its reach across the entire family, including donkeys, mules and even zebras. This presentation explores key milestones and lessons learned from applying assisted reproductive technologies (ART) across multiple equid species, highlighting both the shared biology and species-specific challenges that shape success. Drawing on a decade of research, this talk will cover the production of the first cloned horses in South America and Australia, the first ICSI-generated embryos in donkeys and mules, and the first cloned zebra embryos. By examining how these closely related species respond we can better understand the biological and technical barriers to reproductive success. This comparative approach not only improves outcomes in equid domestic breeding programs but also opens new possibilities for human reproductive medicine and wildlife conservation. From stables to savannahs, ART in equids is evolving and with it, our ability to support reproduction across one extraordinary family.

id #129097

Co-development and implementation of a metabolic care pathway for adults living with cystic fibrosis at a tertiary adult centre

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Aim

With increasing life expectancy in people living with cystic fibrosis (pwCF), new challenges such as obesity are emerging, particularly with the advent of CF modulator therapies. At our adult CF centre, median BMI rose from 23.57kg/m^2 to 25.15kg/m^2 following introduction of Elexacaftor/Tezacaftor/Ivacaftor. (1) This study aimed to co-develop and implement a metabolic care pathway to address the rising prevalence of obesity and associated metabolic complications.

Methods

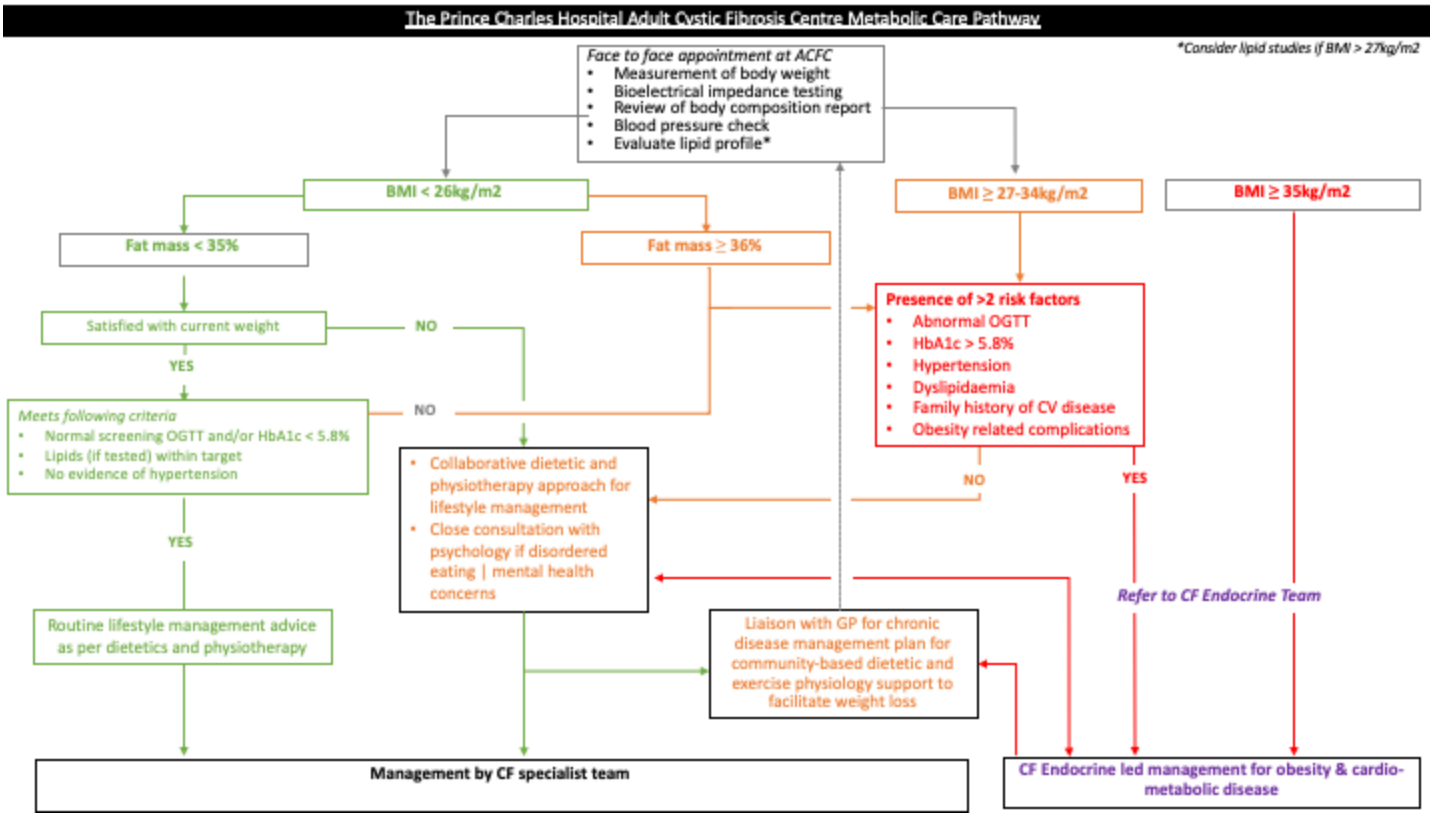
Using the Consolidation Framework for implementation Research, we developed a broad-based survey targeting both consumer (pwCF) and multidisciplinary team (MDT) providers, followed by co-development workshops. These facilitated workshops were face-to-face and comprised respiratory physicians, dietitians, physiotherapists, nurses, social workers and psychologists. Each 60-minute workshop began with a brief presentation of consumer and healthcare provider perspectives gathered from the survey to frame the discussion. Participants were then invited to build consensus on key areas, including what should be continued, barriers to address, opportunities for innovation, and immediate actions to implement.

Results

Stakeholders agreed that (i) obesity is increasingly prevalent in pwCF, (ii) lifestyle optimisation should be first line management and (iii) a lack of CF-specific evidence requires adaptation from general population data. Barriers included limited evidence, fragmented metabolic data collection, cost-related access issues to community providers, and reduced in-person clinic visits. Key innovation included physiotherapy-dietetics co-consultations, routine metabolic screening for all outpatient in-person encounters and pharmacist alerts for anti-obesity medications. A pragmatic, tiered risk stratification approach (low, moderate, high) was co-developed and embedded into routine care using accessible, low cost screening tools.

Conclusion

Through a structured implementation process, we co-developed and embedded a metabolic health pathway into a tertiary adult CF centre. This model of care enables early identification and intervention for obesity and metabolic risk in pwCF, while also providing specialist endocrinology support for pwCF with complex or treatment-resistant obesity.



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id #130892

Novel endocrine links between reproduction and metabolism in females

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The female reproductive system is highly responsive to peripheral endocrine signals, particularly from metabolic tissues. These signals align reproductive function with the body's energy status, meaning that metabolic shifts can influence ovulation, fertility, and reproductive hormone balance. Conversely, fluctuations in ovarian hormones also shape metabolic health. This reproductive–metabolic crosstalk is most evident at puberty, when ovarian activation is strongly influenced by body size and composition, and at menopause, when the loss of ovarian function is accompanied by metabolic disruption.

My research uses innovative technologies to uncover novel endocrine links between reproduction and metabolism in females. Over my 15-year postdoctoral career in reproductive endocrinology, I have progressed from investigating the biochemical mechanisms of ovarian protein hormone synthesis, to developing technologies for manipulating ovarian function, and more recently to preclinical mouse models to advance our understanding of reproductive physiology. In collaboration with early-career researcher and muscle and metabolic physiologist Dr Adam Hagg, my team is now identifying novel endocrine mediators, such as ovarian inhibins, of reproductive–metabolic crosstalk in females. In this presentation, I will describe our serendipitous discovery that ovarian inhibins act as gatekeepers of female metabolic health and outline our emerging interest in how skeletal muscle and myokines contribute as endocrine regulators of female reproduction

id #127053

Obesity risk factors in an autonomous world: unhealthy food access and reduced physical activity

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Rapid advancements in vehicle automation are forecast to bring massive changes in how individuals access food, with implications for both diet quality and levels of physical activity. The aim of this study was to explore consumers' receptiveness to autonomous forms of food delivery, how they perceive their lifestyles would change once these services are widely available, any concerns they have, and preferred regulatory responses to address potential negative health consequences. Eight focus groups were conducted with 54 Australians across five states, with representation across metropolitan and regional areas. Average age was 43 years and 51% of participants were female. A semi-structured interview guide was used to facilitate discussions, with four brief videos (each 58-90 seconds) shown to demonstrate emerging autonomous food delivery methods: drones, street bots, vans, and vending machines. Reactions were generally positive, with participants appreciating the novelty of the services, their greater convenience compared to physically going to the shops, and anticipated lower costs compared to human-driven delivery services. Some expected to eat more unhealthy food and to be more sedentary. Others were concerned about wide-scale job losses among those in driving occupations, the noise associated with drones, and increasing levels of consumerism. Forms of regulation considered acceptable to minimise any negative consequences included the introduction of exclusion zones (mainly around schools), density limits on the numbers of autonomous delivery vehicles permitted within specified areas, curfews on drone deliveries, and the provision of nutritional information at the point of sale. Overall, the identified high level of acceptance of the types of autonomous food delivery services that are emerging around the world highlights the need for proactive consideration of the potential effects on diet quality and physical activity.

id #128333

The Impact of Oocyte-Secreted Factors on Ovarian Cancer Development

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Ovarian cancer is the leading cause of gynaecological cancer mortality in women, with epithelial ovarian cancer (EOC) being the most common subtype. Poor patient survival is largely attributed to a limited understanding of early developmental processes, concomitant with no early detection diagnostic tools. Previously, we observed that the loss of oocytes from primordial follicles enables the transformation of abandoned somatic pregranulosa cells into heterogeneous ovarian tumours in mice [1, 2]. Herein, we further investigate the role of the oocyte in the development of EOC. Based on our previous findings, we hypothesise that oocyte-secreted factors will suppress EOC disease progression.

Using mouse and human EOC cell lines (mOSET2, T2BR and OVCAR-3), we assessed the impact of cumulus-oocyte-complex (COC)-conditioned media or COC co-cultures on cell proliferation (tritiated thymidine incorporation assay) and gene expression of key markers (via quantitative PCR). Both treatment groups reduced cell proliferation and decreased expression of proliferation-related genes *Cdkn1b* and *Ccne1* in the mOSET2 cell line, and *c-KIT* in the OVCAR-3 cell line. Oocyte-secreted factors from COC co-cultures also tended to reduce the expression of EOC markers, *Cdh1* (E-cadherin), *Dab2* and *Muc16,* in the mouse mOSET2 cells, and *CDH1* and *MUC16* in the human OVCAR-3 cell line; however, this was not statistically significant. The anti-mitogenic effects and decrease in epithelial gene markers were not observed when cells were treated with denuded oocytes alone, cumulus cells alone, or recombinant exogenous oocyte-specific secreted proteins, GD9 and BMP15. Thus, the factors within the COC conditioned media responsible for this inhibitory effect remain unknown. However, additional investigation is currently underway by RNA sequencing to elucidate the potential molecular mechanisms.

These results support a novel paradigm in which COCs may play a key role in EOC development. This improved mechanistic understanding will have implications for early detection, prevention and therapeutic intervention of this disease.

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id #129101

Gender Inequality and Socio-Economic Disadvantages Associated with Obesity in Women Compared to Men: A Rapid Review of Observational Studies.

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Aims

To systematically synthesise evidence on whether obesity disproportionately impacts gender inequality and socio-economic disempowerment among women with obesity compared to men with obesity in high-income countries.

Method

A systematic search of Embase, MEDLINE, Web of Science, and Google Scholar for relevant studies. Risk of bias was assessed using the JBI critical appraisal tools.

Results

We identified 17 observational studies published between 2004 and 2021 from an initial 3,495 citations. Studies primarily used a Body Mass Index (BMI) of ≥30 kg/m² to define obesity and consistently identified disproportionate socio-economic disadvantages for women

with obesity compared to those without obesity. These women often earned a lower monthly income (e.g., monthly salary in Finland, €1,464.0 vs. €1,641.5), faced higher unemployment rates (e.g., in Finland, OR=2.266, p<0.01), and had lower personal incomes (e.g., annual income in Canada for 2002: $33,424 vs. $34,686). They also reported greater perceived workplace discrimination (e.g. in the US, 14.5% of women with BMI ≥35kg/m² vs. 1.1% with BMI 19 to 24.9kg/m², p<0.05). Additionally, women with obesity earned lower hourly wages (e.g., in Germany, -0.198 log points, p < 0.01, vs. -0.007 log points) and received smaller bonus payments (e.g., South Korea, OR = 0.501, p < 0.01 vs. 1.305) compared to their male counterparts with obesity. For men with obesity, the findings were less consistent; some studies indicated lower wages (e.g., in Sweden), while others found no significant effect on employment or even higher wages in some cases (e.g., Iceland). Men with obesity reported discrimination, but less consistently across outcomes compared to women.

Conclusion

Obesity is reported to be a significant driver of gender inequality and socio-economic disadvantages, with a more pervasive and detrimental impact on women compared to men with obesity in high-income countries. This emphasises the need for gender-sensitive interventions to address weight-related socio-economic disparities.

id #127822

Three easy ways to positively impact student wellbeing

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Statistics of student wellbeing in university settings both in Australia and internationally remain poor; 25% of students report severe depression, stress or anxiety. This is particularly the case in veterinary science, where 80% of students score highly for stress. This problem is ongoing into early clinical practice, with 54% of veterinary interns and residents reporting moderate to severe depression and 30% experiencing suicidal ideation. This lack of wellness relates directly to students' ability to learn, impacting attention span, cognition and problem solving. In addition, when students fail to develop coping skills while experiencing this stress, they experience more issues when transitioning into clinical practice. The role of the educator in addressing this ongoing 'wellbeing crisis' is clear, given the frequency and quality of staff-student interactions significantly impact student wellbeing. Given that most tertiary teaching staff already have unreasonable workload burdens and limited capacity to change existing university procedures, I suggest 3 simple routes for positively impacting student wellbeing; normalising help seeking, reframing failure and communicating empathetically. These approaches do not add to workload or require system support; they are small changes in teaching practice which create safe and supportive learning environments. Normalising help seeking includes educating students about available support, leading by example and normalising honest conversations about mental health. Reframing failure, based on the work of Carol Dweck, involves framing failure as feedback, distinguishing between the event of failing and the identity of being a failure and normalising failing as learning. Empathetic communication revolves around seeking and actively listening to student feedback, validating students' experiences and actioning a solution where appropriate. These simple strategies can profoundly impact the wellbeing of university students, creating graduates with better coping skills as well as important discipline knowledge.

id #128590

Defining the impact of endometriosis on the hormone responsiveness of human endometrial epithelia utilising endometrial epithelial organoids.

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The inner lining of the uterus, the endometrium, completely remodels in response to ovarian steroid hormones during the menstrual cycle. Endometriosis is a chronic, debilitating gynaecological disorder that affects more than 10% of women (1), with 30-50% of these women suffering from infertility (2) likely due to disruptions in hormone-driven processes critical for receptivity and embryo implantation. The underlying mechanisms of endometriosis-associated infertility remain largely unknown. Our objective was to utilise human endometrial epithelial organoids (EEO) to investigate the impact of endometriosis on the hormone-responsiveness of endometrial glands and their secreted products.

EEO derived from the eutopic endometrium of patients diagnosed with minimal-mild (stages I-II, n=6), moderate-severe (stages III-IV, n=3) and without endometriosis (control, n=3) were treated with either vehicle control, 17β-estradiol (E2), or E2 and medroxyprogesterone acetate (MPA) to mimic menstrual cycle phases. Gene expression of steroid hormone receptors *PGR, ESR1 and ESR2* were examined by RT-qPCR. The basolateral secreted proteome of hormone-treated EEO was analysed by mass spectrometry.

EEO treated with E2+MPA demonstrated progesterone-mediated downregulation of *PGR*, resembling in vivo cycle phase-dependent expression patterns, in control patients (p<0.05) and stage I-II endometriosis (p<0.05) compared to vehicle treatment, but not in patients with stage III-IV endometriosis. 39 significantly differentially abundant proteins were identified in the basolateral secreted proteome of EEO from patients with endometriosis compared to those without endometriosis and between hormone treatments, including, CRISP3 (FC=20.39, p<0.0001), INHBB (FC=8.17, p<0.001), MGAT1 (FC=4.11, p<0.01) and WNT7A (FC=8.46, p<0.05).

EEO from endometriosis patients demonstrate an impaired response to hormones, leading to an altered steroid hormone receptor expression pattern in patients with moderate-severe endometriosis, and an aberrant secreted proteome in endometriosis. These findings are critical in determining the impact of endometriosis on the hormone-driven processes required for endometrial receptivity and embryo implantation and to develop treatments targeting endometriosis-associated infertility.

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id #128079

Habitual dietary intake does not predict micronutrient deficiencies in individuals with Diabetes-Related Foot Ulcers: Analysis from the VITAFOOT Pilot Trial

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Micronutrients such as Vitamin C and Zinc are important in all phases of wound healing, including in collagen synthesis and epithelialisation(1). Deficiencies are common in individuals with Diabetes-Related Foot Ulcers (DFU)(2). The Australian Short Dietary Screener (AUS-SDS) assesses average daily intake across six food groups and is validated in an elderly Australian population(3). We aimed to determine average dietary intake across food groups and correlation to micronutrient deficiencies in individuals with DFU.

The VITAFOOT Study is a pilot randomised control trial investigating the effect of a combination micronutrient supplementation on ulcer healing in patients with DFU. Participant diet across the domains of fruit, vegetables, legumes/beans, cereal/grains, protein and dairy sources was evaluated at baseline using the AUS-SDS(3). Daily equivalent frequencies (DEFs)were calculated for each food group, with 1 DEF representing one serve per day. Plasma Vitamin C and Zinc levels were recorded at enrolment.

Ninety-nine participants completed the AUS-SDS. Median [interquartile range] intakes were 1 [1-1] DEF vegetables, 1 [0.5-2] DEF fruit, 2 [1-2] DEF dairy, 0.07 [0-0.28] DEF legumes/beans, 1 [0.78-0.2] DEF protein sources and 1 [0.89-2] DEF dairy sources. For any food group, less than 40% of participants met intake recommendations (4). Eighty-nine participants had plasma Vitamin C and 96 plasma Zinc levels recorded at enrolment. No significant correlations were observed between reported intake of any food group and plasma Vitamin C or Zinc levels. There was no difference in vegetable (p=0.27) or fruit (p=0.11) intakes between those who were Vitamin C replete versus deficient (plasma Vitamin C <4µmol/L).

Average daily intake of all food groups amongst participants with a DFU was below the recommended intake for Australian adults, indicating suboptimal diet quality(4). The lack of significant correlation between dietary intake and micronutrient levels suggests factors additional to diet contribute to nutritional deficiency in this high-risk population.

	Veg DEF	Fruit DEF	Grain DEF	Legume DEF	Protein DEF	Dairy DEF
Median	1	1	2	0.07	1	1
Quartile 1	1	0.5	1	0	0.78	0.89
Quartile 3	1	2	2	0.28	2	2
Percentage achieving recommended daily serves* (n=99)	5.05% (n=5)	39.4% (n=39)	5.05% (n=5)	N/A	9.09% (n=9)	12.1% (n=12)
***Compared to the NHMRC Guidelines for age and sex**						

Table 1: Median dietary intake of six major food groups in ninety-nine patients with DFU infections and comparison to NHMRC Recommended Daily Intake for age and sex

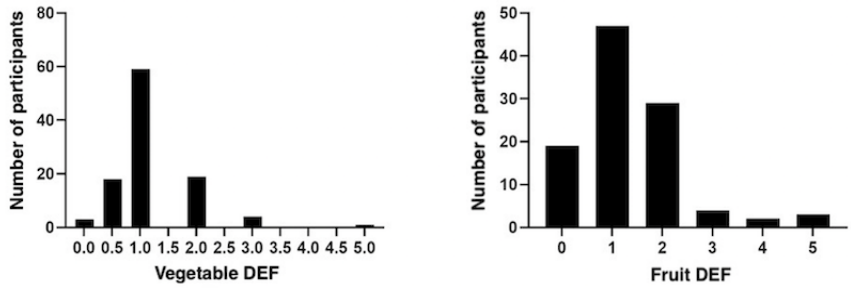

Figure 1: Distribution of daily equivalent frequency consumption of Vegetables and Fruit

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id #132432

Eating Disorders in People Presenting for Obesity Treatment: Treatment Evidence, Practice Wisdom, and Future Directions

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Research examining the treatment of eating disorders in people with obesity remains limited, with most studies focused on binge eating disorder (BED). This presentation will summarise the current evidence base for treating eating disorders in individuals with higher weight, highlighting key treatment approaches evaluated in the literature, including cognitive-behavioural therapy (CBT), interpersonal psychotherapy (IPT), and behavioural weight-loss interventions (BWLI). The session will describe the underlying formulation models, primary treatment targets, typical duration, and treatment outcomes.

Given the scarcity or research in this area, this presentation will draw on clinical experience and expert opinion to explore if, when, and how weight-loss interventions might be safely and effectively provided to individuals with concurrent eating disorders, acknowledging the tensions between weight-focused and weight-inclusive approaches. Practical guidance will be offered regarding identifying and accessing evidence-based eating disorder treatments in Australia.

The session will conclude by outlining key clinical and research gaps, including the need for appropriate screening and assessment tools, trials examining treatment adaptation and treatment integration/sequencing, better understanding of outcomes beyond weight or symptom reduction, and frameworks for co-produced, weight stigma-sensitive care to improve outcomes for people with higher weight and eating disorders.

id #128336

Bioprinted placental organoids as a high-throughput platform for drug screening during early pregnancy

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Preeclampsia is a cardiovascular condition that occurs during pregnancy, associated with placental dysfunction. Without a cure, women and children affected by preeclampsia have an increased risk of chronic health conditions later in life. 3D bioprinted models of the placenta can provide insight into placental development for therapeutic testing. We aimed to assess the effectiveness of aspirin and metformin at abrogating an inflammatory response in first trimester trophoblast organoids.

ACH-3P trophoblast cells were bioprinted in a poly-ethylene glycol (PEG)-based matrix using a RASTRUM bioprinter (Inventia Life Sciences) for 12 days. Organoids were treated with tumour necrosis factor alpha (TNFα; 20ng/mL) with or without aspirin (0.5mM) or metformin (0.5mM). Organoid size, number, and metabolic activity were assessed via live cell imaging and Alamar blue assay. On day 12, culture media was collected to assess inflammation via a C-Reactive Protein (CRP) ELISA. Finally, immunofluorescence staining was performed to assess trophoblast differentiation by confocal microscopy.

There were no statistically significant differences in organoid size or number between conditions. However, from day 9 a statistically significant decrease in metabolic activity was observed in TNF-α ± aspirin/metformin groups compared to the control ($p<0.01$). Aspirin ($p<0.001$) or metformin ($p<0.01$) on their own also reduced ACH-3P organoid metabolic activity. TNFα induced a ~25-fold increase in CRP concentration within organoid media compared to all other groups. Finally, confocal imaging revealed that organoids from all conditions were able to differentiate into extravillous trophoblasts (EVTs; HLA-G) and syncytiotrophoblasts (STBs; β-hCG). Although there were no statistically significant differences in EVT differentiation, STB differentiation was reduced in all groups ($p<0.05$) except TNFα + metformin ($p=0.07$).

In this study, we demonstrate that bioprinted ACH-3P trophoblast organoids can be used as a high-throughput model for drug testing and to determine multiple end points related to placental development in both health and disease.

id #128848

"Lost in the System": Psychological Insights from Lived Experience of Obesity and the Clinical Power of Consent

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Aims This presentation aims to share lived experience perspectives on the psychological burden of chronic obesity and repeated weight loss attempts. It highlights the clinical importance of obtaining consent before discussing weight and explores how systemic and interpersonal barriers affect patient engagement and outcomes. We explore how structural stigma and clinical norms contribute to patient harm. This session is co-designed and delivered by people with lived experience of obesity.

Methods Drawing on qualitative insights from individuals with lived experience, including members of the Weight Issues Network (WIN), we present narrative reflections and thematic analysis of common clinical encounters. These accounts were gathered through community consultation, peer interviews, and advocacy forums. Themes were identified around emotional distress, healthcare avoidance, and the impact of clinician communication styles.

Results Participants consistently reported feeling "lost in the system," where weight was treated as a primary concern without consideration of psychological wellbeing or trauma history. Unsolicited weight discussions were frequently described as triggering shame, reinforcing stigma, and leading to disengagement from care. In contrast, when clinicians sought explicit consent to discuss weight and acknowledged the complexity of obesity, patients reported feeling respected, safe, and more open to collaborative care. Consent-driven conversations were associated with improved trust, adherence, and emotional resilience.

Conclusion For clinicians, the act of asking, "Do you mind if we talk about your weight today?" can be transformative. This simple question signals respect, autonomy, and a willingness to listen—key ingredients in trauma-informed, person-centred care. Embedding psychological insight and lived experience into clinical practice not only reduces harm but enhances outcomes. Clinicians are invited to reflect, listen, and lead change—starting with consent.

id #123729

Investigating acrosome formation under Protamine 2 deficiency using a 3D spatiotemporal approach

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Proper acrosome formation is critical for sperm functionality and morphology, involving dynamic processes such as organelle relocation, repurposing, and reshaping. The cytoskeleton provides essential mechanical support and facilitates intracellular trafficking during this process. Traditional studies utilizing thin histological sections often fail to capture the three-dimensional (3D) context of cells and tissues, potentially leading to information loss.

To address this limitation, we have developed a tissue-clearing protocol based on the CLARITY method, combined with confocal microscopy, to study spermatogenesis in 3D within the seminiferous tubules. Using Imaris software, we reconstruct the surfaces of postmeiotic nuclei and acrosomes at various stages of spermatogenesis (Golgi, Cap, Acrosomal, and Maturation phase) and quantify parameters such as volume, sphericity, and distance from the tubule borders. These quantitative data serve as valuable inputs for computational comparisons and modelling.

Our previous research has identified a link between the nuclear protein Protamine 2 (Prm2) and the cytoskeletal protein Septin 12 (Sanovec et al., 2024). In Prm2-deficient *(Prm2$^{-/-}$)* mice, we observed aberrant acrosome formation and altered localization of Septin 12 and actin, suggesting a disruption in cytoskeletal organization during spermiogenesis (Schneider et al., 2016). Therefore, we aim to apply our 3D imaging approach to analyze acrosome formation in *Prm2$^{-/-}$* mice in detail, focusing on the spatial distribution of actin and Septin 12 as well as the acrosome as a whole organelle. Our findings will be further supported using super-resolution and electron microscopy.

This integrative approach provides a comprehensive understanding of acrosome biogenesis and its perturbations due to Protamine 2 deficiency, offering insights into the molecular mechanisms underlying sperm development and potential causes of male infertility. The newly developing platform can act as a robust pipeline for acrosome analysis in various mouse models, uncovering subtle details in this dynamic process.

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id #123474

Pilot evaluation of the Connecting the Dots program: early childhood health promotion training for primary health professionals

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This study aimed to evaluate the feasibility, acceptability and effectiveness of the Connecting the Dots (CTD) professional development program for primary health professionals (PHPs). CTD embedded key messages from the *Healthy Beginnings* early childhood obesity prevention program into online webinars delivered by Karitane, a not-for-profit parenting service. The evaluation used an action research approach, including both process and impact evaluation. Process evaluation included webinar observations to identify behaviour change techniques and adult learning strategies used by facilitators, and acceptability surveys after webinars. Impact evaluation examined changes in PHPs' knowledge, attitudes, practices and self-efficacy using repeated surveys before and one month following webinars. Interviews with attending PHPs and program facilitators informed process and impact evaluation. From June 2022 to June 2024, CTD delivered 36 webinars, 1,246 PHPs registered and 463 attended live. Facilitators' delivery style reflected adult learning principles, and they used behaviour change techniques that would be expected to influence PHPs' knowledge and skills. The national scope of the program was seen as a strength but posed challenges for dissemination; facilitators reflected on the difficulty of reaching and meeting the needs of a national audience. Acceptability surveys indicated that >90% of PHPs viewed the program favourably; this was echoed in qualitative reflections. PHPs valued practical advice, interactivity of webinars, and provision of program materials to review after sessions. Impact evaluation findings suggested the program supported the development of knowledge and awareness of early childhood health promotion; however, interviewees offered few reflections regarding their clinical application of the content. In future, similar programs should include a more comprehensive impact evaluation, including an examination of changes to clinical practice and child health outcomes. The findings also highlight the need to ensure appropriate investment in promoting such programs to ensure successful scale-up.

id #128598

Exploring and understanding weight stigma in First Nations peoples in the Northern Territory, Australia: a qualitative study

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2. Menzies School of Health Research, Charles Darwin University, Darwin, Northern Territory, Australia

3. Monash University, Melbourne, Victoria, Australia

4. Danila Dilba Health Services, Darwin, Northern Territory, Australia

Weight stigma adversely affects the health and wellbeing of people living with obesity. First Nations Australians experience disproportionately high rates of obesity compared to non-First Nations Australians, yet little is known about how weight stigma affects them. This study aimed to explore the First Nations perspective of weight stigma in the Northern Territory, namely the experiences, responses, and implications of weight stigma on health and wellbeing.

This qualitative study was underpinned by a phenomenological methodology. In-depth interviews were conducted with 16 First Nations adults living with obesity (4 men, 12 women, mean age 42 years), recruited from the Royal Darwin Hospital Weight Management Clinic. Interviews were conducted by SCG, an Aboriginal researcher with lived experience of obesity. Data were analysed independently by AC and AW through two rounds of inductive analysis.

Participants experienced weight stigma across multiple settings, including healthcare, public spaces, and workplaces. In all settings, stigma manifested in the forms of direct (e.g., name-calling), environmental (e.g., not fitting into seats on aeroplanes), and indirect (e.g., non-verbal judgment) discrimination. Responses to stigma varied from internalisation, to confronting perpetrators of stigma. Many participants noted that with increasing age, they developed resilience and were less affected by stigma. The most widely reported implications of weight stigma were that of low self-esteem, strained family dynamics, avoidance of certain activities and places, and feeling like opportunities were limited due to their weight. These in turn led to social exclusion and self-isolation, poor mental health, a sense of powerlessness, and perpetuation of unhealthy behaviours.

These findings highlight the pervasive impact of weight stigma on the health and wellbeing of First Nations Australians living with obesity in the Northern Territory. They underscore the need for comprehensive strategies to reduce stigma and promote inclusivity across multiple settings, to improve health and wellbeing for First Nations people.

id #129878

Gut Microbiota-Derived Metabolites Promoting Healthy Aging Through Enhancement of Mitochondrial Homeostasis

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This talk will highlight the emerging role of gut microbiota-derived metabolites (GMDMs) as pivotal regulators of host physiology and aging. Urolithin A (UA), a first-in-class mitophagy activator derived from microbial metabolism of ellagitannins, has demonstrated significant efficacy in enhancing muscle function, as shown in Nature Medicine (2016) and Nature Metabolism (2019), and was further validated in two independent double-blind, placebo-controlled trials published in JAMA Network Open (adults aged 65–90 years) and Cell Reports Medicine (mean age ~52 years, BMI ~29) in 2022. Building on UA's translational success, we recently identified additional GMDMs with longevity-promoting potential.

In the latter part of this talk, I will present our recent findings published in Nature Communications (2024), which revealed that 3-phenyllactic acid (PLA), a microbial metabolite secreted by Lactiplantibacillus plantarum, extends healthspan in Caenorhabditis elegans by activating energy metabolism and stress resilience pathways in a SKN-1/ATFS-1-dependent manner. Notably, circulating PLA levels inversely correlate with physical performance in individuals with sarcopenia. To assess its translational relevance, we established a composite Healthy Aging Index (HAI) integrating motility, mitochondrial respiration, and ATP levels. These findings support the therapeutic potential of selected GMDMs in mitigating age-related muscle decline and enhancing metabolic resilience in aging populations.

id #131671

Management of Adults with Differentiated Thyroid Cancer – Updates from the New ATA Guidelines 2025

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The management of differentiated thyroid cancer (DTC) has been reviewed in the recently updated by the American Thyroid Association this year, updating the last guidelines from 2015. This talk will cover the initial evaluation and staging, the surgical approach, adjuvant therapies, monitoring, and management of subsequent recurrent disease particularly radioactive iodine refractory (RAIR) disease.

Though there has been an increase in thyroid cancer in the years leading to the previous guideline, the incidence has plateaued in the past few years, due to successful de-escalation of over treatment of low risk disease. There has been a number of new histological subtypes including non invasive follicular tumours with papillary like nuclear features (NIFTP) which are now included in the initial staging. Initial management includes review of the pre operative imaging, molecular testing where possible, and consideration of active surveillance or thyroidectomy. The DATA (Diagnosis, Assessment, Treatment, and Assessment) Framework has been utilised in the management of initial disease, persistent or recurrent disease, and RAIR. The estimated risk of structural recurrence can be estimated at initial review depending on the specific histological subtype, lymphovascular invasion, extrathyroidal extension, and distant metastases, in order to balance the potential for recurrence and residual disease with the adverse effect of a more aggressive initial approach. Tyrosine kinase treatment has revolutionised the care for patients with metastatic disease. Generic VEG-F therapy will be discussed in addition to the benefits of targeted therapy when the molecular driver is identified.

id #128343

Dietetic support provided to adolescents with obesity during an intensive behavioural weight management intervention

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Multi-component lifestyle interventions are the first-line treatment for adolescent obesity; understanding the dietetic resourcing required to deliver such interventions is important for informing future service design. This study aimed to describe the dietetic time, support, and resources provided to adolescents with obesity participating in a behavioural weight management intervention. Fast Track to Health (HREC/17/SCHN/164), a 52-week RCT, recruited 141 adolescents with obesity and related cardiometabolic complications. Adolescents followed a four-week very-low-energy diet (Phase 1) followed by intermittent (IER) or continuous (CER) energy restriction. Frequency of dietetic consults/support reduced between Phase 2 (week 5-16) and 3 (week 17-52). The intervention included 13 dietetic consults and 9 scheduled supports (email/phone/text), and 40 resources were available for distribution. Descriptive statistics summarised dietetic time, scheduled supports used, and number and type of resources provided to participants. Consult time and resources provided were compared by study phase using Friedman and Wilcoxon signed rank tests. Study completers (n=97) spent a mean(SD) of 9.4(2.8) hours in dietitian visits throughout the 52-week trial and were provided 11(3) resources. Median(IQR) time per dietitian visit among all participants (n=141) was 46(16) minutes, with 12(3.5) visits, and 4(4) scheduled supports per participant. Dietitian time per visit was higher in Phase 1 (median(IQR)=50(18) minutes) than Phases 2 (42(19) minutes) and 3 (45(24) minutes) (χ^2=33.9, p<0.001). The number of resources provided per participant decreased over time (Phase 1 – 5(2); Phase 2 – 3(3); Phase 3 – 2(2)) (χ^2=134.3, p<0.001). Frequently used resources included healthy snack and recipe ideas (n=158), low calorie recipes (n=104) and calorie counting guides (n=98). Our results indicate that adolescents require support with food selection and preparation during a behavioural weight management intervention. Despite an intensive schedule of dietetic support, the total contact time with the dietitian did not meet paediatric obesity clinical practice guideline recommendations (≥26 hours(1)).

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id #129879

Collaborating for change: Empowering communities and policy makers to improve food environments

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Creating equitable, health-promoting food environments requires cross-sector collaboration and the translation of evidence into practical policy and community action. This presentation showcases two research initiatives that exemplify collaborative approaches to enhancing food environments in Australia.

The first case study is the WA Food Atlas, a geospatial platform co-designed with local and state governments to map and monitor food outlet access across Western Australia. It provides policy makers with objective, place-based data to inform public health planning, food environment regulation and strategic policy decisions. The tool also fostered cross-sector collaboration and conversations around healthier urban design. Its success—reflected in strong end-user uptake and policy use—led to NHMRC funding to expand it nationally as the Australian Food Atlas, currently under development. Key enablers of its impact include alignment with policy priorities, sustained engagement with government users and adaptability to handle variations in how different local governments collect and organise their data.

The second case study is a community-led intervention in Bridgetown, Western Australia, where local residents and retailers implemented Amped Out—a voluntary ban on energy drink sales to children. Prompted by previous research on the health risks of energy drink consumption among adolescents, the community reached out to our research team for support. A four-month pilot involving all retailers was conducted, with community consultation integrated throughout. The trial received strong local support and led to the permanent continuation of the ban. Multiple regional towns have since expressed interest in replicating the model.

Together, these case studies demonstrate the importance of tailoring research translation strategies to context—whether through policy-focused platforms like the Australian Food Atlas or grassroots mobilisation as seen in Bridgetown. Both initiatives underscore the value of co-design, stakeholder trust and responsiveness to local needs in driving food environment reform.

This presentation offers practical insights for researchers, policy-makers and practitioners seeking to create healthier food environments through collaborative, evidence-informed approaches.

id #128600

Hybrid strains of mice with polygenic mitochondrial complex I insufficiency are obese and display features of cardiometabolic disease

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2. Department of Neuroscience, Monash University, Melbourne, vic, Australia

Mitochondria are present in almost all cells of the body and as such, mitochondrial dysfunction often leads to multisystem disorders, with cardiomyopathies being one of the most prominent manifestations. Due to the genetic complexity and multi-systemic nature of mitochondrial dysfunction, one of the biggest limitations in the field is the lack of suitable research models that recapitulate human disease, particularly those driven by polygenic underpinnings. To this end, our lab recently analysed 107 strains of mice from the HMDP, a panel of genetically diverse inbred mouse strains, and identified four strains which demonstrate robust reductions in mitochondrial complex I abundance. We subsequently bred 2 of these strains (BXD44 and BXD71) and aged cohorts (n=10-16) and controls (C57Bl/6J) to 14 months. Anthropometric phenotyping across this study found that these mice display significantly increased weight gain from 16 weeks of age which is directly related to an increase in fat mass. This obesity phenotype is attributable to reduced activity and energy expenditure and results in glucose intolerance and insulin resistance. Furthermore, molecular analysis performed on the hearts of these mice demonstrated characteristic features of cardiomyopathy including reduced SERCA2 expression, and increase Myh7, while no change in fibrosis markers (colfa3/col1a1) was evident. These results indicate the presence of a cardiometabolic disease phenotype driven by mitochondrial dysfunction. These findings associated with global polygenic complex I insufficiency in these mice, highlight these strains as a useful new model to study cardiometabolic disease in a model organism.

id #129880

Prader-Willi Syndrome – Innovations in Adult Care

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Prader-Willi Syndrome (PWS) is a non-inherited genetic condition that occurs spontaneously in 1 in 15 000 people worldwide. There are at least 1800 people with PWS in Australia. It is due to the loss of gene function of the paternal Chromosome 15 in the critical 'Prader-Willi region' of 15q11 – q13. Nearly every body system can be affected by PWS. The key features include hypotonia, feeding difficulties in infancy, followed by the onset of severe hyperphagia from around age 2-3 years. Hypogonadism is almost universal and most have growth hormone deficiency, manifesting with short stature, low muscle mass and small hands and feet. Hypothyroidism is common but central adrenal insufficiency is rare. Other features include mild to moderate intellectual disability with poor auditory processing, executive function and abstract thinking. Behavioural problems include emotional outbursts, body focused self-harm, repetitive and ritualistic behaviours, rigidity and perseveration. Abnormalities of mental health include situational anxiety (anxiousness), mood instability, affective disorder and, much less commonly, psychosis. Fortunately, there have been significant advances in understanding the genetics of PWS as well as the discovery of treatments that can markedly alter its trajectory. The focus of this talk will be to discuss the important endocrine disturbances that may occur in adults with PWS and the interventions that can change the course of the disease. Some of the newer and investigational therapies for people with PWS will also be highlighted.

id #128345

Health-Related Quality of Life and Cancer Worry in Patients with Multiple Endocrine Neoplasia Type 1 (MEN1)

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Aims

Multiple Endocrine Neoplasia Type 1 (MEN1) is a hereditary tumour syndrome characterised by primary hyperparathyroidism, duodenopancreatic neuroendocrine tumours (pNETs), and pituitary adenomas(1). Given the chronic disease burden and lifelong surveillance requirements, patients with MEN1 are at risk of impaired health-related quality of life (HRQOL). This study aimed to assess HRQOL and cancer-specific distress in MEN1 patients and explore contributing factors.

Methods

This cross-sectional study recruited patients through the Hereditary Endocrine Neoplasia Clinic at Royal North Shore Hospital. Demographics were obtained from medical records. Participants completed the SF-36(2), Cancer Worry Scale (CWS)(3), and Impact of Event Scale–Revised (IES-R)(4). SF-36 scores were compared to Australian normative data. CWS and IES-R outcomes were compared with data from other hereditary cancer syndromes.

Results

Of 28 eligible patients, 24 (86%) completed the questionnaires. The cohort was mostly female (67%), with a mean (± standard deviation) age of 43(±15) years and mean duration of 16(±11) years since diagnosis. All had primary hyperparathyroidism, 67% had pNETs (50% receiving Lanreotide), and 38% had pituitary tumours. Compared to the general Australian population, MEN1 patients had significantly lower HRQOL across all SF-36 domains except Physical Functioning. Cancer-related worry was pronounced, with a

mean CWS score of 19.5(±5.5). 91% scored ≥14, indicating significant fear of disease occurrence (FDO)–higher than rates reported in other hereditary cancer syndromes such as Li-Fraumeni, Von Hippel-Lindau, and familial adenomatous polyposis(5–7). IES-R mean score was 23.7(±18.4), suggesting mild distress overall, though 32% had scores ≥33, consistent with clinically significant post-traumatic stress symptoms. Intrusion was the highest scoring subdomain. HRQOL was lowest in patients with pNETs and post-parathyroidectomy hypocalcaemia.

Conclusion

Patients with MEN1 face significant psychosocial challenges, including impaired HRQOL and elevated cancer-specific worry. These findings highlight the need for integrated psychological support and routine mental health screening in multidisciplinary MEN1 care.

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id #128601

Elevating Ni-Vanuatu women's voices through research on maternal health, nutrition, and adverse birth outcomes

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Aims

Adverse pregnancy, neonatal, and infant outcomes (APNIOs) remain a significant public health concern in Vanuatu, a Pacific lower-middle-income country (LMIC). This study aimed to support local health services by quantifying APNIO incidence, assessing antenatal care (ANC) engagement, investigating antenatal supplementation practices, and evaluating women's knowledge of iron and folic acid in supporting healthy pregnancy outcomes.

Methods

A cross-sectional survey was conducted between July and September 2023. Snowball sampling recruited 586 Ni-Vanuatu women across 27 urban and rural communities on Efate Island. Structured interviews (delivered in Bislama) captured demographic data, pregnancy outcomes, ANC attendance, supplement use, and knowledge. Data were analysed using chi-square, Fisher's exact, Kruskal–Wallis, Spearman's rank correlation, and logistic regression ($p<0.05$).

Results

The cohort reported 1682 births. Among parous women (n=156), 29% experienced at least one APNIO, significantly associated with home region (χ^2, $p=0.003$). Stillbirths (45/1000 births), occured at higher rates in rural areas (64/1000) than urban (36/1000). No significant associations were found between stillbirth rates and education level, region, or food expenditure. ANC initiation varied by age (χ^2, $p=0.0136$), with younger women more likely to attend earlier. While 79% attended ≥4 ANC contacts, only 12% met WHO's recommended 8 visits. Supplement uptake was high (95%), but initiation was delayed, with no women reporting use prior to or during early gestation. Knowledge of iron/folic acid was low (19%), significantly associated with interview location (Exp(B)=18.8, 95% CI [7.4–49], $p<0.001$).

Conclusion

High APNIO rates and suboptimal ANC and supplement practices highlight gaps in maternal health services and literacy in Vanuatu. Strengthening early ANC engagement and nutrition education may reduce APNIOs. Evidence presented here suggests that community-led health promotion is effective in improving maternal health literacy. Future research should explore scalable interventions and policy integration to enhance maternal and child health outcomes across rural and urban Vanuatu.

id #129881

Contemporary Thyroid Nodule Management: Using Ultrasound, Cytology, and Molecular Testing to Optimize Patient Care

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Thyroid nodules are a common condition frequently encountered by practicing endocrinologists. A previous “one-size-fits-all” approach for when to obtain fine-needle aspiration (FNA) biopsy or refer for surgery has been replaced by a more nuanced assessment of available data to create individualized care decisions. Specifically, optimal thyroid nodule assessment demands an understanding of how ultrasound features, FNA cytology diagnosis, and increasing, molecular findings, inform thyroid cancer risks. These discrete results combine with patient factors, such as cancer risk or comorbidities, and patient preference and quality of life considerations, completing a holistic picture to address the fundamental decision: Whether to perform surgical resection for a thyroid nodule, or whether to observe. In recent times, describing ultrasound features has dramatically improved thyroid cancer risk assessment, but has also spawned numerous systems and criteria around the world for doing so, such as Thyroid Imaging Reporting and Data Systems (TI-RADS) from America, Korea, Europe, and others, as well as from the American Thyroid Association. The Bethesda System for Reporting Thyroid Cytopathology is an international standard that provides consistent categories and risk stratification, but undergoes periodic updates to terminology and estimated malignancy risks. Finally, new discovering in the molecular underpinnings of thyroid cancer have led to complex molecular testing platforms, but their use is limited by uncertainties regarding their ideal application and cost-effectiveness, especially globally. Nevertheless, molecular features are undoubtedly a future tool of thyroid nodule evaluation. These aspects represent a changing landscape for thyroid nodule management and can produce uncertainly in providers and patients. This lecture will bring an evidence-based focus to how to employ multimodality thyroid nodule assessment in the clinic and come to well-considered patient care decisions.

id #128346

Male metabolic dysfunction is associated with a higher likelihood of miscarriage

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Obesity is estimated to affect 23-30% of reproductive-aged Australians(1). The negative effects of obesity on fertility and pregnancy loss are well documented(2-4), additionally, female metabolic dysfunction (insulin resistance, dyslipidaemia) is independently associated with poorer pregnancy outcomes(5, 6). The data examining paternal metabolic dysfunction is less robust, although epidemiological data suggests a link with miscarriage(3, 7, 8). We aimed to examine the relationship between male metabolic function and fertility outcomes in a cohort of Australian couples attending a fertility clinic.

A retrospective review of couples undergoing assisted reproduction (ART) at an Adelaide-based fertility clinic was performed. Inclusion criteria: Heterosexual couples >18 years seeking assisted reproduction who undertook measurement of metabolic function (fasting cholesterol, triglycerides, HDL, LDL, insulin, glucose) within 1.5 years of ART. Exclusion criteria: couples requiring donor sperm/oocytes or receiving malignancy related ART. Statistics: A baseline regression model was established via bidirectional stepwise logistical regression incorporating couples’ age, BMI, reproductive comorbidities and number of abnormal female metabolic biomarkers. Subsequent addition of individual male biochemical parameters allowed interrogation of the relationship between paternal biochemical derangements and both pregnancy and miscarriage (conditional on pregnancy).

Between 2020-2025, 388 couples underwent ART, with a mean female age of 37.3 and male age of 38.6 years. Of these, 237 undertook a fresh transfer in an in-vitro fertilisation cycle, and 151 had a frozen embryo transfer (FET). Male BMI and metabolic parameters were not associated with conception, however after adjusting for couples’ BMI, ART intervention and female metabolic state, paternal hypertriglyceridemia (>1.7 mmol/L, OR 2.38, p=0.04) and reduced HDL concentration (<0.9 mmol/L, OR 2.39, p=0.02) were both associated with higher miscarriage risk.

Our findings are consistent with previous epidemiological data suggesting male metabolic function impacts miscarriage risk(8). Further prospective studies and examination of embryo quality are necessary to validate this finding.

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id #129882

Current screening and management tips for Type 2 Diabetes

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Type 2 diabetes in youth is a rapidly rising, aggressive condition linked to increased adiposity. Early detection and treatment are critical for better outcomes. I'll outline the current Australian guidelines to help clinicians identify high-risk individuals and navigate referral pathways to specialist teams. I'll also briefly highlight the evidence for emerging pharmacotherapies and technologies in youth care.

id #127835

Impact of high-fat diet on the elasticity of lipid metabolism in the hypothalamus

Adélaïde Bernard[1], **Kevin Liu**[1], **Yingying Liu**[1], **Jen Xin Fach**[1], **Hanne Woo**[1], **Kevin Huynh**[1], **Natalie Mellet**[1], **Manika Singh**[1], **William Ho**[1], **Peter Meikle**[1], **Brian Drew**[1], **Yi Wang**[1]

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The brain is the second-most lipid-rich organ, with lipids playing essential roles in membrane formation, signalling, inflammation regulation, neurogenesis, energy storage, and protection against oxidative stress. Dysregulation of lipid metabolism is a key factor in obesity-related diseases and neurodegenerative disorders, highlighting the importance of lipid homeostasis for brain function. Despite recent advances in lipidomics technology, how brain lipid metabolism is affected by diet and the energy status of an organism remains poorly understood.

The hypothalamus regulates energy homeostasis by integrating nutrient and hormonal signals to control energy expenditure and feeding behaviour. While high-fat diets are known to disrupt hypothalamic function, whether and how they disrupt lipid metabolism in the hypothalamus remains unclear. This study leveraged lipidomics (quantifying 750+ individual lipid species) and bulk RNA sequencing to examine the impact of short- (3 days) and long-term (8 weeks) high-fat diet on hypothalamic lipid metabolism.

Obesity has recently been shown to reduce the "metabolic elasticity" of peripheral organs, i.e. their ability to respond to energy balance disturbances and return to baseline homeostasis. We applied this concept to the hypothalamus to assess its adaptability to metabolic challenges, such as cycles of fasting and refeeding, under different diet conditions. Originally developed for transcriptome data, we extended this concept to analyse lipidome elasticity. Our findings revealed that just three days of a high-fat diet significantly altered hypothalamic elasticity, identifying pathway perturbations not evident when comparing single metabolic state snapshots in high-fat diet versus chow-fed mice.

Understanding the interplay between obesity, lipid metabolism and brain function is essential for developing new therapeutic strategies. This study shows that metabolic elasticity scoring offers a promising approach to identify novel pathways involved in the neurological aspects of obesity-related metabolic disorders.

id #129883

Embedding sustainment into obesity prevention to achieve lasting impact

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Despite billions invested in community-based obesity prevention, most programs are not delivered long enough to improve population health. Modelling shows interventions must run for at least a decade to impact childhood obesity, yet fewer than 20% of public health programs continue beyond two years. This cycle of promising starts and premature endings is now routine. While implementation science has strengthened program delivery, the field has largely overlooked what happens after programs begin. Sustainment i.e. the continued delivery of effective programs after initial support ends is rarely studied, with less than 1% of public health research addressing it. Guidance on how to plan for and support sustained delivery remains limited. This presentation will identify common system-level threats to program sustainment, synthesise what is known about strategies that support program longevity, and introduce practical tools to help policymakers and practitioners embed sustainment into program design from the outset. By shifting focus from 'getting programs in' to 'keeping programs going', we can help ensure that public health investments deliver on their long-term promise.

id #127068

Effectiveness and cost-effectiveness of community-based interventions to prevent childhood obesity in Australia and the Pacific

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Aims: The Precision Evidence for Childhood Obesity Prevention (PRECIS) project aimed to generate new insights into the effectiveness, cost-effectiveness and broader benefits of child- and adolescent-focused obesity prevention community-based interventions (CBIs) from Australia and the Pacific. This abstract presents findings from this four year project.

Methods: Data from ten large obesity prevention CBIs were collated and harmonised. Individual participant data meta-analyses were conducted to understand intervention effects on measured anthropometric outcomes, self-reported weight-related behaviours, health related quality of life (HRQoL) and subsequent economic impacts. Additionally, qualitative research methods were used to understand the broader benefits of obesity prevention CBIs from the perspective of multiple stakeholders (funders, researchers, community members).

Results: Meta-analysis of participant-level data from six Australian and four Pacific studies (n= 26,003 baseline; n= 22,565 endpoint observations) found no overall intervention effect. Sub-group analysis found CBIs slowed weight gain in Australian studies (BMIz difference: -0.04 (95%CI -0.07, -0.01), and were more effective in students from lower compared to higher socio-economic areas (BMIz difference = -0.10 (-0.18, -0.02)). Additionally, effectiveness was detected in studies with longitudinal design, but not repeat cross-sectional design, and for children within optimal weight range at baseline, but not those with overweight or obesity at baseline. Economic analysis found potential healthcare savings of AUD$496M (AUD$421M-574M) if CBIs were implemented across Australia. Few significant results were found for behavioural outcomes, however CBIs had a positive impact on HRQoL, particularly in younger children, boys and those attending schools in lower socio-economic areas. Qualitative interviews highlighted benefits of CBIs beyond obesity prevention, including social engagement and inclusion, empowering communities, influencing local policies and environmental benefits.

Conclusion: The PRECIS project found obesity prevention CBIs to be effective and cost-effective in some settings, and has highlighted benefits of this approach beyond obesity prevention.

id #128349

Peri-conceptional administration of viral mimetic poly I:C attenuates maternal immune and vascular parameters to impair placental and fetal development

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The uterine immune response during early pregnancy has consequences for embryo implantation, placental and fetal development, and offspring health. In this study, we investigated the cellular and molecular mechanisms underpinning adverse pregnancy outcomes following induction of a mild anti-viral inflammatory response during the peri-implantation window.

Female C57Bl/6 mice mated to C57Bl/6 males were administered a low dose of synthetic viral mimetic poly I:C (10 mg/kg) on gestational days (gd)0.5 and 2.5 and evaluated for effects on endometrial gene expression (gd3.5), uterine leukocytes (gd3.5), placental development and decidual spiral arteries (gd10.5), and placental structure and fetal growth (gd17.5). Flow cytometry of uterine leukocytes on gd3.5 revealed a 6.4-fold increase in conventional T cells, a 9.0-fold increase in regulatory T cells, and a 77% reduction in uterine natural killer (uNK) cells (n=7-9/group, P<0.01). RNA sequencing of the endometrium on gd3.5 identified 223 differentially expressed genes (n=3-5/group, FDR<0.05, logFC=0.485), including many associated with viral inflammatory signalling pathways and NK cell activity. Several genes encoding factors that support implantation and trophoblast invasion, angiogenesis, and vascular function were downregulated. qPCR showed a >3-fold increase in endometrial expression of pro-inflammatory cytokines *Ifng*, *Il6* and *Tnf.* On gd10.5, constrained placental development and impaired decidual artery remodelling was evident, with a 41% reduction in vessel lumen cross-sectional area (n=8-9/group, P<0.001). By late pregnancy (gd17.5) fetuses were growth restricted (~19% reduction in mean weight) and placental weights were increased (n=13-15/group, P<0.001), indicative of placental insufficiency.

These findings provide compelling evidence that even mild viral-associated inflammation during the peri-implantation period disrupts the uterine immune response and dysregulates endometrial gene expression pathways and T cell-uNK cell networks critical for decidual vascular adaptation and trophoblast invasion. These perturbations are implicated as causal mechanisms underpinning compromised placental development and fetal growth, with potential consequences for long-term offspring health and disease susceptibility.

id #128605

Investigating a role for Sirtuin 1 in governing spermatogonial stem cell function

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Spermatogonial stem cells (SSCs) are indispensable for continued male fertility but are exceptionally vulnerable to damage by chemotherapy. SSC destruction is particularly problematic for prepubertal oncology patients, as no mechanism exists to safeguard their reproductive potential, given that they cannot produce sperm for cryopreservation. *In vitro* SSC therapies and treatments to promote regeneration of chemotherapy-resistant SSCs *in vivo* offer promising strategies but require an understanding of molecular mechanisms governing SSC regeneration.

Recently, a proteomic comparison of SSCs and progenitor spermatogonia performed by our group identified expression of 6 SIRT isoforms, and Ingenuity Pathway Analysis (IPA) predicted regulation by SIRT1. Additionally, in an RNAseq dataset that compared undifferentiated spermatogonia in steady-state and regenerative conditions (post-chemotherapy)[1], IPA analysis also predicted SIRT1 as an upstream regulator of the regenerative response. We have produced a novel transgenic mouse line possessing a sirtuin 1-overexpression construct (SIRT1-OE) as well as an *Id4-eGFP* reporter transgene that labels SSCs and progenitor spermatogonia. Immunoblotting analysis confirmed a 2.5-fold increase in SIRT1 expression in the OE testis when compared to controls ($p<0.05$), and immunofluorescence identified SIRT1 expression within the nucleus and cytoplasm of spermatogonia. Breeding studies using SIRT-OE/ID4-eGFP males and control females revealed normal fertility (, and the number of undifferentiated spermatogonia per seminiferous tubule remained equivalent

To explore the effects of SIRT1 overexpression on SSCs in regenerative conditions, chemotherapy exposure and *in vitro* culture studies have been initiated. At 14 days post-busulfan treatment (n=2, ongoing), testis-to-bodyweight ratios remained equivalent between control and SIRT-OE/ID4-eGFP animals. However, a 36% reduction in the total number of spermatogonia in the OE testis has been identified. In undifferentiated spermatogonia cultures, cell counts and the percentage of ID4-eGFP^{Bright} SSCs have remained equivalent over two passages, albeit prolonged studies are required to reveal a true regenerative effect.

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id #128861

Evaluating whole fruit feijoa powder for type 2 diabetes risk prevention: the FERDINAND study

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Publish consent withheld

id #129885

Functional Analysis of HSD17B3-Deficient Male Mice Reveals Roles for HSD17B7 and HSD17B12 in Testosterone Biosynthesis

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Historically, 17β-hydroxysteroid dehydrogenase type 3 (HSD17B3) was thought to be the key enzyme responsible for testicular testosterone production. In humans, loss-of-function mutations in HSD17B3 impair testosterone production during prenatal life leading to impaired development of androgen-dependent tissues in 46,XY individuals. However, male mice with HSD17B3 deficiency exhibit normal testicular testosterone concentrations, normal development of reproductive organs and are fertile, suggesting that mice express other hydroxysteroid dehydrogenase enzymes capable of testicular testosterone synthesis. This study aimed to investigate whether 17β-hydroxysteroid dehydrogenase type 12 (HSD17B12), which can convert androstenedione to testosterone in mice but not in humans, compensates for the lack of HSD17B3 in Hsd17b3 knockout (KO) mice. We used CRISPR/Cas9 to substitute the amino acid in mouse HSD17B12 that is responsible for its ability to convert androstenedione to testosterone with the amino acid of the human enzyme that prevents androstenedione being used as a

substrate. When this Hsd17b12 mutation was introduced into Hsd17b3 KO mice, males exhibited normal reproductive tracts but reduced testicular testosterone production with a consequential reduction in seminal vesicle weight. This suggests HSD17B12 contributes toward testosterone production in the absence of HSD17B3, but other enzymes must also contribute. We therefore quantified other testicular hydroxysteroid dehydrogenases, finding that HSD17B7 mRNA and protein was markedly upregulated in Hsd17b3 KO testes. We confirmed that mouse, but not human, HSD17B7 can produce testosterone in vitro. We conclude that compared to humans, mice exhibit increased plasticity in testosterone production via hydroxysteroid dehydrogenase enzymes to support androgen action and male fertility.

id #128350

Countering sweet deception: the impact of added sugar warning labels on parental perceptions and purchasing preferences for commercial infant and toddler foods.

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Background: Many commercial infant and toddler foods (CITFs) contain added sugars, which contribute to tooth decay, unhealthy weight gain, and lifelong chronic disease risk. CITFs are often marketed as healthy, nurturing and convenient. Displaying front-of-pack Added Sugar Warning Labels (ASWLs) on CITFs with added sugar could help counter misleading marketing and raise awareness of potential product harms.

Aims: Test whether mandatory Added Sugar Warning Labels (ASWLs) prompt parents to select CITFs without added sugar for their infant/toddler to consume.

Methods: In a naturalistic, between-subjects experiment, 533 Australian parents were assigned to an infant or toddler food study arm, then randomly allocated to a warning label condition: no ASWL (control) or ASWL. Within each of three product categories, parents were shown four CITFs (two with added sugars, two without) – with ASWLs displayed accordingly. Analyses examined effects of ASWLs on perceived added and total sugar content, perceived healthiness, purchase intentions and purchasing choices

Findings: Compared to the control condition, ASWLs significantly decreased perceived healthiness of CITFs containing added sugar (M: 3.3 vs. 2.9), increased perceived total sugar content (M = 4.3 vs. 4.9), and increased the likelihood of parents identifying that these products contained added sugar (61% vs. 89%). ASWLs also significantly reduced parents' likelihood of choosing

Conclusions: Displaying ASWLs on CITFs with added sugar increased awareness of total sugar content and the presence of added sugars, and reduced perceptions of product healthiness, curbing parents' preferences and purchasing intentions for CITFs with added sugar. Findings indicate that warning labels offer a promising strategy for discouraging parents from purchasing CITFs with added sugar and reorienting them towards choosing options without added sugar for their children.

id #129887

Bridging Research and Practices in PCOS: Strategic Evidence Synthesis, Clinical Translation, and Global Implementation at Scale

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Polycystic ovary syndrome (PCOS) affects one in eight women globally, yet remains profoundly neglected in clinical research and practice. Traditional research translation from bench to bedside typically requires 10-17 years and often fails entirely, creating critical evidence-practice gaps that perpetuate suboptimal outcomes. This presentation describes a strategic research program spanning epidemiology, evidence synthesis, guideline development, and implementation science to transform PCOS care.

id #127072

Promise and Pragmatism: GPs' Perspectives on GLP-1RAs for Obesity Management in NHS Primary Care

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Publish consent withheld

id #128096

Differential Effects of Exercise Intensity on Muscle-Derived Mediators and Neuroprotective Pathways in Middle-Aged Adults

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Skeletal muscle is an endocrine organ that releases myokines and metabolites acting locally or systemically to influence other tissues, including the brain. These mediators, such as myokines and kynurenine pathway metabolites, are implicated in neuroprotective effects via modulation of inflammation, neuroplasticity, and neurotransmission. However, the role of exercise intensity in regulating these mediators in muscle and blood remains unclear. We hypothesised that high-intensity interval training (HIIT) would be superior to moderate-intensity continuous training (MICT) in increasing muscle and circulating mediators associated with neuroprotection in middle-aged adults. Thirty-two sedentary, middle-aged (45–65 years; 3 males, 29 females) adults completed one of two 12-week, work-matched cardiorespiratory exercise interventions (randomised): MICT (36–48 min, ~60% peak power) or HIIT (4–7 × 4 min, ~90% peak power). Muscle biopsies and blood samples were collected before and after training to assess myokines (FNDC5, BDNF, VEGF, CTSB) and kynurenine pathway metabolites. Both MICT and HIIT improved cardiorespiratory fitness, with significant increases in V̇O2peak (MICT $p < 0.0001$; HIIT $p < 0.0001$; between-group $p = 0.0482$) and Ẇpeak (MICT $p < 0.0001$; HIIT $p < 0.0001$; between-group $p = 0.0192$), favouring HIIT. Skeletal muscle VEGF (both groups $p = 0.0075$) and CTSB (MICT $p = 0.0257$; HIIT $p = 0.0017$) increased in both groups without between-group differences. FNDC5 and BDNF levels were unchanged in muscle and serum ($p > 0.05$). Both interventions elevated serum kynurenine and the kynurenine/tryptophan ratio (time $p < 0.05$). HIIT specifically increased serum kynurenic acid ($p = 0.05$), picolinic acid ($p = 0.0078$), and muscle kynurenine aminotransferase 1 (KAT1; $p = 0.005$), suggesting a greater shift toward the neuroprotective branch of the pathway with higher intensity training. The favourable effect of HIIT as a neuroprotective intervention in middle-aged adults appears mediated by its effects on the kynurenine pathway rather than muscle-derived myokines.

id #128609

Development and successful application of a tool for standardised training in sperm morphology assessment

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Sperm morphology is a critical predictor of fertility in both livestock and human assisted reproduction (1). However, it remains a subjective assessment, vulnerable to human bias and variability unless morphologists adhere to rigorous standardisation protocols. Despite this, there is currently no standardised training tool for sperm morphology assessment, contributing to significant inter- and intra-variation amongst morphologists.

This study developed (2) and evaluated (3) the effectiveness of a novel sperm morphology assessment training tool underpinned by machine learning principles. Specifically, the concept of supervised learning from expert-labelled "ground truth" datasets. The tool presents users with sperm images individually classified by multiple experts and provides immediate feedback on classification accuracy.

Using the tool, novice users were trained to recognise 25 different morphological sperm types and then assessed on their ability to categorise these into four classification systems of increasing complexity (2-, 5-, 8-, and 25-category). Untrained users (n=22) achieved modest accuracy (81.0 ± 2.5%, 68 ± 3.59%, 64 ± 3.5%, and 53 ± 3.69% across the four systems, respectively), while users exposed to a training video and visual aid (n=16) displayed significantly higher accuracy in their initial tests (94.9 ± 0.66%, 92.9 ± 0.81%, 90 ± 0.91% and 82.7 ± 1.05, $p < 0.001$). Continued weekly training further increased accuracies for this latter cohort to 98 ± 0.43%, 97 ± 0.58%, 96 ± 0.81%, and 90 ± 1.38% ($p<0.001$).

Although machine learning may ultimately automate sperm morphology assessment, this study demonstrates that applying its training principles to human users via high-quality, expert-validated image sets and structured, feedback-driven repetition can greatly enhance human diagnostic performance in the interim. This tool represents a scalable, standardised method to improve reproducibility and accuracy in sperm morphology assessment and may serve as a foundation for broader implementation across species and classification systems.

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id #129889

Does salt matter in metabolism?

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Obesity is a global epidemic and is a multifactorial disease associated with an increased risk of serious conditions, including type 2 diabetes, cardiovascular disease (CVD) and certain cancers. It arises from an imbalance between energy intake and energy expenditure. Gaining a deeper understanding of how energy balance is regulated under health and disease is essential for developing better therapeutics for obesity, diabetes and their comorbidities. While much research has focused on how sugar and fat disrupt energy homeostasis, the role of dietary salt, a common yet often overlooked dietary factor, remains poorly understood. In this talk, I will present our recent findings on how high salt intake modulates energy balance, with a particular focus on the critical involvement of the hypothalamic neuropeptide Y (NPY) system.

id #128611

Supporting weight focused discussions in primary care

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Background and Objective: Patients with a higher weight often experience weight stigma in primary care settings. Research to date has focused more on patient experiences of weight-related discussions. This study aimed to understand perspectives of primary care professionals with these discussions, particularly barriers and facilitators.

Methods: Qualified primary care professionals and trainee primary care professionals (*N*=91) at varying career stages within Australia completed an online survey (as part of a larger study) with a series of open-ended questions about their experiences and requirements to facilitate effective weight-related discussions with higher weight patients. Survey responses were qualitatively analysed using thematic and content analysis.

Results: From the analyses, participants recognised their strengths, including non-judgemental and non-blaming attitudes, empathy and providing practical and tailored weight management solutions. Participants also indicated a need for more time and resources to deliver comprehensive, tailored care sensitively. Perceived barriers included appointment length/time and patient financial constraints for extended consultations, limited familiarity with suitable weight management options and challenges prioritising health and lifestyle factors over weight. Participants emphasised the need for resources and multidisciplinary support to facilitate effective weight-related discussions that focused on overall health and wellbeing.

Conclusions: Improving access to and awareness of clinical guidelines and existing resources, along with investing in specialised weight management services, could benefit primary care professionals across the career stage spectrum.

Practice implications: These findings suggest the need for health systems and leadership to support prioritisation of education, training, development of, and access to relevant curricula, tools, resources, and guidelines. This may facilitate primary care professionals (current and future) to raise weight-related discussions sensitively and effectively.

id #128612

Characteristics of participants who regained weight after withdrawal of tirzepatide: A post hoc analysis of SURMOUNT-4

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Aims: In this post-hoc analysis, we investigated the baseline characteristics (week-0) and change in weight and waist circumference at the end of the open-label lead-in period (week-36) associated with varying degrees of weight regain after tirzepatide withdrawal.

Methods: SURMOUNT-4 participants who achieved ≥10% weight reduction with 36-weeks of tirzepatide treatment (maximally tolerated dose (MTD) of 10 or 15mg) and randomized to placebo (N=308) were included in this post-hoc analysis. Participants' baseline characteristics and change in weight and waist circumference were calculated descriptively by the degree of weight regain, from Week 36-88, as a percentage of weight reduction, from Week 0-36.

Results: Participants in the lower weight regain groups exhibited significantly greater mean reductions in weight (%) from the start of the lead-in period to randomization; -23.6%, -23.4%, -22.6% and -18.3% in the <25%, ≥25-<50%, ≥50-<75% and ≥75% groups ($p<.001$). Greater reduction in mean waist circumference (cm) from the start of the lead-in period to randomization was also observed in participants with lower weight regain; -19.6cm, -20.0cm, -17.9cm and –16.2cm in the <25%, ≥25-<50%, ≥50-<75% and ≥75% groups ($p=.022$).

Participants had no significant differences across weight regain groups in demographic or baseline clinical characteristics.

Conclusion: In this post-hoc analysis of participants who were withdrawn from treatment with tirzepatide in the SURMOUNT-4 clinical trial, participants with less body weight regain demonstrated greater reductions in body weight and waist circumference during the initial open-label lead-in period. There were no significant differences in baseline demographic or clinical characteristics across groups with different degrees of weight regain. These findings are consistent with the multifactorial and complex nature of obesity.

id #129892

Incretin-based anti-obesity therapy: will it make you blind? Finding facts and busting myths.

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Each week we are reminded in the media about the benefits and, increasingly, the potential dangers of the new incretin-based obesity modifying medications. We regularly see articles with titles such as: 'What is 'Ozempic personality', and is it real?', 'Ozempic blindness. What Ophthalmologists want you to know' and 'Researchers link popular weight loss drugs to serious digestive problems for 'hundreds of thousands' worldwide'. This session will include a deep dive into some of the proposed dangers of incretin therapy use, with a focus on pancreatitis and other rare gastrointestinal complications, eye damage and changes to our personality.

id #124773

Sex change in fish – what, why, how?

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It is well established that a variety of environmental factors affect sexual development, sexual phenotype, and reproductive function. In fishes, the focus of much of my research, these environmental effects are often pronounced, readily perturbed or manipulated, and thus amiable for study. Among the most striking of these phenomena is the complete female to male sex change during adulthood that occurs in some fishes due to changes in their social environment. Typically, the absence of a dominant male triggers sex change in the dominant female. How male absence initiates such a striking transformation is as mysterious as it is extraordinary. Social position is clearly important, but the behavioural and other cues a female employs to determine her position in the hierarchy and how that influences her decision to change sex or defer to others remain unknown. Here, I will highlight work from my lab that is revealing the behavioural, genetic, epigenetic and physiological underpinnings that enable socially controlled sex change in fish.

id #128101

Evaluating the severity of obesity in adolescents presenting to an intensive behavioural weight management intervention

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This study aimed to determine clinical obesity diagnosis(1) and Edmonton Obesity Staging System for Paediatrics (EOSS_P)(2) severity in treatment-seeking adolescents with obesity.

A cross-sectional secondary analysis was conducted using baseline data from the 'Fast Track to Health' study (2018-2023), which recruited 141 adolescents (13-17years) with obesity and ≥1 cardiometabolic complication from two paediatric hospitals in Sydney and Melbourne. Comprehensive clinical assessments including anthropometry, blood tests, psychosocial questionnaires and paediatrician reviews were used to classify participants according to diagnostic (Lancet) and staging criteria (EOSS_P Stage 0 to 3). Descriptive statistics determined obesity severity and Chi-square tests examined subgroup differences by sex, study site and completion status.

Most participants met the Lancet Commission diagnostic criteria for clinical obesity (n=97, 68.8%) followed by pre-clinical obesity (n=42, 29.8%), and no obesity (n=2, 1.4%). Significant differences were observed by sex, with males more likely to present with clinical obesity (p=0.021). There were no differences by site or completion status. EOSS-P showed most participants were classified as Stage 2 (n=67, 47.5%) or 3 (n=43, 30.5%), indicating the presence of clinically significant health complications. Mental health (Stage 2, n=71, 50.4%) and social domains (Stage 3, n=33, 23.4%) mostly contributed to higher staging. Subgroup differences by sex demonstrated females more likely to be Stage 1 (p=0.011) in metabolic domain. In the mental domain, Pearson's Chi-square was not statistically significant (p=0.52), suggesting no association, however the Likelihood Ratio was significant (p=0.05), indicating a potential association with females more likely to be Stage 2.

The Lancet Commission and EOSS-P frameworks provide clinical insight beyond BMI alone. All participants had cardiometabolic complications associated with weight, yet some did not meet the diagnostic criteria for clinical obesity. There may be unintended bias with females less likely to meet Lancet diagnostic criteria despite no differences in overall severity according to EOSS-P.

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2. Hadjiyannakis S, Buchholz A, Chanoine J-P, Jetha MM, Gaboury L, Hamilton J, et al. The Edmonton Obesity Staging System for Pediatrics: a proposed clinical staging system for paediatric obesity. Paediatrics & Child Health. 2016;21(1):21-6.

id #128357

Androgen receptor genomic structural rearrangements reshape the AR cistrome in castration-resistant prostate cancer

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Prostate cancer cells acquire diverse mechanisms of castration resistance under the selective pressure of treatment. This includes expression of constitutively active androgen receptor (AR) variants. Whether AR variants drive resistance is contested, because they often co-exist with full-length AR. Yet, some tumours with AR genomic structural rearrangements (AR-GSRs) only express AR variants and not full-length AR. Therefore, our objective was to investigate how truncated variants shape the AR cistrome and responses to treatments, with or without full-length AR.

We selected patient-derived xenografts of prostate cancer from the Melbourne Urological Research Alliance (MURAL) cohort. We compared the landscapes of AR binding using chromatin immunoprecipitation sequencing and transcriptomic profiles using RNA sequencing. We also determined the responses of tumours to castration and bipolar androgen therapy *in vivo*.

We identified a distinct group of patient-derived models with structural rearrangements of the *AR* gene. These tumours all expressed ARv567es, a constitutively active AR variant. They had varying levels of full-length AR, depending on the nature of the genomic rearrangements. These tumours had distinctive AR cistrome profiles, gaining some AR binding sites and losing others compared to tumours without AR structural rearrangements. ARv567es-positive tumours also had a different profile of H3K27ac histone marks. Moreover, we defined transcriptional differences, with depletion of canonical AR-regulated gene signatures but enrichment of AR-repressed genes. Consistent with ARv567es having ligand-independent activity, ARv567es-positive tumours were resistant to castration and bipolar androgen therapy. In tumours that co-express full-length AR, this involves disruption of the autoregulatory loop that modulates *AR* levels.

The emergence of ARv567es through *AR* gene rearrangements alters the pattern of AR binding, reprograms the transcriptome, and is associated with resistance to therapies targeting the AR ligand-binding domain. Thus, *AR* genomic structural rearrangements and ARv567es expression are potential markers to guide treatment decisions.

1. Lawrence et al., European Urology Focus, 2025

id #129893

Living with primary aldosteronism

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Primary aldosteronism (PA) is a common but under-recognised cause of hypertension, often diagnosed after years of misattributed symptoms. In this presentation, we will share the journey of a patient with lived experience of PA. Uniquely, the diagnosis was prompted not by clinical suspicion but by personal initiative after hearing a radio interview about PA. We will highlight recurring themes in patient experiences: blood pressure dismissed as "white coat" or stress-related, reluctance among clinicians to test for PA, and a lack of awareness of what to do even after the diagnosis has been made. We reflect on the value of early intervention with medical therapy, the challenges of navigating care, and the importance of recognising non-specific symptoms (e.g. anxiety, fatigue, brain fog) often overlooked in clinical guidelines. The presentation also underscores the need for increased GP and specialist awareness of PA, stronger public education efforts, and routine consideration of PA in all patients with hypertension. Importantly, the role of dietary sodium reduction is emphasised as an empowering but underutilised strategy in patient self-management.

id #122984

Androgen Receptor tumour suppressor activity is defined by GATA3 interaction and enhancer selectivity in ER$^+$ breast cancers

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Our published studies support a tumour suppressor role for androgen receptor (AR) signalling in estrogen receptor positive (ER+) breast cancers and use of a selective AR modulator to treat advanced ER+ disease(1-4). Preclinical studies suggest AR may also sustain tumour suppressor activity in some breast cancers that lack ER(5). AR is a ligand-activated DNA-binding transcription factor that interacts with co-regulatory proteins to influence gene expression programs. Key factors that regulate AR genomic activity in a breast cancer context are largely unknown. Therefore, we employed an unbiased chromatin immunoprecipitation-based proteomic technique to identify AR interacting proteins in cell line models of AR+ER+HER2- (T-47D, ZR-75-1), AR+ER-HER2+ (MDA-MB-453) and AR+ER-HER2- (MFM223) breast cancer. The GATA3 transcription factor was identified and validated as a novel AR interacting protein in all four breast cancer models. AR activation with 5α-dihydrotestosterone (DHT) increased nuclear AR-GATA3 interactions, resulting in AR-dependent enrichment of GATA3 chromatin binding at a sub-set of genomic loci. DHT-induced AR-GATA3 loci were located near genes enriched for luminal differentiation pathways (e.g., *EHF*, *KDM4B*). AR-GATA3 interaction was required for AR-mediated growth inhibition in ER+ and ER- breast cancer cells. We validated AR-GATA3 interaction and its transcriptional consequences in an ER+ patient-derived xenograft model that is growth inhibited by AR agonists. We also observed AR-GATA3 interactions in normal breast epithelial cells and co-localization of AR, GATA3, KDM4B and EHF expression in single cell RNA-seq breast tissue datasets. In conclusion, AR and GATA3 interact to transcriptionally regulate luminal epithelial cell differentiation in AR+ breast cancers regardless of ER status. This interaction facilitates the tumour suppressor function of AR and mechanistically explains why AR expression is associated with less proliferative, more differentiated breast tumours and better overall survival in breast cancer. Our findings implicate AR-GATA3 interaction in normal breast biology, warranting investigation of AR activation for breast cancer prevention.

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id #126056

Abnormal Uterine Bleeding, Obesity and Endometrial cancer - Risks, Management and Challenges

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Abnormal uterine bleeding (AUB) is a common gynaecological presentation that can range from benign hormonal disturbances to malignant endometrial pathology. Among the various risk factors implicated, obesity has emerged as a major determinant linking AUB to endometrial hyperplasia and carcinoma. The pathophysiological nexus between obesity and endometrial cancer lies in chronic unopposed estrogen exposure resulting from peripheral aromatization of androgens in adipose tissue, coupled with insulin resistance, hyperinsulinemia, and chronic inflammation. These mechanisms contribute to endometrial proliferation, atypia, and malignant transformation, particularly in postmenopausal and anovulatory women.

Clinical evaluation of AUB in obese women necessitates a high index of suspicion, with early utilization of transvaginal ultrasonography and endometrial sampling to exclude neoplastic lesions. Management strategies must be individualized, balancing fertility

preservation, metabolic control, and oncologic safety. Medical therapies, including progestin-based regimens and levonorgestrel intrauterine systems, play key roles in controlling bleeding and reversing hyperplasia in low-risk patients. In contrast, definitive surgical interventions, such as hysterectomy, remain indicated for recurrent, refractory, or high-grade lesions.

However, obesity poses significant diagnostic, therapeutic, and anaesthetic challenges. Technical limitations during imaging, reduced accuracy of endometrial sampling, and increased perioperative morbidity complicate management. Furthermore, the rising prevalence of obesity globally underscores an urgent need for preventive strategies, including weight reduction, metabolic optimization, and early screening for endometrial pathology among high-risk populations.

In conclusion, the intersection of abnormal uterine bleeding, obesity, and endometrial cancer represents a critical domain in women's health. Addressing this triad requires an integrated multidisciplinary approach emphasizing early detection, personalized management, and preventive interventions to mitigate morbidity and improve reproductive and oncologic outcomes.

id #128616

New model of care for the management of Aboriginal and Torres Strait Islander Adults with clinically severe and complex obesity.

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Aboriginal and Torres Strait Islander peoples are more likely than non-Indigenous Australians to experience overweight and obesity which contribute to 7.2% of the overall health gap.

The Tharawal Aboriginal Corporation Metabolic Program was developed as a culturally adapted model based on the South Western Sydney Metabolic Rehabilitation and Bariatric Program at Camden Hospital, to improve engagement and outcomes. It is a collaboration between Tharawal Aboriginal Corporation, South Western Sydney Local Health District, Western Sydney University, South Western Sydney Primary Health Network and NSW Ministry of Health that aims to provide multidisciplinary specialist care for the Indigenous community, integrated and located in the Aboriginal Medical Service.

The community-led and designed program offers culturally responsive services, including guidance and support by Aboriginal Health Workers, group education and exercise classes, as well as regular yarning sessions. The additional components provide physical health support in a culturally safe environment, while creating spaces for community connections, storytelling, and peer support.

Of the 29 participants enrolled so far, 82.8% (n=24) were female. Mean age was 41.5 years (range 23 to 65) years, the average BMI 45.88±6.13) and average weight of 128.75kg (SD ± 22.35). Type 2 diabetes was present in 33.3% (n=8) of participants; hypertension and dyslipidemia in 33.3% (n=8) and 19% (n=4) respectively; and GORD in 58.3% (n=14); varying severity of obstructive sleep apnea ranging from mild (2, 9.1%), moderate (1, 4.5%), to severe (5, 22.7%); Polycystic ovarian syndrome in 20% (n=4) female participants.

By embedding culture and connection, the program moves beyond a clinical model to address the broader social determinants of health, which has been shown to strengthen trust, increase participation and retention, and support for holistic wellbeing, illustrating a feasible health program.

We look forward to presenting outcomes in future analysis.

id #129896

Implementing molecular imaging in functional endocrine neoplasia of the head and neck.

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Molecular imaging well suited to the investigation of endocrine disease offering insights into physiology, pathophysiology and receptor expression. Here we explore how molecular imaging has evolved the diagnosis and management of different endocrine disease, illustrated by four clinical cases.

In thyroid disease, molecular imaging has a long history due to the exploitation of the sodium iodine symporter for both diagnosis and therapy. Given the heterogeneity of differentiated thyroid cancer, the radiotracer required is dependent on the individual pathology. This may include: 18F-Fluorodeoxyglucose (FDG), radiotracers targeting somatostatin receptors or various iodine isotopes.

From a pituitary perspective, there have been significant improvement in spatial resolution of molecular imaging, allowing for increased visualisation of small structures including the pituitary gland. The future horizons for pituitary tumour assessment with positron emission tomography will be discussed.

Tumour pathophysiology and genetics is key to understanding the role of PET imaging in phaeochromocytoma and paraganglioma. Molecular imaging is vital to the assessment of tumour burden in metastatic disease and pre-therapy assessment for PPGL which will be shown.

18F-Flurocholine PET/CT has high sensitivity in detection of parathyroid adenoma and hyperplasia in primary hyperparathyroidism despite negative conventional localisation studies. This will be highlighted through a clinical case and discussion of recent Australian experience with the radiotracer.

id #128361

Oocyte epigenetic programming influences neurodevelopment in offspring

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Epigenetic modifications strongly influence gene expression and are vital in maintaining long-term memory of cellular identity and function. As oocytes and sperm transmit both genetic and epigenetic information to offspring, appropriate regulation of epigenetic programming within the male and female germlines is critical for normal offspring development. Oocyte epigenetic programming is highly complex, involving a range of epigenetic modifiers which establish a specific distribution of DNA methylation and histone modifications during oogenesis. Polycomb Repressive Complex 2 (PRC2) is a broadly evolutionarily conserved epigenetic complex which catalyses Histone 3 Lysine 27 trimethylation (H3K27me3) in primary-secondary follicle oocytes. PRC2-dependent epigenetic programming in oocytes is critical for normal developmental outcomes in offspring, including growth, brain and skeletal development. Moreover, *de novo* germline mutations in EED, EZH2 and SUZ12 are associated with Cohen-Gibson, Weaver and Imagawa-Matsumoto syndromes in humans, and are characterised by overgrowth, altered skeletal patterning and intellectual disability, highlighting the importance of also understanding PRC2 function within the human germline. We recently demonstrated that PRC2-dependent programming is coordinated with other chromatin modifications and precedes DNA methylation, reflecting highly organised epigenetic programming in mouse oocytes. Using a mouse model which lacks PRC2-dependent epigenetic programming during oogenesis, we are examining how the oocyte epigenome is established and how PRC2 regulates maternal epigenetic inheritance. We show that offspring resulting from oocytes which lacked PRC2-dependent epigenetic programming have disrupted neurodevelopmental and behavioural outcomes through to adulthood, compared to isogenic offspring which had normal oocyte epigenetic programming. As the mechanisms for these altered developmental outcomes in offspring remain unclear, this work also aims to provide insight into the molecular mechanisms underlying PRC2-dependent epigenetic inheritance. This work is critical in understanding how changes to oocyte epigenetic programming can disrupt epigenetic memory and alter developmental outcomes in the next generation.

id #128617

Modulation of NAD^+ Metabolism by NMNH Improves Obesity-Associated Metabolic Outcomes

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Nicotinamide adenine dinucleotide (NAD^+) is a critical coenzyme involved in numerous enzymatic processes that regulate essential cellular functions, including energy metabolism. NAD^+ levels are known to decline in metabolic disorders such as obesity, in both rodents and humans. Boosting NAD^+ through supplementation with NAD^+ precursors like nicotinamide mononucleotide (NMN) and nicotinamide riboside (NR) has consistently been shown to improve metabolic outcomes in preclinical models. Recently, their reduced forms—NMNH and NRH—have shown greater potency in elevating NAD^+ levels *in vitro* and *in vivo*. However, their long-term effects on obesity pathogenesis remain largely underexplored. In this study, we investigated the impact of chronic NMNH administration on metabolic health in a murine model of HFD-induced obesity. Twelve weeks of NMNH treatment in HFD-fed mice significantly attenuated weight gain, resulting in final body weights comparable to chow-fed controls, while vehicle-treated HFD mice gained approximately 40% body weight. This effect was primarily driven by a reduction in adiposity, independent of food intake. NMNH also enhanced endurance in both dietary groups and improved insulin sensitivity in HFD-fed mice based on an index of insulin sensitivity. Metabolomic analyses revealed that chronic NMNH-treatment sustained elevated skeletal muscle NAD^+ levels up to 24 hours post-treatment. NMNH reduced triacylglycerol (TAG) and diacylglycerol (DAG) accumulation and oxidative stress markers in skeletal muscle, and decreased renal TAG content in HFD mice. Despite no changes in total hepatic TAG and DAG levels, lipidomic analysis revealed a shift toward longer-chain fatty acyl species and reduced levels of C16:0 and C18:0 ceramides in NMNH HFD mice—lipid species implicated in insulin resistance and metabolic disease. Overall, NMNH demonstrates promising therapeutic potential for addressing prevalent metabolic conditions such as obesity and type 2 diabetes.

id #129898

Why Losing Weight Isn't Enough: The Metabolic Truth About Male Fertility

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Male reproductive health is a critical yet often overlooked determinant of fertility, embryo development, and offspring wellbeing. While obesity has long been associated with impaired fertility, emerging evidence suggests that increased adiposity alone is not the primary cause of reproductive dysfunction. Instead, a constellation of metabolic comorbidities including insulin resistance, systemic inflammation, and oxidative stress appears to exert a more direct influence on sperm quality and embryo development.

Key molecular mediators such as sperm microRNAs and reactive oxygen species (ROS) are central to this process. Sperm microRNAs, which are sensitive to metabolic and lifestyle factors, regulate early embryonic gene expression and epigenetic programming. Disruptions in their profiles can impair implantation, placental development, and fetal growth. Elevated ROS levels further compromise sperm DNA integrity and mitochondrial function, contributing to reduced embryo viability and altered offspring health.

Notably, weight loss alone does not appear to reverse these effects. Studies examining bariatric surgery in men show minimal improvement in sperm quality and reproductive outcomes, despite significant reductions in body weight. In contrast, lifestyle interventions such as improved diet and increased physical activity seem to be better at restoring sperm quality and oxidative stress. These findings suggest that it is the metabolic/nutritional recalibration, rather than weight loss per se, that drives reproductive recovery.

Addressing obesity related male infertility through targeted lifestyle strategies offers a more effective and sustainable approach than focusing solely on weight reduction. By understanding the molecular interplay between early metabolic dysfunction and sperm biology, we can better support reproductive success and promote healthier outcomes across generations.

id #128619

Metformin and insulin exacerbate one-carbon metabolism deficits in pregnant growth restricted rats and impacts the placenta, fetal liver and pancreas

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Fetal growth restriction increases the risk of metabolic conditions such as gestational diabetes mellitus (GDM) (1). One-carbon metabolite concentrations are dysregulated in GDM and influenced by antihyperglycaemic medications (2-3). However, it remains unclear if disrupted one-carbon metabolism contributes to GDM onset in growth restricted offspring and if antihyperglycaemic medications exacerbate this dysregulation. We investigated the effects of growth restriction and antihyperglycaemic treatment on one-carbon metabolism in pregnant rats and their fetuses.

Uteroplacental insufficiency (Restricted) or sham (Control) surgery was performed on embryonic day 18 in Wistar-Kyoto rats. Female F1 offspring were mated and Restricted dams received daily metformin, insulin, or vehicle from E13. Maternal and fetal plasma concentrations of one-carbon metabolites were measured using liquid chromatography-mass spectrometry. Liver and placental gene expression of enzymes involved in one-carbon metabolism and associated processes were measured using real-time PCR. Immunofluorescence staining was used to quantify fetal pancreatic β-cell and α-cell area.

Although Restricted dams did not develop metabolic dysfunction during pregnancy, they exhibited reduced one-carbon metabolism with a 71% decrease om their SAM:SAH ratio, indicating reduced methylation capacity. These changes were exacerbated by both metformin and insulin, contributing to a further 41.04% and 79.78% reduction in methylation capacity. In Restricted F2 fetuses, plasma one-carbon metabolites were unaffected despite changes in expression of genes involved in one-carbon metabolism in the placenta and liver. F2 fetuses displayed an elevated pancreatic β-cell:islet ratio. Antihyperglycaemic medications altered expression of multiple one-carbon metabolising enzymes in the maternal liver, the placenta junctional zone and the fetal liver. Metformin also increased pancreatic α-cell area.

This study suggests disrupted one-carbon metabolism may underly programmed metabolic dysfunction and highlights the need for monitoring females born small. Both metformin and insulin induced similar physiological changes indicating that one is not safer than the other. Treatment decisions should consider potential impacts on long-term health.

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id #132204

Community-Driven Public Health Strategies to Improve Aboriginal Perinatal Outcomes

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Despite major investment in maternal and infant health, Aboriginal families in Australia continue to experience higher rates of stillbirth, preterm birth, and perinatal mortality than non-Aboriginal families. These persistent disparities reflect a complex interplay of factors — including unequal access to high-quality care, cumulative exposure to social and economic disadvantage, and system-level barriers that compromise cultural safety.

Emerging evidence demonstrates that culturally safe, Aboriginal-led models of care can transform these outcomes by strengthening trust, continuity, and empowerment throughout the reproductive journey. This presentation explores how community-driven approaches — grounded in Indigenous knowledge systems and supported by robust data — are aiming to advance equity in perinatal health.

Drawing on examples predominantly focused on Noongar Boodja in Western Australia, we highlight initiatives spanning culturally safe maternity care, pregnancy support, and community awareness of pregnancy risks. These include Aboriginal-led projects such as Birthing on Noongar Boodja and culturally responsive doula programs, alongside population-level and community studies such as Jinda Maawit, which illuminate the pathways to safer pregnancies and the importance of approaches that resonate with Aboriginal families. Together, these initiatives show that bridging biomedical and Indigenous worldviews — through Aboriginal leadership, data sovereignty, and culturally grounded public health — is key to improving outcomes for mothers, babies, and families across generations.

id #128364

Higher mRNA Levels of Endometrial Renin-Angiotensin System Signalling Initiators Suggest a Role in Endometrial Repair

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The endometrium is shed and remodelled each menstrual cycle in response to hormonal fluctuations. A system known to be under hormonal control and to drive proliferation and differentiation in tissues is the renin-angiotensin system. Currently, the role of the renin-angiotensin system in endometrial remodelling is unknown. This study aimed to characterise the expression of prorenin, the (pro)renin receptor and angiotensinogen, initiators of renin-angiotensin system signalling, across the menstrual cycle to provide insight into their role.

Endometrial tissue was collected from fertile patients undergoing endometrial biopsies during the proliferative (n=9), mid (n=10) and late (n=10) secretory phases. Prorenin, (pro)renin receptor and angiotensinogen mRNA expressions were determined by qPCR. Proteins were localised by immunohistochemistry and staining intensity (H-score) quantified using HALO image analysis software.

There were no significant changes in mRNA levels of prorenin across the menstrual cycle, with only 3/10 patients in the mid-secretory phase, and 5/10 patients in other phases having detectable prorenin mRNA levels. (Pro)renin receptor mRNA levels were found to be significantly higher in the proliferative phase than the late secretory phase ($p<0.05$), with 8/10 patients having detectable levels in the proliferative and mid-secretory phase, and 5/10 in the late secretory phase. Angiotensinogen mRNA levels were highest in the proliferative phase compared to the mid and late secretory phases ($p=0.0076$ and $p=0.045$, respectively). Seven of 9 patients had detectable angiotensinogen mRNA in the proliferative phase, 5/10 in the mid secretory and 3/10 in the late secretory. There were no significant changes to protein staining intensity across cell types or overall staining intensity within the endometrium.

The high levels of mRNA expression of the (pro)renin receptor and angiotensinogen in the proliferative phase of the endometrial cycle suggest that the renin-angiotensin system is working to drive proliferation to promote endometrial tissue regeneration.

id #129900

Radiofrequency Ablation in the Management of Thyroid Disease

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Over the past 2 decades, use of thermal ablation for the treatment of benign symptomatic thyroid nodules has gained momentum worldwide as a valid and effective non-surgical treatment option for benign nodular disease that is endorsed and supported by all major international Thyroid Associations and Societies. Many patients prefer ablation to surgery as it preserves normal thyroid tissue and does not result in them needing hormonal replacement post treatment. However, although patients may view ablation as the only option for them, careful patient selection for these treatments is critical to optimise safety and post-procedural outcomes. Indications for ablation have now extended into the malignant realm of thyroid disease. The primary objective of this lecture is to provide an update on current indications and uses for thermal ablation in benign thyroid disease, including basic technical factors and long term outcomes. Application to non-benign disease will also be discussed.

id #128621

Early Identification of Adiposity Risk: Longitudinal BMI Trajectory Modelling from Infancy to Adulthood in the Raine Study

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Background

Understanding the early-life development of obesity allows directing public health resources toward at-risk individuals. Distinct childhood BMI trajectories have been associated with cardiovascular risk. This study aims to refine that understanding by identifying critical periods in early life where long-term adiposity risk can be reliably predicted.

Methods

We utilised longitudinal anthropometry from the Raine Study, a population-based birth cohort (n=2,868, 1989-1991), with follow-ups spanning 1-27 years-old. Weight-for-height z-scores were calculated using both the WHO (<2 years) and the 2022 CDC BMI-for-age growth charts (2-20 years). Group-based trajectory modelling identified BMI trajectories across age intervals (1-5, 1-8, 1-13, 1-17, 1-20). Multilogistic regression assessed relative risks associated with maternal exposures and adult outcomes at age 20 and 27.

Results

Five to seven BMI trajectories were identified across all age intervals. Models from 1-5 years-old showed parallel trajectories, while those from 1-8 years and beyond revealed trajectory crossover, suggesting critical divergence before age 8. Three trajectories “very low stable”, “moderately high stable” and “very high stable”, were identifiable by age 5 and reliably tracked into adulthood. At age 8, a further two trajectories were identified, with trajectories having elevated risks of overweight/obesity at age 20 and age 27; “Very high stable” (OR = 21.4, 95% CI: 5.0-58.0), “Rising to high” (OR = 5.2, 95% CI: 2.8-9.6), “Moderately high stable” (OR 2.7, 95% CI: 1.8-4.8).

Conclusions

Models from 1-8 years captured patterns more clearly than those ending at age 5.

Our findings highlight that BMI trajectories become meaningfully distinguishable by age 8, with some risk groups identifiable even earlier. These trajectories are strongly associated with adult obesity and cardiovascular risk. Early trajectory modelling offers a powerful tool for targeted early intervention to prevent obesity.

id #131952

Screening for OSA in children affected by obesity

Adelaide Withers[1]

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Obstructive sleep apnoea occurs in 1-3% of children, but up to 60% with obesity. The mechanisms of OSA in obesity will be reviewed and the importance of screening for OSA in children with obesity will be highlighted. A brief discussion of screening tools including oximetry will be presented, with an outline of referral pathways and investigation of OSA. Lastly, treatment modalities for OSA and the challenges of treatment in this cohort will be discussed.

id #129904

The vaginal microbiome as a modifier of pregnancy outcomes

David MacIntyre[1]

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The vagina is colonised by a dynamic community of bacteria, viruses and fungi, collectively termed the 'microbiome'. In this talk I will describe how vaginal microbiome compositions can modulate host immune and inflammatory responses implicated in key stages of pregnancy, including parturition and labour. I will also present recent findings from our laboratory demonstrating how different vaginal bacteria target glycan structures throughout the reproductive tract to modulate colonisation dynamics and host immune responses. Finally, results from recent studies using live vaginal biotherapeutics designed to modulate the microbiome to improve pregnancy outcomes will be shared.

id #131953

Health and Wellbeing Queensland projects - children and families

Fiona Nave[1]

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Health and Wellbeing Queensland (HWQld) lead on preventive health in Queensland, with a GenQ vision that aims to see the next generation of Queenslanders living healthier lives than their parents, or grandparents. By taking a whole system, multi-strategic approach, HWQld are working in partnerships to develop programs that have been co-designed by the communities that they serve. Initiatives at a strategic, government and local level will be discussed to explore how HWQld are leading the way to improve GenQ.

id #129905

Navigating the Academy: Autistic People's Experiences

Diana Tan[1]

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Research on neurodivergent students in higher education is growing, but most of it looks at coursework students and largely overlooks those in research degrees. In this talk, I'll share findings from a systematic review we conducted on the experiences of neurodivergent research students. We analysed 31 articles - both empirical studies and lived experience accounts - and identified eight themes that shape these students' journeys: academic cultures and expectations, sensory and environmental challenges, executive functioning, supports and accommodations, relationships, ableism and disclosure, mental health, and embracing neurodivergence. While some strengths of neurodivergent thinking came through, the picture was clear: research degree pathways remain full of systemic barriers. I'll discuss what these findings mean for universities, and how we can take concrete steps to build research environments that genuinely support and empower neurodivergent students.

id #130673

Beyond Weight: Building Physical Literacy and Fostering Positive Relationships with Exercise in Children and Young People

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Supporting children and young people to develop lifelong healthy behaviours requires more than simply increasing activity levels, it requires the cultivation of physical literacy: the skills, confidence, and motivation to engage in movement in meaningful and sustainable ways. This presentation explores approaches to building physical literacy among vulnerable or at-risk groups, with a children and young people with emotional and behavioural difficulties, neurodivergence, and/or gender diversity.

Drawing on practical experiences within therapeutic exercise programs in community settings, the discussion will highlight the importance of moving away from weight- or appearance-focused narratives. Instead, interventions centre on fostering positive relationships with exercise, supporting autonomy, and creating environments where all young people can experience success and enjoyment in movement. Through this lens, physical activity becomes a vehicle for enhancing self-efficacy, health, and body confidence, while also addressing the risks of negative body image and disordered behaviours.

Key lessons learned will be shared on tailoring strategies to meet diverse needs, overcoming implementation challenges, and working collaboratively with families, health professionals, and communities. Practical considerations will include how to balance clinical goals with lived experiences, and how to reframe exercise as an enjoyable tool for wellbeing rather than weight management.

id #129138

Postpartum health after gestational diabetes: insights from women on a behaviour change program using digital and coaching approaches

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Gestational diabetes mellitus (GDM) impacts between 10-15% of pregnancies in Australia, yet postpartum care remains under-resourced. Given the increased risk of developing type 2 diabetes after GDM, early intervention is essential. Adapting existing health behaviour change programs may offer a cost-effective solution. This study aimed to explore the experiences of people with lived experience of GDM through participation in the My health for life program. My health for life is a statewide integrated health risk assessment and healthy lifestyle program funded by Health and Wellbeing Queensland and delivered by Diabetes Australia.

Eligible participants had experienced GDM and had at least one child aged two years or younger. Participants were randomly assigned to one of two My health for life program modes – self paced digital or individual telephone coaching. Participants were later invited to join a focus group or semi-structured interview to share their experiences. Demographic data were summarised descriptively; qualitative data were analysed using inductive and deductive content analysis.

Of the 233 people randomised to the digital program, 82 (35%) commenced, 34 (15%) completed half, and 21 (9%) completed the entire program. In the telephone coach group (n=235), 78 (33%) commenced, 27 (11%) completed half, and 23 (10%) completed the full program. Nine individuals joined a focus group, and ten participated in an interview. Analysis identified 16 codes across three themes: (1) Acknowledge and address personal factors impacting engagement, (2) Adapt program elements to ensure relevance, specificity, and digital competence, (3) Integrate aspects of optimal support services. The ideal program design sat at the intersection of these themes.

Participants expressed a desire for a flexible yet clearly defined program to support postpartum behaviour change. Tailoring elements of an existing program using user-centred, collaborative design practices can create an engaging, accessible, and sustainable solution to reduce long-term chronic disease risk.

id #129906

Functional characterisation of human variants implicated in POI

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Although genomic testing for many genetic disorders has become part of routine clinical care, this has not occurred in Australia for the management of female infertility, including premature ovarian insufficiency (POI). POI is a leading form of female infertility affecting up to 4% of women under the age of 40 and characterized by amenorrhea and elevated gonadotropins.

Genetic diagnosis for POI is challenging because 1) it is highly heterogeneous with over 100 causative genes affecting a wide variety of processes, 2) these known genes account for only a minority of patients and 3) most variants remain of uncertain significance until functional validation is performed.

We have studied a diverse cohort of over 200 girls/women with POI using whole exome sequencing, identifying cause in >20%. We have validated or discredited causation of genetic variants using various approaches such as multi-omic analysis of patient cells, modelling in Drosophila, zebrafish or mouse, and in-vitro functional assays. Our approach has led to multiple novel POI gene discoveries, such as TP63, TFAM, MRPL50, HROB, REC8, GGPS1 and more.

Importantly, we have shown that genomic sequencing can alter and improve patient management and outcomes. For example, we identified causative variants in NBN, EIF2B2 and LARS2 in three different patients presenting with apparently “isolated” POI. These genes are usually associated with syndromic POI in the context of cancer predisposition, neurodegeneration, and hearing loss respectively. In each case genomic sequencing identified syndromic POI before its full clinical manifestation. This enabled early intervention for associated co-morbidities, with the potential to improve patient outcomes.

Given the impact of genetic diagnoses on downstream patient care and outcomes, it is critical that variant curation is performed accurately with sufficient functional validation to be confident that variants reported as pathogenic are truly causal.

id #130674

Mapping interactions between dietary macronutrients and sex across the lifecourse

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Understanding mechanisms that define the relationship between diet, physiology, and ageing holds great promise to improve human health despite the complexity of these relationships. Traditional dietary approaches have usually focussed on ‘one-nutrient-at-a-time’ rather than considering the entire nutrient and dietary landscape. In this talk I will discuss how we have employed an integrative

approach called the Geometric Framework for Nutrition (GFN) to explore in unprecedented detail the ways that nutrients and their interactions influence the multiple dimensions of phenotype (spanning molecular interactions to life-history traits) across life.

id #125811

Creating health-enabling supermarkets in Australia: using the Store Scout App in health promotion practice

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Abstract

Objective: To examine the effect of health-enabling changes on supermarket healthiness, the distribution and variation of scores were used to demonstrate this within the participant supermarkets.

Methods: The *Scout App* (*SS-App*) was used to assess the healthiness of supermarkets at baseline vs follow-up in 10 supermarkets (5-implementation, 5-control). The Reach for the Stars program included promotional and informational materials based on the health star rating of healthier products. Two-way analysis of variance (ANOVA) was used to test the effects of time group (implementation vs. control) and their interaction on overall mean *SS-App* scores within the study arm.

Results: *SS-App* scores improved from pre- to post-implementation ($p<0.01$). A larger increase in *SS-App* scores was observed in the implementation group ($M = 8.7$, $SD = 3.7$) compared to the control group ($M = 1.4$, $SD = 6.1$), $t(8) = -2.28$, $p < 0.05$).

Conclusions: The *SS-App* was key in implementing the program by ensuring stores aligned with its goals and objectives, supporting and enhancing retailer participation and sustained engagement.

Implications for Public Health: Community public health practitioners need user-friendly tools to collect real-time data, engage with local food retailers, and customise health initiatives in supermarkets. These technologies can optimise resource allocation and improve outreach.

id #129907

Duplicated paralog of RNA polymerase II associated factor 1 (PAF1) orchestrates male germ line-specific transcription and meiosis in Drosophila.

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Germ line development requires coordination of cell type-specific transcription and preparation for meiosis. In Drosophila spermatogenesis, over a thousand of male germ line-specific genes are transcribed in spermatocytes, before meiosis, in preparation for the post-meiotic spermiogenesis. While doing so, a chromosome-level chromatin reorganisation takes place to pair duplicated chromosomes to successfully pass down each one of the chromosomes to haploid cells after meiotic cell divisions. We identified duplicated paralogs of RNA polymerase II associated factor 1 (PAF1) subunits that are specifically expressed in the testis of fruit flies Drosophila melanogaster; hence we named the complex tPAF. The four core subunits of tPAF, namely, tPaf1, tLeo1, tCdc73, and tCtr9 are each essential for male fertility. RNAseq analysis of the mutant testes did not reveal a large-scale change in the transcription of spermatocyte-specific genes whereas the mutant testes displayed strong defects in meiotic chromosome segregation. Interestingly, we found that tPAF is required for the transcription elongation of the gigantic genes kl-3 and kl-5 on the Y-chromosome. These kl genes are mega-base long, transcribed across two-thirds of the spermatocyte development (~3 days), and the completion of transcription and splicing marks the onset of meiosis. I discuss how the kl gene transcription might act as a timer for spermatocyte development, failure of which leads to a mis-coordination of meiotic chromosome segregation.

id #128628

When the Ground Shifts: Leading an Education special interest group in changing times

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The Education Special Interest group (EdSIG) of the Australian Society for Microbiology (ASM) has been an integral part of the society for more than 15 years. During this time EdSIG has grown significantly to have a dedicated symposium as part of the ASM annual national meeting, has contributed two education-focussed issues of Microbiology Australia (https://www.publish.csiro.au/maa) and since 2014, we have hosted a one- or two-day education-focussed conference (ASM EduCon) either immediately before or after the main national meeting. These education conferences have become vibrant platforms for sharing innovative ideas in education, especially those aimed at enhancing student engagement and participation. They offer a valuable space for educators who have transitioned from research to teaching to reflect on the scholarship of teaching, connect with other educators, and they act as a refresh between semesters, leaving educators genuinely recharged and ready for teaching.

In 2020 as travel halted and communication online became our only connection to the broader community, EdSIG pivoted by launching an online conference, Virtual EduCon. This online format showcased how educators were navigating the new virtual teaching landscape imposed by the pandemic, while also fostering a sense of connection at a time of increasing isolation from both our colleagues and students. The event was a resounding success. We continued with Virtual EduCon in 2021 (just as Melbourne was entering their lockdown) and although we have returned to in-person meetings since 2022, we remain committed to evolving our conference format to respond to the changing needs of educators. The ability to pivot is vital for a group like EdSIG, and the benefits to the educator collective are clear.

Leading change and staying open to new ideas are at the heart of the EdSIG mission, and are important for the support of Microbiology educators across Australia.

id #129908

Womb service: multi-omic insights into the histotrophic nutrition of the fat-tailed dunnart

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Australian marsupials are facing a biodiversity crisis, requiring decisive action to prevent further extinction. Assisted Reproduction Technologies are a promising frontier in species conservation: however, while embryo culture methodologies have been developed for eutherian species, marsupial embryo culture has not yet been optimized. Given marsupial reliance on histotrophic nutrition, close examination of uterine fluid contents is necessary for optimizing embryo culture. Using a model marsupial, we have built a comprehensive molecular profile of the contents of the uterine lumen to understand exogenous cues regulating marsupial embryo development within the uterus.

Uteri from fat-tailed dunnarts (Sminthopsis crassicaudata) were collected each day of the 13.5-day long gestation, capturing every stage of in utero embryogenesis. Endometrial architecture was assessed using histological techniques, and uterine fluid was subjected to proteomic, metabolomic, and lipidomic profiling. Comparisons were drawn between each major stage of embryonic development, highlighting important metabolic pathways necessary for embryo development.

We showed that, in the dunnart, the uterine histotroph is provided by an extensive glandular network. The highly folded endometrial surface transformed across gestation, with adhesion zones between the endometrial epithelium and embryonic trophectoderm evident by day 12. Concurrently, the histotroph protein, metabolite, and lipid profile was altered post-adhesion. Prior to adhesion, when embryo is encased within a porous shell coat, each developmental stage had a unique molecular signature, indicating the dynamic maternal support driving embryogenesis prior to implantation.

It is evident that the marsupial uterus has evolved extensive glandular architecture and dynamic histotrophic cues to maximise the efficiency of their iconic reproductive strategy. The fat-tailed dunnart is an exquisite model for examining maternal-fetal communication and nutrient transfer, and comparative developmental biology. Insights from the molecular milieu presented here will be foundational to the development of marsupial assisted reproduction technologies necessary to combat the extreme rate of extinction faced by these species.

id #128629

“From scratch, to success”- Building a public hospital Aclasta infusion service

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Background:

Osteoporosis (OP) is estimated to affect 3.4% of the Australian population in 2022. One of the treatments for OP includes intravenous Aclasta (Zoledronic Acid) infusion.

In December 2022, Sonic Nurse Connect, one of the largest community Aclasta infusion provider discontinued their infusion service. This had a significant impact on the amount of external Aclasta infusion referrals issued to Endocrine Testing Area (ETA) at St Vincent’s hospital Melbourne (SVHM).

Aim:

- To assess quantity of Aclasta referrals from Victorian Endocrinologists.
- To establish an Aclasta infusion service team at SVHM.
- To promote and improve Aclasta infusion service.

Method:

The ETA nurse initiated a survey which was sent to Endocrinologists across Victoria.

The Diabetes Education and Endocrinology manager proposed to develop an Aclasta infusion service based on government funding availability in the national Weighted Activity Unit (NWAU).

ETA nurse monitors volume of referrals and collect feedback from specialists and patients.

Results:

The survey indicated a drastic increasing number of Aclasta referrals to ETA from Endocrinologists and other specialists.

NWAU funding estimated the Aclasta service captures approximately 10 times more financial source to ETA. Aclasta infusion service opened in April 2024. The ETA service has been well recognised, and the news article was published at SVHM website in October 2024.

In April 2025, the Aclasta team updated procedure protocol to improve infusion service. ETA statistic demonstrates increasing demands of Aclasta referrals. Aclasta service operation expanded from three days per week to four days per week.

Conclusion:

The closure of community infusion service resulted in large volume of Aclasta referrals to ETA at SVHM. NWAU founding has supported the development of Aclasta service. SVHM has become the first hospital in Victoria to have two dynamic ETA nurse on site. Over 700 patients received Aclasta treatment comparing to 120 patients in the previous years.

id #129909

Mitochondrial mechanisms underlying placental dysfunction in fetal growth restricted pregnancies.

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Fetal growth restriction (FGR) occurs when the fetus fails to reach its predetermined growth potential and affects approximately 10% of births in Australia. FGR is characterised by placental insufficiency, with FGR placentae being smaller in size and weight than healthy term placentae and comprising of underdeveloped placental villi – the site of exchange between the maternal and fetal systems. These changes are suggested to arise from poor trophoblast function, although the underlying mechanisms remain elusive. Our recent work has established that mitochondria are essential for optimal trophoblast and placental function. Using cryo-electron tomography and array tomography we have mapped the mitochondrial networks of healthy villous trophoblast cells. This work determined a complex withdrawal of mitochondrial mechanisms accompany cellular differentiation to support cell specific functions in the placental villi. Notably, the abundance of mitochondrial dynamics, structural membrane proteins, and electron transport chain proteins determine mitochondrial morphology, cristae curvature, and thereby function. We have shown that many of these mitochondrial mechanisms are dysfunctional in FGR, resulting in a lack the bioenergetic capacity. We propose these changes precede impaired trophoblast cell growth, leading to poor placental development, and in turn failure of the fetus to grow. A hypothesis supported by genome wide association studies (>250,000 individuals), Sanger sequencing (n=13), proteomics (n=12), western blotting (n=7) and qt-PCR (n=19), which identified altered gene expression and protein abundance in FGR. These findings have provided numerous therapeutic targets and pathways we have begun to investigate within a plate based knockdown model of FGR. Using the Incucyte to assess growth, and Xcelligence to measure invasion of trophoblasts through impedance. We have shown that supporting mitochondrial function improves and restores growth and invasion capacity in trophoblasts. Collectively this work provides insights into the importance of mitochondria to cellular and placental function, highlights their complex role in pathology, and assesses the feasibility of restoring mitochondrial function to aid in placental development and improve growth trajectories in FGR.

id #131958

Metabolic Health in the Care of Transgender Patients

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id #128630

Advancing understanding of the protein composition of human seminal extracellular vesicles

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Seminal extracellular vesicles (SEVs) carry a diverse array of bioactive molecules, including proteins, lipids, and nucleic acids, which influence sperm function and are implicated in modulating the female reproductive tract immune response after intromission. However, the full spectrum of SEV cargo involved in these processes remains incompletely defined. Here, we employed label-free quantitative high-resolution mass spectrometry to characterize the human SEV proteome, identifying 5,079 associated proteins. As the male reproductive tract origins of SEVs are still poorly understood, we first used the Human Protein Atlas Tissue Based Map of the Human Proteome to predict the male reproductive tract origin of the top 20 most abundant proteins. SEV proteins were thereby categorised as seminal vesicle-enriched (5/20 proteins), prostate-enriched (3/20 proteins), or no specific tissue enrichment (12/20 proteins) providing compelling evidence that in addition to the prostate, the seminal vesicles are a major contributor to the SEV pool. To explore the functions of SEV proteins, bioinformatic analysis using Ingenuity Pathway Analysis revealed enrichment in sperm- and immune-related functions, consistent with the predicted roles of SEV in events surrounding conception. Notably, we identified several proteins with established roles in sperm physiology and immune signalling that had not previously been postulated to be SEV signalling mediators. These included; Adenylate kinase isoenzyme (AK)2/9, calcium-binding tyrosine-phosphorylation regulated protein (CABYR), implicated in sperm motility, and immune regulators such as the toll-like receptor 4 ligand, high mobility group protein B1 (HMGB1), and the nuclear factor kappa-light-chain-enhancer of activated B cells (NFκB) inhibitor epsilon (NFκBIE). Interestingly, many other SEV proteins were associated with protein translation functions, potentially contributing to sperm survival and function in the female reproductive tract. Altogether, these findings expand the known SEV proteome and highlight proteins that may influence both male and female reproductive capacity.

id #131703

Lipids, Lipoprotiens and Cardiovascular Health

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<Working Title>

Abstract details coming soon

id #129143

Antenatal ciclesonide does not alter molecular determinants of fluid transport in the fetal lung

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Antenatal corticosteroids (ACS) are routinely administered to pregnant mothers at risk of preterm birth to mature the fetal lung and reduce risk of neonatal respiratory disease. However, ACS also act on other fetal tissues. We hypothesised that ciclesonide (CIC), a prodrug with tissue-specific effects, matures the lung as effectively as existing ACS and examined its impact on molecular determinants of fluid transport.

Preterm lambs (~130 gestational days, gD; term, 150 gD) were delivered from Merino ewes randomised to treatment with saline (control, 48 and 24 h: n=11), betamethasone (standard clinical ACS, intramuscular (i.m.) 11.4 mg, 48 and 24 h: n=11), or CIC (i.m. 11.2 mg, 48 and 24 h: n=10, intraamniotic (i.a.) 0.5 mg/kg, 48 h: n=9, or i.a. 1 mg/kg, 48 h: n=10) before delivery, intubated and ventilated for 60 min, then humanely killed for lung tissue collection. Fetal lung fluid was collected and measured before ventilation. Markers of lung maturation: surfactant-producing type II alveolar epithelial cell (AECII) density, and gene expression of aquaporins (*AQP*) and epithelial sodium channel (*SCNN1*) subunits, were analysed by qRT-PCR. Effects of treatment and sex were analysed using mixed models in SPSS, $P<0.05$ were considered significant.

AECII density was higher in lambs treated with betamethasone ($P<0.001$) and i.a. 1 mg/kg CIC ($P<0.001$) than in controls, consistent with both steroids inducing lung maturation. Lung liquid volume did not differ from control lambs in betamethasone or CIC-treated groups. Expression of *SCNN1G* was lower in betamethasone-treated than controls in female lambs only ($P=0.030$), whereas expression of *AQP1*, *AQP5*, *SCNN1A*, and *SCNN1B* were unaffected by treatment.

Although CIC and betamethasone induce lung maturational changes, including increased AECII density, gene expression of key fluid transporters and lung fluid volumes were not increased by steroid treatments, likely reflecting the variability within the present cohort.

id #129911

Recovering critically endangered and functionally extinct species: a discussion of the ExoUterus system

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The world is undeniably in the throes of a climate crisis which is driving an acceleration in global animal extinction events. The alarming rate of species addition to the endangered list means that numerous species will ultimately find themselves entered onto the critically endangered list followed by functional extinction. Unfortunately, the available set of species recovery tools, based in existing ART, cloning and surrogate birth techniques, are currently incapable of rescuing any functionally extinct species. To date there has been very little success in recovering even critically endangered species. Hence, there is an urgent need to develop new and complementary tools and techniques capable of rescuing a broad range of species from the very edge of extinction.

The ExoUterus project is an ongoing attempt to fill an important gap in our species recovery capability. That gap, stated as a question, is: what can you do when there are no or too few females of a species and no suitable surrogates available to live birth healthy animals? Our proposed solution to this dilemma is gestation within an artificial womb. As such we are developing a functionally modular, exogenous marsupial biosynthetic uterus with the goal of facilitating gestation from zygote to parturition. I will discuss the concept and the underpinning reasoning behind design choices as well as the potential for a broad lateral application across species.

State-of-the-art species recovery methods have no viable answers for the ever-increasing number of critically endangered species. The successful development of a functional artificial uterus is an essential part of the solution to saving these species.

id #131704

Genetics of calcium disorders

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Roderick Clifton-Bligh, Head of Cancer Genetics Laboratory, Kolling Institute, Northern Sydney Local Health District and Faculty of Medicine and Health, University of Sydney.

Blood calcium concentrations are regulated through the co-ordinate actions of parathyroid hormone (promoting renal calcium reabsorption, renal 1-alpha hydroxylation and bone resorption), 1,25-dihydroxyvitamin D (promoting intestinal calcium absorption), and calcium itself (acting on the calcium sensing receptor in parathyroid glands and kidney). Genetic disorders in each of these components lead to either hypercalcaemia or hypocalcaemia; each classified most readily into PTH-dependent and -independent forms, and thereafter into syndromic and non-syndromic categories.

Genetic disorders causing PTH-dependent hypercalcaemia include the Multiple Endocrine Neoplasia (MEN) syndromes 1-5 (arising from pathogenic variants in MEN1, RET, CDKN1B and MAX, respectively), Familial Isolated Hyperparathyroidism (MEN1, CASR or GCM2), Hyperparathyroidism-Jaw Tumour syndrome (CDC73), and Familial Hypocalciuric Hypercalcaemia (CASR, AP2S1, GNA11).

PTH-independent hypercalcaemia can be associated with pathogenic variants in CYP24A1 (causing hypervitaminosis D), ALPL (hypophosphatasia) or SLC34A1 (infantile hypercalcaemia).

Genetic disorders causing PTH-dependent hypocalcaemia include Familial Isolated Hypoparathyroidism (PTH, GCM2), Di George syndrome (TBX1, NEBL), Hypoparathyroidism-deafness-renal syndrome (GATA3), Kenny-Caffey syndrome (TBCE, FAM111A), Kearns Sayre (mitochondrial), Autoimmune Polyendocrinopathy-candidiasis-ectodermal dystrophy (AIRE) and Autosomal Dominant Hypocalcaemia (CASR, GNA11).

Conditions causing PTH-independent hypocalcaemia include Pseudohypoparathyroidism (GNAS1) and Hereditary vitamin D resistant rickets (VDR, CYP27B1).

Genetic causes of PTH-dependent hypercalcaemia should be considered in the presence of multiglandular parathyroid disease, MEN or HPT-JT features, parathyroid carcinoma (or absent parafibromin immunostaining in a parathyroid neoplasm), hypocalciuria or family history of hypercalcaemia; or in any patient younger than 40 y. Genetic causes of PTH-independent hypercalcaemia should be considered when acquired causes have been excluded. Similarly, genetic causes of hypocalcaemia should be considered in any patient if there is no clear acquired cause.

id #128632

Is maternal obesity related complication of gestational diabetes mellitus associated with neurodevelopment, cognitive and behaviour outcomes in children? Insights from individual participant data meta-analysis in ten birth cohorts

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Evidence shows that obesity-related complications in the mother can affect offspring's neurodevelopment. However, results of individual cohort studies have been inconsistent.

Aims: To investigate the association between gestational diabetes mellitus (GDM) with neurodevelopment, cognitive and behaviour outcomes in children.

Methods: Harmonised data (>200 000 mother-child pairs) across ten birth cohorts in Europe and Australia were included where GDM was recorded (yes/no) and >neurodevelopmental, cognitive and behavioural outcome was available in children aged 3 -13. Confounder-adjusted regression models were used to estimate associations between maternal diabetes and child outcomes using individual participant data (IPD) meta-analysis. Estimates (model 1) included adjustments for child sex and maternal age. Full adjustment (model 2) included adjustment for child sex and maternal age, pre-pregnancy BMI, pregnancy weight gain, maternal smoking during pregnancy, plurality, parity, maternal education, and income.

Results: Children (aged 7-10 years) born to mothers with GDM had higher attention-deficient hyperactive disorder (ADHD) symptoms compared to non-exposed controls (model 2, regression coefficient (β) 2.40 (95% CI 0.07, 4.73), P=0.04). Moreover, children (aged 4-6 years) born to mothers with GDM exhibited more externalising problems than those born to mothers without GDM (model 2, β 2.50 (95% CI 0.15, 4.85), P=0.03). In the secondary analysis, maternal history of type 1 and type 2 diabetes mellitus was associated with ADHD symptoms at 4-6 years (model 1, β 8.82 (95% CI 2.21, 15.45, P=0.009) and β 7.90 (95% CI 0.82, 14.98, P=0.02), respectively). The association was no longer apparent in further adjustments.

Conclusions: Children between 4-6 and 7-10 years of age born to mothers with obesity-related complications of GDM have a greater likelihood of developing externalising problems and ADHD symptoms. Overall, this large-scale multi-cohort study suggested that a dysregulated metabolic environment during pregnancy related to maternal obesity may contribute to ADHD and externalising problems in children.

id #129912

YAP/TAZ integrate adipose tissue remodeling with endocrine regulation of energy homeostasis

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Adipose tissue serves dual roles as an energy reservoir and endocrine organ. We identify YAP/TAZ, Hippo signaling pathway effectors, as key integrators of these functions. Mice with adipocyte-specific YAP/TAZ activation develop severe lipoatrophy yet maintain metabolic homeostasis through unexpectedly elevated leptin levels. Mechanistically, we demonstrate that adipocyte YAP/TAZ operates through two distinct transcriptional pathways: inhibiting PPARγ target genes via a YAP/TAZ-PPARγ axis, and directly upregulating leptin expression through YAP/TAZ-TEAD complex binding to a novel Lep enhancer. The physiological relevance of this mechanism is underscored by the finding that adipocyte YAP/TAZ activation correlates with and is required for regulating leptin expression during feeding-fasting cycles and high-fat diet induced obesity. Taken together, these results extend our understanding of the Hippo-YAP/TAZ pathway beyond its canonical role in organ size control, revealing a critical function in integrating adipose tissue plasticity with systemic energy homeostasis.

id #131705

Aboriginal Engagement Lead, Health Consumers' Council presentation

Tania Harris[1]

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The objective of this symposium is to highlight the challenges facing consumers in the health system when seeking support for healthy lifestyle change and/or weight management services. Presenters will share their experiences of how people get "lost in the system", even when proactively asking for help, the stigma and shame associated with asking for support, experiences of racism and bias, and the resultant impact on long-term health. Attendees will hear solutions to these challenges from each of our expert speakers and the role of advocacy.

id #128377

Replacement of angiotensin-converting enzyme 2 (ACE2) *in vitro* can reduce oxidative stress in the human FGR placenta

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Fetal growth restriction (FGR) is a serious pregnancy disorder associated with increased fetal morbidity and mortality. FGR is characterised by placental oxidative stress resulting from impaired placentation and subsequent intermittent hypoxia and reoxygenation (H/R). We previously showed that placental antioxidant angiotensin-converting enzyme 2 (ACE2) mRNA expression is decreased in FGR. This study aimed to characterise placental ACE2 activity in FGR and its relationship to placental oxidative stress. Moreover, using an *in vitro* H/R model in FGR explants, we sought to determine whether ACE2 replacement could mitigate H/R-induced placental oxidative stress.

Placental villous tissue was collected from control (n=35) and FGR (n=15) pregnancies. Of the FGR tissue, n=4 were dissected into villous explants and cultured for 24hrs under normoxia (8% O_2) or H/R conditions (6hr cycles of 1% and 8% O_2) and treated with or without recombinant human (rh)ACE2. ACE2 activity and markers of oxidative stress were assessed in both whole tissue and explants.

ACE2 activity was significantly decreased in FGR placentae compared with controls (p=0.006), which was accompanied by increased pro-oxidative xanthine oxidase activity (p=0.004) and reduced antioxidant catalase activity (p=0.011). When determining the effect of H/R on FGR explants, ACE2 activity was significantly decreased following exposure to H/R compared with normoxia (p=0.045). While H/R had no significant effect on xanthine oxidase, H/R significantly reduced catalase activity in FGR explants compared with normoxia (p=0.044). Treatment with rhACE2 during H/R partially reversed these effects by significantly increasing FGR explant ACE2 and catalase activity (p=0.037 and 0.015, respectively) compared with H/R alone.

This study demonstrates that FGR placentae exhibit reduced ACE2 activity and that this is associated with oxidative stress. Moreover, replacing ACE2 *in vitro* during H/R insult to FGR explants partially reversed the effects of H/R, a finding that offers unique potential for treating pregnancies with FGR.

id #131706

ORCHID Study

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Background

Detecting HIP is complex, requiring a two-hour 75g OGTT at first antenatal presentation for women with risk-factors (early), and between 24–28 weeks' gestation (routine). Only 50% of rural and remote women in WA complete routine screening. Of those screened ~62% of HIP is missed due to preanalytical glucose measurement error. The ORCHID Study aims to improve HIP screening and management in rural and remote WA.

Methods

Setting: Kimberley ACCHOs introduced a first antenatal visit HbA1c (2017) and replaced fluoride-oxalate (FLOX) with fluoride-citrate (FC) tubes (2019). Retrospective audit (2018-2023): 1340 Kimberley ACCHO antenatal records (98% Aboriginal). Outcome measures: maternal characteristics, early HbA1c, OGTT (≥24-weeks' gestation) pre- (T1) and post- (T2) FC tube implementation, HIP management, birth outcomes. Co-design management strategies: 47 research yarns (21 Aboriginal community members; 26 clinicians). Analysis: ADIPS 2025 OGTT diagnostic criteria; HbA1c rule-in threshold for HIP by OGTT (specificity >90%); FPG (mmol/L) triage: <4.7 low-risk; 4.7-5.2 indeterminate risk; ≥5.3 HIP. Aboriginal and non-Aboriginal researchers identified barriers and enablers for self-management, and acceptability of using technology and other resources.

Results

Audit: Most (86.7%) women presented <20-weeks gestation. Only 178/1132 women with HIP risk-factors had an early OGTT; 89 ≤14-weeks gestation;715 had an early HbA1c at 8.6±4.4 weeks gestation. An early HbA1c ≥5.7% had 94.9% specificity (95% CI 90.5-97.6) for HIP by routine OGTT (FC tubes). Only 378/830 eligible women completed a routine OGTT: 196 T1; 182 T2. The 1.9-fold T2 HIP increase (14.2% v 27.5%) was largely due to the fasting sample (39.3% v 78.1% of cases, P =0.001). Seven-fold more women were recommended pharmaceutical management (2.6% T1 v 17.6% T2, P <0.001). FPG triage would identify most of these women and reduce OGTTs (>50%). Co-design management themes: GDM screening is challenging; understanding GDM takes time; GDM management is individualised; Culturally safe holistic care is valued; care and support is provided by partners, extended family and friends; post-delivery it's all about the baby.

Conclusions

Early and routine OGTT screening remains poor for remote Aboriginal women. Diagnostic equity could be addressed by reducing the early pregnancy HbA1c cut-point (5.7%) and removing OGTT confirmation. Addressing glycolysis improved identification of women requiring pharmaceutical intervention. FPG triaging would identify most of these women and reduce the burden of OGTTs. Pilot sites will host Aboriginal health navigators, who will provide support to Aboriginal women with GDM, from screening to 6-months post-partum.

id #126586

Why a guideline for hypertension in Australian children?

Nicholas Larkins[1]

1. Perth Children's Hospital | Nutrition & Health Innovation Research Institute ECU, Nedlands, WA, Australia

Dr Larkins will be discussing the significance of hypertension among children and adolescents as a predictor of future cardiovascular and kidney events. Obesity is the strongest predictor of blood pressure in childhood, and the impact of increasing obesity on prevalence of essential hypertension will be presented provoking discussion about optimal care of children with multiple cardiovascular risk factors and preventative healthcare for children in Australia more broadly. This presentation occurs in the context of the forthcoming first Australian Guidelines for the Identification and Management of Hypertension among Children and Adolescents.

id #127098

Psychosocial outcomes after 6 and 12-months of gender affirming hormone treatment in transgender and gender diverse individuals.

Christopher A Muir[1]

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Background: Gender affirming hormone treatment (GAHT) is safe and can significantly improve health-related outcomes. However, there is limited prospective data assessing psychosocial outcomes of transgender and gender diverse people receiving GAHT.

Methods: Interim analysis of a prospective, observational study of adolescents and adults commencing GAHT in Sydney, Australia. Surveys assessing dysphoria (*Transgender Congruence Scale; TCS*), depression (*Beck Depression Inventory; BDI*), and anxiety (*Generalized Anxiety Disorder 7; GAD-7*) were administered at baseline, 6-, 12-, and 24-months after commencement of GAHT. Interim baseline, 6- and 12-month data will be presented.

Results: To date, 139 participants have been enrolled (study recruitment ongoing). Median age of study participants was 22-years (range 14-51). Birth-assigned sex was male (41%) and female (59%), respectively. Gender identity was varied and self-reported as non-binary (39%), male (25%), female (22%), fluid (6%), and other/unspecified (8%). Self reported psychological comorbidity was high at baseline with prevalent diagnoses of depression (32%), ADHD (30%), anxiety (26%), and ASD (12%).

TCS (scored out of 5, higher scores equate to greater congruency between an individual's appearance and gender identity) measured 2.4±0.5 at baseline. Following 6- and 12-months of GAHT, TCS improved to 3.2±0.7 and 3.4±0.7 respectively, indicating lower levels of dysphoria (p<0.001). Mean baseline BDI measured 21±11, indicating moderate levels of depression. Following 6-months of GAHT, BDI improved to 14±10, indicating mild depression only (p<0.001). Improvements in BDI were durable and persisted at the 12-month assessments (BDI 14±10). Baseline GAD-7 score measured 9±6, indicating moderate anxiety, improving to 7±6 after 6-months of GAHT (p<0.001).

Conclusion: Interim analyses of an ongoing study in treatment naïve individuals commencing GAHT demonstrated that survey measures of dysphoria, depression, and anxiety improve significantly following commencement of GAHT across a diverse spectrum of gender identities.

id #129914

Abnormal LFTs in Children with Obesity.

Emma Turner[1]

1. Perth Children's Hospital, CAHS, Claremont, WA, Australia

Metabolic dysfunction- associated steatotic liver disease (MASLD) is the most common paediatric liver disease, affecting 10% of children. Paediatric MASLD has specific perinatal influences that, along with genetic predisposition and early onset, can exacerbate disease severity, increasing the lifetime risk of major adverse liver outcomes such as liver cancer and end stage liver disease requiring liver transplantation. There are additional disease factors in the pathogenesis of steatotic liver disease, only 1 in 4 patients with obesity will develop MASLD. The approach to assessing Liver Function Tests in children with obesity will be discussed, including the role of the primary care physician and referral pathways.

id #131708

Perth Children's Hospital/Telethon Kids Institute Presentation

Tim Jones[1]

1. Princess Margaret Hospital, Perth, WA, Australia

From Lab to Clinic: Automated Insulin Delivery

Most people living with T1D do not reach accepted glycaemic goals placing them at risk of long-term diabetes complications. In addition, many remain at risk of severe hypoglycaemia and experience psychological distress resulting from the burden of T1D and its treatment. Feedback control of insulin delivery has long been proposed as an effective approach to achieving glycaemia closer to levels seen in those without T1D but the technology to enable this was not available until recently.

The availability of insulin pumps that can deliver precise doses of insulin along with the development of accurate wearable glucose sensors (CGM) that can measure ambient glucose levels continuously led to efforts to achieve feedback control. The addition of the third essential component, mathematical control algorithms, led to production of effective insulin delivery systems that were tested initially in silico and then in humans firstly in clinic and eventually in a free-living situation.

The first commercially available product was released in 2017 and since then a range of devices have rapidly become available. All currently available systems require a meal bolus and are designated as Hybrid Closed Loop (HCL). Multiple RCTs and a large body of real-world data have demonstrated significant improvements in glycaemia and hypoglycaemia rates along with improved quality of life in users of automated insulin delivery systems. Health economic analyses have confirmed cost effectiveness.

Challenges and improvements remain. A key challenge in Australia is ensuring equity of access, outside of philanthropy access to insulin pumps requires an individual to have top level private health insurance which is limiting access for the disadvantaged.

Further enhancements under investigation include the development of fully closed loop systems that do not require meal bolusing. Personalization of devices with learning algorithms and AI is likely in the future. Systems aimed at special groups (the elderly,

pregnancy) are under development and their use in T2D is under trial. Overall automated insulin delivery has been a major transformative innovation that is now the recommended means of insulin delivery in T1D in many jurisdictions.

id #132476

Preclinical and clinical obesity: implications for practice, policy and research

Christina Pollard[1]

1. Curtin University, Bentley, WA, Australia

Preclinical and clinical obesity: implications for public health policy

Christina Pollard1 2

1. School of Population Health, Curtin University, Perth, WA, Australia

2. Public Health Advocacy Institute, Curtin University of Western Australia, Perth, WA, Australia

Public health is an interdisciplinary field concerned with understanding psychosocial, behavioural and biomedical science, knowledge and techniques relevant to health and illness, and applying this knowledge and techniques for health of the population. Its mission is to prevent (ill health), protect and promote health. This evidence-informed practice first and foremost aims to do no harm. Policy makers require intelligence to inform their practice, from defining the problem and its determinants, to appraising options, and implementing and evaluating portfolios of interventions. Monitoring and surveillance of risk factors at a population level e.g., Body Mass Index have provided the evidence to support a focus on obesity prevention strategies. Calls for a nuanced and de-stigmatising definition of obesity was based on many factors, particularly to ensure the right people have access to treatment, primary care, prevention etc. Additional measures are required to define clinical obesity with the aim of facilitating treatment pathways.

The first step in policy cycle requires a clear definition of the problem and its determinants, understanding its extent and impact on health of the population (e.g., pandemic, epidemic, local issue). How an issue is framed determines the response. This information helps to decide what the public health response (with do nothing always an option based on the precautionary principle or when intervention is not warranted.) Taking action from a public health perspective must be evidence-informed, feasible, equitable, timely and requires political amenability. This presentation explores the perspectives of a career public servant turned academic, on the potential impact of refining the definition to distinguish between clinical and non-clinical obesity on public health interventions.

id #126844

Metabolic Syndrome Identifies a More Inflammatory Asthma Phenotype in Adults with Obesity

Tamara Blickisdorf[1], Lisa G Wood[1], Sarah R Valkenborghs[1], Anne E Dixon[2], Jay C Horvat[1], Natasha A Weaver[1], Serene Yoong[3], Bronwyn S Berthon[1], Evan J Williams[1], Alexandra C Brown[1], Christine R Jenkins[4], Meagan M Morissey[1], Peter A Wark[1], Katie Wynne[1], Christopher L Grainge[1], Emad M El-Omar[5], Lily Williams[1], John D Brannan[1], Hayley A Scott[1]

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Obesity-related asthma is a distinct and increasingly common clinical phenotype, characterised by poor symptom control, corticosteroid resistance, and systemic inflammation.[1] Metabolic Syndrome (MetS), prevalent in individuals with obesity, may amplify these features through metabolic and inflammatory pathways.[2] However, the impact of MetS in asthma is underexplored.[3] This cross-sectional study aimed to examine whether MetS is associated with poorer lung function and heightened inflammation in adults with obesity and asthma.

40 adults (56.75±11.71 years old, 57.5% female, BMI 34.82±5.71 kg/m^2) with physician-diagnosed asthma and obesity were stratified by MetS status according to the International Diabetes Federation criteria.[4] Assessment included lung function (FEV_1, FVC, FEV_1/FVC), asthma control, systemic and airway inflammation (CRP, blood and sputum neutrophils), and metabolic markers (fasting glucose, HOMA-IR). Between-group differences were assessed using appropriate parametric and non-parametric tests, and multivariable regression.

MetS was present in 65% of participants and was associated with significantly greater CRP (p=0.017), blood neutrophils (p=0.024), and inhaled corticosteroid use (p=0.036). Although lung function did not differ significantly by MetS, glucose was inversely correlated with FEV_1 (r_s=-0.359, p=0.038), FVC (r_s=-0.348, p=0.044), and blood neutrophils (r_s=-0.359, p=0.038), indicating that metabolic dysfunction may be associated with both pulmonary impairment and systemic inflammation. There was a correlation between higher fasting blood glucose and airway inflammation (sputum %neutrophils) in females (r_s=0.550, p=0.035) but not males (r_s=-0.035, p=0.913), suggesting sex-specific effects.

Metabolic Syndrome is associated with increased systemic and airway inflammation in adults with obesity and asthma, suggesting it may contribute to a more severe, metabolically influenced asthma phenotype. Effects appear to be sex-dependent, warranting further research exploring drivers. These findings highlight the clinical relevance of MetS as a treatable trait in obesity-related asthma and underscore the importance of integrated metabolic and respiratory care in this high-risk group.

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id #128124

Exploring intercellular communication in testicular cells with volumetric imaging

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Cell-cell interactions between germ cells and the essential somatic supporting cells, Sertoli cells, are essential for the maintenance of male fertility. Intracellular calcium (Ca2+) signaling controls many processes in mammalian physiology, including important aspects of fertility and reproduction. Importantly, disruption of Ca2+ channels in mice can result in infertility. Despite the clear importance of this pathway in male fertility, it remains unknown exactly which cells in the male gonads express the Ca2+ channels that are indispensable for normal gonadal function, how these channels are activated by components of the extracellular environment and whether Ca2+ signals are propagated between neighboring cells and cell communities. Therefore, this project has two aims: 1) to visualize intercellular Ca2+ signaling between both germ cells and Sertoli cells and, 2) to define the 3D architecture of testicular cells with a focus on cellular connections. To do this, we use genetically engineered mouse models that express fluorescent sensors in either germ cells or Sertoli cells and visualize stable and dynamic signals by confocal microscopy. Preliminary results show that upon agonist stimulation Sertoli cells exhibit robust intracellular Ca2+ signals, which can propagate across defined regions of the tissue through mechanisms yet to be elucidated. Through volumetric imaging we have also started to map cell-cell connectivity patterns at various regions of the seminiferous tubules. Overall, our study is working toward defining cellular connectivity in the testis, shedding important insights into mechanisms of cellular information flow. Ultimately, this work will provide critical new knowledge on normal mammalian reproductive development and cell synchronization and may provide new avenues for modulating male fertility.

id #130940

Long life and fertility: ovarian metabolism as a target for reproductive ageing

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The molecular biology of ageing has captured the public imagination, with the idea that within our lifetimes, new drugs could improve late-life health and even extend human lifespan. In reality, the clinical translation of basic discoveries in this field are hampered by the practical realities of clinical trial design, leading to trials for new geroprotective drug interventions in age-related indications such as cardiovascular disease, dementia and other common conditions of ageing. These ignore a much earlier event in the life history of mammals: female infertility, with declining oocyte quality occurring far earlier than declines in any other tissue due to the non-renewable nature of the ovarian reserve. Here, I will cover my lab's key findings in the biology of reproductive ageing, including our discovery of declining levels of the redox cofactor NAD+ in age-related female infertility, and its subsequent clinical translation, and applications in other aspects of reproductive health, including chemotherapy induced ovarian toxicity. I will also describe new mechanistic insights in NAD+ metabolism from stable isotope tracing, and its applications in clinical translation. Finally, I will present the age-mismatched re-aggregation of "heterochronic cumulus oocyte complexes" as a new, unbiased approach for discovering factors that could rejuvenate oocyte quality during ageing, and answer fundamental "chicken and egg" questions around the role of somatic versus germ cell ageing in reproductive decline.

id #131709

Everything Everywhere All at Once: Transition challenges in endocrinopathies

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The complexity of transition of paediatric patients to adult care is well recognised, with a multidisciplinary approach widely agreed to be essential. In practice, however, many obstacles still exist for patients, their families, and practitioners alike.

Many endocrine conditions have a genetic or epigenetic basis, but childhood-onset acquired conditions may also have highly specific and complex presentations that evolve over time. These may be less familiar to adult practitioners, particularly given the breadth and volume of adult endocrinology, and with dual expertise in paediatric and adult practice becoming increasingly rare. Barriers to effective communication between paediatric and adult practitioners need to be addressed, both at individual and systems level, in order to optimise continuity of care.

With a rapidly increasing number of childhood cancer survivors filtering into adult clinics, care and surveillance for late effects of cancer therapies represents a growing – and relatively recent - challenge for effective transition. The complexity, interaction, and ongoing evolution of endocrinopathies in these patients is compounded by neurocognitive, psychosocial, and physical comorbidities, which

impact their capacity to engage and follow through with care. In this session, clinical knowledge gaps, potential practical pitfalls, and management strategies for both paediatric and adult clinicians will be discussed, highlighting aspects that may be unfamiliar in adult practice.

id #128381

Does long-term calcium supplementation increase the risk of dementia? A post-hoc analysis from a 5-year randomised clinical trial of calcium supplements to prevent fractures in older women

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Abstract

Calcium supplementation is commonly adopted to prevent and treat osteoporosis. Previous concerns around calcium supplements exacerbating vascular calcification and cardiovascular disease (CVD) have led to speculation around the potential negative impacts for dementia; given the strong nexus between vascular and cognitive health. However, data supporting such concerns are limited to observational studies (1, 2). This post-hoc analysis of a 5-year randomised controlled trial of calcium supplements evaluated its effect on the long-term risk for dementia in older women.

1460 dementia-free community-dwelling Australian women aged ≥70 years took part in the Calcium Intake Fracture Outcome Study (CAIFOS) in 1998. Women received either 1200 mg of calcium carbonate per day (n=730) or an identical placebo (n=730) for 5 years. The effects of calcium supplementation on dementia outcomes were examined using unadjusted and multivariable-adjusted Cox regression analysis under both intention-to-treat (ITT) and per-protocol criteria (PP, ≥80% annual tablet compliance, n=830). Dementia outcomes were obtained from linked hospital and mortality records from baseline over the next 14.5 years.

Mean age of women at baseline was 75.2 ± 2.7 years. Over 14.5 years, 269 women (18.4%) suffered a dementia event, comprising of dementia-related hospitalisations (n=243, 16.6%) and dementia-related deaths (n=114, 7.8%). Compared to placebo, calcium supplements were not associated with increased hazards for any of the dementia outcomes in unadjusted and multivariable-adjusted ITT and PP analysis (**Fig 1**). No significant differences in the cumulative dementia-free survival rates were observed between women randomised to calcium supplements or placebo for any dementia outcome (log-rank test, all $p>0.05$).

Five-years of calcium supplements did not increase the long-term risk for dementia in older women. Our findings support the safety of calcium monotherapy in relation to cognitive health in a population most likely to use and benefit from it due to their high risk for osteoporosis.

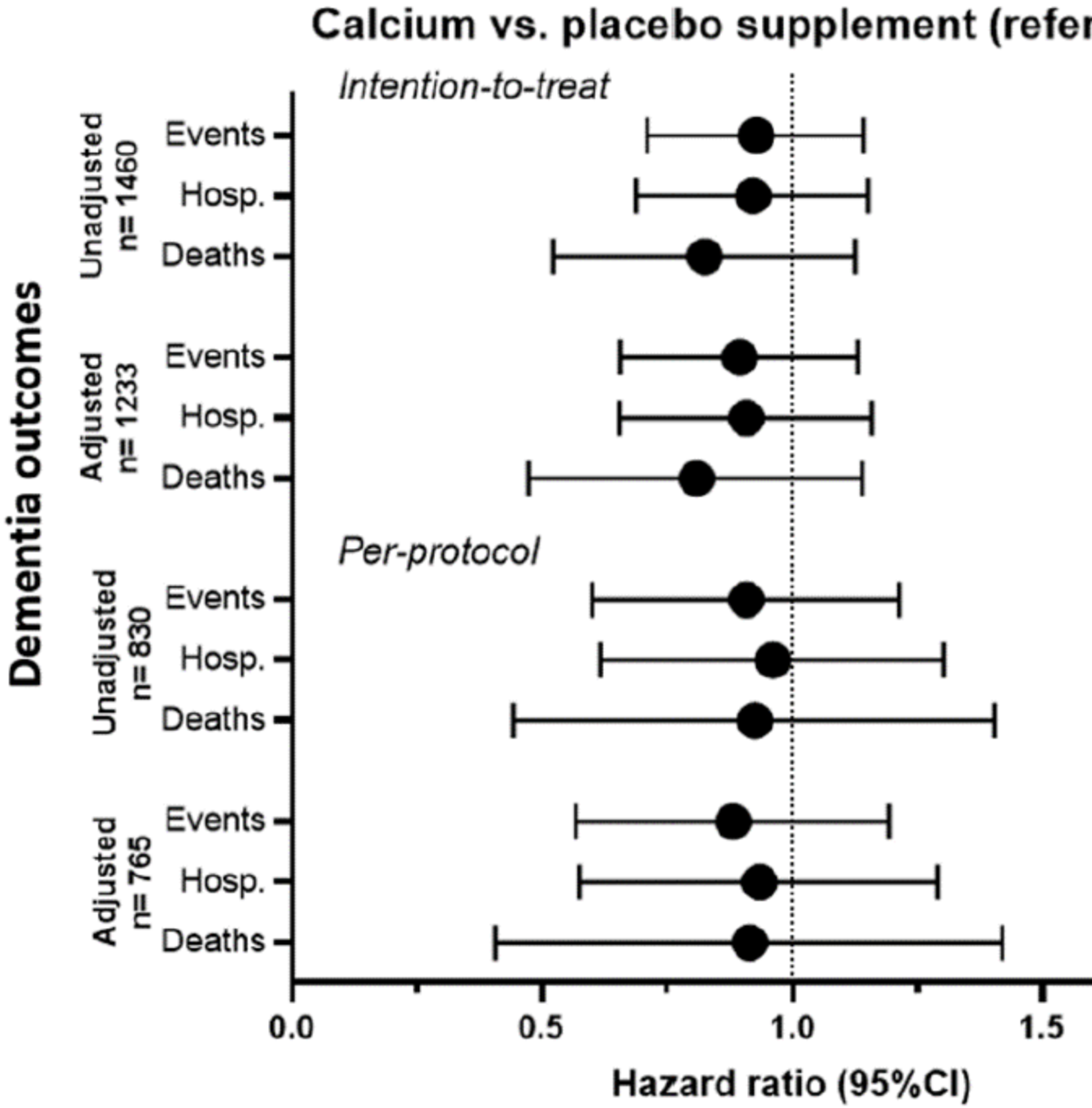

Fig 1. Hazard ratios (95%CI) for dementia events, hospitalisations and
provided with calcium supplements (●) compared to placebo. Adjusted m
BMI, apolipoprotein E, systolic blood pressure, prevalent diabetes, stati
prevalent ASVD, dietary calcium, smoking status, physical activity, a
socioeconomic status. Only women with complete data for all covariates
adjusted analysis.

id #131710

A public health perspective on childhood food insecurity in Australian communities

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In 2023-4 the Australian Bureau of Statistics reported that 34% of lone parent households and 16% of family households with dependent children in Australia experienced food insecurity. Childhood experiences of food insecurity can impact growth and development and have lifelong consequences for health. Improving the food security of people living in rural and remote communities is both a public health priority and a poisoned chalice for Australian Governments. Many of the actions that are needed to address the determinants lay outside of the health sector. Food security in remote Indigenous communities is particularly challenging resulting in a disproportionate burden from preventable diet-related diseases in these communities. Improved food security will result in health gains. Interventions aim to achieve a secure, sustainable, safe, nutritious and culturally appropriate food supply in these communities and changes to dietary patterns a major outcome. Public health action must address supply and demand, and infrastructure to create environments to support change. Public health needs to advocate for suitable and effective interventions. Gleaning insights from the last three decades, this presentation explores a range of actions that are the most effective in the real world – from cross sector regulatory instruments to health 'education' in a clinical setting. Sustained action across all sectors and governments are required to address the structural and systemic problems that have resulted in poor food security for many communities.

id #128638

Mediating immune tolerance of sperm in sheep: Identifying factors in ram seminal plasma responsible for facilitating sperm neutrophil evasion

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Seminal plasma (SP) is a complex immune modulator within the female reproductive tract of several species [1]. In sheep, it can restore the fertility of cryopreserved sperm [2] and is necessary for the fertility of epididymal sperm [3] following cervical artificial insemination. We have also shown it capable of protecting cryopreserved sperm from polymorphonuclear leukocyte (PMN) binding *in vitro* [4]. Thus, we hypothesise SP, and its components confer immune protection to sperm following deposition in the ovine cervix and that sperm cryopreservation disrupts this delicate sperm-female interaction.

To delineate the influence of soluble or extracellular vesicle (EV) derived SP components on sperm-PMN binding, a series of PMN binding assays were conducted using frozen-thawed ram spermatozoa (FT; n=3 rams). Firstly, blood-derived PMNs from Merino ewes (n=2) were incubated (120min;37ºC) with FT supplemented with either whole SP, EV-depleted SP, isolated EVs or PBS (n=3 replicates). EVs were separated from a pool of SP (n=24 rams x 3 ejaculates) via ultracentrifugation [5]. While SP treatments (24.17±0.29%, 23.91±0.21%, 20.15±0.23%) reduced PMN-binding compared to the control (38.22±0.47%; $p<0.01$), there was no significant difference between SP treatments, suggesting the protective effect is both soluble and of EV origin.

To further elucidate the role of soluble SP components, FT was incubated (120min;37ºC) with SP fractionated into 5 molecular weight treatments (<10, 10–30, 30–50, 50–100, >100 kDa), whole SP and PBS (n=3 replicates). Binding was significantly reduced in 30–50 (22.44±0.65%), and >100 (21.67±0.55%) kDa fractions, compared to PBS (58.83±1.36%), but was similar to whole SP (20.67±0.49%), suggesting these fractions may harbour key immunoregulatory factors.

Mass spectrometry will now identify quantitative differences between treatments, linking protein and/or vesicle cargo expression with protective effect. These results enhance our understanding of SP-mediated immune modulation in sheep and may identify candidates to restore immunotolerance and fertility of cryopreserved ram sperm.

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id #128383

Are we still ignoring the male? Reframing male fertility in research, clinical care, and conservation

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Despite rising concern around reproductive decline in both humans and wildlife, male fertility remains critically underrepresented in research, diagnostics, and public discourse. In human reproductive medicine, female factors are rightly prioritised due to the biological constraints of ovarian ageing — yet male fertility is often assumed to be stable, secondary, or easily bypassed with assisted reproduction technologies. Similarly, in wildlife conservation and animal breeding programs, male reproductive assessments are frequently cursory, despite their importance to population viability and genetic management.

This presentation explores the shared cultural and scientific blind spots that contribute to the persistent marginalisation of the male factor across species. Drawing on clinical and laboratory experience in human and animal andrology, I reflect on how sperm deemed "normal" by conventional parameters — particularly motility — may carry significant functional impairments, including oxidative damage, DNA fragmentation, or poor fertilising capacity. Emerging insights from both clinical data and wildlife reproductive programs suggest that these overlooked factors can undermine reproductive success, even in cases where sperm appear morphologically or kinetically normal.

By challenging our reliance on reductionist semen analysis criteria and drawing attention to underutilised functional diagnostics, this talk advocates for a broader, more nuanced understanding of male fertility. Whether in the fertility clinic or the conservation lab, improving how we evaluate male gametes is essential to achieving successful, sustainable reproductive outcomes.

id #123265

Diet quality and physical activity trajectories in pregnancy and associations with maternal characteristics

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Background/Aims: Maternal changes in diet quality and physical activity (PA) throughout pregnancy are unclear. This study described the changes in diet quality and PA (i.e., trajectories) during pregnancy and examined their associations with maternal characteristics and gestational weight gain (GWG).

Method: Dietary intake and PA were collected through surveys at 18-, 28-, and 36-week gestation among pregnant women (n=688) recruited from three health sectors in New South Wales. Diet quality was assessed by Dietary Guideline Index (DGI) with higher score representing greater adherence. Multi-trajectory modelling identified joint trajectories of DGI and PA. Multivariable logistic regression assessed maternal determinants of DGI and PA trajectories and their association with GWG.

Results: Most women (58.0%) exhibited a "high-stable DGI low-stable PA" trajectory, 34.5% followed the "low-increasing DGI low-stable PA" trajectory, and 7.5% of the women had a "mid-stable DGI high-decreasing PA" trajectory. Higher maternal age (OR 1.07, 95%CI 1.04, 1.11), being married (OR 3.26, 95%CI 1.66, 6.42) and the diagnosis of gestational diabetes (OR 2.79, 95%CI 1.55,5.03) were associated with higher odds of being in the "high-stable DGI low-stable PA" than the "low-increasing DGI low-stable PA" trajectory. Women who were not working (OR 0.56, 95%CI 0.36, 0.86), identified as Aboriginal or Torres Strait Islander (OR 0.48, 95%CI 0.25, 0.94) and with high school (OR 0.27, 95%CI 0.18, 0.43) or certificate/diploma education (OR 0.50, 95% 0.34, 0.74) showed a lower likelihood of following the "high-stable DGI low-stable PA" trajectory. Maternal age, working status, education and gestational diabetes were also associated with the "mid-stable DGI high-decreasing PA" trajectory. No evidence of an association was found between DGI and PA trajectories and GWG.

Conclusions: Three heterogeneous joint-trajectories of DGI and PA were identified during pregnancy. Maternal age, marital status, gestational diabetes, education level and working status were identified as significant determinants of DGI and PA trajectories.

id #128642

Role of maternal NAD+ reserve in determining embryo development

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Nicotinamide adenine dinucleotide (NAD+) is an essential metabolic co-factor regulating energy synthesis and developmental processes in oocytes and early embryos. Oocyte NAD+ levels decline during reproductive ageing, which is linked to suboptimal embryo development. We showed previously that oral supplementation with the NAD+ precursor, nicotinamide mononucleotide (NMN) in aged mice restores reproductive function. Here, we hypothesized that NAD+ synthesis and accumulation in oocytes is important for embryo development. Firstly, we inhibited NAD+ synthesis with 30 μM FK866 in mouse GV oocytes either during in-vitro maturation (IVM) and/or in mature oocytes during IVF. Depletion of NAD+ in oocytes during IVM significantly reduced day 5 blastocyst rates by 30%, whereas depletion during IVF had no effect. This suggests sufficient oocyte NAD+ reserves are required for healthy embryo development. We investigated this further by supplementing oocytes from aged mice with NMN during IVM, which improved blastocyst development by 10% compared to untreated aged oocytes. To explore the underlying mechanisms, we investigated NAD+ turnover in oocytes and embryos by conducting a pulse-chase experiment using liquid chromatography-mass spectrometry (LC-MS).

Deuterium-4 labelled nicotinamide was supplemented to either GV oocytes, 2-cell embryos or compacted embryos for 16 hours. Our data revealed that oocytes accumulate excess NAD+ and its precursors during meiotic maturation, with ~30% of total NAD+ in blastocysts derived from maternal stores. Previous studies have shown that NAD+ is rapidly consumed in the first 24 hours of embryo development. Our LC-MS data show that embryos can replenish NAD+ levels but only after reaching the two-cell stage. Together, our findings demonstrate that maternally stored NAD+ and its precursors are critical for supporting embryo development. This work also further highlights the potential NAD+ supplementation strategies for women of advanced maternal age undergoing IVF.

id #130946

Targeting energy expenditure with the mitochondrial uncoupler BAM15: effects on exercise performance and metabolic function in mice

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Losing 5-25% body weight can decrease onset and mortality from diseases including type-2-diabetes. Current obesity treatments focus on reducing calorie-intake through diet, surgery or drugs; however, these approaches are often ineffective long-term or have significant side effects. More than 65% of Australian adults remain overweight or obese, underscoring the need for new approaches. Exercise is a cornerstone weight loss strategy; however, few patients can achieve long-lasting weight loss with exercise alone. Mitochondrial uncoupling is an alternative mechanism to increase energy expenditure through decreasing caloric efficiency at the inner mitochondrial membrane. In this talk I will discuss efforts to target energy expenditure with uncouplers, and our studies investigating if the metabolic and weight loss benefits of exercise can be enhanced by combination treatment with BAM15, a mitochondria-selective mitochondrial uncoupler.

id #127875

Genome-wide CRISPR screen identifies C1orf35 as a novel regulator of hepatic lipid metabolism

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Metabolic dysfunction-associated steatotic liver disease (MASLD) has served as a major driver of Hepatocellular carcinoma (HCC) due to its great potential for increasing cirrhosis. MASLD is characterised by defective lipid metabolism, which causes hepatic steatosis and inflammation, key events that precede and contribute to fibrosis and are essential for disease progression. Hence, tackling early metabolic defects (i.e., inhibiting hepatic steatosis) is likely to prevent the development of MASH and metabolic co-morbidities.

To systematically uncover novel genes required for hepatic lipid accumulation, we performed five independent, pooled genome-wide screens in HepG2 cells using the human GeCKO CRISPR library. Cells were treated with or without excess fatty acid (FA) to mimic chronic lipid overload, followed by Bodipy lipid staining and fluorescence-activated cell sorting. In Control cells, we selected the highest 10% of cells to identify mutants that retained high levels of lipid due to defects in lipid processing. In contrast, for the FA-treated cells, we selected the lowest 10% of cells, thereby screening for cells bearing mutations in genes necessary for FA-induced lipid accumulation.

Using single gRNA knockout combined with functional assessment of lipid accumulation, we identified C1orf35 (Chromosome 1 open reading frame 35) as a novel regulator of hepatic lipid metabolism.

Deletion of C1orf35 in HepG2 cells reduces lipid accumulation by >80% by suppressing lipogenesis and fatty acid uptake and enhancing triglyceride secretion. The restoration of C1orf35 expression in C1orf35$^{-/-}$ cells brings the triglyceride content back to baseline, indicating a dynamic response to changes in C1orf35 expression. Mechanistically, C1orf35 acts as a master transcriptional regulator of key lipid metabolism enzymes, including SREBP1, FASN and CD36. The role of C1orf35 in metabolic reprogramming was further validated in 3D liver organoids derived from patients. Future studies aim to investigate whether the deletion of C1orf35 in the liver may confer protective benefits in MASLD.

id #131716

Hypertension management in 2025 – what's new?

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<Working title>

Abstract content coming soon

id #128132

Progressing cross-sector collaboration for people with eating disorders and higher weight: Priority actions from an expert roundtable

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7. Centre for Eating, Weight and Body Image, Melbourne, VIC, Australia

8. National Eating Disorder Collaboration, Melbourne, VIC, Australia

We aimed to establish collaborations and relationships across the fields of obesity and eating disorders and develop shared understandings, goals and priority actions. Multidisciplinary researchers and clinicians working in the fields of obesity, eating disorders or both, and people with lived experience of higher weight and eating disorders (n=28) held a round table in November 2024. The National Eating Disorder Collaboration Stepped System of Care Framework guided identification of key challenges for people experiencing eating disorders with higher weight. For each challenge, participants identified existing initiatives (services, programs, resources, research) and opportunities for the future. Participants then identified five priority areas of action arising from the roundtable. Cross-cutting themes across the System of Care included creating a professionally safe environment for this work to occur, addressing weight stigma, cultural safety and intersectionality. The five priority areas are: Health Campaigns (building awareness of the occurrence of binge-type and restrictive eating disorders in people with high weight, use of appropriate language, health literacy); Screening and Assessment (developing standardised eating disorder assessment protocols embedded across healthcare settings); Primary Healthcare (supporting the use of MBS items for extended eating disorder consults and access to allied health services); Tailored Treatment Pathways (growing the evidence base for eating disorder treatment programs and models of care and identification of eating disorder treatment pathways for people with higher weight); and Workforce Capacity (upskilling of broad workforces to prevent, identify, respond and treat people with eating disorders and higher weight). To drive progress in the five priority areas and cross-cutting themes, working groups have been established. These groups will champion key initiatives, share information, and promote Australian efforts aimed at enhancing prevention and care for individuals experiencing eating disorders and higher weight.

id #128900

Lipidomics of mouse uterine fluid reveals vast fluctuations in several lipid classes across gestation

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Uterine fluid (UF) consists of lipids, metabolites, proteins and hormones, and is secreted by the endometrial glands. While UF is essential for early embryo development and blastocyst implantation, its importance post-implantation, i.e. after placenta formation, is not well understood. Hence, it is routine to grow mouse zygotes up to the blastocyst stage in culture, but the factors required for achieving development beyond this stage remain unknown.

Lipids are essential for embryo development through their involvement in maintaining cell structure, cell signalling, neuronal development, steroid biosynthesis and are an energy source. We have characterised the lipidome of mouse UF across gestation (6 timepoints) using mass spectrometry, which identified 971 lipid species. Principal component analysis demonstrates that early stages cluster together, while mid- and late-stages cluster individually, indicating a shift in the lipidome post-implantation. Significant changes were detected in total levels of sphingolipids, glycerophospholipids, glycerolipids, and sterols in mid- and late-stages of gestation, indicating the need for different lipids at specific timepoints.

For example, glycosphingolipids such as hexosylceramides (HexCer) and dihexosylceramides (Hex2Cer) are involved in cellular processes such as cell proliferation, differentiation, migration and angiogenesis and are required for embryo survival post implantation. Accordingly, our data demonstrate that total levels as well as specific species of hexosylceramides and dihexosylceramides progressively increase in UF post-implantation with up to 23-fold higher levels in late- compared to early-gestation. Glycosphingolipids are synthesised by the glucosyltransferase enzyme (UGCG) and its expression in the uterus across gestation will determine if the endometrial glands are the source of the increased glycosphingolipids.

In summary, our data provide insight into the role of each lipid class and how lipids in the UF impact embryo development. This will allow for the identification of components that can be supplemented into *ex utero* culture media to prolong culture of early-, mid- and late-stage embryos.

id #130436

The paternal RNA contribution to the embryo and offspring

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Sperm RNAs delivered to the zygote during fertilization have emerged as important non-genetic contributors to embryo development and offspring health. Interestingly, small RNAs are delivered to sperm during post-testicular maturation in the epididymis. Moreover, this developmental window is vulnerable to environmental stressors, leading to a reprogramming of the sperm RNA code, with significant post fertilisation consequences. Despite this knowledge, there remains limited understanding of the specific RNAs delivered to sperm during epididymal transit or how paternal exposures influence the remodelling of the sperm RNA landscape.

Focusing on a subclass of small RNAs, microRNAs (miRNAs), we utilised *Cre:lox* conditional genetics to selectively ablate *Dgcr8*, a key protein involved in miRNA biogenesis, in the epididymal epithelium to investigate the function of sperm miRNAs in the embryo. Small RNA sequencing of populations of sperm revealed reduced abundance (~5-fold decrease) of 27 miRNAs. Moreover, embryos fertilized by sperm from these mice displayed significantly increased expression of 184 genes ($P < 0.01$). Remarkably, however 65% of these gene changes were rescued when embryos were supplemented with purified epididymal miRNAs, linking reduced sperm miRNA levels with transcriptomic dysregulation in the early embryo. Further, we have established that the epididymis mounts a response to multiple different paternal environmental exposures, leading to an altered sperm RNA profile. Indeed, exposure to increased ambient temperature led to the accumulation of RNA changes in sperm from exposed mice that are causally linked to accelerated embryo development, changes in embryonic gene expression and increased fetal:placental weight ratio. Ultimately, this work aims to deepen our understanding of the establishment and modulation of the sperm RNA profile and its subsequent post fertilisation consequences.

id #131717

The Healthy Lifestyle Program: Lessons learned

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The Healthy Lifestyle Program is a family-based pilot program hosted by Child and Adolescent Community Health, in Western Australia. It supports children and young people aged 4–16 years and their families to make sustainable, healthy lifestyle changes. The multidisciplinary team includes Healthy Lifestyle Coordinators, Dietitians, an Exercise Physiologist, Psychologist, and Paediatricians, who provide comprehensive, evidence-based care that integrates physical, nutritional, and psychosocial wellbeing.

The program was co-designed with Aboriginal community members, Elders, and consumers with lived experience, ensuring cultural safety, accessibility, and continuous evolution through family and community feedback.

There are two key features embedded in the program. The first is the Healthy Lifestyle Check, a community/home-based screen that assesses growth, nutrition, physical activity, and related health indicators at baseline, six months, and twelve months. These checks guide tailored support and provide valuable outcome data.

Families then participate in weekly community-based group sessions (currently in Midvale and Armadale) over six months, focusing on fun, practical, and interactive learning for both children and caregivers. The sessions promote achievable, family-wide behaviour change through hands-on nutrition education, physical activity, and wellbeing strategies.

Since its launch, the program has welcomed over 110 families, with strong participation from Aboriginal and Torres Strait Islander families and those experiencing significant socioeconomic disadvantage.

Supported by research, the Healthy Lifestyle Program contributes to a growing evidence base for equitable, community-based approaches to paediatric weight management and prevention. Its collaborative design and holistic family-focused approach positions it as a feasible and equitable model for multidisciplinary, culturally responsive child health care in Western Australia.

id #123269

Efficacy of Gonadotrophin Treatment to Induce Spermatogenesis and Fertility in Men With Congenital or Acquired Gonadotrophin Deficiency

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Gonadotrophin treatment to induce spermatogenesis for gonadotrophin-deficient men is the only medically treatable cause of male infertility. However, time-dependent analyses of fertility outcomes in large cohorts are lacking. We aimed to evaluate the time to, and determinants of, fertility outcomes in men with pathologic gonadotrophin-deficiency undergoing gonadotrophin treatment.

Consecutive infertile men (n=99) with congenital or acquired pathologic gonadotrophin deficiency were treated according to a standardised protocol between 1983 and 2024, including 161 cycles of treatment with urinary or recombinant hCG and FSH. Kaplan-Meier and multivariate Cox regression analyses examined time to pre-specified sperm density thresholds, pregnancy, and impact of urinary vs recombinant gonadotrophin.

Men aged 35±1 years with female partners 30±1 years had mostly prepubertal onset (73%) of gonadotrophin deficiency. The proportion (%) and median time (months) to achieve sperm thresholds of >0, >2, >5, >10, and >20 million sperm/mL was 82% (4

months), 59% (10 months), 51% (12 months), 39% (22 months), and 27% (37 months) respectively. Higher baseline testes volume was independently associated with earlier appearance of sperm (HR 1.04, 95% CI 1.01-1.07; p=0.01). The major determinant of successful pregnancy was the presence of adverse fertility factors in the female partner (HR 0.24, 95% CI 0.12-0.49; p<0.001), with time to pregnancy also significantly increased by the presence of adverse female fertility factors (15 vs 43 months; p<0.0001). Median sperm concentration and sperm output associated with partner pregnancy was 4.0 (0.4, 16.9) M/mL and 12.8 (0.7, 50.4) M/ejaculate, respectively, with and without adverse female factors. Time to >0 and >2 M/mL sperm thresholds was significantly faster for recombinant vs urinary hCG, with no difference in time to higher sperm concentrations.

Most men with pathological gonadotrophin deficiency treated with hCG/FSH will achieve sperm output and fertility within a year, with greatest impact on fertility outcomes being detrimental female fertility factors.

id #126597

ANZ Joint Society Consensus on Genetic Testing for Monogenic Diabetes in Adults

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Monogenic diabetes accounts for 2-5% of all diabetes and has clear treatment implications. For example, GCK-hyperglycaemia typically allows cessation of all treatment/monitoring, and HNF1A/HNF4A-diabetes is exquisitely sensitive to sulfonylureas which often obviate the need for insulin. A molecular diagnosis can also guide family planning, cascade testing and surveillance for other manifestations. Despite the frequency and significance of monogenic diabetes, >80% of cases are missed. This relates to the complexity of genetic testing in monogenic diabetes, the varied and overlapping phenotypes between monogenic diabetes subtypes and with other forms of diabetes, and access to testing, although the latter is rapidly improving.

Noting these missed opportunities in diabetes care in Australasia, a collaboration was formed in 2023 between the Australian Diabetes Society (ADS), Endocrine Society of Australia (ESA), Human Genetics Society of Australasia (HGSA), New Zealand Society for the Study of Diabetes (NZSSD) and Royal College of Pathologists of Australasia (RCPA) to generate world-first guidelines on genetic testing for monogenic diabetes in adults. Coinciding with publication of this joint society consensus statement in the Medical Journal of Australia, this talk will outline testing recommendations along with their evidence base and implications for day-to-day practice.

id #130437

Bright Bodies: A Family-Based, Intensive Lifestyle Intervention for Childhood Obesity

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With one in three U.S. children affected by overweight or obesity, there is an urgent need for accessible, evidence-based interventions. Bright Bodies (BB) is a structured, multicomponent intensive health behavior and lifestyle treatment (IHBLT) for children and adolescents aged 7–16 years and their parents or caregivers. The program typically includes twice-weekly group classes delivered in successive 12-week sessions, combining supervised physical activity, nutrition education, and behavioral strategies to promote healthy lifestyle changes. Parents or caregivers participate in parallel or joint sessions to reinforce these behaviors at home.

Developed at Yale, BB demonstrated efficacy in a diverse urban population in a randomized trial two decades ago. Participants achieved reductions in %BMIp95 of −10.7% at 6 months and −11.9% at 12 months compared with standard clinical care, with improvements maintained up to two years post-intervention. Additional benefits included improved body composition, insulin resistance, and self-concept scores, particularly among children with low baseline self-concept.

Recent studies demonstrate cost savings compared with usual clinical care and confirm real-world effectiveness beyond the original trial, despite adaptations due to funding and staffing constraints. The curriculum, SmartMoves™, has been disseminated to over 40 heterogenous sites in the U.S. and globally, though barriers to broad implementation and sustainment persist and limit access. To address these barriers, we recently conducted a mixed-methods formative evaluation and user-centered design process to optimize both the intervention and its implementation package. Concurrently, recent investments by the U.S. Centers for Disease Control and Prevention (CDC) have supported implementation of six CDC-endorsed, proven-effective Family Healthy Weight Programs, including BB, to further expand access to effective IHBLT.

Bright Bodies illustrates a feasible, family-centered, and evidence-based approach to pediatric obesity care that is adaptable to diverse populations and settings.

id #131718

Insights from the TOBOGM Randomised Controlled Trial: Time for a Lifecourse Approach to Gestational Diabetes Mellitus

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Over the last 30 years, the management of gestational diabetes mellitus (GDM) has evolved from an almost randomised controlled trial (RCT) “evidence-free” condition, to a much studied, and discussed, clinical entity with varied guidelines around the world, focusing on GDM at 24-28 weeks gestation. However, GDM diagnosed early in pregnancy (30-70% of all GDM) is associated with worse outcomes than pregnancies with GDM developing later in pregnancy. The Treatment Of BOoking Gestational diabetes Mellitus

(TOBOGM) study is the only international RCT of treatment of GDM in early pregnancy that involving masked controls. Participating women had diabetes risk factors and an oral glucose tolerance test (OGTT) before 20 weeks' gestation. Those with GDM by WHO-2013 criteria (n=802) were randomised to either treatment or a repeat OGTT at 24-28 weeks gestation. Nested studies allowed comparison of pregnancy outcomes among women with GDM with higher and lower glucose values, and before and after 14 weeks gestation. Women without early GDM form an epidemiological cohort. The TOBOGM results clearly showed that early treatment reduced a primary outcome composite of important neonatal complications; babies had less fat and days in the special care unit were down 0.8 days. Quality of life and breastfeeding were significantly improved. Early testing and treatment of those with early GDM was A$5500 cost saving if before 14 weeks' gestation. However, TOBOGM also showed that caution is needed in selecting thresholds for early treatment, with a 75% increased risk of small for gestational age babies, with the potential for long term consequences. This evidence has been used in the latest ADIPS-25 recommendations to raise the threshold for diagnosing GDM and promote more early pregnancy testing. It is now clear that GDM represents pre-existing metabolic abnormalities with implications that GDM should now be seen as a lifecourse, not solely a pregnancy-related condition.

id #130438

Incretin therapy and eating disorders: Friend or Foe?

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Incretin therapy in the form of GLP1 receptor agonists or GLP1/GIP dual agonists (GLP1-RA) are established in the management of Type 2 diabetes (T2D) as well as the management of overweight/obesity. There is also increasing evidence that people with overweight/obesity and T2D are at a higher risk of eating disorders. However, screening for eating disorders is not usual practice for health care professionals prescribing these medications. This means that there are potentially a large number of people with eating disorders or at high risk of eating disorders that are taking these medications. There are a lot of opinions (some very strong), on whether or not people with eating disorders (or at risk of eating disorders) should be offered these medications that have been demonstrated to greatly benefit glycaemia and assist in weight loss. While there are a lot of posts on social media and many podcasts for either side of the argument, there is limited scientific evidence to support either the use or avoidance of these medications. The evidence around the possible use or danger of using GLP1-RA for binge eating disorders will also be discussed. Given the emerging pipeline of medications that are likely to result in even greater weight loss, and the wider use of incretin therapy, this talk will discuss the evidence around the safety as well as the pros and cons of using GLP1-RA in people with or at risk of an eating disorder.

id #130694

300 Adrenal Vein Samplings and counting- observations, tips and tricks after all these years

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The adrenal vein sampling (AVS) service at Royal Prince Alfred hospital (RPAH) has developed over the past 19 years from a handful of tests yearly to a comprehensive service that continues to grow exponentially. From a few blood samples sent to the lab, it has developed into an experienced multidisciplinary team dedicated to providing excellence and more importantly successful cannulation and diagnosis.

Over three hundred and twenty AVS have been performed with an explosion in the past 5 years (even through the Covid-19 pandemic). The same nurse has been present for 98% of these and the experience gained has allowed others to also develop the skills required to perform successfully within the team and at other centres.

The need for the test is forever increasing with recent diagnostic guidelines for primary aldosteronism1 continuing to require the AVS as a part of best practice for the diagnosis pathways. Major AVS centres throughout Australia and New Zealand provide the majority of AVS services to the referring clinicians. A successful AVS not only requires correct cannulation but also best patient preparation, skilled AVS interventional radiology team, efficient and knowledgeable laboratory staff and experienced clinicians to manage the medical care and interpret results.

Coordinating from start to end the endocrine nurse at RPAH has supported patients to navigate through the workup, assisted interventionalist to correctly identify adrenal veins, has helped develop a dynamic testing protocol that minimizes risk of error and has created a unique reporting program that makes understanding the results clearer for clinicians and patients alike.

This presentation will describe the RPAH AVS service, its key achievements, identify problems faced and suggestions that may make the difference.

1. Gail K Adler, Michael Stowasser, Ricardo R Correa, Nadia Khan, Gregory Kline, Michael J McGowan, Paolo Mulatero, M Hassan Murad, Rhian M Touyz, Anand Vaidya, Tracy A Williams, Jun Yang, William F Young,
2. Maria-Christina Zennaro, Juan P Brito, Primary Aldosteronism: An Endocrine Society Clinical Practice Guideline, The Journal of Clinical Endocrinology & Metabolism, Volume 110, Issue 9, September 2025, Pages 2453–2495, https://doi.org/10.1210/clinem/dgaf284

id #131719

AI for Everyday Research: Workflows That Save Time, Avoid Burnout, and Get Results

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1. Andy Stapleton YouTube Channel, PLYMPTON, SA, Australia

1. Why This Isn't Just About ChatGPT
2. Build Your AI Workflow Stack

- Literature Review & Idea Generation
- Reading & Multi-document Understanding
- Writing, Editing & Grant Crafting
- Light-touch Data Curation & Automation

3. Using AI Safely and Responsibly
4. Action Plan: Start Simple
5. Q&A; and Live Prompt Challenge

id #128135

Association of Health-Related Quality of Life and Weight Status throughout Childhood and Adolescence

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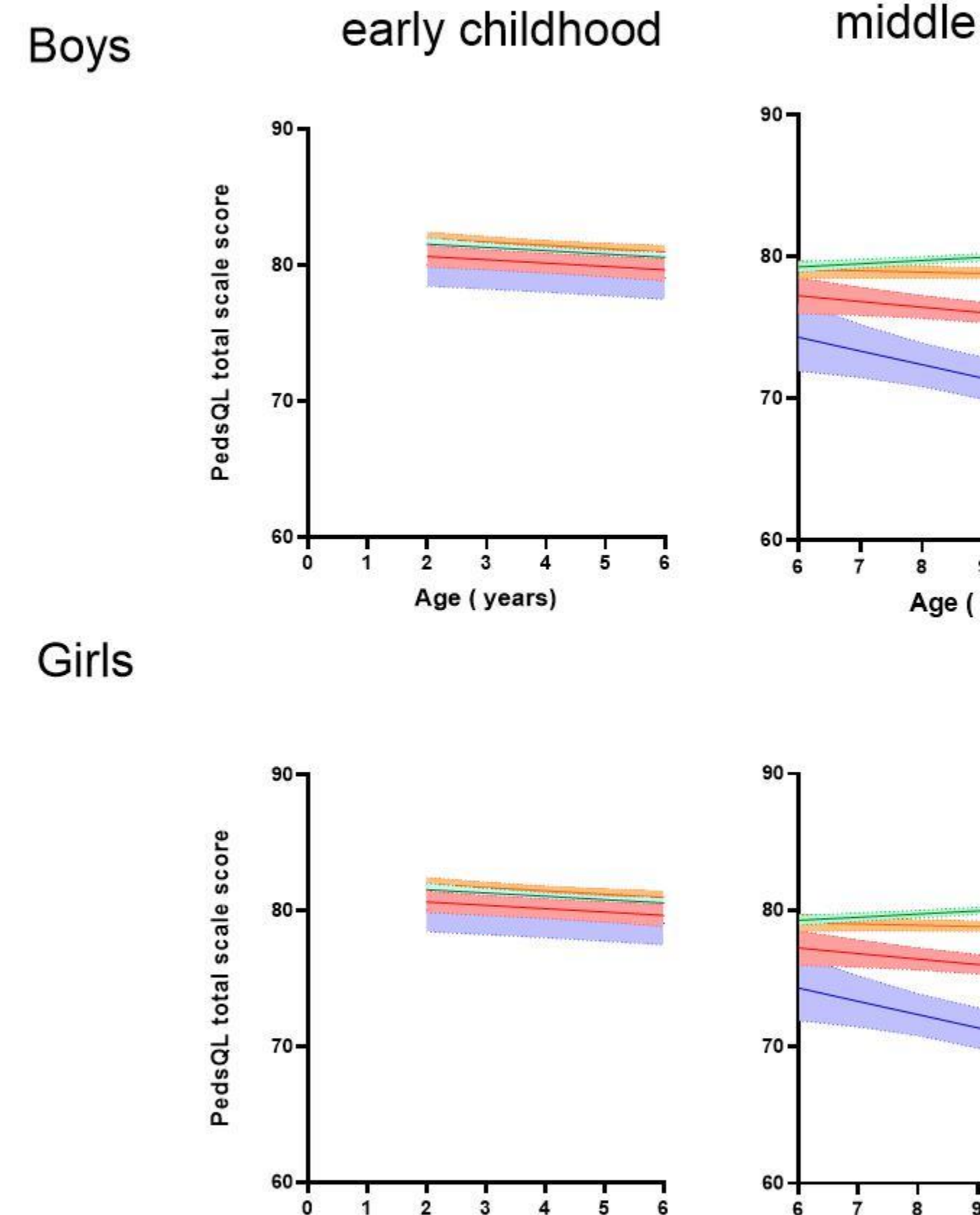
The aim of this study was to examine health-related quality of life (HRQoL) during the child and adolescent life-course and how it is impacted by weight status and sex. We used data on 9745 children from the Longitudinal Study of Australian Children aged between 2 and 17, that included quality of life and weight status collected biennially. HRQoL was measured with the parent-reported Pediatric quality of life inventory (PedsQL), on a 0-100 scale. Height and weight were objectively measured and BMI-z was categorized into healthy, overweight, obesity or severe obesity, using WHO cut-points. We investigated the association of child HRQoL with weight status and sex, during 3 periods of childhood corresponding to age: 2-5 years (early childhood), 6-11 years (middle childhood) and 12 -17 years (adolescence). Analyses controlled for socioeconomic position and for continuous age to account for age effects within the groups.

The negative association of HRQoL and weight status strengthened with increasing age and higher weight status. For example, the mean (95%CI) differences in PedsQL total score between healthy weight and obesity in early childhood, middle childhood and adolescence were respectively: -0.9(−1.7 to −0.2) p= 0.028, -3.6 (-4.4, to -2.9) p<0.001 and -5.5 (-6.4 to -4.6) points (p<0.001). Middle childhood was a critical time for development of weight-related inequalities in HRQoL. Weight-associated loss of HRQoL was greatest for adolescents with severe obesity at −10.5 points. There were no significant differences between girls' and boys' HRQoL in early or middle childhood (p>0.05). Weight-related loss of HRQoL in adolescence was similar for girls and boys, but independent of weight, girls' HRQoL declined with age whilst boys' HRQoL did not, resulting in a 5-point difference in PedsQL score at 17 years. This study highlights the important contribution of weight status and sex to declining HRQoL in childhood and

adolescence.

Figure 1. PedsQL quality of life by weight st



id #130440

Maternal immune–vascular interactions shaping pregnancy outcomes

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Vascular remodelling of the uteroplacental circulation is critical for placental perfusion, fetal growth, and maternal cardiovascular adaptation. Using experimental models of immune dysregulation, including maternal C1q deficiency and regulatory T cell depletion, we demonstrate that impaired immune regulation disrupts spiral artery remodelling, uterine artery blood flow, and placental development, leading to fetal growth restriction, pregnancy loss, and—in the case of Treg deficiency—long-term cardiometabolic risk in offspring. Complementary human studies integrate advanced vascular imaging and immunophenotyping to define immune–vascular interactions in high-risk pregnancies. Ongoing preclinical therapeutic investigations aim to restore immune and/or vascular function in complicated pregnancies, including evaluation of biological therapies, vascular-targeting agents, and lifestyle-based interventions such as exercise. These findings underscore the immune–vascular interplay in pregnancy and its relevance to improving maternal and fetal outcomes.

id #131721

New mechanisms of mineralocorticoid signalling in non-epithelial tissue - a role for the circadian clock

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The mineralocorticoid receptor (MR) is a high-affinity corticosteroid receptor that is central to electrolyte and fluid homeostasis via actions in epithelial tissues (kidney and colon). The MR is a known regulator of cardiac and renal tissue remodelling and failure and MR antagonists (MRA) such as spironolactone are now one of the four pillars of therapy for heart failure. MRA also show benefits for chronic kidney disease (CKD). However, steroidal MRAs are limited by adverse effects including hyperkalemia and renal impairment. Non-steroidal MRAs (e.g., finerenone, esaxerenone)are now available and are proposed to have improved safety profiles.

The MR is widely expressed in non-epithelial tissues including the inflammatory cells, adipose tissue, brain and skin, where its actions are highly context dependent. Emerging research reveals novel molecular mechanisms of MR regulation, including ligand-responses, transcriptional coregulators and MR-specific DNA binding sequences. Our recent work using a series of transgenic animal models identified bidirectional regulation between MR and the molecular circadian clock in cardiac and inflammatory cells and identified time-of-day-dependent MR modulation of clock genes (Per2, Cry1, REV-ERBα), inflammatory mediators (NOS2, IL-1β, CCL2), and metabolic regulators with sex-specific differences. Aldosterone and corticosterone were shown to directly influence clock gene oscillations in bone marrow-derived cells and cardiomyoblast cells. These findings suggest MR contributes to temporal regulation of inflammation and other cell functions and may underlie sex-based differences in cardiovascular disease. This presentation will explore MR signalling in the heart and inflammatory cells, its integration with circadian biology, and implications for MR-targeted therapies.

id #128650

ATF3-Regulated Eosinophils Drive Adipose Tissue Angiogenesis Via VEGFA Expression

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Adipose tissue eosinophils regulate the activation of thermogenic beige adipocytes, which could be harnessed to reduce obesity. Despite being destructive in diseases such as asthma, eosinophils have a protective role in the adipose tissue. Here we asked critical questions to enable translation to anti-obesity therapies: which genetic regulators switch eosinophils from being destructive to protective? And, how do adipose eosinophils play this protective role in metabolic health?

We previously performed the first bulk RNA-seq of adipose-resident eosinophils. We found that adipose eosinophils are transcriptionally distinct from circulating eosinophils and identified Activator Protein 1 (AP-1) proteins as key transcriptional regulators of the adipose eosinophil transcriptomic profile.

Next, we took a functional genomics approach, using CRISPR/Cas9 genome editing to individually knock-out the identified transcription factors in human eosinophilic EoL-1 cells. RNA-seq and Chromatin Immunoprecipitation (ChIP) analyses revealed AP-1 member protein Activating Transcription Factor 3 (ATF3) as a key regulator of adipose eosinophil gene expression.

We found that IL-5 transgenic mice, with elevated numbers of adipose eosinophils, had higher vascular endothelial growth factor A (VEGFA) levels and enhanced adipose tissue vascularisation. VEGFA is critical for adipose tissue angiogenesis, a process essential for maintaining tissue health and promoting the conversion of adipose tissue to thermogenic beige fat. We showed that VEGFA expression is regulated by ATF3 in adipose tissue eosinophils. Deletion of ATF3 in eosinophils in cell culture models and in mice led to reduced VEGFA expression, increased pro-inflammatory gene expression, and impaired adipose tissue vascularisation and thermogenesis.

These findings establish ATF3 as a key regulator of adipose eosinophil function that we propose drives the switch from destructive to protective adipose eosinophil phenotypes. This study also reveals a previously unrecognised mechanism by which eosinophils can support metabolic health through driving angiogenesis. This work therefore provides new insights into potential therapeutic targets for obesity.

id #130442

Simplifying the diagnosis of primary aldosteronism

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The diagnosis of primary aldosteronism (PA) can be time-consuming and this can delay definitive management. This is exacerbated by the need for adrenal vein sampling (AVS) to determine the subtype of PA and therefore inform treatment. Use of clinical algorithms to predict the subtype is an under-utilised tool that could help to streamline the path to treatment for patients and enable more selective use of AVS as an invasive and resource-intensive investigation.

id #128395

Increasing livestock production through the isolation and *in vitro* culture of bovine ovarian follicles

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Assisted reproductive technologies are being increasingly utilised by the agricultural industry to meet the growing demand for animal protein (1). Commercial *in vitro* production of bovine embryos uses oocytes from the antral follicles of donor cow ovaries collected via ovum pick-up (2-3). However, only ~25 antral follicles are present per ovary, resulting in low oocyte yields per cow (4). The number of follicles from earlier stages is greater with ~4,000 secondary and ~250 tertiary follicles per ovary (5-6), and thus are a promising way to increase oocyte yield. This study aims to isolate viable secondary and tertiary follicles from fresh bovine ovarian tissue and develop a culture system that allows for successful follicular growth and oocyte maturation *in vitro.* Follicles were successfully cultured from the secondary to preovulatory stage, with the addition of insulin-transferrin-selenium to culture medium being beneficial for secondary follicle growth from Day 1 to 21 and for tertiary follicle growth during early culture. To further improve this growth, Factor A and Factor B were added in addition to insulin-transferrin-selenium. The addition of Factor A to culture medium was beneficial for secondary follicle growth during late culture and for tertiary follicle growth from Day 1 to 21. The addition of Factor B to culture medium had no effect on secondary follicle growth but was beneficial for tertiary follicle growth from Day 1 to 21. In conclusion, isolation and culture of secondary and tertiary follicles to produce mature oocytes offers a favourable approach for the *in vitro* production of bovine embryos to produce large numbers of high-quality livestock.

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id #128651

Gene expression dynamics during early gonadal differentiation in the tammar wallaby

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Ovaries and testes develop from a bipotential gonad. Tammar wallabies deliver a highly altricial young, and while the bipotential gonad is formed at day 21 of the 26.5 day gestation, the testes and ovaries remain undifferentiated at birth (1). By 2 days postpartum (dpp), testicular cords enclosing germ cells are distinct in males. In females, ovarian differentiation starts later, with ovigerous cords and germ cell nests starting to form in the ovarian cortex between 2-4 dpp (1, 2). Expression profiles of key eutherian gonadal differentiation regulators, including *FOXL2*, *WNT4*, *SOX9* and *AMH*, have been assessed in tammar gonads (3-5) and after exposure to estrogen and bisphenol A (2, 5). However, to identify novel candidate regulators, we focussed on 2 dpp and 8 dpp in both ovaries and testes.

We performed RNA-seq on tammar gonads collected at 2 and 8 dpp, the period of gonadal differentiation, and profiled differential gene expression. From 2-8 dpp, there was a developmental increase in known testicular markers (*HSD17β3, CYP17A1, INSL3, ATRX*), as well as in novel genes including *NWD1*, a gene associated with prostate cancer and *Interleukin-1 receptor type 2*. In ovaries, there was a developmental increase in *DDX4* coinciding with the postnatal germ cell proliferation. Developmental changes in the ovary were enriched for gene ontology terms associated with cell cycle regulation, germ cell development, piRNA processing, morphogenesis and neuronal development. Based on significant changes in expression potential regulators of early ovary development include, for example, *Serpin B2* and *Suppressor of glucose autophagy associated 2*.

The function of these genes in gonadal development is as yet unknown, but the long period of differentiation after birth in the tammar allows us a unique opportunity to define their action to further understand the control of mammalian gonadal development.

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id #128652

Purinergic Receptor Inhibition Impairs Trophoblast and Trophectoderm Outgrowth During Early Placentation

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Early placentation relies on tightly coordinated trophoblast differentiation, adhesion, migration and invasion. Purinergic signalling is an understudied but exciting area due to the ability of extracellular nucleotides, including ATP and UTP to act as rapid messengers, enabling swift cellular responses to environmental cues via surface purinergic receptors. Thus, purinergic signalling offers a novel avenue to explore mechanisms driving early placentation. However, specific purinergic signalling function during early placentation remain unclear. This study aimed to determine functional actions of purinergic receptors P1A1 and P2Y6 on trophectoderm and trophoblast migration, invasion and expansion.

Spatial transcriptomics on human placentas (n=13; 5–13 and ≥38 weeks) was undertaken to assess the purinome across gestation. First trimester placental tissue (7–12 weeks) was cultured on collagen and treated with antagonists to P1A1 (DPCPX) or P2Y6 (MRS2578) for 48 hours. Outgrowth area was measured to assess trophoblast migration and expansion. Mouse blastocysts were also cultured on fibronectin with the same antagonists for 96 hours to evaluate trophectoderm/trophoblast outgrowth.

Spatial transcriptomic analysis revealed low expression of *P1A1* across samples assessed. *P2YR6* expression was abundantly detected in cytotrophoblasts and syncytiotrophoblasts, suggesting a trophoblast specific function. Inhibiting both receptors significantly reduced first trimester placental outgrowth, suggesting their effects in early trophoblast expansion. P2Y6 inhibition also caused altered differentiation and increased cell death in placental explants, indicating a potential disruption in trophoblast function. Preliminary findings suggest that mouse blastocysts treated with both P1A1 and P2Y6 antagonists showed reduced trophectoderm outgrowth compared to control, suggesting these receptors may play a critical role in early trophoblast function.

Collectively, these findings suggest that dysregulation of P1A1 and P2Y6 in early trophectoderm and trophoblast may disrupt placental development. Therefore this may contribute to placental dysfunction in major pregnancy complications, including preeclampsia and fetal growth restriction.

id #130444

Set-Domain Proteins in Epigenetic Inheritance

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Over the last two decades it has become clear that epigenetic modifications acquired by an individual during its lifetime can be inherited for multiple generations. We have developed a transgenerational epigenetic inheritance sensor in the model organism Caenorhabditis elegans in which RNAi-induced silencing of a GFP transgene is robustly inherited for multiple generations.

Using this model, we identified a network of proteins involved in epigenetic inheritance, classifying them into three groups: those involved in establishment, maintenance, or both. This distinction has implications for how epigenetic signals are maintained not only in the context of transgenerational epigenetic inheritance, but in epigenetic memory throughout development as well.

Most of the proteins we identified have homologs in mammals and two of particular interest are SET-9 and SET-26, homologs of KMT2E/MLL5. Although poorly studied, KMT2E/MLL5 has been implicated in many diseases including cancer, immune regulation and autism, and was recently identified as the cause of O'Donnell-Luria-Rodan (ODLURO) syndrome. Symptoms of ODLURO syndrome include global development delay, ASD and epilepsy. We have shown that SET-9 and SET-26 are defective in epigenetic inheritance and show progressive sterility. SET-9 and SET-26 bind H3K4me3 with high affinity in vitro. Mutation of SET-9 and SET-26 causes widespread disruption of H3K4me3, leading to activation of genes that should be silenced. We hypothesise that this disruption to the global epigenome when KMT2E/MLL5 is mutated in humans causes ODLURO syndrome, and leads to the development of cancer.

id #124046

Beyond autism awareness and towards understanding, supports, acceptance and inclusion: insights from camouflaging and burnout autism research

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We need to move beyond knowledge and awareness of autism and Autistic people, to achieve understanding, acceptance, supports and inclusion across higher education, work, community, and society more broadly. In this talk, I present findings from camouflaging and burnout autism research which illustrate how current pressures harm autistic and neurodivergent people, what needs to change and how we can do better.

id #127374

Ready, set, react: A hybrid lab for the next generation of scientists

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Practicals are an important component of education in STEM disciplines. They not only teach physical laboratory skills but also time management and downstream analytical skills. However, with growing enrolments, there are pressures on the availability of physical laboratory space, reagents and teaching staff which restricts students' ability to expand or repeat experiments.

One solution that enables students to practice their skills is to create a hybrid practical environment. We have developed an authentic Virtual Lab, which incorporates random variability and errors, that allows students to repeat and expand on experiments done in physical laboratories. It encompasses a suite of common experiments in molecular biology, biochemistry, physiology and microbiology.

The hybrid laboratory has been deployed in several second- and third-level biological science courses to specifically support learning in each course. It has been used to allow students to familiarise themselves with a technique by repeating it and then designing their own experiment to be conducted in the physical laboratory. The Virtual Lab allows students to learn new techniques not available in

the physical laboratory due to high costs, and to expand on the original experimental plans (e.g. by increasing the assay duration, sample number and/or concentration ranges). The Virtual Lab can also be used to generate results when students are absent from practicals.

The implementation of the hybrid environment has resulted in a 7% increase in the average mark for practical-related questions on exams, improved student confidence in the wet lab, and reduced anxiety when wet lab experiments fail or when students have been unable to attend. In addition, students have been able to virtually learn techniques that previously were demonstrated only.

Therefore, the hybrid laboratory environment supports and expands student learning and is highly adaptable while reducing the strain on scarce resources.

id #128398

Tirzepatide improves adverse liver outcomes in a mouse model of concurrent type 1 diabetes and obesity

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The incidence of obesity in people with type 1 diabetes (T1D) is rising at an alarming rate, and obesity is associated with insulin resistance and poorer glycaemic control. The enhanced metabolic dysfunction, coupled with lipid accumulation, increases the risk of metabolic dysfunction-associated fatty liver disease (MAFLD), which is already increased in T1D. MAFLD can progress to severe stages of liver disease such as fibrosis and cirrhosis. Given weight loss is the gold-standard treatment for MAFLD, there is a need for therapies beyond lifestyle intervention, often particularly challenging in the setting of T1D. This study aimed to assess the effect of tirzepatide, an incretin-based therapy which facilitates weight loss, on liver outcomes in a mouse model of concurrent T1D and obesity.

C57BL/6J mice received intraperitoneal 55mg/kg/day injections for 5 days of vehicle-matched control (CON) or streptozotocin (STZ) to achieve beta cell depletion and insulin-dependent diabetes. After 2 weeks, once hyperglycaemia was established (≥14 mmol/L), mice that received STZ were split into: chow diet (DM), high-fat diet (HFD; DMO) or HFD with tirzepatide (DMO-TZP). Tirzepatide was administered thrice weekly at maximum dose of 40nmol/kg s.c. for 24 weeks. Mice were sacrificed and livers harvested for histology and immunohistochemistry.

Total histological scoring for liver steatosis, inflammation and ballooning was elevated in the DMO group, compared to DM ($P < 0.01$), indicating a MAFLD phenotype. Tirzepatide significantly reduced scores (DMO vs DMO-TZP, $P < 0.01$). Hepatic lipid accumulation was significantly lowered in tirzepatide-treated mice (DMO vs DMO-TZP, $P < 0.05$). There were no differences in fibrosis between groups.

These findings underscore the potential of tirzepatide to promote weight loss and improve MAFLD-related liver outcomes in individuals with T1D and obesity. Our T1D and obesity mouse model resembled early-stage MAFLD; longer studies are needed to assess whether tirzepatide can prevent progression to advanced liver disease.

id #128911

Application of a novel long-acting biotherapeutic targeting the growth hormone receptor in melanoma

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Aims: Localised expression of growth hormone (GH) and its receptor (GHR) has been identified in various human malignancies and is associated with poor survival outcomes in certain types of cancer. Despite evidence from published literature, preclinical studies investigating the anticancer efficacy of growth hormone inhibition have been difficult to undertake due to the limited availability of suitable pharmacological tools for *in vivo* studies. Pegvisomant, the only clinically available GHR antagonist, is difficult to access for research so novel GHR antagonists are needed to investigate the role of GHR signalling in cancer. Here the preclinical efficacy of a novel long-acting GHR antagonist (GHA2) was investigated in melanoma.

Methods: Recombinant GHA2 protein was expressed and purified from *E. coli* and conjugated with polyethylene glycol (PEGylated) to extend the *in vivo* circulating half-life. *In vitro* bioactivity was confirmed using cell-based assays and inhibition of GHR-dependent signal transduction. For tumour growth studies, melanoma xenografts (NZM79) grown in immunodeficient NIH-III mice were treated daily with vehicle or GHA2 (30 mg/kg/day) ± human GH (2 mg/kg/day) for 2 weeks.

Results: In melanoma cell lines, high *GHR* mRNA expression was observed across a panel of 24 New Zealand metastatic melanoma (NZM) cell lines. 16/24 cell lines were GH responsive (STAT5 phosphorylation) and responded to GHR antagonism. GH promoted cell proliferation in GHR-positive cell lines. In xenograft studies, serum IGF1 decreased by 51% with GHA2 treatment ($p<0.001$). GHA2

treatment also significantly decreased the growth rate of NZM79 tumours versus vehicle ($p<0.05$), and reduced tumour expression of the proliferation marker Ki67.

Conclusion: GHA2 effectively antagonised GH signalling in melanoma cell lines and slowed melanoma tumour growth, highlighting its potential as a therapeutic strategy for treating melanoma.

id #127377

The Lancet Commission on clinical obesity – rationale, diagnostic criteria and implications for practice

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In what situations could obesity be considered a disease in its own right? The 2025 Lancet Commission on the Definition and Diagnosis Clinical Obesity (1) defined clinical obesity as a chronic, systemic illness characterised by alterations in the function of tissues, organs, the entire individual, or a combination thereof, due to excess adiposity.

The Commission recommended a move away from a sole reliance on BMI to define obesity. Instead, excess body fat should be confirmed by either direct measurement of body fat, or at least one anthropometric criterion (e.g. waist circumference, waist-to-height ratio) in addition to BMI, using validated methods and appropriate cutoff points. People with confirmed obesity status should be assessed for clinical obesity. The diagnosis of clinical obesity requires one or both of the following criteria: evidence of reduced organ or tissue function due to obesity (i.e. signs, symptoms, or diagnostic tests showing abnormalities in the function of one or more tissue or organ system; 18 criteria for adults and 13 for children/ adolescents); or substantial, age-adjusted limitations of daily activities reflecting the specific effect of obesity on mobility, other basic activities of daily living, or both. Pre-clinical obesity was defined as being present when there is excess body fat but no associated health problems. Note that the definition of obesity as a standalone disease does not depend upon the presence of another disease.

The new definition means a move away from a strict epidemiological definition to one that is more clinically nuanced. People with clinical obesity should receive timely, evidence-based treatment, aiming to improve clinical manifestations of obesity and prevent progression to end-organ damage. People with preclinical obesity should receive evidence-based health advice, monitoring over time, and, where appropriate, more intensive therapy depending upon individual risk. All people with obesity (clinical or pre-clinical) should have equitable access to therapies.

1. (1) Rubino F, et al. Definition and diagnostic criteria of clinical obesity. Lancet Diabetes Endocrinol. 2025 Mar;13(3):221-262.

id #131730

Obesity prevention in Australia – where are we now?

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Obesity remains a considerable burden to individuals, communities and the health system. Despite investment in a range of health initiatives over past decades, rates of obesity remain unacceptably high. The implementation of strategies to prevent obesity in children has been recommended in obesity strategies globally. Evidence supporting the effectiveness of these in reducing obesity child obesity prevalence, however, has been mixed. This presentation will describe the evolution of efforts to prevent obesity in Australia over the past 2 decades characterising different approaches and perspectives over this period. Despite significant advances in knowledge, technology, and perspectives on prevention, the translation of effective interventions into health policy and practices remains a persistent impediment to reducing population prevalence of obesity prevention programs. The novel application of scientific disciples including implementation science, methods and technologies will be discussed as potential means of improving the impact of investments in obesity prevention.

id #124051

Kingdom of reproductive life; core sperm proteome

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Reproductive biology is often considered in three siloed research areas; humans, agriculture and wildlife. Yet, each demand solutions for treatment of subfertility, fertility biomarkers, development of assisted reproductive technologies and effective contraception. To efficiently develop solutions applicable to all species, we must improve our understanding of the common biology underpinning reproductive processes. Accordingly, we integrate proteomic data from 29 publicly available datasets (>2 TB of data) to characterize mature sperm proteomes spanning 12 vertebrate species, identifying 13,853 proteins. Although human and mouse have relatively well-annotated sperm proteomes, many non-model species rely heavily on predicted or homology-inferred identifications. Despite variation in proteome size, composition and reproductive strategies, comparative analyses revealed that vertebrates share a fundamental molecular framework essential for sperm function. A core set of 45 species-level and 135 order-level conserved proteins mapped to critical processes, including energy generation, acrosome function, as well as novel signalling pathways (BAG2 and FAT10). Utilising knockout mouse models, we further validate the significance of these conserved proteins, demonstrating that their disruption impairs sperm motility and fertilization capacity. Moreover, we discovered loss-of-function variants of two additional core sperm proteins in clinical samples, linking them to severe sperm defects. Intriguingly, in-silico analysis reveals function-driven, context-dependent diversity surpassing evolutionary patterns. Collectively, these results highlight the value of integrating publicly available datasets and underscore the need for improved genome/proteome annotation in non-model species in mammals. This work provides a foundation for developing cross-species strategies to enhance fertility treatments, assisted reproductive technologies, and conservation efforts. All data is available via ShinySpermKingdom (https://reproproteomics.shinyapps.io/ShinySpermKingdom/).1

id #131734

The effect of semaglutide on weight, reproductive and metabolic outcomes in adolescents with PCOS and obesity

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Polycystic ovary syndrome is one of the most common endocrinopathies in women, can present with anovulation in adolescence, and is often accompanied by cardiometabolic disease. In many patients with PCOS, reproductive dysfunction is related to excess weight. Trials that induce weight loss through lifestyle interventions have demonstrated some effectiveness in improving reproductive measures. The effects reproductive and metabolic effects of glucagon-like peptide-1 receptor agonist therapy induced weight loss in patients with PCOS will be reviewed, in particular data from newer GLP1 RA and in the adolescent population.

id #127894

A potential biological link between lactational mastitis and risk of breast cancer

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Aims: There is an emerging body of epidemiological literature suggesting that mastitis is associated with increased risk of breast cancer, however little is understood of the underlying biology that could link these two breast conditions (1). Interestingly, the association appears to be independent of the breast in which mastitis occurred, suggesting there may be factors that increase risk of both conditions, rather than mastitis having a causal effect on breast cancer risk (2). The aim of this study was to investigate whether factors in breastmilk may mediate this association.

Methods: Breastmilk samples from healthy multiparous women with a history of mastitis whilst feeding a previous infant (high-risk; n=10) and no history of mastitis (low-risk; n=10) were cultured at 100 µg/ml with breast cancer and macrophage cell lines (MDA-MB-231 and RAW264.7, respectively). RT-qPCR was used to assess the expression of proinflammatory genes in macrophages and epithelial–mesenchymal transition (EMT) markers in breast cancer cells. To evaluate crosstalk activity, breast cancer cells were treated with conditioned media from macrophages treated with breastmilk, followed by analysis of EMT markers, cell viability, wound healing, transwell migration, and invasion assays.

Results: Despite high variability in gene expression in macrophages treated with individual breastmilk samples, high-risk breastmilk induced overall higher expression of proinflammatory markers in macrophages compared to low-risk breastmilk (p = 0.001). Breast

cancer cells treated with macrophage-conditioned media derived from selected high-risk breastmilk exhibited increased mesenchymal marker *CDH2*, enhanced cell viability, migration, and invasion.

Conclusion: This study suggests there may be factors in breastmilk from women with a history of mastitis that indirectly promote breast cancer development and progression through macrophage-mediated mechanisms. Further research is required to explore the potential biological association between mastitis and breast cancer risk.

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id #128663

The effects of acute and chronic exercise on lipocalin-2 in middle-aged and older adults

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Lipocalin-2 (LCN2) is a mechanoresponsive hormone involved in bone-muscle-fat crosstalk. Chronically elevated circulating LCN2 levels are implicated in poor energy regulation, increased cardiometabolic disease risk and poor physical function. Exercise is known to improve the aforementioned factors, but whether LCN2 is implicated in this relationship is not clear. We examined the effect of acute and chronic exercise on serum LCN2 levels and whether this relates to glucose regulation, body composition and physical function.

Thirty-three middle-aged and older adults (45 – 84 years, 72.73% female, median BMI 26.21kg/m^2) completed a single acute high intensity interval exercise session (HIIE) (4 x 4 mins at 90 – 95% Heart Rate Reserve). Participants were then randomised to four weeks of high intensity interval training (HIIT) or control in a parallel groups design. LCN2, insulin, glucose and homeostatic model assessment for insulin resistance (HOMA-IR) were analysed in serum at baseline and immediately, 1 h and 3 h post-HIIE, and four weeks post-intervention. Urinary LCN2 was assessed pre and post four weeks of HIIT at rest. Linear mixed-modelling was used to assess change in LCN2 post-acute and chronic exercise.

A main effect for time for serum LCN2, insulin, glucose and HOMA-IR was detected after acute HIIE ($p < 0.001$). Circulating serum LCN2 levels increased significantly immediately post-HIIE compared to baseline ($p < 0.001$) and returned to levels similar to baseline by 60 and 180min post-HIIE. Four weeks of HIIT improved VO_{2peak} yet had no significant effect on urinary and serum LCN2 levels or physical function.

Acute HIIE, but not four weeks of HIIT, transiently increased circulating LCN2 and improved insulin sensitivity in middle-aged and older adults. Whether the transient increase in LCN2 is related to post-exercise appetite suppression and long-term glucose regulation following exercise training should be explored further.

id #126872

Understanding the experience of living with obesity: A co-design photovoice exploration with obesity lived experience consumer group

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3. Weight Issues Network, Sydney

Background: Obesity is a complex, individualized, and often stigmatizing experience. Including consumer voices in policy, programs, and research has been established as essential for generating positive health outcomes. However, limited research has been conducted in a co-designed manner where consumers directly voice their experiences to improve obesity-related healthcare.

Objective: This study explores the real-world experiences of living with obesity, as described by consumer experts, to identify key areas for healthcare improvement.

Method: Twenty-four self-identified obesity lived experience experts participated in semi-structured interviews, guided by a self-designed image or hand-drawn picture representing their experience.

Design: A photovoice qualitative study co-designed with obesity lived experience experts and obesity health researchers. Interviews followed photovoice methodology and were analysed using Braun and Clarke's thematic analysis.

Results: Three overarching themes emerged: (1) regular dehumanizing experiences; (2) the need for holistic obesity healthcare; and (3) raising awareness about the complexities of living with obesity. Participants described pervasive obesity discrimination across daily life, contributing to internalized stigma and, in severe cases, dehumanization. Obesity was characterized as interconnected and

complex, requiring a holistic, person-centred healthcare approach for better outcomes. Participants advocated for public, tertiary, and healthcare education to highlight the difficulties of living with obesity and challenge the harmful nature of obesity stigma.

Conclusion: Stigma's harmful impact was central to participants' experiences, demonstrating how systemic, interpersonal, and internalized biases contribute to further health complications. These findings align with international literature but highlight the under-recognized severity of obesity stigma as a major barrier to improving health outcomes. Future research should focus on developing co-designed obesity education initiatives for public, tertiary, and healthcare sectors to raise awareness and reduce stigma for individuals living with obesity.

id #129688

Five-Year Retrospective Audit of Endocrine Dynamic Testing in a Tertiary Hospital: Trends, Outcomes, and Implications

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INTRODUCTION

Endocrine dynamic tests are essential for diagnosing various endocrine disorders. In endocrinology, the foundation of diagnosis involves demonstrating hormone dysfunction through biochemical tests, followed by imaging. These dynamic tests are also crucial for follow-up and management, as they help assess treatment response (Goyal et al. 2019). However, with advancements in laboratory methods that are more sensitive, accurate, and rapid, the use of some dynamic tests has decreased over time.

AIM

Our objective is to establish a comprehensive registry of endocrine dynamic tests, facilitating future research initiatives for both the nursing and medical teams within the department. This registry will serve as a valuable resource for data collection, trend analysis, and clinical evaluations, contributing to ongoing advancements in patient care and endocrinology research. Additionally, it will support the optimisation of workflow processes and provide a structured approach to estimating the time investment of junior doctors involved in conducting these tests, thereby enhancing efficiency and resource allocation within the department.

METHOD

This study presents a retrospective analysis of data extracted by the Service 1 Business and activity analyst team via Webpas. It includes all patients who attended the Day Medical Procedure Unit at FSH for Endocrine Dynamic Tests between January 2020 and December 2024. Each patient's Digital Medical Record (DMR) was reviewed to confirm that the scheduled Dynamic Tests were conducted as planned.

RESULTS

- The Short Synacthen Test is the most frequently performed endocrine dynamic test at the FSH Day Medical Unit.
- The Seated Saline Suppression Test ranks as the second most common endocrine test conducted at FSH DMP.
- The overall number of dynamic tests has been steadily increasing.
- The monthly count of tests is variable.

CONCLUSION

Regular clinical audits are integral to driving continuous improvement in service delivery and implementing evidence-based modifications to enhance operational efficiency.

id #130712

Fractures, Frameworks, Frontiers

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Osteoporosis care has seen major advances through clinical trials and the development of bone-targeted therapies. Yet, conventional treatment approaches rely on short-term, single-agent regimens, overlooking the complexity of long-term management—sequential therapy, treatment cessation, and individual variability in response. This presentation will explore real-world insights in sequential and combination therapies in osteoporosis, ethnic variations in skeletal drug response, bone loss following acute spinal cord injury, and the establishment of the Westmead Hospital Fracture Liaison Service, a service designed to support high-risk and underserved populations in Western Sydney.

id #128409

Embedding play and puzzles into reproductive science curricula

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Play-based and simulation-style learning are known to enhance student engagement and support the development of transferable skills (1,2). However, theory-heavy science curricula often struggle to incorporate these approaches, as they do not naturally lend themselves to immersive, simulated environments. In 2022, assessment reinvigoration within our faculty prompted a shift away from traditional exams that prioritised recall, toward more authentic assessments focused on the application of knowledge and skills to

"real-world" scenarios. In response, we developed tasks that embedded reproductive science content within creative, applied contexts to assess not only content mastery but also critical thinking, teamwork, and real-time problem-solving.

In our postgraduate reproductive science program, we introduced a series of puzzle- and play-based activities during in-person tutorials throughout the semester, culminating in a 90-minute escape room assessment that replaced a final exam. In this assessment, learners worked collaboratively to solve five interconnected challenges aligned with the unit's learning outcomes, applying theoretical knowledge to unique scenarios, all embedded within a cohesive narrative.

Feedback on these activities has been overwhelmingly positive. Learners reported preparing for the escape room as seriously as they would for an exam but found the experience more engaging, less stressful, and more reflective of real-world problem-solving. Educators gained direct insight into students' reasoning and teamwork, allowing for a more nuanced evaluation of their understanding and skills.

While effective, the design and implementation of these activities require significant upfront investment and may be difficult to scale in larger cohorts without adequate staffing or resources. Nonetheless, escape rooms and structured play have become a valued part of our curriculum. We offer our approach as a template for integrating simulation into science education and invite others to adapt and extend it within their own teaching practice.

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id #128665

Investigating regulation and misregulation of Cripto in fetal germ cells: balancing pluripotency and meiotic progression

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Publish consent withheld

id #129689

Demystifying TFTs – when the numbers don't add up

John Walsh[1]

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An overview of thyroid function tests, including typical patterns of thyroid dysfunction (hyperthyroidism and hypothyroidism) and how to approach unusual or discordant results.

id #131482

Improving our understanding and management of obesity: advantages and constraints of animal models

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Animal models have been indispensable in advancing understanding of the mechanisms underlying human obesity, by providing a controlled framework in which genetic, environmental, and behavioral determinants of disease risk can be systematically examined. Rodents have been widely used, due to their well-characterized genomes, short reproductive cycles, and suitability for genetic manipulation. Seminal discoveries regarding appetite regulation and energy homeostasis emerged from murine models, perhaps most notably the ob/ob mouse, lacking the gene encoding leptin, which develop profound obesity and metabolic disturbances. Further work using rodents has elucidated the interplay between neuroendocrine circuits, adipose tissue, and peripheral metabolic organs, thereby providing insights into the pathophysiology of obesity-related conditions such as type 2 diabetes and non-alcoholic fatty liver disease. Diet-induced obesity (DIO) models have also been widely utilized to replicate human obesogenic environments. Feeding rodents high-fat or high-sugar diets induces weight gain, insulin resistance, and systemic inflammation, thereby recapitulating the metabolic syndrome observed in humans. Such approaches have clarified how nutrient excess disrupts cellular signaling pathways and contributes to chronic low-grade inflammation. Nonhuman primates share physiological and behavioral similarities with humans, particularly in fat distribution and diet-related pathologies, making them valuable for translational studies. Zebrafish, despite their evolutionary distance, have proven useful for high-throughput metabolic studies.

Nevertheless, animal models have limitations. No single model fully captures the complexity of human obesity, which is influenced by cultural, psychological, and socioeconomic factors impossible to recapitulate in laboratory settings. Rodent metabolism, for example, differs from humans in aspects of fat distribution, thermogenesis, and gut microbiota, potentially limiting translational scope. Thus, animal models remain fundamental to obesity research, offering critical insights into genetic, metabolic, and behavioral drivers of

disease, while facilitating the development and testing of therapeutic strategies. Despite their shortcomings, they constitute an essential component of translational obesity research.

id #132506

Aboriginal Engagement Lead, Health Consumers' Council presentation

Mel Robinson[1]

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The objective of this symposium is to highlight the challenges facing consumers in the health system when seeking support for healthy lifestyle change and/or weight management services. Presenters will share their experiences of how people get "lost in the system", even when proactively asking for help, the stigma and shame associated with asking for support, experiences of racism and bias, and the resultant impact on long-term health. Attendees will hear solutions to these challenges from each of our expert speakers and the role of advocacy.

id #128411

Preventing childhood obesity through physical activity intervention: Lessons learnt from the Play Active program

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Energetic play is essential for children's development, to set lifelong positive health behaviours, and curb obesity and chronic disease. Yet only one in ten children aged 3-5 years get the recommended 60 minutes of daily energetic play. Early Childhood Education and Care (ECEC) is an important setting for supporting children's physical activity. Play Active is an evidence-informed physical activity policy intervention with implementation strategies to enable ECEC services to successfully implement their policy. Play Active is backed by 10 years of research with leading (inter)national research institutions, ECEC providers and peak bodies and organisations working in child physical activity and health.

In 2021-22 a pragmatic trial to test the effectiveness and implementation of Play Active was conducted with 81 ECEC services (646 educators) in Perth, WA. There was a significant increase in the uptake of policy physical activity practices during the 3-month implementation period. There was high awareness of the policy recommendations (90%). Acceptability was high for both educators (83%) and directors (78%) and, fidelity and reach were high for most implementation support strategies (75%-100%).

Play Active supports services to meet the Australian ECEC national standard: "Each child's health and physical activity is supported and promoted". Play Active received a further $2million to be scaled up nationally and was launched by the Federal Minister for Early Childhood Education and Youth, the Hon. Dr Anne Aly MP in April 2024. More than 80,000 Australian children from 700 ECEC services across nationally are expected to benefit through improved physical activity and health. A key focus is equitable implementation of Play Active for ECEC services who work with priority population groups. The presentation will include the process for embedding current policy environments and industry practices into research and lessons learned for implementing interventions at scale and working with community and stakeholders.

id #128159

Wnt-egrating developmental insights: an atlas of cross-species Wnt/WNT signalling in placental development and preeclampsia

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Wingless-related integration site (WNT) signalling regulates cell fate, proliferation and differentiation in embryonic development. However, its component temporospatial expression in early placental development remain incompletely characterised, limiting understanding of WNT-related contributions to placental insufficiency, including preeclampsia. We sought to characterise Wnt expression dynamics across mouse placental development and dysregulation in human placentas with preeclampsia. Wnt-related components were proposed to localise to defined placental compartments during normal placental development, with dysregulations in preeclampsia.

To generate an atlas, 59 Wnt-related genes were profiled by qRT-PCR /*in* situ hybridisation across key developmental stages in wild-type C57BL/6 mouse placentas (n≥3 litters across 7 timepoints, E8.5-E18.5). Public spatial transcriptomic datasets access provided comparison/validation (E7.5-E14.5) (1-3). In human placentas, qRT-PCR assessed orthologous genes in <34-week preterm controls (n=17) versus preeclampsia (n=83); and across gestation in first trimester (n=11), early preterm (n=9) and term (n=11), with validation using an independent transcriptomic database (4).

In mice, 36 Wnt genes increased, 14 were stable, and 9 decreased across gestation. *In situ* hybridisation revealed distinct stage-/compartment-specific patterns. *Axin1*, *Lgr5*, *Ror2*, *Tcf7l1* were enriched in labyrinth trophoblast progenitor populations. 21 genes exhibited broader localisation across trophoblasts, the junctional zone, vasculature and stroma. Most patterns validated with public datasets, although discrepancies existed for low abundance genes.

In human placentas, across gestation, *FZD10* and *GSK3a* increased from first trimester to term ($p<0.0159$, $p=0.0005$), *sFRP1* displayed a U-shaped pattern ($p<0.0420$), and *WNT3* declined ($p=0.0058$). *FZD10*, *GSK3a* and *sFRP1* were significantly upregulated with preeclampsia ($p=0.0029$, $p=0.0137$, $p=0.0157$). *DKK2*, *DVL3*, *GPR177*, *WNT2, WNT3* and *WNT7A* were downregulated ($p=0.0002$, $p=0.0398$, $p=0.0001$, $p=0.0470$, $p=0.0129$). In human snRNA-seq data, many dysregulated genes also mapped to broader roles than trophoblasts in regulating placental progenitor niches.

These findings underscore the value of temporospatial profiling to define Wnt-related molecules coordination of placental morphogenesis and identify conserved genes susceptible to disruption in preeclampsia.

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id #128416

Capacitation Conundrum: Are Oxidative Defences Sabotaging Equine IVF?

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Achieving *in vitro* capacitation in stallion sperm remains a key barrier to the large-scale commercialisation of IVF in horses. One proposed explanation is that elevated antioxidant defences in stallion sperm, while protective against oxidative damage, may suppress the ROS-mediated signalling required for capacitation. Unlike human sperm, which rely on glycolysis, stallion sperm use OXPHOS, generating more ROS and requiring robust antioxidant defences. In the context of IVF, stallion sperm must survive a 22-hour incubation at 38.2 °C under capacitating conditions, making it critical to understand how long-term redox balance impacts sperm viability, motility, and functional competence. Motility (CASA), viability (PI), intracellular H_2O_2 (DCF), and DNA integrity (halo assay) were assessed following exposure to increasing H_2O_2 concentrations (0–2000 µM). Catalase activity was selectively inhibited using 3-amino-1,2,4-triazole (3-AT) to evaluate its role in stallion sperm redox regulation (n=18). Stallion sperm showed high resilience to oxidative stress, with IC_{50} values for progressive motility exceeding 2000 µM, compared to 251.9 µM in humans. Interestingly, despite accumulating more intracellular H_2O_2 (e.g. at 2000 µM H_2O_2, stallion sperm DCF fluorescence was 5825±1047 AU vs. 3333±184 AU in human; $p \leq 0.05$), stallion sperm exhibited no increase in DNA fragmentation. In contrast, human sperm showed significant DNA damage at 2000 µM H_2O_2 (12.9±2.2% vs 41.5±7.1%; $p=0.0062$). Catalase inhibition significantly increased intracellular H_2O_2 in stallion sperm (250 µM: 3.0±1.2% vs 302.4±65.5%; $p \leq 0.0001$) and reduced progressive motility (18.9±1.9% vs 5.9±3.7%; $p=0.021$). While the presence of catalase in mammalian sperm cells is contentious, RT-PCR confirmed catalase expression in stallion sperm, and immunocytochemistry localized it to the post-acrosomal region. Interestingly, sublethal H_2O_2 exposure (250 µM) increased viability (66.5±2.8% vs 71.3±2.9%; $p=0.003$), consistent with oxidative eustress. These findings highlight redox balance as a critical factor for developing IVF protocols and suggest catalase inhibition as a potential target to enhance equine sperm capacitation outcomes.

id #128672

A global analysis of critical shifts in infertility treatment from 30 years of ART reporting

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Infertility affects 1 in 6 people globally, with tremendous health, economic, and social consequences. To treat infertility, assisted reproductive technologies (ART) are increasingly employed, resulting in ~10-13 million births worldwide. However, gamete quality remains the largest barrier to ART success, driving advancements to bypass this limitation. This study aimed to analyse 30 years of ART data to examine key trends and industry shifts in infertility treatment.

Clinical data were extracted from publicly available annual reports and databases spanning 1991-2022, across 66 countries including Australia and New Zealand, Canada, Japan, Latin America, United Kingdom, United States, and Europe (subdivided into Central + Eastern, Northern, Southern, and Western regions). Patient demographics, treatment cycles, and outcomes were evaluated regionally and collectively to identify global trends.

Over three decades, global ART uptake rose from 3.0 to 23.0 cycles/10,000 inhabitants, totalling >29 million reported cycles. Among these cycles, striking shifts were observed in fertilisation procedures and oocyte/embryo preservation. IVF use declined 2.8-fold, while adoption of ICSI (intracytoplasmic sperm injection) escalated to comprise 69.9% of all fertilisations in 2022. This represents over double the number of ICSI fertilisations (2.4-fold higher) than those performed for male-factor infertility, the primary clinical indication for ICSI. From 2010, oocyte and embryo cryopreservation “freeze-all” cycles increased 6.1-fold, constituting 33.2% of cycles in 2022. Subsequently, thaw cycles (using cryopreserved eggs/embryos) overtook fresh cycles, comprising 41.2% of cycles in 2022.

This analysis highlights growing reliance on ART and shifting treatment paradigms, prioritising ICSI and cryopreservation to maximise patient success. These technologies may enable use of lower-quality gametes or exert additional cellular stressors, raising concerns about how short-term success impacts future offspring health trajectories. This study underscores the need to minimise excessive ICSI use, evaluate long-term cryopreservation safety, and strengthen ART reporting to encourage ethically responsible practices for improved global ART outcomes.

id #128162

Early-onset preeclamptic extracellular vesicles induce endothelium-dependent vascular dysfunction in spontaneously hypertensive rats

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Placental extracellular vesicles (pEVs) are known to cause endothelial cell activation in vitro[1] and are heavily implicated in the development of preeclampsia[2]. Early-onset preeclampsia is associated with postpartum arterial stiffness, microvascular dysfunction and chronic hypertension; however, it is unknown whether pEVs are responsible for these lingering vascular changes. This study aimed to evaluate the effects of pEVs on maternal vascular function in spontaneously hypertensive rats (SHRs).

pEVs were isolated from cultured human term-placenta explants from either normotensive (n=7) or early-onset preeclamptic pregnancies (n=5). Each rat received 5 intravenous injections (315 µg protein each) of EVs obtained from one placenta, between days 8-18 of pregnancy. Two weeks postpartum, the function of second and third-order mesenteric arteries were evaluated using wire myography.

Resistance arteries from SHRs that received pEVs from early-onset preeclamptic pregnancies were more responsive to the vasoconstrictor U46619, a thromboxane A_2 analogue, than vessels from the normotensive group (p<0.0001). There were no differences in vessel response to vasoconstrictors, phenylephrine or endothelin-1 (p=0.2735 and p=0.1590, respectively). Vessels from SHRs in the early-onset treatment group were less responsive to the vasodilator acetylcholine than the normotensive treatment group (p=0.0112). There was no difference in response to the vasodilator sodium nitroprusside (p=0.6215).

U46619 and acetylcholine both act on the vasculature in an endothelium-dependent manner. Whereas phenylephrine, endothelin-1 and sodium nitroprusside are endothelium-independent. These results suggest that preeclamptic pEVs interact with endothelial cells during pregnancy to produce lasting negative effects on the maternal vasculature. Ongoing effects of preeclamptic pEVs in early postpartum may be an indication of long-term changes to the maternal vasculature after a preeclamptic pregnancy. Further investigation will be required to establish whether EVs from preeclamptic placentae are, at least partly, responsible for the increased risk of vascular dysfunction and hypertension after pregnancy in women affected by early-onset preeclampsia.

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id #128418

Population snapshot: Exploring knowledge and consumption of sugar-sweetened beverages across audience segments to inform public health messaging

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The LiveLighter® healthy lifestyle program aims to motivate adults to adopt healthy eating habits. Funded by the Western Australian (WA) Department of Health and delivered by Cancer Council WA, LiveLighter® uses a TV-led integrated communications strategy to promote diet-related knowledge and behaviour aligned with this aim. This study examined these population-level outcomes related to sugar-sweetened beverages (SSBs) among key audience segments, to inform future campaign messaging.

A cross-sectional non-probability online survey of 754 WA adults aged 25-64, with population weighting, was undertaken in Nov/Dec 2024 following the LiveLighter® '13 Cancers' campaign, which focuses on reducing SSB consumption. Multivariable logistic regression assessed whether gender, age-group, body mass index (BMI), location (metro/regional), education, health care card and SSB consumption were differentially associated with SSB knowledge and behaviour.

Males (cf. females) and younger respondents (aged 25-34 cf. 35-64) reported higher intake of SSBs with males less likely to drink adequate water daily (p<0.05). Males also lacked confidence to reduce their SSB intake, despite being more concerned and to have contemplated the health risks (p<0.05). There was no difference in SSB intake by indicators of disadvantage (education, low income; p>0.05), while a low income was associated with less confidence and motivation to reduce consumption (p<0.05). In contrast, those with a higher body weight (cf. BMI<25) were more likely to report concern, urgency and intention to reduce their SSB consumption (p<0.05). Regional (cf. metropolitan) residents were more likely to choose a non-sugary drink (p<0.05).

Findings reveal males, younger respondents and SSB consumers would benefit from additional messaging about the health effects of drinking too many SSBs and the benefits of reduced consumption. Population-level messaging about SSBs that promotes self-efficacy through behavioural strategies should benefit all audience segments - especially people living with overweight - by helping them translate knowledge and intentions into reduced SSB consumption.

id #128674

Evaluating the feasibility of mental health screening in adolescents presenting for obesity treatment

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The aim of this study was to evaluate the feasibility of mental health screening in adolescents presenting to a tertiary weight management program.

This service improvement initiative included data collected between October 2022 to June 2025 from adolescents, 13-17 years, presenting to The Children's Hospital at Westmead multidisciplinary weight management program. Questionnaires were administered using an iPad, and included Rosenberg Self-Esteem Scale (scores 10-40), Severity Measure for Depression (scores 0-27; severe scores ≥20), Generalized Anxiety Disorder (scores 0-21; moderately severe/severe scores ≥15), Pediatric Quality of Life (scores 0-100), and Eating Disorder Examination Questionnaire (scores 0-6; cut-off ≥2.7). Caregivers completed Depression Anxiety Stress Scales (scores 0-42; severe scores: Depression ≥21, Anxiety ≥15, Stress ≥26). Descriptive statistics were reported as median (interquartile ranges, IQR), with cut-offs calculated using counts and percentages.

Of 98 adolescents who presented, 45 completed screening (47% female; 15% Aboriginal/Torres Strait Islander). The most common reasons for non-completion were telehealth integration barriers (n=25) and missed appointments (n=8). The median (IQR) score for self-esteem was 27.0 (3.0), quality of life 63 (33.7), depression symptoms 9.0 (10.0) with 20.5% scores ≥15, anxiety symptoms 6.5 (10.0) with 20.5% scores ≥15. For eating disorder risk, the score was 2.40 (1.7) with 41.9% scores ≥2.7, however, this cut-off is not well validated and should be cautiously interpreted. In caregivers, median score was 4.0 (10.0) for depression symptoms (5.4% scores ≥21), 4.0 (10.0) for anxiety symptoms (8.1% scores ≥16), and 10.0 (12.0) for stress symptoms (5.4% scores ≥26).

Half of adolescents presenting for weight management were unable to complete mental health screening. Barriers including telehealth integration must be addressed to facilitate screening. One in five adolescents presented with symptoms of depression or anxiety and 40% required further assessment for disordered eating. These results highlight the need for mental health screening to guide appropriate care pathways.

id #130979

RNA Processing factors as gatekeepers of mitochondrial Translation and metabolic integrity

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2. UWA/The Kids Institute, Nedlands, WA, Australia

Mitochondrial gene expression requires RNA processing and ribosome assembly to support oxidative phosphorylation. We investigated the hepatocyte-specific roles of MRPP3, the catalytic subunit of mitochondrial RNase P, and PTCD1, a pentatricopeptide repeat protein required for rRNA maturation. Liver-specific deletion of either factor caused early lethality with profound mitochondrial hepatopathy. Mechanistically, MRPP3 loss blocked tRNA processing, while PTCD1 loss destabilized 12S and 16S rRNAs, impairing mitoribosome biogenesis. Both knockouts abolished mitochondrial translation, depleting mtDNA-encoded OXPHOS subunits and

collapsing respiratory function. Proteomics revealed depletion of mitoribosomal proteins and compensatory induction of nuclear-encoded stress markers. Transcriptomics showed remodelling of oxidoreductase pathways, while metabolomics uncovered accumulation of amino acids and TCA intermediates, energy depletion, and altered bile acid metabolism, with evidence of compensatory anaplerotic flux. Together, these findings establish MRPP3 and PTCD1 as essential gatekeepers of mitochondrial translation and highlight how their loss drives metabolic collapse and organ-specific pathology.

id #128164

Socioeconomic differences in the cost-effectiveness of a telephone-based intervention for obesity prevention in early childhood

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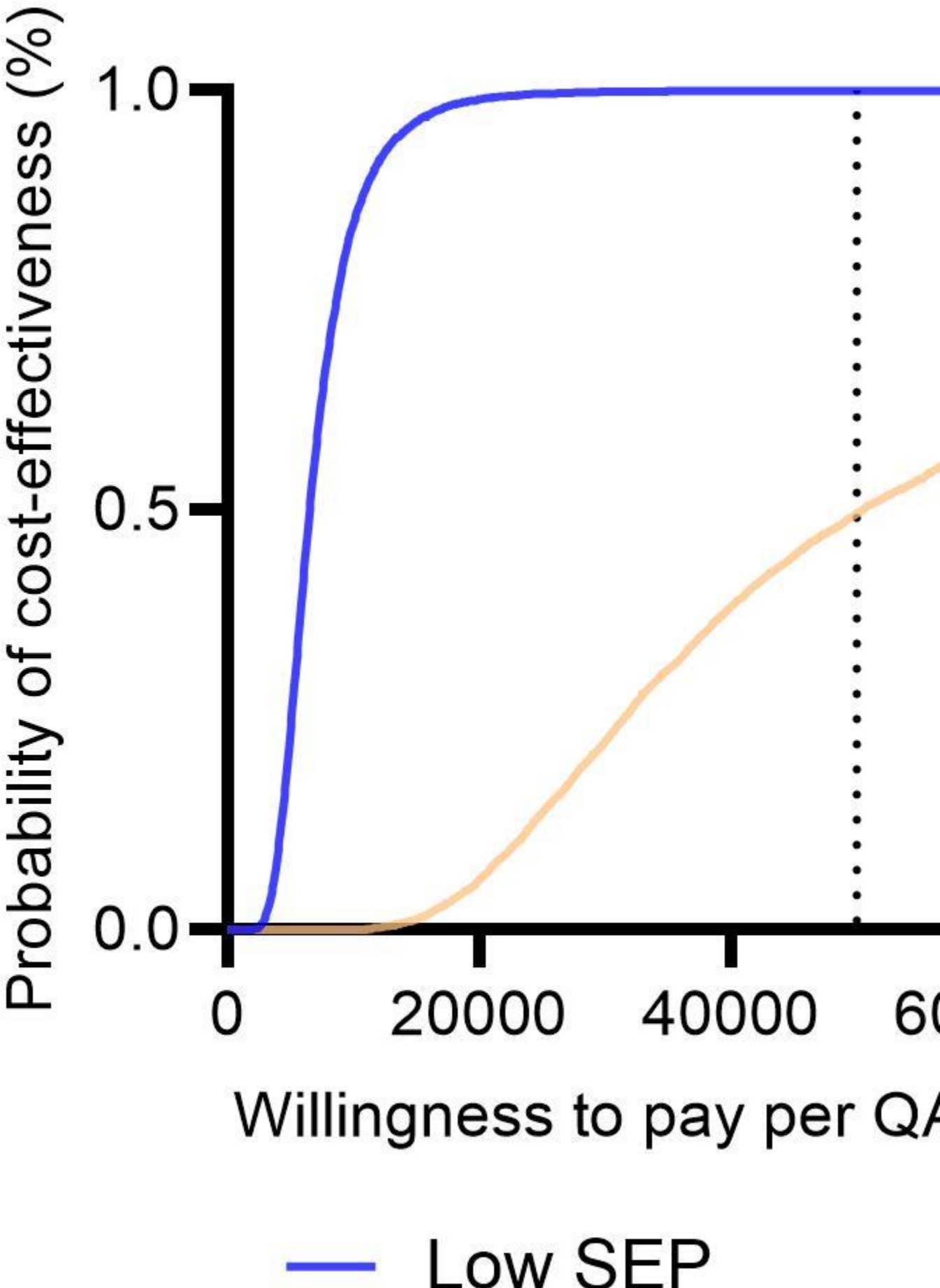
The aim of this study was to investigate in different socio-economic groups, the cost-effectiveness of an early childhood obesity prevention intervention providing telephone and short message service (SMS) support to mothers of children aged 2-4 years (1). Socio-economic position (SEP) was defined as high or low, based on annual household income. A modelled SEP-specific economic evaluation of the intervention was conducted, using a microsimulation model (2) to predict SEP-specific body-mass index (BMI) trajectories, prevalence of overweight and obesity, quality-adjusted life years (QALYs) and health care costs until 17 years of age. SEP-specific intervention costs and effects at age 5 years were derived from the trial data and applied to a cohort of 4- to 5-year-old Australian children. Incremental cost-effectiveness ratios (ICERs) and acceptability curves were derived for each SEP group, using 2023 Australian dollars.

The model predicted, at age 17 years, that the intervention could reduce overweight and obesity in the low SEP group from 58% to 40% and in the high SEP group from 52% to 49%. From an Australian health payer perspective, the ICERs for the low-SEP group were $131 per BMI unit avoided and $6,549 per QALY gained, compared to the high-SEP group at $1,161 per BMI unit avoided and $41,462 per QALY gained. Results were robust to sensitivity analyses varying the intervention effect size, intervention costs, healthcare costs, discount rate and disutility from overweight. The probability that the intervention was cost-effective at a willingness-to-pay threshold of $50,000 per QALY gained was extremely high in the low-SEP group (99.7%) and marginally cost-effective in the high-SEP group (49.6%) (Figure). The greater cost-effectiveness in the lower SEP group suggests that prioritizing families from socioeconomically disadvantaged backgrounds for this service will represent good value for money and may reduce healthy weight inequalities in childhood.


Probability of cost-effectiveness (%)
1.0
0.5
0.0
0
20000
40000
Willingness to pay per QA
Low SEP

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id #128676

Increase in serum copeptin following treatment of hyponatraemia with tolvaptan: Secondary analysis of an open-label, randomised, clinical trial

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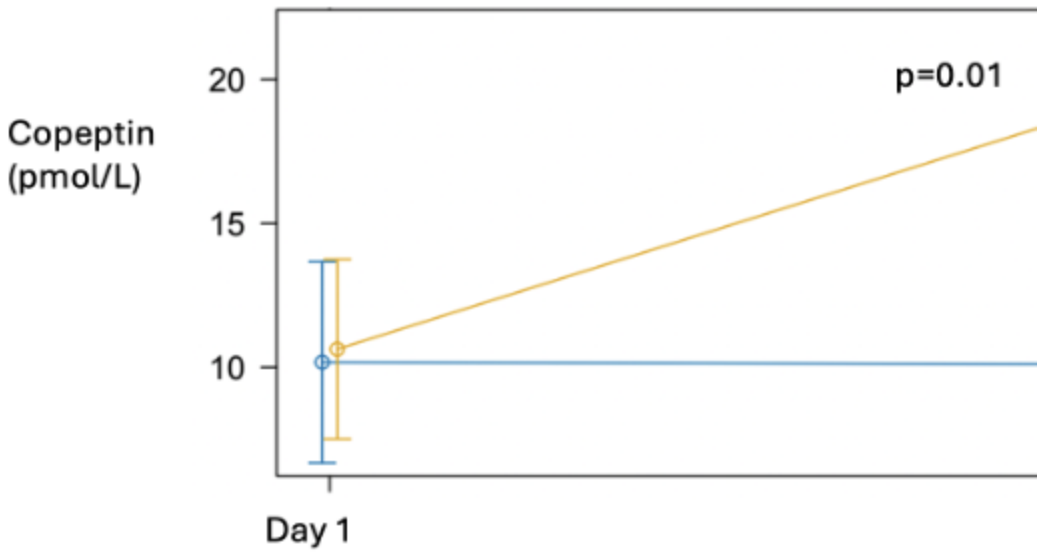
Hyponatraemia is a common electrolyte disorder with significant morbidity, often driven by excess arginine vasopressin(AVP)(1). Copeptin is co-secreted with AVP but more stable and easily measured. Copeptin is not routinely measured in hyponatraemia as it is not useful in differentiating between common causes(2). It is not known whether hyponatremia treatment impacts copeptin concentration, or whether higher baseline copeptin may be associated with risk of overcorrection of plasma sodium(pNa) in patients treated with tolvaptan, an AVP-V2 receptor antagonist.

We conducted a three-day, randomised, single-centre, open-label trial comparing two hyponatraemia therapies, Tolvaptan and Fluid Restriction(FR), in hospitalised patients with pNa 115-130mmol/L. Copeptin measurement was performed on Day 1 and Day 4 on frozen serum using the BRAHMS Copeptin proAVP Kryptor assay from Thermo Fisher Scientific at Northern Health Pathology, Victoria.

Fifty-four patients with mean pNa 123.8mmol/L were enrolled and randomised to tolvaptan (n=28) or FR (n=26). Serum copeptin was higher at baseline in participants randomised to tolvaptan (13.1 vs. 7.0pmol/L) by chance. Plasma sodium increased over 3 days in both arms, but significantly more with tolvaptan than FR (p.overall<0.001) as previously reported. Copeptin significantly increased in the tolvaptan group at Day 4, but remained stable with FR. The mean adjusted difference in copeptin between groups at Day 4 was 8.4pmol/L (95% CI 2.1-14.6,p=0.01)(**Fig 1**). There was no association between baseline copeptin concentration and rapid pNa rise, observed in 5 tolvaptan recipients.

Tolvaptan was associated with in an increase in serum copeptin that was not seen with fluid restriction, despite increased pNa in both groups. This suggests that AVP receptor blockade increased AVP production, but this did not compromise improvement in pNa. Contrary to expectation, higher baseline copeptin did not predict rapid pNa rise following tolvaptan. Further research is required to determine if there is clinical utility in measuring copeptin in hyponatraemia.

Figure 1: Serum copeptin at Day 1 and Day 4 (or discharge) in p
tolvaptan versus fluid restriction, with levelled baseline



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id #128423

Challenges and Pitfalls with Pituitary Dynamic Testing

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Dynamic endocrine testing plays a vital role in diagnosing pituitary and hormonal disorders. The Harmonisation of Endocrine Dynamic Testing in Adults (HEDTA), a joint initiative of ESA/AACB/RCPA, provides protocols to standardize these procedures and ensure reliable interpretation of test results. A specialised endocrine testing facility is crucial, particularly for evaluating complex pituitary conditions. Close collaboration between clinicians and laboratory services is essential to ensure proper patient preparation, sample handling and provision of timely and accurate results. Additionally, understanding differences in immunoassay methodology can support clinical decision making.

At Sir Charles Gairdner Hospital, all requests for synacthen stimulation test (SST) are referred to the Endocrinology Registrar or Chemical Pathology Registrar at PathWest Laboratory Medicine. Morning bookings are made for referrals from Specialists and ideally patients not on corticosteroid therapy. The Endocrinology Resident Medical Officer (RMO) supervises the testing.

Glucagon Stimulation Test (GST) is the investigation of choice for assessment of adult growth hormone deficiency. This is well tolerated and risk of hypoglycaemia is low. This procedure is supervised by the Endocrinology RMO in the Immunology Testing Unit. Insulin tolerance test is rarely performed.

The challenges and pitfalls associated with SST and GST will be highlighted in case-based discussion.

id #128679

Engineering potent anti-Müllerian hormone analogues for *in vivo* testing in female domestic cats

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Anti-Müllerian hormone (AMH) is a member of the transforming growth factor-β superfamily. In females, AMH is produced by the granulosa cells of small growing ovarian follicles, where it suppresses several stages of folliculogenesis. As such, AMH is considered an attractive therapeutic to address diverse reproductive needs, including fertility preservation and/or contraception. We set out to characterise the molecular mechanisms that govern the synthesis and activity of human AMH, to then generate potent analogues. By introducing an optimised furin cleavage site, we enhanced processing of the AMH precursor from <10% to >90%, corresponding with a dramatic increase in signalling activity. Based on species differences across the AMH type II receptor-binding interface, we introduced a series of double mutations ($Gln^{484}Met/Leu^{535}Thr$ or $Gln^{484}Met/Gly^{533}Ser$) into human AMH that enhanced potency 5- and 10-fold, respectively. Subsequently, we showed that similar mutations also enhanced the activity of murine and feline AMH.

As recent studies in mice and cats have indicated that AMH overexpression results in durable contraception; by preventing primordial follicle activation in mice and breeding-induced ovulation in cats, we envisaged that our potent AMH analogues would be more efficacious. Adeno-associated viral vector delivery to female cats increased serum AMH levels >1000-fold, with supraphysiological activity confirmed via ELISA and *ex vivo* signalling assays throughout 9 months of measurements. High serum AMH was associated with non-follicular ovarian cyst formation and a progressive decline in antral follicles, however, the few surviving large follicles continued to ovulate. As such, most cats conceived during a breeding trial, but none of the cats within the AMH overexpression group gave birth. Our findings highlight the complexity of AMH signalling on reproductive physiology.

id #128425

Metabolism and Reproduction – Beyond ATP

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When scientists consider metabolism and reproduction, their thoughts are drawn to energy balance and ATP synthesis. However, over the past decade our perception of the role of metabolites and co-factors as functional players in ATP formation and biosynthesis has shifted as they have been determined to be epigenetic regulators. This phenomenon, referred to as “Metaboloepigenetics”, is helping to elucidate how culture conditions and diet regulate preimplantation embryo development and viability.

Typically considered an end product of anaerobic glycolysis, lactic acid has been shown to have key roles in the initial phases of implantation, being involved in the breakdown of the endometrial extracellular matrix, the induction of angiogenesis, and modulation of local immune function through the formation of an “acid cloud” by the blastocyst, with both lactate and pH controlling events at peri-implantation. Lactic acid has also been shown to affect gene expression through a novel epigenetic modification of both histone and non-histone proteins, a process known as lactylation. NAD+, a key cofactor in the conversion of lactic acid to pyruvate, and whose cytosolic concentration is regulated by the ration of pyruvate:lactate in an embryo culture medium, also serves as a potent epigenetic regulator, being an activator of histone deacetylases (sirtuins).

Research on the impact of diet on gamete function and embryo development has focussed primarily on high fat/high sugar intake, but one of the fastest trending diets worldwide is the ketogenic diet (KD). Characterised by elevate levels of circulating ketone bodies (KBs; b hydroxybutyrate and acetoacetate), the KD has been shown to be effective in managing weight loss and even in the treatment of certain cancers. However, it transpires that KBs not only perturbs blastocyst metabolism, but also modifies histone acetylation leading to persistent female-specific alterations in fetal development. Other examples of metabolic regulation and their impact on embryo viability and the development of embryo culture systems will also be considered in the lecture.

id #128682

A Retrospective review of Radioactive Iodine Avidity in a Cohort of Patients with Oncoytic Thyroid Carcinoma; A Single Centre Review

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Oncocytic thyroid carcinoma (OTC), previously termed Hürthle cell carcinoma, represents 5% of all thyroid cancers. This follicular cell-derived neoplasm was recategorised as a distinct thyroid cancer subtype due to its unique molecular and pathologic characteristics. Clinical outcomes for OTC patients are worse than other forms of differentiated thyroid cancer (DTC). Widely invasive OTC subtype

has been shown to have extensive vascular invasion and OTC was found to be less radioactive iodine (RAI) avid than other forms of DTC.[1] RAI remains controversial in OTC and its utility is largely dependent on minimally or widely invasive phenotype.[2]

We conducted a retrospective study, reviewing our electronic records to assess the response to RAI in patients with an OTC diagnosis, treated at our quaternary referral centre.

Data analysis revealed 49 patients with a diagnosis of OTC between 2012-2020, who underwent treatment with RAI. Mean tumour size was 38.1 mm (8–110mm) with 81.6% (40/49) showing vascular invasion. Extra thyroidal extension was seen on histology in 7 cases(14.3%). 26 cases(53.0%) received 4GBq of RAI activity, with the remainder receiving either 1,2,6 or 8 GBq of RAI activity based on risk stratification. Initial RAI ablation in 45 cases showed only residual iodine uptake in the thyroid bed, the thyroglossal duct tract or was reported as physiologic uptake. Four cases (8.2%) showed focal uptake away from these sites. 3/45(6.7%) cases, had proven metastatic disease on imaging or histology, which was not RAI avid. Six cases received repeat RAI treatment due to a rising thyroglobulin or disease progression. None (0/6) of these cases showed any focal iodine uptake away from the thyroid bed, despite this progression.

Our data on patients with OTC shows high rates of vascular invasion, and a RAI-refractory profile. As has previously been suggested, OTC warrants tailored patient care that differs from that of other DTCs.[3]

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2. 2. Yang Q, Zhao Z, Zhong G, Jin A, Yu K. Effect of adjuvant radioactive iodine therapy on survival in rare oxyphilic subtype of thyroid cancer (Hürthle cell carcinoma). PeerJ. 2019;7:e7458.
3. 3. Bischoff LA, Ganly I, Fugazzola L, et al. Molecular alterations and comprehensive clinical management of oncocytic thyroid carcinoma: a review and multidisciplinary 2023 update. JAMA Otolaryngology–Head & Neck Surgery. 2024;150(3):265-272.

id #128683

Characteristics and treatment patterns of people with obesity and high cardiometabolic risk: An Australian chart review study

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Aims: Obesity is a prevalent chronic illness with high morbidity. Despite its prevalence, there are limited real-world insights on how people with obesity (PwO) are treated and managed. This study sought to understand obesity management in Australia.

Methods:A retrospective, multi-centre, web-based chart review was conducted with 27 Australian primary and specialist healthcare professionals (HCPs) involved in management of PwO in public and private clinics. HCPs provided deidentified, patient-level data for up to 5 PwO (Body Mass Index [BMI] ≥30 kg/m^2) with high cardiometabolic risk. Eligible patients first presented between 01 January 2022 - 31 December 2022, and attended for treatment on ≥3 occasions. Patient background and obesity treatment delivered as first, second and third line of therapy were collected.

Results: Data from 132 PwO were collected. Average age was 45.4 years (SD=12.2) and 54% were female. Mean BMI was 40.3 kg/m^2 (SD=7.7) and 45% of patients had a BMI ≥40 kg/m^2. Obesity-related conditions were prevalent, with 60% reporting hypertension, 58% dyslipidaemia, and 39% type 2 diabetes. More than 3 obesity-related conditions were reported for 75% of patients with a BMI ≥40 kg/m^2. Non-pharmacological intervention was received by 98% of PwO as first line treatment, 57% as second line and 34% as third line. Pharmacological intervention was received by 43% of PwO as first line treatment, 66% as second line and 55% as third line. Surgical intervention was received by 5% of PwO as first line treatment, 11% as second line and 34% as third line.

Conclusions: Australians with high cardiometabolic risk managed in obesity clinics had a very high BMI and multiple obesity-related conditions. Non-pharmacological intervention was prioritised as first line therapy, despite the high BMI and prevalence of obesity-related conditions in this cohort. There is a need for early, evidence-based, highly effective therapy to address the immense burden of obesity in Australia.

id #126892

TGFB1 in the follicular fluid play a role in DNA methylation and subsequent embryonic development

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Aims: Embryos produced in vitro are used in human assisted reproductive technology and animal industries. However, the quality and epigenetic landscape of these embryos differ from those of embryos collected from the uterus. Follicular fluid (FF) influences the oviduct and regulates its environment. In the present study, we examined the effects of short-term exposure of early-stage embryos to low concentration of FF

Methods: Experiment-1. In vitro-fertilized embryos were cultured with 1% FF from 18 to 48 h post-insemination (pi), and DNA methylation (5mC) and blastulation rates were examined. Experiment-2. Embryos treated with FF (48 h pi) were subjected to RNA-seq to predict upstream regulators. Experiment-3. 5mC and histone modifications were examined in TGFB1-treated embryos, which were then subjected to RNA-seq. Experiment-4. FF collected from individual cows was rated based on the concentration of TGFB1, and the effects of TGFB1-rich or -poor FF on 5mC and embryonic development were examined. Experiment-5. Granulosa cells corresponding to rich or poor FF were subjected to RNA-seq.

Results: Experiment-1. FF improved embryonic development and reduced the levels of 5mC in the 8-cell and blastocyst stages. Experiment-2. Differentially expressed genes (DEGs) revealed that TGFB1 was a significant upstream regulator. Experiment-3. TGFB1 reduced the levels of 5mC in the 8-cell and blastocyst stages, increased the levels of TET3 and H3K4me3, and decreased the levels of H3K9me3 in the 8-cell stage. Pathways enriched by DEGs included focal adhesion pathways. Experiment-4. TGFB1-rich FF improved embryonic development and reduced 5mC compared to poor FF. Experiment-5. DEGs of granulosa cells revealed that the top upstream regulator of rich FF granulosa cells was TGFB1.

Conclusion: TGFB1 plays a major role in follicle formation, induces DNA demethylation, and improvement of development.

id #127148

Feeding the Feed: How Social Media Shapes the Digital Food Environment for Young People

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Publish consent withheld

id #123053

Do wireless communication technologies pose a threat to male fertility?

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The societal benefits of wireless communications technologies are arguably only outshined by their absolute presence in our modern environment. The electromagnetic energy medium used to communicate mindboggling magnitudes of digital data, is also a very new physical exposure for biology. Ever-present exposures, coupled with our naive biology have given rise to concerns about the potential safety of such technologies, concerns which are further amplified by gaps in our biophysical understanding of how this non-ionising energy may interact with our health. These concerns extend a spotlight on the externalised parts of the male reproductive tract which may be subject to higher rates of exposure, and coupled with the inherent vulnerabilities of the spermatozoon, the influence of wireless communication on male fertility is a central part of the debate. In a controversial field, we and others have shown that even at moderate levels of exposure across both animal models and those applied directly to spermatozoa, there are clear effects on fertility potential. Here we present an overview of the molecular impacts of wireless communication electromagnetic energies on spermatozoa which are tightly linked to hallmarks of oxidative stress. While this depth of understanding is a key step toward assessing the risk on male fertility, these data also provide a rational for elucidating the potential mechanisms of how such a low energy factor may interact with our health more generally.

id #128173

Faecal Microbiome Transplantation From Rats Fed High-Fat, High-Sugar Diets Do Not Impair Spatial Memory In Rats Fed Healthy Chow.

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Aims: High-fat, high-sugar diets are associated with impaired cognitive function and altered gut microbiome composition. Research on the 'gut-brain axis' indicates that specific microbial taxa and metabolites in the gut can alter behaviour and brain function. However, whether diet-induced alterations of the gut microbiome directly cause cognitive impairments remains unclear. This experiment investigated the mechanistic relationship between diet-induced changes in gut microbiota and cognitive outcomes using faecal microbiota transplantation (FMT).

Method: Adult male Sprague-Dawley donor rats were fed a healthy chow or high-fat, high-sugar 'Cafeteria' (CAF) diet for 12 weeks. Faecal samples were collected from individual donor rats, processed anaerobically, and frozen for later use in FMT. Recipient rats were fed chow throughout experimental procedures. Chow-fed recipient rats were treated with antibiotics to deplete the endogenous microbiome and subsequently received FMT from chow (Chow-FMT, n = 18) or CAF-fed (CAF-FMT; n =18) donors over 3 weeks (oral gavage 3x/wk).

Results: CAF-fed donor rats showed significantly increased body weight, adiposity and blood glucose, impaired spatial memory and

altered microbiome composition. In recipient rats, no significant changes in short-term memory (place and object recognition tests) were observed across FMT with performance intact in both groups, despite differences in recipient microbiome composition. Conclusions: Results suggest that high-fat high-sugar diet-induced cognitive impairment are not driven by altered microbiota composition. Further work is needed to explore potential protective effects of the chow diet fed to recipient rats, which may select for specific microbial strains provided during FMT.

id #128685

Molecular Insights into Ovine GDF9 and BMP15 *Fec* Mutations

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Publish consent withheld

id #127919

Centrosomes and cilia require delta tubulin during embryonic development

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2. Australian Regenerative Medicine Institute, Monash Univeristy, Clayton, Victoria, Australia

Centrioles are the core structural component of centrosomal microtubule organising centres and are essential for cell division, differentiation, and maturation during mammalian embryogenesis. Delta tubulin has been implicated in the stability of centriole triplet microtubules in unicellular species (1) and is required for mammalian spermatogenesis (2), but its *in vivo* role during early embryogenesis has remained unknown. Herein, we leveraged the process of *de novo* centriole formation in mouse embryos to examine the function of delta tubulin at centrosomal and non-centrosomal microtubule organising centres.

Through creation of a whole-body knockout mouse model of its gene, *Tubd1*, we reveal that delta tubulin gradually localises to the developing mouse centrosome at blastocyst stages ($p = 0.0028$) and is essential for early embryogenesis. Loss of delta tubulin function leads to developmental arrest and embryonic lethality at mid-gestation and importantly, the function of other tubulin proteins (alpha, beta, gamma, epsilon) cannot compensate for its absence. We identify a 91.4% reduction in centrosome number within delta tubulin knockout embryos ($p < 0.0001$) and a complete absence of cilia. Moreover, we show that delta tubulin is needed for the progression and completion of centrosome-dependent mitosis during post-implantation development. Lastly, we reveal that delta tubulin's function is restricted to the centrosome and that non-centrosomal microtubule structures are not perturbed in its absence. This work provides a necessary insight into delta tubulin's cellular function, enhances the understanding of how abnormalities within the microtubule cytoskeleton contribute to defects in early embryogenesis and may inform tubulinopathies and ciliopathies associated with various disease manifestations.

1. 1. E. T. O'Toole et al., Three-dimensional organization of basal bodies from wild-type and delta-tubulin deletion strains of Chlamydomonas reinhardtii. Mol. Biol. Cell 14, 2999-3012 (2003).
2. 2. G. G. Stathatos et al., Delta tubulin stabilizes male meiotic kinetochores and aids microtubule remodeling and fertility. J. Cell Biol. 224 (2025).

id #128431

Common herbal fertility supplements disrupt central carbon metabolism and nucleotide signalling pathways in Sertoli and Leydig cells

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This study aimed to investigate the changes to metabolism, nucleotide signalling and oestrogen concentration that occur in the Leydig and Sertoli cells of the testes after exposure to herbs commonly included in 'fertility' supplements.

Murine Leydig and Sertoli cells were cultured with 0.1 or 1.0 mg/mL ginseng, maca or green tea extract (GTE), or selected ginsenosides (Rg1 and Compound K [100 mM]) or catechins ((-)-epicatechin, (+)-catechin hydrate, (-)-epigallocatechin gallate and (-)-epigallocatechin [80 mM]) for 48 h. Cells were separated from the culture media, and intracellular concentrations of the nucleotides cyclic adenosine monophosphate (cAMP) and cyclic guanosine monophosphate (cGMP), and of 17-b-oestradiol were measured using enzyme-linked immunosorbent assay (ELISA). Cells exposed to ginseng, maca or GTE also underwent untargeted metabolomics analysis, using gas chromatography-mass spectrometry (GC-MS), to assess changes to the metabolome.

cAMP, cGMP and 17-b-oestradiol concentrations were altered from controls in both cell types after some of the treatments, in some cases several-hundred-fold higher. Marked changes to sugars, amino acids and metabolic intermediates, including several involved in the tricarboxylic acid (TCA) cycle, were also observed. These results indicate that disruption to energy metabolism, nucleotide signalling and hormone regulation may occur with use of these supplements. Dietary supplement and herbal medicine use is widespread in Australia, and ginseng, maca and GTE are popular ingredients in those marketed for fertility but also weight loss,

immune and general ‘wellbeing’ products. These products should be used with caution until the translational relevance of this in vitro analysis is further elucidated.

id #128687

ANZ interdisciplinary survey of non-functioning pituitary adenoma management: areas of variability and common practice

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2. University of Adelaide, Adelaide, SA, Australia

3. Radiation Oncology, Central Adelaide Local Health Network, Adelaide, SA, Australia

4. Rhinology, Central Adelaide Local Health Network, Adelaide, SA, Australia

5. Neurosurgery, Central Adelaide Local Health Network, Adelaide, SA, Australia

6. Endocrinology, Waikato Hospital, Waikato, New Zealand

7. Endocrinology, Wellington Regional Hospital, Wellington, New Zealand

8. Endocrine and Metabolic Unit, Central Adelaide Local Health Network, Adelaide, SA, Australia

Aim:

To determine ‘real-world’ current practices in NFPA investigation and management across Australia and New Zealand (ANZ), comparing to the recent consensus guidelines from the Pituitary Society on pituitary incidentalomas and helping guide future initiatives.

Methods:

An anonymous online survey comprising four clinical scenarios (23 questions total) was disseminated to ANZ consultant endocrinologists, neurosurgeons and rhinologists via the ANZRS, ANZSB, ESA, NSA and NZSE.

Results:

99 endocrinologists and 25 surgeons (11 neurosurgeons, 14 rhinologists) across ANZ responded (Fig.1).

In relation to intrasellar microadenomas:

- Gadolinium was requested for MRI assessment by 66% of all responders[#]
- Hormonal evaluation included cortisol, FSH, LH, androgens (for males), TSH, fT4, prolactin and IGF-1 by > 90% of endocrinologists. ACTH was requested by 61%[#] (Fig.2)
- Growth hormone was regularly requested (87% surgeons vs 42% endocrinologists)*[#]
- Repeat MRI evaluation was requested at 2+ years by 6% of total responders[#]
- Surgeons requested formal visual field testing more frequently (52%[#] vs 19%)*

For asymptomatic macroadenomas clear of the optic chiasm:

- 16% of all responders organised repeat imaging at 12 months[#]

For macroadenomas with associated visual deficit:

- Surgeons referred more often for MDT evaluation (72% vs 47%[#])*
- Cortisol was most consistently checked day 3 post op
- Full post operative hormonal evaluation was performed at 4-6 weeks (46% surgeons vs 89% endocrinologists)*
- Repeat was most commonly requested 3 months post operatively (64% surgeons vs 39% endocrinologists)*

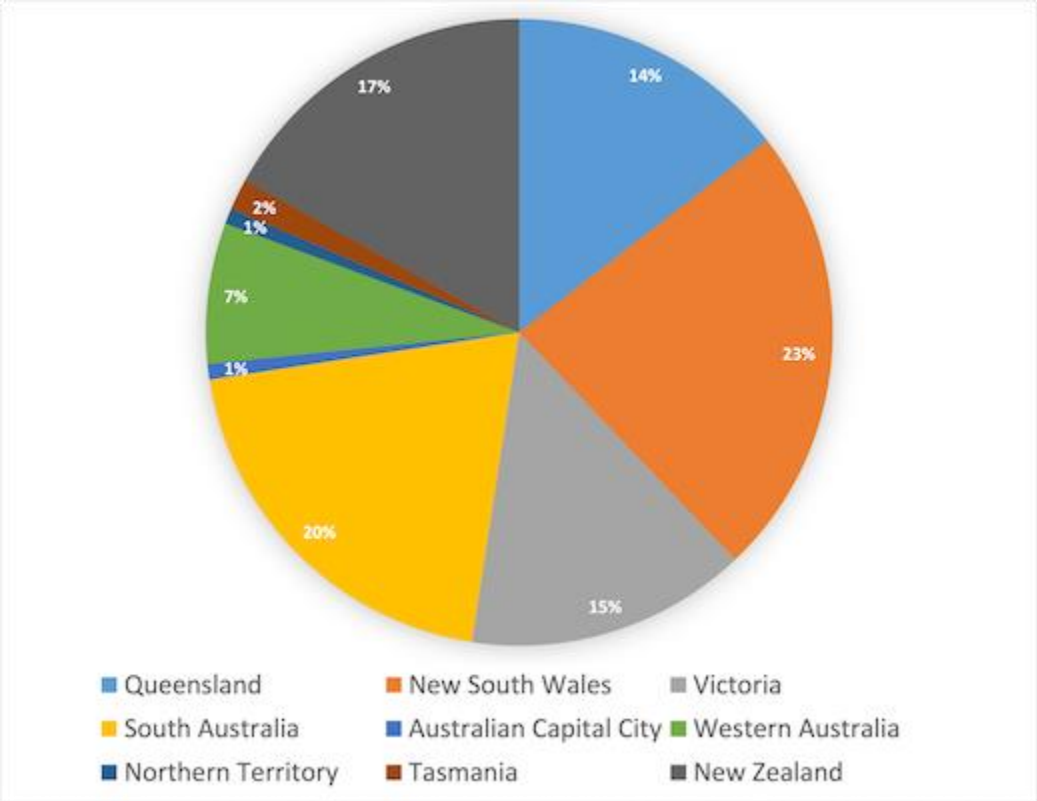
Statistically significant variability also existed between endocrinologists who attended regular pituitary MDTs and MDT clinics vs general endocrinologists.

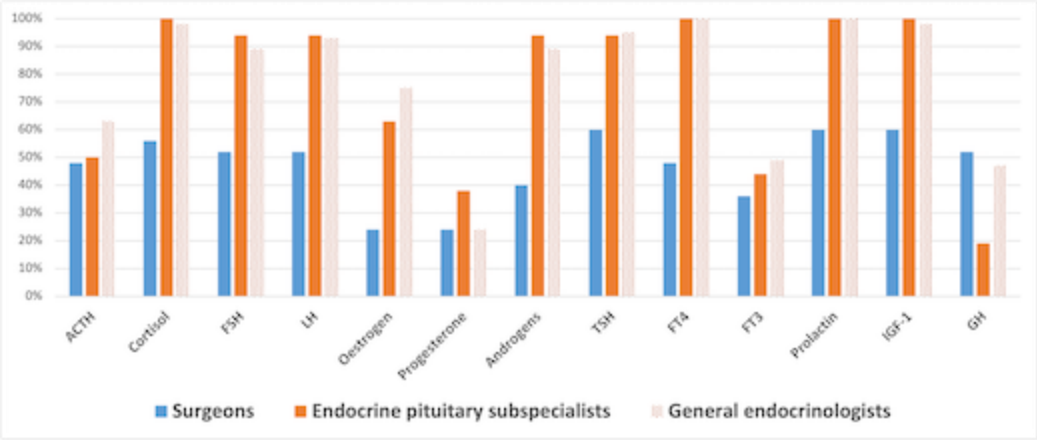
[#] Areas of discordance with consensus recommendations

* Areas with statistically significant differences between specialists

Conclusions:

This large survey dataset (*n*=124) identifies areas of deviation and concordance in real-world practice from recent guidelines, highlighting areas for improvement as well as unmet needs within current recommendations.





id #128943

Insights from 35 years of the Raine Study; Metabolic and Endocrine Influences on male infertility.

Roger Hart[1]

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The Raine Study was commenced in 1990 as a long term follow up of children who underwent serial ultrasound examinations *in-utero.* These children have been followed-up as part of the Generation 2 Raine cohort. The men underwent a full reproductive assessment at aged 21 years of age and are currently undergoing a reproductive assessment at 33-35 years of age. This data will not be available for presentation as data collection is not complete. The focus of this talk will be the early life influences on male reproductive function when they were assessed at 21 years of age. They underwent hormone assessment, testicular ultrasound examination and a detailed semen analysis.

id #128688

Barriers and enablers to assisted reproduction in Aotearoa New Zealand: a Pacific perspective.

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Infertility is increasing amongst Pacific peoples in Aotearoa New Zealand (NZ), however the rate of access to assisted reproductive technologies (ART) and fertility services remains low within this community. The decision to access ART services is complex. For some Pacific people, ART is a foreign technology that sits in direct opposition with their religious beliefs and cultural norms. For others, ART is a blessing from God and represents a chance to start their own family – to receive the 'gift' of a child.

We wanted to explore the varied perspectives of Pacific people who had experienced infertility or accessed ART. Over a year, we facilitated talanoa (qualitative Pacific research method, meaning 'mutual conversation') with Pacific people (N=18) to understand the barriers and enablers to accessing ART services. As a Pacific research team, we were also guided by epistemological frameworks that allowed us to respond to cultural nuances in the talanoa environment.

Participants emphasised an overwhelming desire for children and this allowed them to endure tumultuous journeys through infertility. Unsurprisingly, their family and church community were central supports and enablers for ART access. However, family and religion could also be the greatest barriers to accessing ART services and contributed to feelings of isolation and fear. Clinical experiences were also highly varied which indicates a clear need for standardised and culturally-competent clinical care.

These insights allow us to identify opportunities to better engage with, and support Pacific peoples experiencing infertility and accessing ART. Given the role that Pacific health professionals play as trusted sources of information within Pacific communities, we are currently recruiting Pacific health professionals for talanoa to tease apart the challenges that Pacific peoples face in fertility care.

This research was support by a Health Research Council of New Zealand - Pacific Project Grant (23/348) awarded to ZLC and EF.

id #128944

The influence of obesity on female fertility

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As well as having significant impact on maternal and neonatal outcomes for women when pregnant, obesity has a negative impact on the ability to conceive naturally, fertility outcomes when they embark on fertility treatment and the woman's risk of miscarriage. This talk will discuss this in detail, including discussing the positive impact of weight loss strategies.

id #128177

The development of nanoparticle technology to regulate endocrine systems

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Reproduction and fertility rely on endocrine hormones. Treatments for endocrine dysfunction involve pharmacological agents to regulate hormone production or action, but many involve off-target effects, the need for long-term use and close clinical monitoring. We aimed to develop novel gene delivery systems that specifically target endocrine cells to safely and efficiently modulate endogenous *in vivo* hormone production. Our team has developed nanoparticle-based, endocrine-targeting technologies and validated them in mice. We have validated the following components: 1) An ionisable lipid nanoparticle sphere that encapsulates a DNA payload. The nanoparticles are made from FDA-approved excipients and are low-immunogenic and of a customisable, uniform size. They are rapidly synthesised on a platform that can be scaled for clinical translation. They are administered via intraperitoneal injection and are highly stable in circulation. Once the nanoparticles reach their target cell, they cross the plasma membrane, and the DNA payload is released. The nanoparticles can carry large (up to 14 kb) genetic payloads. 2) The nanoparticle surface can be coated with targeting peptides that bind to an extracellular receptor on the target cell to customise cell-specificity. 3) The DNA payload can be further customised for specificity by the inclusion of a cell-specific promoter. 4) The DNA payload can be customised to drive (cDNA) or suppress (shRNA, miRNA) gene expression in the target cell. Finally, we have administered this system to mice to target the adrenal and testis and have demonstrated its ability to drive changes in hormone production. We conclude this customisable system can be used to rapidly generate transgenic models from adult wildtype mice within 4-8 weeks, with an 85-90% cost reduction compared to traditional transgenic lines, and with significant advantages for animal welfare. This technology offers a myriad of opportunities to regulate or treat endocrine and reproductive disorders with a clear clinical needs-gap.

id #128689

Evolving morbidities and transition challenges for survivors of childhood posterior fossa tumours

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2. Stem Cells and Development, Monash Biomedicine Discovery Institute, and Department of Anatomy and Developmental Biology, Monash University, Clayton, Victoria, Australia

3. Peter MacCallum Cancer Centre, Parkville, Victoria, 3052

4. Department of Paediatric Endocrinology & Diabetes, Monash Children's Hospital, Clayton, Victoria, 3168

5. Department of Endocrinology & Diabetes, Royal Children's Hospital Melbourne, Parkville, Victoria, 3052

6. Murdoch Children's Research Institute, Parkville, Victoria, 3052

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Aims

Medulloblastoma and ependymoma comprise the commonest childhood infratentorial malignancies. Most patients receive cranial/craniospinal irradiation, surgery, plus combination chemotherapy. Sequelae include multiple pituitary hormone deficiencies, disinhibition of hypothalamic restraint on puberty, risks of thyroid malignancy, reduced fertility, neurocognitive impairment, and later second malignant neoplasms (SMN). Care is usually undertaken in tertiary survivorship clinics, but awareness of complications and their management is increasingly important for clinicians outside this setting. We aimed to characterise long-term outcomes and identify unmet needs in patients treated for posterior fossa malignancies in childhood or adolescence.

Methods

Audit of long-term health outcomes for 136 patients with medulloblastoma (N=106) or ependymoma (N=30) treated at the Royal Children's Hospital and Peter MacCallum Cancer Centre, referred to endocrinology 1980-2025.

Results

Amongst 118 5-year survivors, most developed ≥1 pituitary hormone deficiencies. Growth hormone (GH) deficiency occurred in 55; significant functional benefits were reported by 25/27 treated in adulthood. TSH and ACTH deficiency were frequently reported. In females, primary ovarian insufficiency (32) manifested as pubertal failure/arrest, or post-pubertal failure. In males, biochemical evidence of impaired fertility was frequent and oligoazoospermia observed on semen analysis; 10 required treatment for androgen deficiency. Malignancy was found in 17/39 patients who developed thyroid nodules. Other SMN occurred in 16, most commonly sarcomas, high-grade gliomas, haematologic malignancies and skin cancers (4); 10 developed meningiomas and 9, bowel polyps. 10 patients had strokes. Educational outcomes were poorer than the general population; many patients derived self-reported benefits from low-dose stimulant therapy (34/37).

Conclusions

We report a high burden of complex and evolving morbidity requiring multidisciplinary care and life-long surveillance, underlining the need to educate and support adult practitioners caring for these patients. Additionally, our data suggests that adult GH replacement and the use of stimulants may significantly improve neurocognitive function and quality of life.

id #128434

Identification of biomarkers in breastmilk associated with risk of lactational mastitis

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Aims

Lactational mastitis is a common inflammatory breast condition affecting 1 in 5 women within the first six months postpartum [1]. Although the presence of pathogenic bacteria can be a feature of mastitis, research suggests the host inflammatory response is a key determinant of disease [2]. Women with a past history of mastitis are at increased risk of experiencing another episode, and we hypothesised that there may be factors in breastmilk that increases risk of inflammation [3]. This research aimed to identify proteins in breastmilk associated with mastitis risk and investigate how these might affect immune signalling.

Methods

Breastmilk samples were collected from multiparous healthy women with full-term infants, stratified into high-risk (n=20) and low-risk (n=20) of mastitis based on past history of mastitis whilst feeding a previous infant. Samples were collected at week 2 and week 8 postpartum, proteins were identified and quantified using mass spectrometry and validated with ELISA. The impact of breastmilk on immune cell activity was investigated using the RAW264.7 mouse macrophage cell line.

Results

Using data-independent acquisition proteomic analysis, 36 proteins were differentially expressed between the high- and low-risk mastitis groups. Several upregulated proteins are associated with immune regulation. Macrophage migration inhibitory factor is a pleiotropic proinflammatory cytokine and was validated by ELISA to be upregulated 1.6-fold in breastmilk from high-risk mastitis breastmilk (p=0.035). Immunoglobulin kappa was also significantly upregulated (3.6-fold) and confirmed by ELISA (p=0.039).

Breastmilk from high-risk women upregulated expression of proinflammatory chemokine C-C motif ligand 2 (CCL2) in macrophages compared to low-risk breastmilk (p=0.049).

Conclusion

Increased abundance of proteins associated with inflammation in the breastmilk of healthy women with a past history of mastitis suggests that host factors could in part be responsible for mastitis. This research provides new opportunities to identify women at risk of mastitis and develop new treatment options.

id #128690

Unravelling the fate of paternal mitochondria during mammalian development

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The uniparental inheritance of mtDNA is an evolutionary conserved feature in mammals. One of the key drivers of uniparental inheritance is to prevent the coexistence of two different mtDNA haplotypes within offspring, or *heteroplasmy,* a state that can compromise overall organismal fitness. As such, safeguarding uniparental inheritance involves a biased transmission towards maternal mitochondria and the selective elimination of paternal mitochondria. The mechanisms surrounding the elimination of paternal mitochondria comprises mtDNA elimination during spermatogenesis, followed by selective removal of paternal mitochondria during early embryo development. However, the underlying molecular mechanisms that govern uniparental inheritance, and more importantly how paternal mitochondria are eliminated remains unclear. To investigate these questions, we use a combination of molecular biology and imaging techniques. We show in mice that mtDNA gradually decreases between the spermatocyte and round spermatid stages of spermatogenesis. As a consequence, mature spermatozoa isolated from the epididymis harbour mitochondria lacking intact mtDNA. Consistent with recent findings, the decline in mtDNA correlates with the loss of a major mtDNA-binding protein, mitochondrial transcription factor A (TFAM) from the mitochondria. After fertilisation, sperm mitochondria are gradually degraded throughout early embryo development and are largely undetectable by blastocyst stage. We show that this process is regulated by mitochondrial fission factor, Dynamin-related protein 1 (Drp1), as evident by a delay in the degradation of sperm mitochondria in Drp1 knockout oocytes. Further studies are in progress to understand how mtDNA are degraded during spermatogenesis, and whether the selective elimination of sperm paternal mitochondria during embryo development is of physiological significance.

id #128438

New generation antiplatelet agent prasugrel upregulates antioxidant and reduces anti-angiogenic pathways in primary human first trimester placenta

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Preeclampsia is a serious obstetric complication, and a leading cause of maternal and neonatal death. Aspirin, an old antiplatelet agent has been found to have limited prophylactic effectiveness. We identified that new generation antiplatelet agents, clopidogrel, prasugrel and ticagrelor mitigate key aspects of preeclampsia pathogenesis, including enhancing antioxidant cytoprotective pathways and downregulating anti-angiogenic factors in term placenta. Here, we specifically evaluate the safety of these agents in first trimester placenta, and their effect on key antioxidant and anti-angiogenic pathways in early placental development.

First trimester placental tissue was collected at surgical termination of pregnancy (6-13 weeks' gestation). Placental explants and isolated cytotrophoblast cells were treated with 100μM Aspirin, 1-100μM clopidogrel, 1-100μM prasugrel, or 0.5-25μM Ticagrelor for 48h. Cytotrophoblast viability was measured via MTS assay. Regulation of NRF2 pathway antioxidants (GCLC, HO-1, NQO1, TXN) and anti-angiogenic soluble fms-like tyrosine kinase (sFLT1) were assessed (qPCR/ELISA). Placental villous tips (2-3mm) were plated on collagen, treated for 72h, and outgrowth assessed.

Cytotrophoblast viability was unaltered with aspirin, prasugrel and ticagrelor treatment, but 100μM clopidogrel reduced cell viability (n=5; thus excluded from further studies). Prasugrel (100μM) increased NQO1 expression in explant tissue (n=4), and increased cytotrophoblast expression of GCLC, HMOX-1, NQO1, and TXN, while decreasing sFLT1 secretion (n=3). Ticagrelor reduced cytotrophoblast NQO1 expression. However aspirin, clopidogrel and ticagrelor did not alter other antioxidant genes nor sFLT1 secretion in either tissue or cytotrophoblast cells. Treatment with antiplatelet agents did not impair first trimester villous outgrowth compared to control; further studies are underway to determine whether treatment affected specific cellular proliferation, differentiation and outgrowth.

Collectively these data demonstrate prasugrel safety in early placental tissue, and its potential to enhance cytoprotective antioxidant pathways that will mitigate early placental dysfunction associated with preeclampsia. These data are essential to progressing prasugrel to clinical trials to prevent preeclampsia.

id #128695

Liraglutide ameliorates pathogenic changes in cardiac tissue proteins in female mice of reproductive age

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Background: Obesity increases the risk of cardiovascular disease among women of reproductive age, highlighting the need for intervention strategies to address this understudied population. GLP-1 receptor agonists, such as liraglutide, are effective therapeutic options for weight reduction, yet their cardiovascular impacts in women of reproductive age remain understudied.

Aim: To employ untargeted proteomic analysis to characterise the protein differences in cardiac tissue in female mice of reproductive age, exposed to an obesogenic environment.

Methods: 6-week-old female C57BL/6 mice were allocated to either a high-fat-diet (HFD) or chow-diet (CHOW). After 8-weeks, the HFD-fed group was further randomised to receive subcutaneous injections of liraglutide (LIRA), 0.3mg/kg daily, or matched saline. Mice were sacrificed after 4-weeks of treatment with LIRA or saline and the hearts were perfused with phosphate buffered saline before being snap frozen whole. After homogenisation and sample preparation, proteomic analysis was completed on cardiac tissue using data-dependant acquisition, liquid chromatography mass spectrometry. Statistical analysis was completed in Spectronaught and R.

Results: In total 46 proteins were significantly different between the HFD and CHOW groups. Of these 37 were upregulated, and 9 were downregulated (Adj.p<0.05). Immunoglobulin-heavy-constant-gamma 3 was 1.6-fold lower in HFD vs both CHOW and LIRA (p<0.05). Both Immunoglobulin-heavy-constant-gamma 2C and Immunoglobulin-heavy-variable 1-77 were >2-fold higher in HFD vs both CHOW and LIRA (Adj.p<0.05). Furthermore, 32 proteins that were significantly different between CHOW and HFD were not significantly different in the LIRA group compared to CHOW or HFD suggesting some level of amelioration. These proteins were significantly associated with the regulation of triglyceride metabolic process (p<0.05).

Conclusion: Our findings indicate that 4-weeks treatment with liraglutide modulates specific protein expression, indicating potential mechanisms for its cardiometabolic benefits. Given the heightened cardiovascular risk in women of reproductive age with obesity, further study of GLP-1 receptor agonists in this group is warranted.

id #129207

Cost-Effectiveness of Subtyping Primary Aldosteronism using Predictive Algorithms: a Markov Model Analysis

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Publish consent withheld

id #128440

The weighty topic of obesity and health impacts diet and exercise impacts in the context of metabolic dysfunction-associated steatotic liver disease MASLD

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The diagnostic criteria for MASLD has evolved to incorporate the definition of hepatic steatosis with inclusion of cardiometabolic risk factors. Current management guidelines recommend lifestyle interventions, such as dietary changes and increased physical activity, supported by a multidisciplinary team (MDT). However, real-world data on the effectiveness of MDT-led care for MASLD remains limited, despite the growing prevalence of MASLD alongside rising obesity rates. This study aimed to evaluate the impact of multidisciplinary input, including dietetics and an exercise physiologist support, on MASLD and its associated biochemical markers. A retrospective cohort study was conducted on patients presented for weight excess management under endocrinology, with access to multidisciplinary care. Inclusion criteria required evidence of hepatic steatosis and at least one cardiometabolic risk factor (elevated BMI, HbA1c, hypertension, or dyslipidaemia). Outcomes were assessed before and after a minimum of six months of MDT involvement, focusing on changes in liver ultrasound, weight, HbA1c, and fasting lipid profile. In a total of 50 patients, 21 received MDT input: all saw a dietitian, 17 consulted an EP, and 5 met with a bariatric surgeon. Fifteen patients attended more than one follow-up session for both diet and exercise. Participants with MDT input experienced greater weight reductions (115.54kg to 100.07kg, change of 15.48kg; p=0.01) and BMI (41.26kg/m² to 36.00kg/m², change of 5.27kg/m²; p= 0.02). While HbA1c improvement was smaller in the MDT group (6.21% to 5.81%, change of 0.39%; p=0.22), reductions in hepatic steatosis grading were greater (2 to 1.56, change of 0.44; p=0.61). Our findings support the value of structured MDT care in achieving meaningful clinical improvements in MASLD. Longitudinal patient engagement appears key, highlighting the importance of integrating MASLD management into broader obesity and metabolic health strategies.

id #128441

Clues to the underlying pathophysiology of low-renin hypertension using steroid profiling

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Publish consent withheld

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id #129209

An observational study on the use of semaglutide in type 1 diabetes

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Obesity and being overweight are common in patients with type 1 diabetes mellitus (T1DM), which contributes to multiple cardiometabolic complications (1,2). Adjunct therapies used in type 2 diabetes, including GLP-1 receptor agonists, have shown promise in T1DM (3). Limited data exist on the specific impact of semaglutide in this population (1,2). The aim of this study was to examine the effect of semaglutide use on glycaemic control as measured by HbA1c and time in range [blood glucose level 3.9-10 mmol/L] on continuous glucose monitoring (CGM), body weight and body mass index (BMI).

We conducted a retrospective review of medical records from patients with T1DM treated with semaglutide for a minimum of 3 months during endocrinology consultations at Royal North Shore Hospital. Patient age, duration of diabetes, HbA1c, weight, BMI, BP and fasting lipid profile within 3 months prior to semaglutide initiation and within 3 months after date of follow up were collected. CGM metrics from two weeks before semaglutide initiation and before the follow-up appointment were analysed.

23 individuals were included, with mean age 50 +/- 14 years, weight 92.1 +/- 14.4kg, BMI 33.7 +/- 5.2 kg/m^2, HbA1c 8.1 +/- 1.3% and SBP 132 +/- 12.1mmHg, with mean duration of semaglutide use 204.7 +/- 107.1 days. Semaglutide was associated with a significant reduction in body weight (mean change 6.72 +/- SE 4.4kg), BMI (mean change 2.5 +/- SE 1.6), HbA1c (mean change 0.53 +/- SE 0.36), and systolic blood pressure (12.5 +/- SE 3.6 mmHg) sustained for over six months. CGM data showed a reduction in time spent above range. There was a reduction in total cholesterol and LDL-C. No severe hypoglycaemia, diabetic ketoacidosis (DKA) or hospital admissions were reported.

Semaglutide was safe and effective in patients with T1DM and obesity, improving glycaemic control and cardiometabolic markers without increased complications.

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id #127675

Mapping the effects of chronic and acute activin A elevation on spermatogonial fate throughout life: implications for male fertility

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This study addresses the hypothesis that the risk of developing testicular cancer and/or male infertility is heightened by exposure to elevated activin A (AA), which occurs in pathological conditions throughout life (pre-eclampsia[1], infections[2], cachexia[3]). AA influences somatic and germ cell proliferation and viability, limits steroid production, and governs somatic cell differentiation in fetal mouse testes[4,5,6,7]. Here we examine AA cell-specific actions in fetal, neonate and adult testes, and highlight consequences for germ cell development.

We performed single-cell RNAseq (scRNAseq) on testes from E13.5, E15.5, P0 and P6 (n=2/age/genotype) *Inha*KO mice (chronic unopposed/elevated AA signalling[8]). To study acute effects, E17.5 WT testis fragments were cultured (72hr) with 50ng/mL AA or 10μM SB431542 (activin/TGFβ/Nodal inhibitor; n=5-7 fragments/treatment). Spermatogonia were examined using immunofluorescence and RNAseq in neonate (P0, P3, P6; n>3/age/genotype) and adult *Inha*KO testes, and cultured adult WT undifferentiated spermatogonia (5, 25ng/ml AA or BMP4, 6/24hr; n=4/treatment/timepoint).

*Inha*KO testes lose 50% of fetal germ cells by E15.5. Amongst surviving germ cells, scRNAseq identified cell cycle defects (Ccnd2 & Cdk1 retention) at E15.5 and premature cell cycle re-entry (Mki67+) at P0. Evidence of advanced development includes early expression of differentiation genes (Stra8, Sohlh2) and higher germ cell migration in E17.5 testis cultured with AA. At P6, when the SSC population is fully established, more spermatogonia in *Inha*KO testes were GFRA1+, indicating enhanced SSC formation. Surprisingly, SSC-associated transcripts were unaltered in AA-cultured spermatogonia, while BMP4 elevated several (Id1-3), and altered Wnt signalling potential. A greater abundance and proliferation of SSCs in adult *Inha*KO testes suggests chronic AA elevation promotes a niche that supports long-term SSC self-renewal.

These data indicate elevated AA exposure in early life may increase the risk of testicular cancer/infertility by disrupting germ cell maturation. Ongoing scRNAseq interrogation is focussed on revealing candidate niche factors regulated by AA that determine spermatogonial fate.

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id #132284

Obesity in Pacific children and young people in the Pacific Islands – a large and growing problem

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The Pacific Islands has been described as the 'epicentre' of the global epidemic of obesity. Pacific adults are among the most obese in the world. The World Health Organization estimates that more 90% of adults in Nauru and Tonga are overweight or obese. In recent years, childhood obesity has increased dramatically and despite multiple global and regional plans and strategies, there are no signs of decline. UNICEF estimates that Niue had one of the highest rates of obesity in children aged 13-15 years in the Pacific. Childhood obesity is a reflection of dietary patterns where almost all food items consumed are imported highly processed items.

Despite the best efforts of Pacific Islands Governments, regional and global organizations, there has been little impact on the growing obesity problem in the region. There are multiple global and regional commitments to NCD prevention and control in the region, including the Pacific ECHO – a regional version of the WHO 2016 Ending Childhood Obesity Commission framework.

There is an urgent need for better implementation of the global and regional commitments, enhanced advocacy, strengthen community engagement and civil society participation. Advocacy can be an effective if affected communities are fully engaged and interventions are evidence based and culturally appropriate. Effective advocacy is an important counter-measure to lobbying by food, alcohol, tobacco industries and global advertisers especially in small island jurisdictions where the regulatory and policy environments are often ignored. The situation requires all stakeholders to intervene at local, regional and global levels.

The presentation will discuss the growing problem of childhood obesity in the Pacific islands and ways of scaling up efforts to prevent and control childhood obesity. Regional organizations need to place limits on the food trade and ensure that the health of children is protected.

id #128700

Observational study on hypothyroid patients with gastric disorders in treatment with liquid L-T4 therapy

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Aims: We performed an observational and retrospective study involving patients with hypothyroidism and gastric diseases in treatment with liquid levothyroxine (L-LT4) or tablet L-T4 (T-LT4). We assessed and compared TSH stability in these patients.

Methods: Eighty-four patients were in treatment with L-LT4, and 120 patients with T-LT4. The patients were affected by many types of gastric disease. In the T-LT4 group, 74 patients with chronic gastritis (CG), 4 with gastrectomy for gastric cancer (GTx) and 42 with gastro-plastics (GP), whereas in L-LT4 group, 60 with CG, 3 with GTx and 21 with GP ($p>0.05$). In the T-LT4 group 66% of the patients were chronically treated with PPI, against 51% in the L-LT4 group ($p>0.05$). The frequency of Helicobacter Pylori infection was 17% in both T-LT4 and L-LT4 groups. Gender distribution, mean age and body weight were comparable in the two groups ($p>0.05$). In the T-LT4 group the L-T4 mean dosage at the basal evaluation was 1.22+/-0.27 µg/kg/die, whereas in the L-LT4 group was 1.36+/-0.22 µg/kg/die ($p>0.05$).

Results: The basal evaluation reported a prevalence of patients with a TSH > 3.5 µIU/mL in the T-LT4 group of 36%, whereas in the L-LT4 group was of 46% ($p<0.05$). The patients were re-evaluated in an interval of 5-9 months, for 4 times, over period from 23 to 31 months.

The prevalence of patients with a TSH>3.5 µIU/mL in the T-LT4, or in the L-LT4 groups were respectively: a) at first revaluation 13%, 13%; b) at second revaluation 26%, 13%; d) at third revaluation 19%, 9%; d) at fourth revaluation 18% and 5% ($p<0.05$ for all comparisons). Mean FT4 and FT3 circulating levels were not significantly different in the two groups.

Conclusion: We demonstrated that liquid L-T4 ensures more stable long-term TSH control than L-T4 tablets in hypothyroid patients with gastric disorders.

id #128446

Enrichment and long-term culture of marsupial spermatogonia: A foundation of next generation conservation technologies.

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Ongoing declines in Australian marsupial populations highlight the limitations of conventional conservation strategies and the need for innovative approaches. Spermatogonial stem cells (SSCs), the source of the male germline, have been used in advanced techniques that may prove valuable for marsupial conservation efforts, including SSC transplants, *in vitro* spermatogenesis, and derivation into induced pluripotent stem cells. However, marsupial SSCs, and the techniques required to utilise them, are not defined. This research aimed to establish reliable methods to culture and enrich marsupial spermatogonia to advance marsupial SSC-based research and conservation technologies.

Fat-tailed dunnart (*Sminthopsis crassicaudata*) testis cells were cultured under various common eutherian SSC conditions. Antibody-based cell sorting and differential adhesion were assessed for spermatogonial enrichment and subsequently cultured for spermatogonia colony formation. Spermatogonial enrichment, colony formation and maintenance were evaluated using gene expression analysis (RT-PCR, RNAseq) and immunofluorescent staining for germ cell (UCHL1, DDX4) and somatic cell (GATA4) markers.

ITGA6-based cell sorting and differential adhesion resulted in a 13-fold and 8-fold increase in spermatogonial gene expression (*ID4, UCHL1, GFRA1*), respectively, with the assessment of colony formation in enriched fractions currently ongoing. Dunnart spermatogonial culture was most robust under serum-free DMEM/F12 when compared to StemPro-34-SFM and MEMα. These conditions supported spermatogonia for ~50 days and through passage, suggesting continual support of the stem cell population. Differences between conditions were more pronounced after passage, with DMEM/F12 show up to 10-fold higher expression ($p<0.0001$) of key spermatogonial regulatory genes (*ID4, ETV5, GFRA1*) relative to MEMα.

This study significantly advances our knowledge of the enrichment methods and culture conditions needed for isolation and extended *in vitro* expansion of marsupial spermatogonia, enabling developments towards dunnart SSC transplants and investigations into marsupial SSC regulation. This also provides essential tools for developing advanced SSC-based applications that will be invaluable for marsupial research and conservation.

id #132543

Aldosterone, Mineralocorticoid Receptor and Cardiometabolic Disease

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The goal of this presentation is to better understand the contribution of aldosterone and its receptor, the mineralocorticoid receptor, to the pathophysiology of cardiorenal injury. Excess aldosterone/mineralocorticoid receptor activity is common in hypertension, obesity (especially obesity with metabolic syndrome components), heart failure, diabetes and persons with HIV. Preclinical and clinical studies demonstrate that blocking the mineralocorticoid receptor or reducing excess aldosterone reduces renal injury and improves arterial inflammation and coronary microvascular dysfunction, key mechanisms underlying cardiovascular disease.

id #128447

Investigating the role of β-adrenergic signalling in triggering adipose-resident eosinophils to promote beiging

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Weight loss for the treatment of obesity requires skewing the balance between energy intake and expenditure. Existing anti-obesity pharmacotherapies drive this through a reduction in intake. An alternative approach to pharmacological weight loss could instead target expenditure. Increasing energy expenditure in the adipose tissue through the upregulation of thermogenic beige fat holds promise as a targeted treatment strategy. Cold exposure is a strong natural stimulus for beige fat activation, mediated by β-adrenergic signalling that directly induces thermogenesis in adipocytes. Additionally, adipose-resident eosinophils are essential for harnessing the full thermogenic capacity of the adipose tissue during cold exposure, seemingly by secretion of pro-beiging factors we term eosinokines. Currently, it is not well understood how adipose eosinophils become activated to promote beiging.

We aimed to determine whether β-adrenergic signalling during cold exposure drives adipose eosinophils to secrete pro-beiging eosinokines. We have found that adipose eosinophils highly express the β2-adrenergic receptor (*ADRB2*). Using human EoL-1 cells as a model, we have shown that eosinophils are responsive to β-adrenergic signalling via this receptor. Furthermore, we have generated an *ADRB2* knock-out cell line using CRISPR/Cas9 genome editing to assess the importance of this receptor during cold signalling and adipose eosinophil activation. We have used RNA-sequencing to examine differential gene expression between cells unstimulated or stimulated with a β-adrenergic agonist, as well as wildtype and knock-out cell populations. This has shown that eosinophils' response to β-adrenergic signalling is largely mediated by ADRB2. Additionally, this dataset is enabling the identification of candidate eosinokines, which will be screened using established *in vitro* beiging assays. Promising candidates will be further assessed *in vivo*.

Understanding the mechanism of eosinophil activation following a cold stimulus and how this promotes beiging in the adipose tissue may reveal novel targets or pathways for the development of anti-obesity pharmacotherapies that drive energy expenditure.

id #128703

Using genetics to understand drivers of obesity-linked endometrial cancer

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Endometrial cancer is the most common gynaecological cancer in developed countries and the cancer type most strongly linked to obesity. Up to 60% of endometrial cancer cases can be attributed to excess weight, yet the biological reasons for this relationship remain poorly understood. Not all obese women develop endometrial cancer, and not all women with endometrial cancer are obese — suggesting that individual risk is shaped by both environment and genetics.

To better understand how obesity contributes to endometrial cancer, we used data from the largest genome-wide association study (GWAS) of endometrial cancer to date (involving over 17,000 cases) alongside multiple measures of obesity, including BMI, body fat percentage, and adipose distribution. Our goal was to separate genetic factors that increase endometrial cancer risk because of obesity, from those that act independently of body weight.

We identified two distinct sets of genetic signals. The majority were independent of obesity and may reflect other biological pathways involved in endometrial cancer development. A smaller set of signals appeared to act specifically in the context of obesity and were enriched near genes involved in metabolism, inflammation, and hormonal regulation. Several of these were located at regions of the genome previously linked to both obesity and cancer risk.

These findings provide new insight into the biology that connects obesity to endometrial cancer. Understanding these pathways could help identify women most at risk, improve prevention efforts, and support the development of treatments that target obesity-related cancer mechanisms.

id #128448

Development of adipose-derived eosinophil cell lines to uncover novel pro-beiging factors for treating obesity

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While existing obesity therapeutics target energy intake, novel approaches that instead aim to increase energy expenditure hold significant therapeutic promise. Adipose tissue contains both energy storing white adipocytes, which contribute to the development of obesity, and thermogenic beige adipocyte, which can burn energy as heat. Activation of these thermogenic beige adipocytes has been shown to have beneficial metabolic effects in both mice and humans, including improved glucose tolerance, enhanced insulin sensitivity and leanness. Identifying endogenous mechanisms that drive beige adipocyte activation is critical to realising the therapeutic potential of this tissue in treating obesity.

Eosinophils residing in adipose tissue can promote beige adipocyte activation through the secretion of pro-beiging proteins, making these immune cells a promising therapeutic target for stimulating thermogenesis and increasing energy expenditure. However, progress in this area is limited by the lack of suitable *in vitro* models of adipose eosinophils. Primary adipose eosinophils are difficult to isolate, low in abundance and short lived in culture, while existing eosinophil cell lines such as EoL-1 cells are derived from human peripheral blood and may not recapitulate an adipose-specific phenotype.

To address this gap, we are developing immortalised eosinophil cell lines derived from mouse and human adipose tissue. Primary eosinophils will be isolated and transduced with viral vectors to deliver a range of immortalising transgenes. Detailed downstream characterisation will be performed to select lines that best model adipose eosinophils. These adipose-derived eosinophil cell lines will enable the identification of novel eosinophil secreted proteins that promote beige activation and energy expenditure. By uncovering new molecular drivers of adipose tissue thermogenesis, we aim to identify therapeutic targets with high translational potential for the treatment of obesity.

id #129729

Transforming Public Obesity Care: Nurse-Led, Multidisciplinary and Digitally Enabled Innovation at CALHN

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To address escalating obesity rates and fragmented care delivery, the Central Adelaide Local Health Network (CALHN) undertook a major service reform by amalgamating two previously siloed services at the Royal Adelaide Hospital and Queen Elizabeth Hospital. This integration led to the establishment of the **CALHN Metabolic and Bariatric Clinic (CMBC)** in 2025—a unified, nurse-led, multidisciplinary service combining endocrinology, surgery, dietetics, psychology, and exercise physiology.

A cornerstone of this transformation is **OPTIMAP** (Online Pathway from Triage to Individualised Metabolic Action Plan), a purpose-built digital platform that supports streamlined triage, automates documentation and pathology workflows, and delivers **consumer education modules** across domains such as nutrition, physical activity, sleep, mental health, and chronic disease management. OPTIMAP also enables an **active waitlist model**, fostering patient engagement and behavioural readiness before first clinical CMBC touch point, and facilitates **real-time tracking** of progress toward bariatric surgery eligibility.

This presentation will describe the co-design, implementation, and evaluation phases of both CMBC and OPTIMAP, including early outcomes in access, efficiency, and patient activation. It will also explore opportunities and challenges in scaling digitally enabled, team-based obesity care models across public health systems

id #128194

Decoding the epi-regulatory puzzle contributing to the pathophysiology of PCOS

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Polycystic ovarian syndrome (PCOS) is the most common gynecologic-endocrine disorder and leading cause of anovulatory infertility. Ovarian function is shaped by complex interaction of genetic, hormonal and environmental factors, which trigger epigenetic modifications. DNA methylation and miRNAs are critical epigenetic regulators of hormone synthesis and folliculogenesis. Beyond these, mRNA undergoes epitranscriptomic N6-methyladenosine (m6A) methylation, adding further complexity to the regulation of gene expression in PCOS. These epigenetic modifications have been independently associated with PCOS; however, their cross-layer interaction is sparsely investigated.

We investigated how DNA methylation influences miRNA regulation in dysregulated pathways associated with PCOS. Through *in-silico* reanalysis of seven GEO microarray datasets, we identified differentially expressed genes (DEGs) and curated differentially expressed miRNAs (DE-miRNAs) from studies focused on the follicular environment in PCOS. Functional enrichment analysis identified “Regulation of Actin Cytoskeleton” as the top disrupted pathway, and further network analysis revealed hub genes *ARPC1B, ACTR2, RAC2, PIP5K1B*, and *IQGAP*. In granulosa cells (GCs) of women with PCOS, we found significantly altered expression of hub genes and their regulating miRNAs: miR-196a-5p, miR-377-5p, and miR-424-5p. Further, using pyrosequencing, we found these

miRNAs are regulated by differential DNA methylation. Disrupted cytoskeletal dynamics could impair steroidogenesis and cumulus expansion, contributing to aberrant folliculogenesis.

The interplay between m6A modification and miRNAs in PCOS is largely unexplored. We observed increased global m6A levels, with upregulation of "writers" like *METTL3, METTL14, WTAP, VIRMA*, downregulation of "erasers" such as *FTO, ALKBH5* and dysregulation of readers (*YTHDF1/2/3, YTHDC1*) in GCs of PCOS. Notably, miR-20b and miR-607, which target *METTL3* and *FTO*, showed differential expression, suggesting altered miRNA expressions regulate m6A modifications in PCOS. The strong correlations we observed between m6A levels, *METTL3/FTO* expression, and androgen indices indicate an androgen-m6A regulatory loop in PCOS.

Our study sheds light on the complex epi-regulatory network underlying ovarian dysfunction in PCOS.

id #131013

Early and multiple doses of zoledronate mitigates rebound bone loss following withdrawal of RANKL inhibition

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Rebound bone loss following denosumab discontinuation is a significant challenge in long-term treatment of skeletal disorders. This is driven by increased osteoclastic bone resorption following the offset of RANKL inhibition, and sequential osteoclast-directed therapy has been utilized to mitigate this. However, current sequential treatment strategies intervene following the offset of RANKL inhibition and this approach fails to consistently prevent bone loss. Our previous work, using a mouse model of denosumab discontinuation, has shown that the processes that drive the rebound phenomenon occur earlier than when bone loss is detected, namely a rise and overshoot in serum tartrate-resistant acid phosphatase (TRAP). We identified that these changes in serum TRAP may provide an earlier window of opportunity to intervene with sequential therapy following RANKL inhibition withdrawal.

We show that early treatment with zoledronate (10 mg/kg, 3 weeks following the last dose of OPG:Fc), preceding the rise and overshoot in serum TRAP, effectively mitigates rebound bone density loss through preventing the overshoot in serum TRAP. Further, we show that multiple doses of zoledronate (early treatment and during anticipated BMD loss) is superior in consolidating bone density gains made with RANKL inhibition and preventing rebound BMD loss as measured by DXA. Importantly, we demonstrate the efficacy of early and multi-dose zoledronate strategy in preventing bone loss in both growing and skeletally mature mice. MicroCT analysis showed improved trabecular bone structure in both the femur and lumbar vertebrae with zoledronate treatment compared with control. These increases in bone mass translated to increased fracture resistance in skeletally mature mice.

These findings support a novel sequential therapy approach: early and multi-dose zoledronate treatment strategy following withdrawal of RANKL inhibition can more effectively prevent rebound bone loss. This has significant implications for clinical management of patients who discontinue denosumab therapy.

id #127942

Unlocking the potential of koala spermatogonial stem cells for conservation: optimising isolation, characterisation, and culture approaches

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The koala (Phascolarctos cinereus), an iconic Australian marsupial, faces escalating threats from habitat loss, disease, and climate-related disasters, leading to its endangered status in several states. Preserving male germline potential through spermatogonial stem cell (SSC) biobanking offers a promising avenue for long-term fertility preservation and assisted breeding programs. However, the limited understanding of SSC biology in marsupials hinders the development of such technologies.

This study aimed to characterise koala SSCs and develop protocols for their isolation and in vitro maintenance. Using immunohistochemistry on paraffin-embedded testis sections, we identified 8 stages of the seminiferous epithelium based on acrosome development (PNA-lectin labelling). Upon identifying the conserved expression of 4 spermatogonia markers in the koala testis we defined the distribution of undifferentiated (PLZF+) and differentiating (STRA8+) spermatogonia across the seminiferous cycle as well as their proliferation via co-staining with PCNA.

In addition, transmission electron microscopy has been used to investigate the ultrastructure of koala germ cells within the seminiferous tubules. This revealed defining morphological features of different germ cell types and the presence of cytoplasmic bridges between dividing spermatogonia, providing novel insights into spermatogonial morphology and behaviour in situ.

To support downstream applications, several SSC enrichment methods have been tested, including differential plating, Percoll gradient separation, and magnetic-activated cell sorting (THY1+), with assessments of enrichment efficiency underway via quantification of PLZF+ cells. Trials of short-term in vitro culture of koala spermatogonia are in progress, using both feeder-free (laminin) and feeder-dependent (mitotically inactivated embryonic mouse-derived fibroblasts) systems in serum-free and FBS supplemented medium, with and without growth factors (GDNF, FGF2). Cultures are being monitored for viability, morphology, and marker expression (PLZF, STRA8, DDX4, UCHL1, PCNA, EPAS1).

Together, these approaches bring us closer to establishing SSC-based conservation tools for koalas, laying a critical foundation for SSC biobanking and assisted reproduction in endangered marsupials.

id #128710

Food for thought: the impact of diet on endometrial decidualisation and embryo implantation

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We postulate that maternal diet induced obesity is a complex, but modifiable, contributing factor to the burden of spontaneous early pregnancy loss which reportedly occurs in up to 15% of clinical pregnancies[1]. High levels of adipose tissue are linked to dysregulation of decidualisation[2,3]; a crucial cell transformation in the uterus that facilitates embryo implantation and provides the maternal component of the placenta. We are using mouse models to investigate how a high fat diet impacts decidualisation and embryo implantation.

C57BL/6 mice were fed a high fat (HFD), high sucrose (HSD) or control diet for 8 weeks and mated before being culled on gestational day (GD) 5.5 or 7.5. Body composition was measured using minispec NMR. The number of implantation sites were recorded, and uteri were taken for histology and immunohistochemistry for markers of vasculature, proliferation, apoptosis, senescence and immune cells. Serum was collected to determine progesterone, prolactin, leptin and adiponectin levels.

After 6 weeks, the high fat group had significantly higher fat composition (HFD=27.8±1.23; HSD=19.2±0.82; control=17.0±1.04) and less lean mass than other diet groups ($p<0.0001$). There was no significant effect of diet ($p=0.86$) or GD ($p=0.79$) on the number of implantation sites, and no significant interaction effect ($p=0.13$). Histological and serum analyses of the tissue are currently underway.

Although no embryo loss was observed at the time points examined, we predict there will be impacts on decidualisation that may negatively impact embryos should pregnancy have progressed. Our ongoing studies will elucidate the subtle effects of high fat and/or high sucrose diets on endometrial processes. Such studies are fundamental if we are to further understand the mechanisms responsible for early pregnancy loss.

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id #128456

OPTIMAP: A Digitally Enabled Model to Transform Public Obesity Care in South Australia

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Background

South Australia reports one of the highest obesity rates in Australia, with 13% of adults experiencing severe obesity (BMI >35). Until recently, the Royal Adelaide and Queen Elizabeth Hospitals operated siloed obesity services with a combined waitlist of over 700 patients and wait times exceeding seven years. In 2024, stakeholder engagement facilitated the unification of these services into a

single multidisciplinary model—the CALHN Metabolic and Bariatric Clinic (CMBC), launched March 2025. The new model offers in-person and telehealth options, small group sessions (“My Healthier Life”), community-based exercise physiology, and fortnightly multidisciplinary team meetings.

Aim

To develop a sustainable, cost-effective digital model of care to improve access, service delivery, patient empowerment, and health outcomes.

Methods

Phase 1 – Discovery: An earlier prototype software (OBEMAN, CI-Wittert 2010) was assessed but not adaptable. Stakeholders (CMBC, CALHN Digital, Digivate Health) agreed to co-design a new solution: **OPTIMAP**.

Phase 2 – Design: OPTIMAP (Online Pathway from Triage to Individualised Metabolic Action Plan) is a first-of-its-kind digital platform that:

- Triages patients by online questionnaire
- Provides pre-appointment education and coaching
- Generates GP-facing personalised "My Health Summaries"
- Delivers tailored content on diet, activity, sleep, mental health, medications, comorbidities and goal setting
- Automates documentation and pathology workflows
- Tracks real-time patient progress and surgical readiness

Phase 3 – Implementation: OPTIMAP launched in May 2025 following user testing.

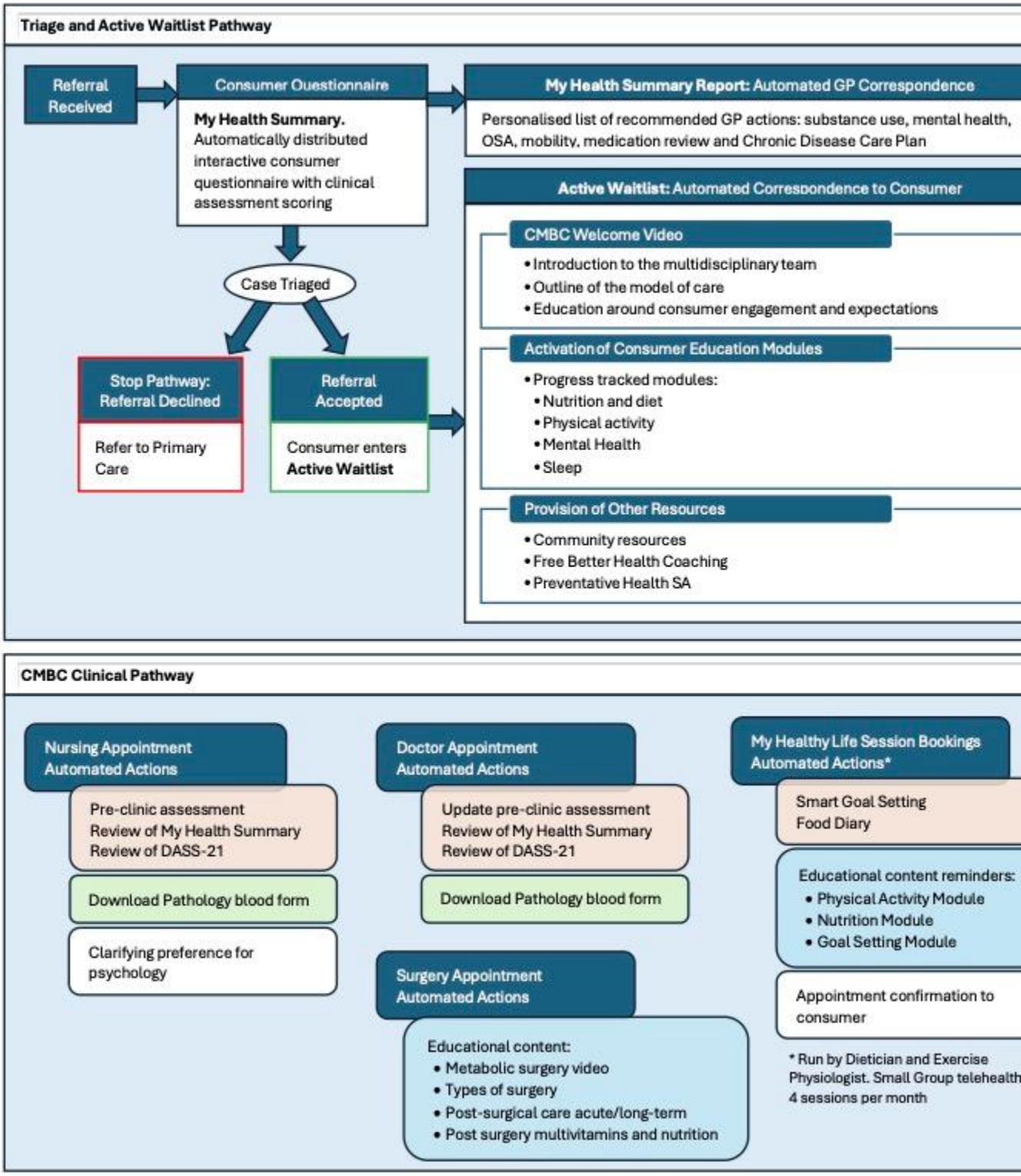
Results

Within three months, the CMBC and OPTIMAP achieved a fivefold increase in physician and nursing activity and tripled dietetic capacity. First-appointment waitlist fell by 8.7%, maximum wait time reduced by two years, and failure-to-attend rates dropped by 65%. OPTIMAP improved referral compliance, clinical documentation and readiness tracking.

Conclusion

OPTIMAP and CMBC model represent a scalable, digitally enabled solution addressing systemic barriers in public obesity care. Ongoing KPI evaluation will inform future sustainability, equity and the broader health system impact.

Complex Metabolic and Bariatric Clinic (CMBC) – Online Pathway from Triage to Individualised Metab



id #123337

Improving The Environmental Sustainability Of Insulin Prescribing

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Introduction: Insulin pens come in reusable and disposable forms. The average patient with diabetes uses 75 disposable pens annually. Reusable pens generate less waste and are available in various designs

Objective: This study aimed to identify factors influencing patients' decision making between reusable and disposable insulin pens, with the goal of improving patient-centred care while promoting environmentally sustainable insulin prescribing.

Methods: Forty-eight inpatients at Alfred Hospital, Melbourne, were recruited and categorised into three groups: insulin-naïve (Group 1), insulin-experienced (Group 2), and those who switched to reusable pens due to the shortage of Ryzodeg FlexTouch pens (Group 3). Participants completed a questionnaire on insulin pen preferences. Preferences were compared with their discharge prescriptions.

Results: Most participants prioritised ease of use ($p=0.06$), while aesthetics were largely considered unimportant ($p=0.18$). Environmental sustainability was deemed at least moderately important by the majority ($p=0.93$), with preferences consistent across age, gender, and diabetes type. Notably, six patients who preferred reusable pens were prescribed disposable ones upon discharge ($p<0.01$).

Conclusion: Education about pen types influenced some patients to choose reusable pens, citing ease of use and environmental sustainability as key factors. Insulin-naïve patients equally preferred both pen types, highlighting an opportunity to promote environmentally sustainable prescribing practices.

		Group 1 Insulin-naive	Group 2 Insulin experienced	Group 3 Reusable Ryzodeg	Tota
Preferred choice of pen n (%)	Disposable	12 (50.0)	10 (76.9)		22 (
	Reusable	12 (50.0)	3 (23.1)		15 (
Primary reason for choice n (%) (n of preferred disposable)	Ease of Use	18 (75.0) (12)*	11 (84.6) (8)*		29 (
	Environmental Sustainability	3 (12.5) (0)	0		3 (8
	Storage Space	1 (4.2) (0)	0		1 (2
	Aesthetics	0	0		0
	Other	2 (8.3) (1)	2 (15.4) (2)		4 (1
Most convenient pen n (%)	Disposable	15 (62.5)	9 (69.2)	3 (37.5)	27 (
	Reusable or no difference	9 (37.5)	4 (30.8)	5 (62.5)	18 (
Discordance of script on discharge n (%)	Given disposable, wanted reusable	3 (12.5)	3 (23.1)	0	6 (1

*p value significant (<0.05) within group

id #128714

The contribution of mitochondrial complex I in oocyte development and maturation

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Oocytes rely on the mitochondrial electron transport chain and oxidative phosphorylation to produce energy and metabolites for their growth and maturation. Mitochondrial respiration also generates potentially damaging reactive oxygen (ROS) species, in part as a by-

product of complex I activity. In vitro studies indicate that long-lived human and Xenopus early-stage oocytes are insensitive to complex I inhibitors and mitigate the risk of ROS generation by excluding complex I from the respiratory chain. Here we have utilised an in vivo approach to further investigate the role of complex I activity in the function and viability of mouse oocytes during their growth and maturation. Ndufs4 is a complex I subunit which in other systems is essential for complex I formation and function. We developed an oocyte-specific Ndufs4 knockout mouse using the GDF9-Cre/LoxP system to investigate the contribution of complex I in developing oocytes in vivo. In two-month-old mutant mice, there was a minimal impact on the early-stage follicles, however, there was a significant decrease in the number of large antral follicles. In isolated fully-grown oocytes, Ndufs4 deletion markedly decreases mitochondrial membrane potential (MMP), mitochondrial ROS, mitochondrial FAD^{++}, and ATP. Ndufs4 KO oocytes displayed delayed germinal vesicle breakdown (GVBD) and had a lower polar body extrusion (PBE) rate compared to control oocytes. Proteomics data revealed that Ndufs4 deletion markedly increased the expression of protein phosphatase Ppp1cb, providing a potential link between cell cycle defects in Ndufs4 KO oocytes. These findings demonstrate that functional complex I is critical for oocyte development and maturation.

id #128203

Use of microchannels to add selective efficacy to a functionalised surface sperm selection device.

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In natural fertilisation, stringent selection mechanisms favour genetically competent spermatozoa. In contrast, current spermatozoa preparation protocols used in assisted reproductive technologies (ART) lack the ability to select highly competent spermatozoa with similar precision. Conventional methods like swim-up and density gradient centrifugation are limited in removing apoptotic or DNA-damaged spermatozoa, affecting fertilisation success and embryo viability. Therefore, biomimetic approaches are urgently needed to improve ART outcomes.

We developed and validated a surface-engineered spermatozoa selection device incorporating a microchannel-based architecture that mimics natural selection processes in the female reproductive tract, including immune-mediated clearance. Microchannels (~50 µm deep, ~100 µm wide) were patterned onto glass slides using a diamond saw to promote directional motility and limit passive drift of compromised spermatozoa. Surfaces were coated with plasma-polymerised polyoxazoline, a biocompatible interface characterised via X-ray photoelectron spectroscopy and ellipsometry. Gold-nanoparticles were covalently attached to enhance surface topography and spermatozoa interaction.

To enable selective elimination of apoptotic spermatozoa, anti-phosphatidylserine (anti-PS) antibodies were immobilised near the channel inlet, simulating immune cell recognition. Progesterone also adsorbed at the outlet facilitated chemotactic retrieval of competent spermatozoa, showing time-dependent release from GNP-coated surfaces peaking at 20.7± 6.3 ng/mL at 60 minutes (competitive ELISA).

Optimising surface chemistry, geometry, and topography led to enrichment of spermatozoa with high DNA integrity. After 45 minutes of processing, spermatozoa collected at the outlet showed significantly improved spermatozoa motility and lower DNA fragmentation (0.6± 0.5% vs. 16.6± 1.6% in swim-up; $P<0.0001$, $N=3$). Annexin V-positive spermatozoa were also significantly reduced (3.9± 0.2% vs. 15.7± 4.6% in swim-up, $P<0.05$, $N=3$). Addition of microchannels provided a substantial improvement compared to previous models without microchannels, where DNA fragmentation rates averaged 4.5± 1.5% ($N=5$).

These data highlight the added value of microchannels in a channeled-slide format and support the translational potential of this non-invasive, efficient spermatozoa selection platform for ART.

id #128459

Integrating lived experience into service model of care planning for severe and complex obesity in Western Australia

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Drivers of obesity are systemic and varied, with most outside of people's control (1). In 2022, a third of Australian adults were living with obesity; and between 2011-12 and 2022, class 3 obesity prevalence increased by 48% (2, 3). Despite being a treatable condition, people experiencing the greatest burden of obesity lack access to low or no-cost specialist medical services in Western Australia (WA) (1). This study aims to describe the East Metropolitan Health Service project to develop an evidence-based patient-centred service model of care for adults with severe and complex obesity (service model). To inform the draft service model, the literature, obesity

services guidelines, and existing obesity services were reviewed. The project design incorporated partnership principles, and stakeholders with lived experience of obesity informed service model development. Aboriginal health consumers' views were integrated via a separate mechanism (not reported here). We identified key health consumer stakeholders and created a project process to enable them to provide direct input to the service model development. Health consumer views were contributed via: 1) including a Health Consumers Council WA (HCCWA) representative on the service model reference group; 2) a HCCWA-led health consumer workshop; 3) a HCCWA presentation and participation in the service model clinician workshop. Consumer feedback strengthened the service model, including by adding a peer-navigator role, improving referral and discharge processes, and prioritising patient-centred, trauma-informed care with a focus on overall patient health and wellbeing. Integrating partnership principles enabled the consumer voice to be incorporated making the service model fit-for-purpose.

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id #128715

Preserving female fertility & offspring health after chemotherapy by inhibiting PUMA

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Cancer therapies frequently cause irreversible ovarian damage, depleting the finite reserve of oocytes and leading to infertility and premature menopause in female survivors. This presents a major health challenge for the increasing number of young women surviving cancer, as no current strategies protect both fertility and long-term health post-treatment[1]. Our previous landmark studies revealed chemotherapy directly damages oocyte DNA and induces apoptosis[2], with PUMA identified as the key mediator of oocyte loss[3]. Notably, our recent work presented at ESA-SRB-ANZBMS-2024 demonstrated that small molecule PUMA inhibition robustly protects oocytes in preclinical mouse and human models. Here, we assessed the impacts of PUMA inhibition on chemotherapy efficacy, and whether oocyte quality and offspring health are preserved long-term.

To test if blocking PUMA-mediated apoptosis affects tumour cell survival, human breast cancer cells (MDA-MB-231) were incubated with PUMA inhibitor (PUMAi; 0-250μM) ± an IC_{50} concentration of cyclophosphamide derivative 4-HC (5μM). After 48h, 4-HC alone reduced viability to 54% ($p<0.0001$) and co-treatment with PUMAi did not increase cell survival, with viability remaining at ~50% across all concentrations. Similarly, patient-derived breast cancer organoids (HBC14) were exposed to PUMAi (0-100μM) ± 4-HC (5μM) on days 1, 3 and 5. After 48h, no changes in viability were observed after PUMAi co-treatment, confirming that PUMA inhibition does not compromise chemotherapy efficacy *in vitro*.

To evaluate fertility and offspring health, mice (n=10/group) received 150mg/kg cyclophosphamide ± 10mg/kg PUMAi, and were bred for three litters. While average litter sizes were similar, cyclophosphamide alone dramatically impacted offspring health, with only 28% of pups surviving past PN5 versus 69% from control-treated dams ($p<0.001$). Strikingly, PUMAi improved survival to 54% ($p<0.05$), indicating oocyte quality and offspring health are effectively preserved.

Together, these data demonstrate that PUMA inhibition is a promising avenue for oncological fertility preservation, strongly warranting further investigation with other chemotherapeutic agents.

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id #128716

Exposure to an estrogenic endocrine disruptor alters methylation in the male germ line

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The incidence of DSDs has increased significantly in the last few decades, and this rise is attributed to our increased exposure to endocrine disrupting chemicals (EDCs). Prenatal exposure to the estrogenic endocrine disruptor Diethylstilbestrol (DES), a prescribed drug given to millions of pregnant women worldwide, led to multiple reproductive effects in exposed offspring. We have previously shown the effects of DES across four generations of male mice, including a significant reduction in anogenital distance, reproductive organ weights and fertility, and an increased incidence of DSDs through to the F4 generation. To determine the mechanism behind these transgenerational impacts, we investigated DNA methylation in male germ cells from three generations of DES exposed mice. Male mice were exposed to DES during gestation, and germ cells collected from control, F1, F2 and F3 DES exposed generations at day 21 post partum. Whole genome bisulfite sequencing analysis was conducted to identify differentially methylated regions (DMRs) between treatment and control germ cells. We identified 128 genes with DMRs that were common across F1, F2 and F3 generations, and had at least 20% difference in methylation compared to controls. One of the genes in which a DMR was identified was antizyme inhibitor 2 (Azin2) a modulator of ornithine decarboxylase (ODC), a key enzyme in polyamine biosynthesis and polyamine uptake. Azin2 has an important role in testicular cells, modulating polyamine concentrations, testosterone synthesis and sperm function. In control germ cells Azin2 was 74% methylated, but this was reduced to 5% in F1, F2 and F3 generations. Methylation changes in Azin2 are therefore a potential mechanism through which DES causes transgenerational effects in exposed males. These results not only demonstrate epigenetic effects following DES exposure but also provide insights into the mechanisms through which estrogenic endocrine disruptors more broadly are impacting human fertility and reproductive health.

id #128975

Grow.Cook.Eat.: Supporting a community living with disadvantage to build food literacy and connection

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Rising living costs, poor access to affordable healthy food, and being swamped with unhealthy options pose major health challenges to the Norlane community (the most disadvantaged area in Victoria, Australia). The Good Neighbourhood Project, a community-led placemaking organisation, takes a whole-of-neighbourhood and whole-of-person approach to create healthy, sustainable, inclusive, and resilient communities. Their strategies include: social enterprise cafés, an urban farm, a community garden, neighbourhood meals, and a food co-operative. Community feedback in 2022 revealed a demand for food literacy skill-building.

In response, The Good Neighbourhood Project partnered with Deakin University **to co-design, deliver and evaluate a pilot food literacy program Grow.Cook.Eat.** Weekly sessions were held at a social enterprise café adjacent to a community garden. The free program helped residents to build practical cooking and gardening skills, increase nutrition knowledge via growing, cooking and sharing a meal; and via monthly *Healthy Conversations* interactive workshops. A mixed-methods evaluation in 2024 included pre/post surveys, weekly session evaluations and follow-up interviews. Thematic analysis is underway.

Early interview feedback at follow-up reveals enjoyment and strong engagement of participants with Grow.Cook.Eat. Participants improved food knowledge (labels, healthy swaps), confidence, cooking skills. Participants were more motivated and creative with cooking, cooked more and increased fruit and vegetable intake. Social connections were fostered via shared meals. Gardening engagement was lower, possibly due to weather, limited growing space at home, and mobility challenges.

In conclusion, co-designed, place-based food literacy programs can build community trust and engagement while addressing local needs such as food security and food literacy skills. Embedding opportunities for social connection into food literacy programs enhances impact beyond empowering community members with nutrition knowledge by fostering a healthier more connected community.

id #127698

Active school commuting and obesity prevention: a mixed-methods exploration with schoolchildren, parents, and other stakeholders in regional Australia

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Aims

Active school commuting (ASC) is a form of incidental physical activity that contributes to childhood obesity prevention, yet remains underexplored in regional areas. This study examined its prevalence and key determinants among primary schoolchildren in northwest Tasmania, a state with the highest obesity rate in Australia. Perspectives of children, parents, school and local government stakeholders were explored to identify context-specific barriers and opportunities for promoting ASC.

Methods

A convergent mixed-methods design was used: (1) an online parental survey collecting school commuting behaviours, sociodemographic, and commuting route attributes of 213 children; (2) semi-structured interviews with 11 parents and 13 children about their school commuting experience and views on ASC; and (3) semi-structured interviews with 7 school and local government representatives about their views on ASC and its promotion.

Results

Only 21% of children commuted actively. Longer perceived commuting duration and more frequent parental accompaniment were associated with lower ASC likelihood, whereas greater street connectivity and land-use diversity increased ASC. While children described ASC as an enjoyable experience that fostered confidence and independence, parents prioritised concerns about safety, adverse weather, time constraints, and highlighted the convenience and social norm of driving as major barriers. Interventions that enhanced safety and enjoyment, such as crossing guards and walking school bus programs, were potentially effective strategies. Institutional stakeholders recognised ASC benefits but reported that car dependency, competing school priorities, and limited organisational capacity made ASC promotion difficult. Responsibility for ASC was often viewed as outside the remit of schools and local governments.

Conclusion

ASC in northwest Tasmania is shaped by a complex interplay of individual, social, environmental, and institutional factors. While children's enthusiasm and parental openness offer opportunities for change, effective ASC promotion to prevent obesity requires co-designed, context-specific interventions supported by infrastructure investment, policy alignment, and shifts in cultural norms around car dependency.

id #127954

Clinical Impact of Endocrinologist Involvement in Inpatient Glucose Management

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Background: Specialist involvement in inpatient diabetes management may enhance glycemic outcomes, but real-world evidence remains limited. This study evaluated the impact of endocrinologist involvement on glycemic control in hospitalized patients receiving insulin therapy.

Methods: We retrospectively analyzed adult inpatients with diabetes hospitalized at Seoul St. Mary's Hospital between July 2023 and July 2024 who received insulin therapy. Patients were grouped based on whether their inpatient care involved an endocrinologist. The primary outcome was the change in hemoglobin A1c (HbA1c) between admission and the first post-discharge outpatient follow-up.

Results Among 1,099 patients, 266 (24.2%) received care involving an endocrinologist. Although the endocrinologist group had a higher baseline A1c (7.7 ± 1.9% vs. 7.3 ± 1.6%, p = 0.001), they showed greater HbA1c reduction after discharge (–0.8 ± 1.5% vs. –0.2 ± 1.6%, p < 0.001), and a lower follow-up A1c (6.9 ± 1.4% vs. 7.1 ± 1.4%, p = 0.027). Age and BMI were similar between groups. In multivariable regression adjusting for age, sex, BMI, baseline A1c, admission duration and cost, department group, and OHA use, endocrinologist involvement remained independently associated with greater A1c reduction (β = –0.260, 95% CI –0.435 to –0.086, p = 0.003).

Conclusions: Involvement of an endocrinologist in the inpatient care of patients receiving insulin was independently associated with improved glycemic outcomes. These findings support implementing structured inpatient glucose management systems led by endocrine specialists.

id #128467

Diagnostic Utility and Cost Analysis of Pragmatic Sequential Transcription Factor Immunohistochemistry in Adenohypophyseal-Immunonegative Pituitary Adenomas

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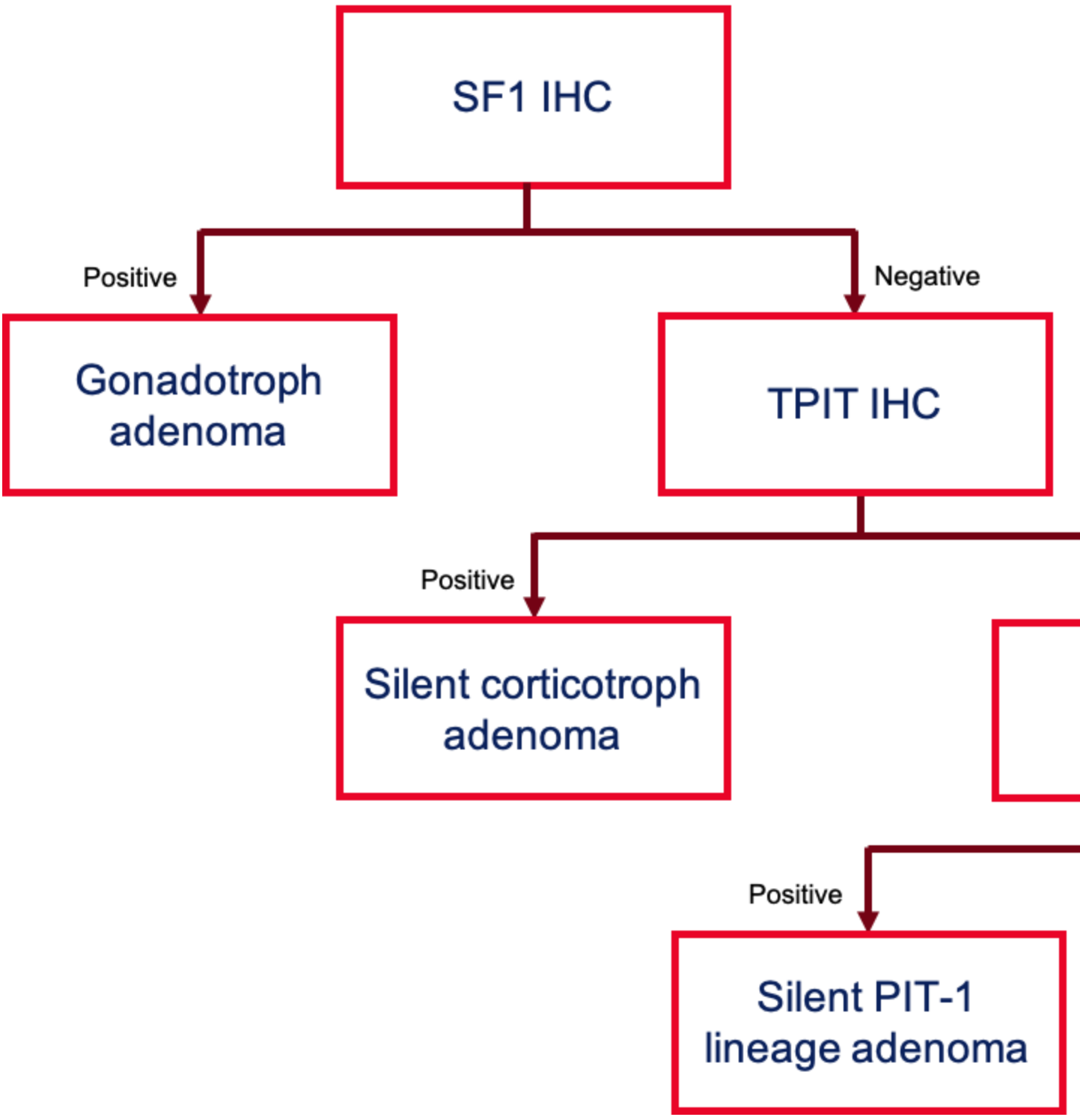
Background: Since 2022, transcription factor (TF) immunohistochemistry (IHC) has been recommended for pituitary adenoma subtype identification.[1] However, the routine use of TF IHC in clinical practice is variable due to financial and laboratory resource limitations.[2] Our pilot study demonstrated that gonadotroph adenoma was the most prevalent revised diagnosis after retrospective additional TF IHC in adenohypophyseal-immunonegative pituitary adenomas.[3] We aimed to conduct a validation study, perform a cost analysis of our proposed pragmatic sequential TF IHC approach, and quantify the routine use of TF IHC in clinical practice.

Methods: In the most recent 100 patients diagnosed with null cell adenomas without prior TF IHC at our tertiary pituitary hospital, SF1, TPIT, and PIT-1 were performed. The diagnostic accuracy of our pragmatic sequential TF IHC approach (SF1, followed by TPIT, then PIT-1) was simulated (Figure 1), with a cost analysis comparing it to traditional TF IHC. A telephone survey of hospitals performing pituitary surgery across Australia and New Zealand was conducted to assess the routine TF IHC use.

Results: Ninety-six patients labelled as null cell adenomas were available for retrospective additional TF IHC. The most commonly revised diagnosis was gonadotroph adenomas (56.3%), followed by corticotroph adenomas (15.6%), plurihormonal adenomas (11.5%), and PIT-1-lineage adenomas (1.0%). The pragmatic sequential TF IHC approach yielded 88.5% diagnostic accuracy, with a cost reduction of $6,150 (48%) compared to the traditional TF IHC approach. The telephone survey revealed that 42.9% (n=9/21) of hospitals do not perform routine TF IHC.

Conclusion: We validated our finding that the majority of the adenohypophyseal-immunonegative pituitary adenomas are gonadotroph adenomas. Three years post-diagnostic paradigm shift, over 40% of hospitals do not routinely perform TF IHC. In resource-limited settings, our pragmatic TF IHC approach may accurately subtype adenohypophyseal-immunonegative pituitary adenomas in approximately 90% of cases at nearly half the cost of traditional methods.



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id #128725

Evaluation of Time Dependent Oxidative Stress in Equine Oocytes During In Vitro Holding

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Intracytoplasmic sperm injection(ICSI) plays an important role in equine embryo production. Commercially, immature equine cumulus-oocyte complexes(COCs) are collected from mares via oocyte pickup and placed into holding media for transportation to the ICSI facility, with a recommended upper limit of 24h.However, the effect of prolonged in-vitro holding on oocyte viability and oxidative stress remains unknown.This study aimed to evaluate the effects of holding duration on oocyte viability, oxidative stress, and oxidative DNA damage.

COCs were removed from abattoir-derived ovaries 4-8h post-slaughter, washed, and placed in M199(Hanks salts) supplemented with 3% BSA and held for 0h, 12h, 24h, or 36h at room temperature to mimic commercial conditions.At each time point, COCs were denuded, and oocytes were stained with Live/Dead Violet(viability) and CellROX Green (ROS marker), then fixed in 4% paraformaldehyde. Oocytes were permeabilized with 0.25% Triton X-100, blocked using 3% BSA, and incubated with antibodies against 4-hydroxynonenal(4HNE; lipid peroxidation) and 8-hydroxy-2'-deoxyguanosine(8-OHdG). Samples were mounted for fluorescence microscopy, and images were analysed using ImageJ.

Data were analysed using one-way ANOVA to ascertain the percentage of viable oocytes and the mean fluorescence intensity(FI) of oxidative stress and DNA damage markers compared to the initial(0h) time point. Normality of the data was assessed using the Shapiro-Wilk test. The percentage of viable oocytes decreased significantly at 36h ($P \leq 0.05$). Mean FI for 4HNE increased significantly by 12h ($P \leq 0.05$) and then decreased significantly by 24h ($P \leq 0.05$). The mean FI for CellROX was significantly higher after 24h ($P \leq 0.05$). No significant difference in mean FI was observed for 8OHdG at any time point. In conclusion, prolong holding of equine oocytes negatively affects viability and oxidative stress, though no increase in DNA damage was observed. These results suggest that the upper limit for holding time ought to be reduced to 12h to reduce lipid peroxidative damage and adverse ICSI outcomes.

id #128470

The tubulin glutamylase TTLL1 is required for spermatid differentiation and male fertility in mice

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Microtubules (MTs) are core cytoskeletal filaments that play a vital role in spermatogenesis, including in germ cell division, spermatid remodelling and flagella formation. How MTs achieve this incredible diversity of function however is poorly understood. Emerging data suggests that posttranslational modifications to the MT surface, the 'tubulin code', are essential for MT function acting as instructional signposts for MT regulatory enzymes including MT severing enzymes. Herein we aimed to define a key aspect of the tubulin code, MT glutamylation, in spermatogenesis and the role of a key MT tubulin glutamylase, TTLL1.

Using antibodies targeting different glutamylation modifications, we first defined the precise tubulin glutamylation pattern during male germ cell development, revealing tubulin glutamylation is predominantly distributed in the later steps of spermatogenesis, with a majority localised to the manchette and the sperm axoneme.

To explore how tubulin glutamylation is encoded and its functions during spermatogenesis, we then characterised a TTLL1 whole-body knockout mouse model. *Ttll*1 null male mice were sterile, and our analysis revealed this was due to defects in sperm morphology and number. Daily sperm production were reduced by 35%, and epididymal sperm were significantly decreased. Moreover, histological analyses revealed TTLL1 KO sperm had abnormal head shapes and shortened or entirely absent sperm flagella. Immunostaining on testis sections and Western blots revealed significantly decreased broad-, poly- and beta tubulin mono-glutamylation. Together, our data reveals that TTLL1-dependent tubulin glutamylation is required for microtubule dynamic changes during spermatogenesis by playing a critical role in spermatid reshaping, notably in sperm tail formation and head shaping.

id #128728

Distinct macronutrient ratios optimize offspring survival, growth and maternal glucose tolerance across mouse reproduction

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Pregnancy and lactation are reproductive periods that require major energy and nutrient investment by the mother. Dietary perturbations over reproduction can impair offspring development and increase the risk of metabolic disease for the mother. However, how the intake of specific macronutrients, independent of total calorie intake, influence maternal reproductive investment and metabolic health remains poorly understood. To understand the role of protein, carbohydrate and fat intake in influencing these parameters we fed mice one of ten isocaloric diets that differed systematically in their macronutrient make-up. We allowed females to breed and observed striking effects of different macronutrients on fetal development, with protein intake having strong positive effects on offspring survival, accompanied by major shifts in the morphological structure of the placenta and placental lactogen production. However, maternal glucose tolerance was strongly impaired by high protein intake during pregnancy, with reproductive females more

susceptible to the effects of these macronutrients than non-pregnant animals. During lactation, we also observed that offspring development was optimized by a different ratio of macronutrients compared to during pregnancy. These results highlight the importance of optimizing macronutrient intake during pregnancy to ensure optimal health for the mother and her offspring.

id #132059

The Whānau Pakari experience: over a decade on

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Background

Whānau Pakari (WP) was created in 2012 and has since drawn on it's integrated research base to evolve the service to cater to our Taranaki whānau (families) to improve equity, acceptability and applicability.

Aim

To highlight learnings and resultant growth and change over the 12 years WP has been operating.

Methods

Research has guided service development to ensure appropriate and equitable support for the whānau referred, who are often over-represented statistically in terms of low socioeconomic status; autism, intellectual disability and ADHD, which pose barriers to accessing/utilising care. Research into barriers and facilitators to accessing the service highlighted the need for home-based only support for those struggling with transport or who are time-poor through high stress home environments.

Results

Initial research suggested the large age range created a learning gap, so WP developed the service to provide a workshop for rangatahi. Barriers to accessing weekly sessions resulted in offering more home-based Dietitian and Physical Activity Advisor visits to set whānau-focused goals. As a response to increasing numbers of neurodiverse children and adolescents we have increased staffing ratios and changed content to tailor to our changing needs of the whānau we support. Feedback from whānau around the element of fear and past trauma with healthcare creating barriers to attending weekly sessions has led us to create a friendly and relaxed "Meet the Team" session at the start of each term of weekly sessions to grow relationships and trust with staff prior to starting the term.

Key take-home messages/Discussion

WP is an ever-evolving service model for addressing weight-related issues for tamariki (children) and rangatahi (adolescents) within the Taranaki community. Future research has focussed on developing and integrating an online whānau-friendly, holistic assessment to further increase ease and acceptability of the service.

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id #127707

Critical role of brainstem NPFF neuronal circuits in the control of torpor-like states

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Energy conserving strategies such as torpor and hibernation are important survival mechanisms that endothermic organism utilise to deal with environmental challenges like starvation and cold exposure. While neuronal circuits in the brain have been implicated in this process the exact underlying mechanism of initiating and controlling torpor-like states is still unknown. We have now identified that selective chemogenetic activation of a brainstem NPFF neuronal circuit induces a hypothermic and hypometabolic state in mice, characterised by a rapid drop in brown adipose and whole-body temperature, reduced locomotor activity and altered glucose metabolism. Interestingly, although body temperature and oxygen consumption are low in this state, the mice are still able to adjust body temperature to environmental temperature fluctuations. Mechanistically, NTS NPFF neuronal activation modulates neurons in the lateral parabrachial nucleus (PBN) and median preoptic area (MPO) to reduce body temperature as well as alters parasympathetic outflow to control glucose metabolism. Taken together, our results reveal a specific neuronal circuit in the brain stem that serves as a major regulator of torpor, which may also be explored as potential intervention point in metabolic diseases.

id #128475

Activin A antagonizes BMP signaling via receptor competition in early human placental development

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Publish consent withheld

id #128476

Move Way More: Evaluating two waves of the LiveLighter® digital media campaign

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LiveLighter® is a comprehensive healthy lifestyle promotion and education program, funded by the Western Australian (WA) Department of Health since 2012, and delivered by Cancer Council WA. To address the low proportion of WA adults meeting Australian physical activity (PA) guidelines, Cancer Council WA developed 'Move More' – a LiveLighter® digital media campaign focusing on the intrinsic and short-term benefits of PA.

Eight videos were developed for the campaign across two waves of advertising (2024 and 2025); the videos included community members describing what motivates them to move. 'Move More' aimed to represent people not often shown in PA promotion and inspire people to find personally motivating reasons to maintain movement in their routine. Intrinsic benefits of PA such as improving mental health, increasing energy and social connection were highlighted. Both waves ran across digital channels, including catch-up TV, YouTube, Meta, TikTok, on relevant websites, and digital audio, and were evaluated through two post-campaign non-probability online surveys (T2, T3) with population weighting.

Respondents at T2 and T3 with campaign awareness were significantly more likely than those without awareness to intend to be more physically active (T2 66% cf. 44%; T3 66% cf. 48%); and to have been physically active for longer than usual (T2 21% cf. 12%; T3 20% cf. 10%). Respondents at T2 with campaign awareness were significantly more likely than those without awareness to have met the overall Australian PA guidelines (27% cf. 43%). Respondents at T2 and T3 with campaign awareness reported significantly increased participation in vigorous physical activity and meeting the vigorous PA guideline than those without awareness.

The development of a digital media campaign involving community members that highlights co-benefits of PA achieved positive changes to behaviour. Given the importance of PA to health, learnings from the development of campaigns such as this are important.

id #128988

Urinary Aldosterone for Diagnosis of Primary Aldosteronism – Comparison Between Immunoassay and Liquid Chromatography-Mass Spectrometry (LC-MS/MS) Analyses

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Background: Primary aldosteronism (PA) is the most common endocrine cause of hypertension associated with high cardiometabolic risk. Identification of PA is important as specific management can reduce the excess risk and potentially lead to cure. We have recently reported that urinary aldosterone excretion measured over 24 hours (24hr-UAE) by LC-MS/MS in the setting of 24-hour urinary sodium (24hr-UNa) ≥190 mmol/24h can confer high sensitivity and specificity to identify PA cases diagnosed by the standard seated saline

suppression test (SSST). Most centres however use immunoassay to measure aldosterone, and 24hr-UAE cut-offs in current practice are based on immunoassay measurements.

Aim: To compare the diagnostic performance of 24hr-UAE measured by immunoassay (24hr-UAE-IA) versus LC-MS/MS (24hr-UAE-LCMS) for diagnosing PA.

Methods: We analysed 182 prospectively-collected 24hr-urine samples from 167 patients who had hypertension with elevated aldosterone-renin ratio or had adrenalectomy for unilateral PA, 24hr-UNa measured and SSST performed, at a tertiary centre over 5 years. Patients were off interfering medications and on unrestricted dietary sodium. 24hr-UAE was analysed by LC-MS/MS in 182 samples, and by a concurrent Immunoassay in 121 stored samples. The performance of 24hr-UAE-IA in diagnosing PA was assessed by receiver operating characteristic (ROC) analyses, and compared with 24hr-UAE-LCMS, using SSST as the reference test.

Results: Among patients with 24hr-UNa ≥190 mmol/24h, a 24hr-UAE-IA cut-off of ≥24.5 nmol/24h yielded 92.3% sensitivity with 66.7% specificity. Increasing the cut-off to ≥35.5 nmol/24h improved specificity to 77.8% but reduced sensitivity to 73.0%. In contrast, 24hr-UAE-LCMS cut-off of ≥23.5 nmol/24h in the setting of 24hr-UNa ≥190 mmol/24h achieved 92.1% sensitivity and 82.6% specificity. The correlation between 24hr-UAE-LCMS and 24hr-UAE-IA was modest (r=0.352, P<0.001).

Conclusion: 24hr-UAE analysed by immunoassay offers inferior specificity compared to LC-MS/MS. These findings highlight the limitations of immunoassay-based cut-offs and support the broader use of LC-MS/MS for accurate diagnosis of PA.

id #128733

Premature placental ageing contributes to Late Onset Preeclampsia

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Late Onset Preeclampsia (LOPE) is a serious condition affecting ~6% of Australian pregnancies, accounting for ~85% of all preeclampsia cases[1]. It develops after 34 weeks' gestation and remains incurable, threatening the health of mother and baby, until delivery. Placentae from LOPE pregnancies show histopathological signs of ageing[2], however the mechanism by which this occurs remains unknown.

Placental tissue (n=3/LOPE or healthy pregnancy, per gestational week 36,37,38,39,40,41; total n=36) was assessed for telomere length using TESLA assay and markers of ageing (gH2AX, 8-OHdG) using immunofluorescence. Trophoblast stem cells were isolated from placenta biopsies (n=3/LOPE or healthy, per gestational week 37/40; total n=12) and grown as placental organoids for 4 weeks, with or without treatment using antioxidant superoxide dismutase, anti-inflammatory compound JNUTS013 or antisense oligonucleotides to sequester Telomeric Repeat-containing RNAs (TERRAs; non-coding RNAs that protect from telomere degradation). Telomere, senescence (senescence-associated b-Galactosidase assays), damage and morphometric analyses were performed along with appropriate statistical tests.

Placentae from LOPE had shortened telomere length (p=0.0253) and increased expression of ageing markers (p=0.0021, p=0.0050) significantly earlier in gestation compared with healthy controls. Placental organoids were confirmed to age in culture at a similar rate to placentae *in vivo*. Treatment with superoxide dismutase and JNUTS013 delayed, and treatment with antisense oligonucleotides expedited, telomere shortening, senescence and DNA damage (results shortened for brevity; all p<0.05) with no significant change in organoid morphometry. Treatment with antisense oligonucleotides had the largest effect on placental organoid ageing, with treated organoids ageing ~2 weeks faster than untreated.

In summary, the LOPE placenta experiences premature placental ageing, likely due to multiple biological mechanisms. Our investigation into 3 proposed mechanisms confirmed that all contributed to premature placental ageing, with inflammation contributing the least and TERRA depletion contributing the most. These findings highlight potential therapeutic targets to delay placental ageing in LOPE, improving pregnancy outcomes.

1. 1 Heart Foundation, Australia.
2. 2 Kujoth GC, Science, 2005

id #128222

Mental health treatment utilisation among transgender and gender-diverse people following gender affirming hormone therapy: evidence from whole-of-population Australian administrative data

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Aims: Gender affirming hormone therapy (GAHT) is associated with improved self-reported mental health outcomes in transgender and gender-diverse (TGD) individuals, yet limited evidence examines mental healthcare utilisation changes after GAHT initiation.

Methods: Using Australian administrative data (2012–2024), we identified TGD individuals initiating estradiol-based (e-GAHT) or testosterone-based GAHT (t-GAHT). We applied a dynamic difference-in-differences model to estimate within-individual changes in mental health services (general practitioner, psychiatrist, psychologist and other allied health professionals) and prescriptions (antidepressants, anxiolytics), using future GAHT recipients as controls. Effects were estimated relative to individuals' utilisation 2 years before GAHT initiation, up to 5 years post-initiation, and stratified by age (15-24, ≥25 years) and baseline mental healthcare engagement (above/below mean mental health prescription use).

Results: 21,073 individuals initiated e-GAHT and 11,418 initiated t-GAHT (median follow-up 4.5 and 3.8 years, respectively). Prior to initiation, e-GAHT recipients had lower engagement with mental healthcare. For both regimens, mental health service use rose at initiation but declined sharply thereafter. Five years post-initiation, t-GAHT and e-GAHT recipients used 2.59 (95%CI 1.87;3.31) and 0.29 (95%CI -0.03;0.60) fewer mental health services per year, respectively. Mental health prescription use among e-GAHT recipients initially rose but fell to 0.53 (95% CI 0.20; 0.86) at 5 years, while t-GAHT recipients used 1.02 (95%CI 0.31;1.72) fewer prescriptions per year at 5 years. Reductions in mental healthcare were more pronounced for individuals with higher baseline mental healthcare engagement as well as e-GAHT recipients aged ≥25 years.

Conclusion: GAHT initiation is associated with dynamic changes in mental healthcare use. While use increases around the time of initiation – particularly among younger e-GAHT recipients and those with limited prior mental healthcare engagement – use declines substantially over time. Altogether, GAHT may help address unmet mental health needs and contribute to longer-term reductions in mental healthcare use and associated costs among TGD individuals.

id #128478

Examining the anti-obesogenic effects of a novel ceramide synthase inhibitor

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Ceramide, a sphingolipid, has a causal role in cardiometabolic disease. Ceramides containing saturated acyl tails of 16 and 18 carbons are particularly deleterious, due to frequent association with metabolic diseases. Ceramide synthase (CerS), the enzyme catalysing ceramide production, has six isoforms, each demonstrating specific fatty-acid substrate preference and tissue localisation. Selective pharmacological inhibition of CerS isoforms producing deleterious ceramides, could prevent cardiometabolic disease. Our study aimed to characterise the anti-obesogenic effects of ET2.39, a novel CerS inhibitor.

HEK293 cells were treated with ET2.39 and effects on ceramide levels and cell viability were evaluated. A 4 week high-fat diet (HFD) study was undertaken with male C57BL/6 mice provided Chow, HFD, or HFD + ET2.39 (~10 mg/kg/day) and physiological measurements (weight gain, fat and lean mass, glucose tolerance) taken throughout. Subcellular fractions were extracted from muscle and liver using ultracentrifugation and an iodixanol gradient. Enrichment was verified via western blotting. Lipids extracted from cells, whole tissue lysates and subcellular fractions, were analysed via targeted liquid chromatography-mass spectrometry. ET2.39 significantly inhibited C16:0 and C18:0 ceramide production in HEK293 cells, without impacting cell viability. Dietary administration of ET2.39 prevented HFD-induced weight gain, but not glucose intolerance. ET2.39 slowed fat accretion, significantly decreasing epididymal and inguinal fat pad mass in mice.

Subcellular fractions demonstrated unique sphingolipid composition, with greatest sphingolipid content in the membrane and nucleus. HFD significantly increased deleterious ceramides across all fractions. ET2.39 treatment significantly reduced C18 ceramides in quadriceps (50% reduction), with similar trends across cellular fractions. There was no observed impact of ET2.39 on C16:0 ceramides in tissues from mice. Different sphingolipid distributions exist across cellular fractions, and can be altered by diet and pharmacological inhibition. Our novel CerS inhibitor, ET2.39 demonstrates significant anti-obesogenic effects in HFD-fed mice and could limit the accumulation of deleterious C18:0 ceramides in key metabolic tissues.

id #128992

GLP-1RA Use for Obesity in Australia: Access, Affordability, and Support Gaps

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Background: Glucagon-like peptide-1 receptor agonists (GLP-1RA) are an effective weight management treatment but are expensive with limited government subsidisation for individuals with obesity and access largely restricted to costly private prescriptions. Concerns exist about equitable access, affordability, and adequacy of supportive care. This research explored Australian GLP-1RA medication use, focusing on usage barriers and support systems to inform strategies for safe and improved access for individuals with obesity without diabetes.

Methods: A cross-sectional survey online survey was used to collect a convenience sample of participants via Facebook/Instagram. Participants were asked about patterns of weight loss injection usage and support accessed while using the medications. Eligibility included living in Australia and aged >18 years old. Key variables measured included demographics, access to medications, prescribing practitioner and self-reported perceptions of nutritional, physical activity, and behavioural support. Data were descriptively analysed and univariate logistic regression used to identify factors associated with perceptions of support.

Results: N = 1311. The sample was predominantly female (90.1%), English-speaking (95.5%), with participants evenly distributed across socioeconomic quintiles. Most participants (72.9%) had obesity, with 58.1% reporting current GLP-1RA use (mainly semaglutide 55.9%), predominantly prescribed by GPs. Affordability was a significant barrier with 58.3% of users finding GLP-1RA 'difficult/very difficult' to afford. Despite clinical guidance promoting multidisciplinary support, several support gaps were identified: only 44% received sufficient dietary support, 36% physical activity support and 34% behavioural/psychological support. Only 22.6% reported referral to other healthcare professionals (mostly dietitians). Greater need for support was reported by those with higher obesity classes and lower socioeconomic status.

Conclusion: GLP-1RA use for obesity appears to be widespread, but high cost and under-provision of multidisciplinary support underscore significant equity and sustainability challenges. Support needs of users are not being adequately met, indicating urgent need for integrated, patient-centred approaches to improve access and health outcomes.

id #128225

Inflammation and Fertility in Cattle

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The immune system plays an integral role in female fertility. Uterine inflammation due to infection or extrinsic stress have immediate and long-term implications for fertility. Common, acute postpartum uterine infections in cattle are associated with decreased fertility long after the resolution of disease. We hypothesize that uterine inflammation causes long-term alterations to tissues of the reproductive tract that compromise fertility after disease resolution. Using models of spontaneous uterine disease and induced uterine inflammation we have demonstrated long-term changes to the competence of uterine tissues to recognize and support early embryo development and facilitate pregnancy recognition. In parallel, granulosa cells of the developing ovarian follicle are exposed to pathogen components like lipopolysaccharide during uterine infections. Consequently, granulosa cells create an inflammatory environment in which oocytes develop. We have shown that oocytes collected from cows weeks after the occurrence of uterine inflammation have a decreased capacity to develop preimplantation stage embryos. Similarly, if oocytes are matured in an environment that mimics ovarian follicle inflammation, they too have a decreased capacity for further development. Granulosa cell inflammation also alters ovarian endocrine function. The capacity of granulosa cells to produce estradiol is diminished when exposed to pathogen components, and long-term steroidogenic capacity of subsequent luteal tissue is altered even after the resolution of disease. Collectively, we have demonstrated that inflammation of the female reproductive tract has both immediate and long-term implications for the capacity to generate and support future pregnancies long after the resolution of disease. While these discoveries are important in improving food security in animal agriculture, they also have implications for human fertility where sexually transmitted infections are common.

id #128481

Phenotype-resolved proteomic profiling of placental tissue reveals cell-type-specific dysregulation in Fetal Growth Restriction

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Publish consent withheld

id #128738

Decision Support Tools for Active Surveillance of Low Risk Cancers: A Scoping Review

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Background: Evidence for the role of active surveillance (AS) as an alternative to surgery in the management of low-risk thyroid cancer is well established. Despite this, many clinicians do not feel comfortable in identifying patients who are appropriate for AS.

Aims: This scoping review explores key features that underpin decision support tools or aids looking at AS in prostate, breast and thyroid cancer. This information will be utilised to help refine a pilot clinical decision support tool for low-risk thyroid cancer.

Methods: PubMed, MEDLINE, EMBASE and Cochrane databases were searched. No limits were put on publication date, including studies from inception to January 2023. Studies were imported into Covidence software. Duplicates were removed, then screening of abstracts and titles eliminated further articles.

Results: The search identified 3542 unique studies; 3457 were excluded on review of abstract and title. 85 studies underwentfull text review and 25 studies were included in final analysis. Eight studies were randomised control trials, six were systematic reviews, five were cohort studies, four were qualitative research and two were cross sectional. Twenty one studies addressed prostate cancer, two addressed ductal carcinoma in situ, one addressed thyroid cancer and one looked at all cancers suitable for AS. Themes explored in studies included clinician acceptability of the decision aid, patient knowledge on their cancer, rates of decision conflict and treatment choice. Overall, the use of decision aids reduced decision conflict and demonstrated treatment choice concordant with decision aid recommendations. Web based tools were found to be a feasible tool for both patients and clinicians to streamline the treatment decision process.

Conclusion: This scoping review has identified a framework of the key features of decision aids designed to assist both patient and clinician in approach to treatment of low risk cancers in which active surveillance is a management option.

id #130532

Trafficking of RNAs and organelles regulating preimplantation embryogenesis

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The transformation of a mammalian embryo from a tiny soccer ball-like structure into a newborn with four limbs, a beating heart and big bright eyes is one of the most remarkable and fundamental processes of life. Inside the soccer ball-like embryo resides a handful of “all-rounder” cells, known as pluripotent cells, which can give rise to any type of cell in the adult body.

Until recently the inimitable potency of pluripotent cells has been known to be regulated by a combination of genetic, epigenetic and external factors. We were the first to discover that pluripotent cells develop and mature into distinct cell types also based on the functions of their inner scaffolding, the microtubule cytoskeleton, which was until then widely regarded as disorganised and its contribution to cell fate specification was largely ignored.

Inside a cell, organelles and proteins are usually not randomly distributed but are assigned to regions where they are needed. The cell utilises the microtubule cytoskeleton as the road map to localise organelles and to trigger the relay of signals intra- and intercellularly. By performing innovative live imaging of preimplantation mouse embryos, we discovered an unprecedented form of non-centrosomal microtubule organisation required for the formation and maintenance of pluripotency. Dependent on the microtubule anchor and nucleator Calmodulin-Spectrin associated protein 3 (CAMSAP3), this form of non-centrosomal microtubule organisation orchestrates the asymmetric distribution of cell adhesion proteins, RNAs and organelles which results in an unequal inheritance of information, and differential cell fate decisions of daughter cells.

Our discoveries comprehensively address the cell biological hallmarks of pluripotency during mammalian embryogenesis, orchestrated by the microtubule cytoskeleton. By addressing this knowledge gap, we can harness our discoveries to develop novel therapeutics for regenerative medicine and fertility.

id #128742

Pre-pregnancy liraglutide does not prevent the post-pregnancy adverse cardiovascular effects of maternal obesity in a murine model of obesity

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Background: Obesity during pregnancy heightens cardiovascular disease (CVD) risk in women by compounding the physiological demands of pregnancy, such as increased blood volume and altered cardiac output. Current recommendations advise pre-pregnancy weight loss. GLP-1 receptor agonists show promise in weight management with improved cardiovascular outcomes, but their use pre-pregnancy remains understudied.

Aim: To characterise the effects of pre-pregnancy liraglutide treatment on post-pregnancy cardiac protein expression in a murine model of high-fat diet–induced obesity.

Methods: Female C57BL/6 mice were allocated to either a high-fat-diet (HFD) or chow-diet (CHOW). Liraglutide treatment (LIRA) commenced for a subset of the HFD group, after 8-weeks of diet commencement, at a dose of 0.3mg/kg. All other mice received volume matched saline. Female mice were co-housed with male mice until pregnancy was achieved, and after birth and lactation they were sacrificed (n=4/group/timepoint). Hearts were perfused with phosphate buffered saline before being snap frozen whole. After homogenisation and sample preparation proteomic analysis was completed on cardiac tissue using data-dependant acquisition, liquid chromatography mass spectrometry. Statistical analysis was completed in Spectronaught and R.

Results: In total 31 proteins were significantly different post-pregnancy between the HFD and CHOW groups. Of these 15 were significantly up-regulated and 16 were significantly down-regulated (Adj.p<0.05). Whilst both tensin 1 and Succinate-dehydrogenase-assembly-factor 3 were approximately 2-fold increase in both the CHOW and LIRA groups comparted to HFD (Adj.p<0.05), 17 of the proteins dysregulated between HFD and CHOW followed the same pattern when comparing LIRA to CHOW (Adj.p<0.05). These proteins were significantly associated with several metabolic and oxidative pathways (p<0.05).

Conclusion: Pre-pregnancy liraglutide treatment led to minimal changes in cardiac protein expression, suggesting limited cardioprotective effects after pregnancy. In contrast, the chow-fed group showed widespread alterations in protein expression, highlighting the greater impact of baseline metabolic health on postpartum cardiovascular outcomes.

id #128487

Inhibition of mtDNA replication by oocyte specific deletion of *Polg* leads to premature ovarian insufficiency in mice

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Publish consent withheld

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id #132584

Environmental determinants of diet quality: implications for public health policy

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Momentum and action: National Dietary Surveys of Australian adults (1983) and school children (1985) set the scene for government action (e.g.,; Nutrition Taskforce of the Better Health Commission (1987); National Food and Nutrition Policy (1992); National Dietary Guidelines for Australia (1991), for Children and Adolescents (1995) and Older Australian (1999); National Goals and Targets for Australia's Health (1993); Strategic Intergovernmental Nutrition Alliance (SIGNAL), Eat Well Australia and the National Aboriginal and Torres Strait Islander Nutrition Strategy and Action Plan (2000-2010)). Key principles addressed environmental determinants – social justice, quality of the food supply, community participation and accountability, food and nutrition system and wider interaction, and ecologically sustainable development. In the late 1980's, the Department of Health in Western Australia and New South Wales implemented social media campaigns to encourage consumption consistent with dietary guidelines. Deakin University's Food and Nutrition Program (1991) ambitious intervention framework to improve public health nutrition to addressed determinants of dietary intake, nutrition status, and health outcomes. Addressing the food supply (e.g., availability, cost and composition), consumer characteristics as drivers of demand (e.g., knowledge, beliefs, values and attitudes) and other environmental influences (e.g., income, family, health services). In 2013, the increasing non-communicable disease attributable to diet led to the global International Network for Food and Obesity/NCDs Research, Monitoring and Action Support (INFORMAS). focussing on healthy food environments to reduce obesity. Specifically, the unhealthy food environment supply-side 'push' of energy-dense, nutrient-poor, widely available, relatively inexpensive and heavily promoted processed food products. Importantly, monitoring food environments, access, and sovereignty. *Political amnesia:* A potted history about the memory of politics and policymaking in public health nutrition in Australia with a focus on key lessons and turning points in addressing the environmental determinants of diet quality.

id #123115

Choosing to Be Seen: Rethinking Autism Disclosure

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Disclosure of an autism diagnosis or identity is a deeply personal decision that can shape an autistic person's access to support, sense of safety, and experience of inclusion. Yet disclosure can also invite misunderstanding, stigma, or discrimination. This presentation draws on a program of co-produced research exploring the complexities of autism disclosure across contexts, methods, and identities, using innovative approaches such as social media analysis and experience sampling methodology (ESM). Findings from an analysis of over 3,000 social media posts revealed that autistic people often feel compelled to weigh the potential benefits of disclosure against widespread societal misunderstandings of autism—particularly in workplaces, healthcare, and interpersonal relationships. A second study demonstrated that disclosure is more likely among autistic adults who hold a strong sense of autistic or sexual identity, while other identity dimensions (e.g., ethnicity, gender) showed no clear association. Finally, a real-time ESM study captured 231 disclosure and nondisclosure experiences, highlighting how disclosure decisions are shaped by perceived contextual safety, anticipated energy costs, and the desire to be authentic, educate others, or advocate for change. Across these studies, one message is clear: disclosure is not a single, simple decision, but a continuous, complex negotiation. While often framed as a personal choice, our research supports a shift in focus toward systemic responsibility—creating environments where disclosure is safe, supported, and not always necessary for respect or inclusion. This talk will offer practical implications for educators, clinicians, and researchers interested in adopting neurodiversity-affirming practice and fostering inclusive environments where autistic people can thrive—whether or not they choose to disclose.

id #128492

Direct effects of survodutide on liver endpoints beyond weight loss: insights from a phase 2 trial of the glucagon receptor/glucagon-like peptide-1 receptor dual agonist survodutide in people with metabolic dysfunction-associated steatohepatitis and fibrosis

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We evaluated weight-loss (WL) direct and indirect effects of survodutide, a GCGR/GLP-1R dual agonist, on liver endpoints in a phase 2 trial in people with biopsy-confirmed MASH and F1–F3 fibrosis (NCT04771273).

A total of 295 participants were randomised to once-weekly s.c. survodutide 2.4, 4.8, 6.0 mg or placebo. Participants with fibrosis stage F2/F3 and paired baseline and end-of-treatment biopsy readings (N=170) were included, survodutide arms were pooled. Mediation analysis explores how an intermediate variable explains the pathway between an exposure and an outcome. This analysis assessed the proportion of the effect of survodutide on liver endpoints attributable to a direct/indirect effect mediated by WL. Liver endpoints assessed at Week 48 included resolution of MASH without worsening of fibrosis, improvement in fibrosis without worsening of MASH, absolute change in ELF™ score, relative change in PRO-C3, FAST score, LSM (FibroScan), and MRI-PDFF. Model included treatment and percentage change in bodyweight, with baseline bodyweight, type 2 diabetes status, and fibrosis stage as covariates. Total treatment effect (TE) or total odds ratios (OR), percentages mediated (proportion mediated by WL [indirect effect of changes in bodyweight in relation to the total effect]) and 95% CI are presented.

Liver endpoints that were highly mediated by WL were resolution of MASH without worsening of fibrosis (response rate: 62.9 vs 13.0% for placebo; OR: 14.70), or changes in MRI-PDFF (TE: −50.3 [−60.1, −40.5]). Endpoints for which WL had a lower attribution were ELF™ (TE: -0.64 [−0.83, −0.45]), improvement in fibrosis without worsening of MASH (response rate: 52.6 vs 25.9% for placebo; OR: 3.68), LSM (TE: −38.78 [−49.08, −28.49]), FAST (TE: −65.16 [−79.13, −51.18]), and PRO-C3 (TE: −28.63 [−36.38, −20.88]).

Survodutide had a direct (WL-independent) effect on liver endpoints related to improvement in inflammation and fibrosis via direct glucagon agonism in the liver.

id #130796

The healthy weight service (HWS): A hospital perspective

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The Healthy Weight Service (HWS) at Perth Children's Hospital delivers tertiary-level outpatient care to children experiencing severe (>150% of 95th percentile BMI) or complex obesity. HWS provides comprehensive, evidence-based support tailored to the needs of each family.

Children <16 years may be referred to HWS with pre-diabetes, significant obesity-related complications, age under 24 months with concerning weight patterns, or complex contributing factors.

Our team includes Endocrinologist, Paediatrician, Nurse, Social Worker, Mental Health Nurse, Dietitian, Physiotherapist, Exercise Physiologist and Clinical Psychologist.

Our family-centred intervention begins with psychosocial telephone screening followed by a comprehensive in-person triage involving all team members. Ongoing care typically includes three-monthly follow-ups over the course of a year.

We offer personalised dietary and activity modification programs, support for neurodiverse children, families facing financial or social barriers, pharmacotherapy when clinically indicated and collaboration with other medical specialties to manage coexisting conditions.

HWS has historically (prior to GLP-1 agonist uptake) achieved a change in BMIz of -0.19 (95% CI -0.26, -0.13, $p < 0.001$, N = 464). Preschool (aged 2-5), child (aged 6-12) and adolescent (aged 13-16) subgroups comprised 25%, 49% and 26% respectively. Within our cohort 1.3% have known monogenic causes. Dietetic assessments show 100% of families improve their food choices and eating behaviours. Younger age and higher baseline BMIz were independently associated with larger reductions in BMIz. Analysis stratified by age subgroup showed a worse outcome in the child sub-group (coefficient B=0.36, 95% CI 0.16, 0.56, $p < 0.001$, n=227) during COVID (2020).

A strength is the rapport, trust and sustained engagement established with families. We face significant challenges due to high demand and limited staffing capacity. Despite this, we remain committed to expanding our reach by partnering with GPs and clinicians across Western Australia to deliver shared care for children and adolescents living with severe obesity-related complications.

id #128749

Early pregnancy metabolic syndrome, micronutrients, placental hormones and risk of pregnancy complications in the STOP Study

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We have previously shown that maternal metabolic syndrome (MetS) in early pregnancy increased risk for GDM (4-fold) and preeclampsia (2-fold) in the international SCOPE Study. In separate analyses we have also shown increased folate status and vitamin D deficiency increased risk for GDM. Here we aimed to investigate the combination of these factors and placental hormone secretion in the STOP Study. Maternal MetS was assessed using IDF criteria at 11-16 weeks' gestation. Circulating red cell folate, serum B12, homocysteine, vitamin D, PRL, hPL and GH2 were also quantified at this time. Logistic regression models were adjusted for maternal BMI, age and socioeconomic index. Splines were used to model non-linearity of continuous variables to assess interactions in pregnancy outcomes.

Data were available for 1208 women of whom 112 (9%) had MetS. Women with MetS were significantly more likely to develop GDM (38.2% vs 13.5%), preeclampsia (18.5% vs 8.9%) and gestational hypertension (14.4% vs 6.1%) than those without MetS. SGA and spontaneous preterm birth were similar between the two groups.

In women with MetS, serum vitamin D was significantly lower ($p<0.005$) with more women deficient or insufficient in this secosteroid hormone. Serum folate was higher while red cell folate (RCF) was not different in women with MetS but the ratio of RCF to vitamin D was higher in women with MetS ($p<0.001$). hPL was also significantly lower in women with MetS than those without it ($p<0.0008$). Both PRL and GH2 were lower in women with MetS but these were not significant.

MetS, independent of maternal BMI, appears to have important impacts on pregnancy outcomes and their mediators. MetS is also a risk factor for long term cardiometabolic diseases. Therefore, reducing its incidence and severity is essential for pregnancy planning and future health.

id #127982

A novel mechanism of sperm midpiece epididymal maturation and the role of CCDC112 in sperm midpiece formation and establishing an optimal flagella waveform

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The mitochondrial sheath is a key requirement for sperm function, providing structural support and the energy necessary for motility. While many of the key steps of sperm mitochondrial sheath formation have been described at a cytological level, the molecular processes required for its assembly and function remain poorly understood. Recently, poorly characterised coiled coil domain containing protein, CCDC112, has been identified as a likely regulator of cilia and sperm tail formation via roles in the assembly, maintenance, and remodelling of the centrosome. Herein, using a *Ccdc112* loss-of-function mouse model, we tested this role and show that CCDC112 is essential for male fertility. We demonstrated a critical role for CCDC112 in mitochondrial morphogenesis and remodelling during mitochondrial sheath formation, where loss of CCDC112 resulted in sperm with highly abnormal mitochondrial sheath architecture and stiffened midpieces with limited flexibility (p <0.0001 compared to wildtype). Consequently, loss-of-function sperm possessed an irregular flagellar waveform, with significantly diminished mitochondrial ATP production and mechanical power, resulting in a significantly reduced ability for progressive motility and swimming speed. Ultimately, given their inability to sufficiently traverse the female reproductive tract, loss-of-function sperm exhibit reduced fertilisation capabilities, with impaired penetration of the zonae pellucidae of oocytes and poor sperm-oocyte fusion. We identified that these defects were in part explained by CCDC112 acting as a component of the distal appendages of the mother centriole. Using this mouse model, we also identified a previously unrecognised process of epididymal mitochondrial sheath maturation that occurs during epididymal sperm maturation. These findings suggest that upon sperm release from the testis, most sperm midpieces are structurally immature, with maturation continuing as sperm transit through the epididymis from caput to cauda. Collectively, we show that CCDC112 is an essential regulator of sperm midpiece assembly and function and reveal a novel form of epididymal sperm maturation.

id #130802

Epigenetic inheritance as a mediator of paternal stress exposure and its multigenerational modification of behaviour

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Epigenetic inheritance is the transmission of non-genetic, environmentally-induced epigenetic changes from parents to their offspring. In some instances, this leads to inter- (F0 to F1) or trans-generational (F2/F3 and beyond) modifications of offspring traits and behaviour. The impacts of maternal influences on offspring health are well-documented and studied. By comparison, there have been far fewer investigations of the paternal influence. In this presentation, I will describe the development of a preclinical model of generalised daily stress that our lab then used to investigate the impact of paternal stress on the sperm epigenome and on the behaviour of F1 and F2 PatCORT offspring. We have found that this mild exposure to stress was sufficient to alter the non-coding RNA content of sperm, including microRNA and long non-coding RNAs (Short et al., 2016). More recently, using long-read DNA sequencing methods, we have also demonstrated alterations to sperm DNA methylation in this mouse model (Hoffmann et al., 2023). Validation of miRNA-regulated target genes such as insulin-like growth factor 2 (Igf2) confirmed sexually-dimorphic impacts of igf2 expression in the brains of male and female F1 PatCORT offspring. Paternal stress exposure resulted in male F1 PatCORT offspring exhibiting behavioural responses associated with anxiety and depression. Assessments of rodent naturalistic behaviours further revealed intergenerational shifts in subordinate displays towards other male mice and receptivity from female mice. Expansion of our studies to other preclinical models of paternal stress (early-life maternal separation) have uncovered significant changes to the neural activation patterns in male F1 offspring linked to greater risk taking, implying that brain development is prone to paternally-mediated intergenerational influence. Finally, I will describe our studies of the intergenerational influences of paternal physical activity and our separate attempts to document the earliest intergenerational impacts on offspring development.

id #127988

The genomic landscape of juvenile granulosa cell tumours of the ovary

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Juvenile granulosa cell tumour (jGCT) is a rare, hormonally-driven ovarian tumour that primarily affects girls and young woman. While early-stage disease often has favourable outcomes, prognosis is poor for patients with advanced or recurrent disease. Unlike adult GCT, which is uniformly characterised by the *FOXL2*^{C134W} mutation, the genomic drivers of jGCT remain poorly defined, limiting the development of targeted therapies.

To address this, we performed whole genome sequencing (WGS) on tumour and matched germline DNA from six patients with histologically confirmed jGCT. Sequencing data was processed using the nf-core/Sarek pipeline with two variant callers (Mutect2 and Strelka2), followed by stringent multi-layered filtering, and variant prioritisation through a customised variant ranking framework.

Consistent with previous reports, the pathognomonic *FOXL2*^{C134W} mutation, was absent in all cases. The known jGCT-associated somatic *GNAS* hotspot mutation was identified in two patients, and a pathogenic *IDH1*^{R132} mutation was observed in one tumour. Mutations in *AKT1* and *DICER1* were not detected. Each of three cancer-related genes (*PLEC*, *TGFBR1/ALK5*, *TP53*) harboured somatic variants, with each variant detected in two different patients.

Of particular interest, a previously unreported heterozygous missense mutation in *TGFBR1/ALK5*, a valine substitution at a highly conserved glycine residue, was found in both *GNAS*-mutated tumours. This variant predicted to activate SMAD2/3 signalling, was functionally validated using a TGFBR1-SMAD transactivation assay. The *TGFBR1/ALK5* mutation induced constituent receptor signalling and then enhanced further following ligand binding. Strikingly, an equivalent variant in orthologues *ACVR1B/ALK4* gene was also identified in a separate tumour, suggesting activation of ALK/SMAD signalling as a potential oncogenic mechanism in jGCT.

These findings highlight the genetic heterogeneity of jGCT and uncover ALK/SMAD signalling as a recurrently altered pathway. Our study underscores the need for personalised molecular profiling in jGCT and lays the groundwork for exploring novel targeted therapeutic strategies for this rare and understudied tumour.

id #127990

Weight-independent benefits of semaglutide on histology and non-invasive tests in participants with biopsy-defined MASH: *Post hoc* analysis of the ESSENCE trial part 1

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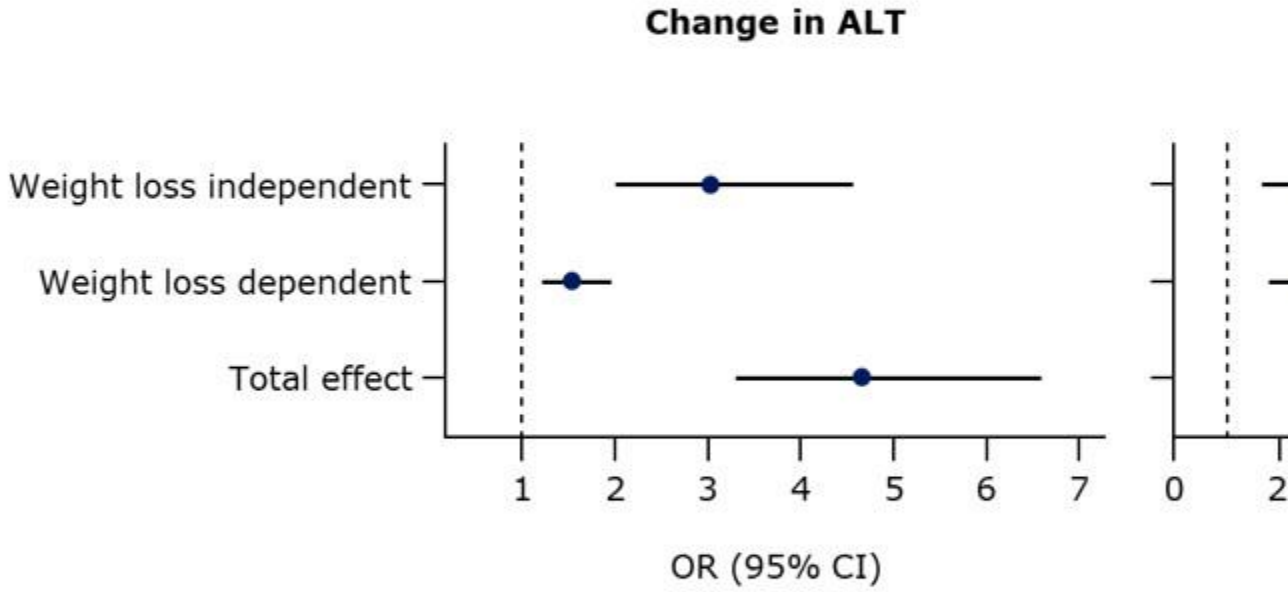
Aim: The phase 3 ESSENCE trial (NCT04822181) reported positive interim results in 800 randomised participants with F2/F3 MASH receiving once-weekly semaglutide 2.4 mg vs placebo. In this *post hoc* analysis, we assessed the weight dependency of the effects of semaglutide 2.4 mg on non-invasive tests (NIT)s & histology after 72 weeks, using weight loss-independent & -dependent pathways as covariates.

Methods: NITs & biopsies were assessed at baseline & week 72. MASH-related NIT responder endpoints were change in ALT(≥17-unit reduction) & FibroScan-AST (FAST) score (≥0.22 reduction). Fibrosis-related NIT responder endpoints were change in liver stiffness measurement (VCTE -30%) & Enhanced Liver Fibrosis (ELF) score (≥0.5-unit reduction). Histologic endpoints included MASH resolution & improvement in fibrosis. All endpoints were assessed using logistic regression at week 72 with treatment as exposure, % weight loss from baseline to w72 as mediator, baseline T2D status, fibrosis stage, & body weight as covariates. The total & weight loss-independent & -dependent effect sizes were calculated as odds ratios (ORs), & missing data were omitted. Data are based on the full analysis set from the on-treatment observation period.

Results:

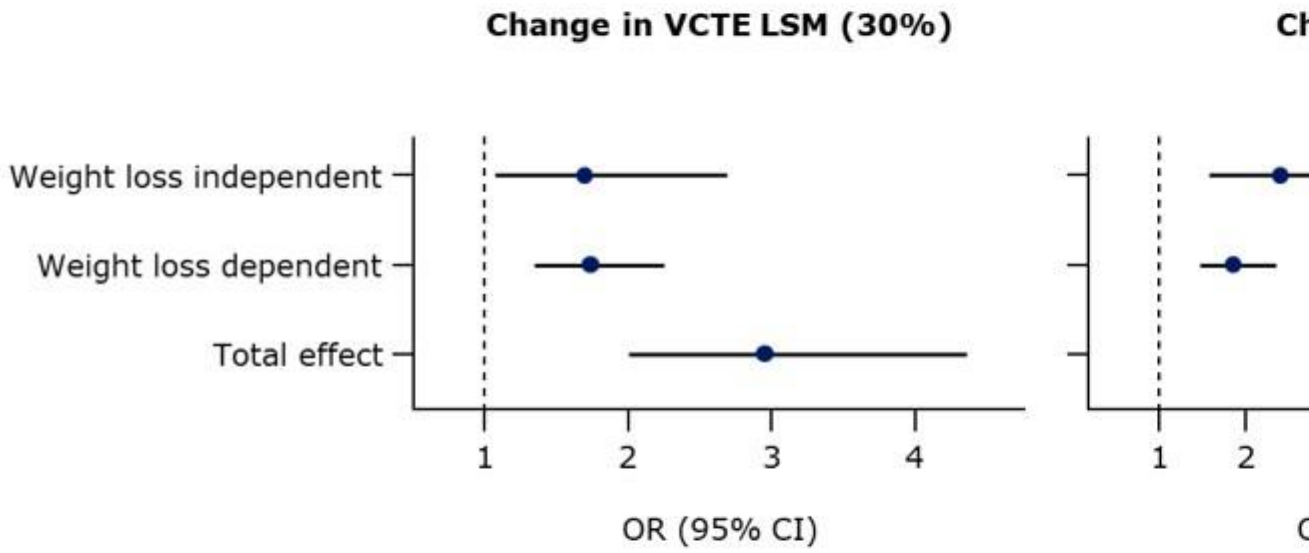
Figure 1. MASH-related endpoints



Data are based on the full analysis set from the on-treatment observation period.
All endpoints were assessed for weight loss-independent effects (where the char
effect on the mediator [body weight]) and weight loss-dependent effects (where t
the mediator [weight loss]). Effects were considered statistically significant if the
Responder definitions: ALT reduction ≥17 U/L, FAST score reduction ≥0.22 and
inflammation).

ALT, alanine aminotransferase; CI, confidence interval; FAST, FibroScan-aspart
steatohepatitis; NAS, nonalcoholic fatty liver disease activity score; OR, odds rati

Figure 2. Fibrotic-related endpoints



Data are based on the full analysis set from the on-treatment observation period.
All endpoints were assessed for weight loss-independent effects (where the chan
effect on the mediator [body weight]) and weight loss-dependent effects (where th
the mediator [weight loss]).
Effects were considered statistically significant if the lower bound of the CI exceed
Responder definitions: VCTE LSM reduction 30%; ELF score reduction ≥0.5 units
CI, confidence interval; ELF, Enhanced Liver Fibrosis; MASH, metabolic dysfunct
vibration-controlled transient elastography liver stiffness measurement.

Conclusion: Semaglutide 2.4 mg improved MASH-related histological & NIT endpoints & fibrosis-related NIT endpoints through equal contributions of weight loss-independent & -dependent metabolic mechanisms, with effects beyond weight loss.

id #128246

Tarnishing the health halo: How warning labels and removal of nutrition content claims influence parental perceptions and purchases of commercial infant and toddler foods with added sugar.

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Background: Many commercial infant and toddler foods (CITFs) contain added sugars, posing health risks to consumers. Front-of-pack nutrition content claims can create a 'health halo' over sugary products, whereas warning labels could be effective in raising awareness of potential harms.

Aims: Test whether displaying Added Sugar Warning labels ('warning labels') and removing nutrition content claims on sugary CITFs helps parents evaluate products and prompts purchasing of CITFs without added sugar.

Methods: Using an online shopping experiment, 1,017 Australian parents of infants and toddlers (6 to <36 months) were randomly assigned to one of four conditions, using a 2 (warning label: control/warning) X 2 (claims: absent/present) between-subjects design. Parents viewed screens displaying twelve infant/toddler CITFs (six with added sugar, six without), featuring labels and claims reflecting their condition. Regression analyses tested effects of warning labels and no claims on product perceptions, purchasing choices and intentions.

Results/findings: Significant main effects (all p<0.05) showed that cf. control condition, warning labels: reduced parent's likelihood of choosing CITFs with added sugar (82% vs. 53%); mean purchasing intentions (M: 4.93 vs. 3.80); perceptions of suitability (M: 4.65 vs. 3.70), naturalness (M:4.55 vs. 3.82), healthiness (M: 4.48 vs. 3.76), and fibre content (M: 4.44 vs. 4.05); but increased perceptions of the level of added sugar (M: 4.70 vs. 5.70), total sugar (M: 4.62 vs. 5.07) in CITFs with added sugar, irrespective of whether nutrition content claims were displayed or not (no main effects or interactions with warning labels).

Conclusions: Displaying warning labels on CITFs containing added sugar detracts from parents' perceptions of the healthiness and suitability of these products and reorients their purchasing preferences towards lower sugar options, even in the presence of nutrition content claims. Warning labels offer a promising policy option to inform parents about added sugars in CITFs, nudging them towards healthier choices.

id #128502

Characterising the immune response driven by seminal extracellular vesicles in human primary cervical epithelial cells

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Introduction: Seminal plasma interacts with epithelial cells lining the female reproductive tract (FRT) to activate proinflammatory responses that facilitate pregnancy. Seminal extracellular vesicles (SEVs) are postulated to contribute to this process, although their signalling capacity is poorly understood.

Aims: To explore the immune-signalling capacity of SEVs in human primary cervical epithelial cells.

Methods: SEVs were isolated using an established density gradient ultracentrifugation protocol and EV concentration was characterised using nanoparticle tracking analysis. SEVs or matching seminal plasma from normozoospermic donors (n=14) was co-incubated with primary human cervical epithelial cells using media-treated cells as control. Intra-donor SEV signalling capacity was assessed by comparing normozoospermic (n=3) and non-normozoospermic (n=3) SEV samples from the same donor. Pro-inflammatory cytokines were quantified in cell culture supernatants by Luminex microbead assay.

Results: Seminal plasma significantly increased secretion of chemokine (C-C motif) ligand (CCL5), interleukin (IL)1A, IL4, IL6, IL8, IL22, macrophage colony-stimulating factor (MCSF), vascular endothelial growth factor (VEGF)A and suppressed secretion of IL1B (all p<0.05 compared to control). IL8 and IL22 were induced to an equivalent extent by SEVs (p<0.05 compared to control), suggesting their secretion was driven by SEV exposure. Additionally, CXCL1 was significantly induced following SEV co-incubation (p<0.05 compared to control). Pearson's correlation analysis of SEV-regulated cytokines showed SEV number was not associated with CXCL1 or IL22 secretion but was negatively correlated with IL8 (r=-0.48, p=0.051). SEVs from non-normozoospermic samples showed a reduced capacity to induce CXCL1, IL8, and IL22 compared to those from normozoospermic samples.

Conclusion: In addition to seminal plasma, SEVs elicit FRT cytokine induction in primary epithelial cervical cells, providing evidence for a physiological contribution during the peri-conception period. Our future studies are exploring SEV effects across different regions of the FRT, with preliminary data showing SEVs interact with vaginal (n=7), endometrial (n=5) and fallopian tube (n=7) epithelial cells.

id #126711

A healthier commute: Restricting unhealthy food advertisements on public transit assets

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The commercial determinants refer to the various economic factors and business practices that influence health outcomes. Commercial players have a significant impact on population dietary intake, creating conditions which drive the consumption of highly processed unhealthy food and drinks. Marketing practices, such as advertising are one example of a strategy used by the food and drink industry to shape consumer behaviour and health choices by influencing purchasing behaviours and dietary consumption. As such, these determinants are a critical area for public health action.

In 2024, Preventive Health SA in partnership with the South Australian Department for Infrastructure and Transport undertook exploratory work to develop an understanding of the various policy options to restrict unhealthy food and drink advertising on government owned assets. A public consultation period was held seeking feedback on a proposed policy position for South Australia, attracting feedback from a variety of stakeholders including the alcohol industry, food and beverage industry, media and advertising sector and public health sector. Following consolidation of consultation findings, the Government of South Australia announced in January 2025 approval of a policy to restrict the advertising of unhealthy foods and drinks on government owned buses trams and trains, and that the Government wide policy would take effect from 1 July 2025.

This policy to restrict unhealthy advertising on South Australian transit assets is a small step towards action on the commercial determinants of health. Collaboration is difficult but essential, recognising that intersectoral action is critical to achieve population health outcomes by creating environments that support the population to make healthy choices and be free from commercial influence. This presentation will reflect on the journey through the policy development phase, key learnings from policy implementation, and the critical success factors for public health policy.

id #131576

Lost in the System – Pacific children and young people in Aotearoa/New Zealand; disproportionately affected but poorly supported

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Obesity disproportionately affects Pacific and indigenous Maori children and adolescents, as well as those of lower socioeconomic status in Aotearoa/New Zealand. A review in 2019 showed that more than 33% of children and young people aged 2-14 years were overweight or obese. The prevalence of childhood obesity is highest in Pacific children (22.3%). More than two thirds of young Pacific women in Aotearoa/New Zealand are obese. Much of the underlying factors relate to socioeconomic disadvantage, poor access to health information and health care, and the influence of the global food and advertising industries.

Support for Pacific children and their families who are overweight or obese in Aotearoa/New Zealand is limited. There are no Child Obesity Clinics in Auckland, our largest city. Children can be seen in a General Paediatric Clinic with/without a dietician and referred to community programmes which are also limited. Often kids are seen with another condition and obesity is noted and addressed with lifestyle advice and/or referred to the dietician clinic. Kids with complications e.g. T2D can be seen by Endocrine Clinic or we will be seen in General Paediatrics or Youth Clinic with advice from Endocrinologists and others. The dietician clinic sessions are very limited due to lack of resources. The entire health system is severely stretched and not meeting the needs of those most in need.

There is an urgent need to address obesity in children and young people in Aotearoa/New Zealand with special attention to those most affected. Obesity prevention is the priority but there is also immediate need for improvements in management support, including;

1. Specialist Child and Youth Obesity clinics with multi-disciplinary teams (MDT) including Nutritionist, Paediatrician, Adult physician (and Endocrine support) and capability/capacity to use (and explore and research) the new technologies plus subspecialty clinic to address serious morbidities

1. Community based and facing MDT clinics that partner with community programmes with capacity to work with whole families and households – ie in the community and ability to link into subspecialists if needed but also back-up and work with teams in the field.

Acknowledgements to Dame Teuila Percival DNZM QSO FRACP FCPHM (Hon)

id #129528

Liver glucagon signalling effects on metabolic control and body composition

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Glucagon is known as an important metabolic hormone but has also recently emerged as a efficacious agent in obesity and metabolic disease therapies. However, despite being discovered over 100 years ago, we still don't understand how it works to regulate metabolism and beyond. During this presentation, I will give an overview about our own and others recent discoveries on how glucagon signals within liver hepatocytes to regulate almost all aspects of metabolism. This new knowledge will have implications on the use, and possible refinement, of glucagon-based therapies for obesity and metabolic diseases.

id #128249

Exploring the protective role of the CREBRF rs373863828 variant on maternal metabolic health and gestational diabetes mellitus in a mouse model

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Gestational Diabetes Mellitus (GDM) is a rising global concern that has been linked to maternal diet, with a prevalence of approximately 6% in Aotearoa New Zealand. The CREBRF missense variant rs373863828, common among Māori and Polynesian populations , is associated with a reduced risk of GDM and type 2 diabetes. However, the mechanism for these protective effects is poorly understood. We explored this effect of the variant and diet on maternal metabolic health, using a novel CRISPR/CAS9 knock-in (KI) mouse model with a human equivalent CREBRF variant (ARG458Gln).

KI and wild-type (WT) female mice were placed on normal protein (21%) or high protein (42%) isocaloric diets and grouped by reproductive status(Pregnant /Virgin). On gestation day 17.5, an intraperitoneal glucose tolerance test (GTT) was performed, followed by body composition analysis and organ collection. We observed that high-protein diet influenced impaired glucose tolerance and increased weight of the liver and pancreas during pregnancy, suggesting that a high-protein diet during pregnancy could be a risk factor for GDM. However, this effect was unaffected by genotype. This indicates that maternal physiological adaptations are influenced by diet, but not the CREBRF genetic variant, in specific conditions. Our results suggest that, while the CREBRF rs 373863828 variant may not affect maternal glucose intolerance directly, diet is highly influential. Further studies are warranted to investigate tissue and pregnancy-specific mechanisms through which the CREBRF missense variant may exert protective metabolic effects.

id #128505

Understanding menstrual fluid for pathophysiology and diagnosis of endometriosis

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Endometriosis, characterised by the presence of endometrial-like lesions outside of the uterus, is a debilitating and incurable gynaecological condition(1). Current diagnosis relies on invasive laparoscopic surgery(2). None of the proposed mechanisms thus far definitively explain the pathophysiology of the disease, nor have they been beneficial for non-surgical diagnostic methods(3). We aim to investigate menstrual fluid and its components as a non-invasive tool to better understand endometriosis and identify and utilise them as biomarkers for early diagnosis.

Menstrual blood was collected from women diagnosed with endometriosis (Endo,n=5) and healthy women (no symptoms of endometriosis, Ctrl,n=3) on day 2 of menses using a menstrual cup. Menstrual fluid supernatant was separated, and protein levels quantified. The abundance of 105 cytokines in menstrual fluid was assessed using multiplex array kits. Pixel density per cytokine signal was quantified, and statistical difference of the relative change in cytokine levels between groups was analysed using the two-tailed Mann-Whitney test with a confidence level of 99%.

Acrp30, C5/C5a, CHI3L1, IGFBP-3, IL-1β, MMP-9, OPN, PECAM-1, PF4, Serpin E1, SHBG, TFF3, THBS1, VCAM-1, VDB and VEGF were highly abundant in the menstrual fluid from both groups. Also present in lower abundance in both groups were interleukins (6,11,17A,18BPa and 19) and chemokines (CXCL9, CCL2, CCL20). These factors are associated with inflammation, decidualisation, tissue breakdown, blood loss regulation and tissue regeneration, supporting menstruation as a pro-inflammatory piecemeal event(4, 5). C-Reactive Protein (linked to infection), BAFF (B-cell activating factor), lipocalin-2 (released by neutrophils), IL-8 (a pro-inflammatory cytokine and chemokine for neutrophils), and angiogenin (pro-angiogenesis) were highly expressed in menstrual fluid from women with endometriosis compared to control groups, supporting the pro-inflammatory nature of endometriosis and the bacterial association of endometriosis(3, 6-9).

Menstrual fluid may serve as a minimally invasive diagnostic tool and provides valuable resources for biomarker identification for early diagnosis of endometriosis.

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id #129529

Cancer Immunotherapy-related Endocrinopathies

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Immune therapies, such as checkpoint inhibitors, have revolutionized cancer treatment by producing dramatic and durable tumor responses in many types of advanced malignancies. Unfortunately, nearly two-thirds of patients treated with checkpoint inhibitor therapies will develop autoimmune disease in healthy tissues as an unwanted side effect. Endocrine organs (thyroid, pancreas, pituitary) are among the most commonly affected, and usually result in permanent tissue injury requiring life-long hormone replacement (e.g. insulin for ICI-diabetes). The clinical presentation and optimal management of these endocrine immune related adverse events (irAEs) are distinct from spontaneous autoimmune endocrinopathies, as reflected in changing practice guidelines. Furthermore, no treatments currently exist to prevent or reverse endocrine irAEs, but recent studies have shed light on the immune mechanisms and potential new therapeutic targets. With the expanding use of cancer immunotherapies, clinicians and researchers need to aware of this emerging class of endocrinopathies.

id #128506

Diabetes-related major amputations: a ten-year audit of patient characteristics and mortality outcomes

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Background: Major amputation(MA) secondary to diabetes-related foot disease (DFD) is a significant health burden. To our knowledge, there is minimal research on the determinants of MA and subsequent outcomes in a modern Australian population.

Aim: To describe the burden, determinants and outcomes of MA associated with DFD at a tertiary Victorian hospital between 2013-2022.

Methods: Inpatients aged >18 years with diabetes mellitus and a MA (occurring at/above the ankle joint) were identified by ICD-10AM codes. Demographic, mortality (recorded until June 2025) and comorbidity data were extracted from the hospital electronic database. Ethnicity was determined by birth country and coded according to the ABS classifications(1). Socioeconomic status (SES) was coded by postcode and grouped according to ABS IRSAD scores(2).

Results: At Western Health, 133 individuals underwent a MA between 2013-2022. Majority were male (77.4%) with a mean age of 65±11.8 years. Overseas-born cases comprised 43.6% of the cohort, primarily from South-Eastern Europe (18.0%), followed by North-Western Europe (11.3%). Only one patient identified as First Nations, with no mortality in this group. Majority had a diagnosis of T2DM (90.2%), with a mean HbA1c and LDL of 8.3±1.9%, 1.6±0.7mmol/L, respectively. SES was denoted by a mean IRSAD score of 2.7±1.3 (mode 3). Neuropathy, PVD and prior minor amputation were recorded in 68.4%, 73.7% and 39.1%, respectively. Wound chronicity of ulcers demonstrated 31.5% present for <1 month and 25.6% present for >6 months. A significant mortality burden was identified, with a mean Charlson Comorbidity Index of 7.2±2.9, all-cause mortality of 51.1% and a 2-year mortality of 31.5%. Median time-to-death was 483.5 days (IQR 1110). The most common causes of death were sepsis (17.6%), cardiac arrest (17.6%) and end-stage renal disease (10.2%).

Conclusion: Individuals with DFD-associated MAs have significant all-cause mortality risk. Further research to understand the determinants of MA and mortality is currently underway.

Table 1. Demographics and Outcomes

Demographics	N=133
Gender, %	
F	22.6
M	77.4
Age, mean	65
Ethnicity, %	
Oceania	57.1
-First Nation	0.7
Southeastern Europe	18.0
Northwestern Europe	11.3
North African and Middle East	2.3
South East Asia	2.3
North East Asia	0
Southern and Central Asia	3.8
Americas	1.5
Sub-Saharan Africa	1.5
IRSAD, mean	2.7
Co-morbidities	
T2DM, %	90.2
T1DM, %	9.8
CCI, mean	7.2
Neuropathy, %	68.4
PVD, %	73.7
Prev Minor Amp, %	39.1
Biochemistry, preceding 3 months	
HbA1c, mean	8.30%
LDL, mean	1.6 mmol/L
uACR, median	42.7mg/mmol
Chronicity of wound	
Under 1 month, %	31.5
1-3 months, %	16.5
3-6 months, %	6
>6 months, %	25.6
Outcomes	**N=133**
Mortality	
Total all-cause mortality, %	51.1
2-year mortality, %	31.5
Median time-to-death, days	483.5
Cause of mortality, %	
Unknown	36.7
Sepsis	17.6
Cardiac arrest	17.6
ESRD	10.2
ARDS/APO	7.3
Limb ischaemia	6
Pneumonia	5.9
CVA	4.4
UGIB	2.9
Biochemistry, subsequent 3 months	
HbA1c, mean	8.70%
LDL, mean	1.6mmol/L
uACR, mean	67.3 mg/mmol
eGFR, mean	43

1. (1) Australian Bureau of Statistics Standard Australian Classification of Countries (SACCC) - https://www.abs.gov.au/statistics/classifications/standard-australian-classification-countries-sacc/latest-release
2. (2) Australian Bureau of Statistics Census of Population and Housing: Socio-Economic Indexes for Areas (SEIFA), Australia, 2021- Socio-Economic Indexes for Areas (SEIFA), Australia 2021

Impact of temperature and incubation in 6%CO_2 in air on testicular sperm motility. Part 1: TESA sperm

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This work aims to ascertain the usefulness of incubating overnight TESA spermatozoa (TS) in HEPES-buffered flushing medium (FM) at 37°C in the gaseous phase (6% CO_2 in air).

After maceration in FM, the testicular tissue was divided into four equal portions for individual treatments (Tx). The suspensions are held overnight at either room temperature (RT) or 37°C with or without incubation gas (6% CO_2 in air) as follows: (i) without CO_2@RT; (ii) without CO_2@37°C; (iii) with CO_2@RT; with CO_2@37°C. The tubes are capped tightly with incubation gases sealed within the tube, and kept at RT or 37°C (in the incubator) overnight. Statistical analyses performed were Chi-square, Pearson's correlation studies, paired-T test, and two-by-two tables.

A significant proportion of TS (21.4% vs 5.3%, $p<0.001$) became motile after Tx's, indicating that physiological temperature (37 °C) and physiological pH (attained by overnight incubation in 6%CO_2 in air) induced motility in and retained the viability of the TS. The differences between Tx's were statistically highly significant ($p<0.001$), indicating the critical impact of both physiological temperature and physiological pH on TS viability and motility induction. There was a significant strong interaction ($p=0.0000$) between Tx's and positive correlations between the Tx's ($p<0.001$; highly significant).

Physiological temperature and pH appear critical for retaining the viability of and for initiating motility in TS. It is safer to induce motility with physiological temperature and pH than with embryotoxic pentoxyfylline or theophylline. When exposed to ambient temperature and air, the HEPES medium drifted toward the alkaline phase, making it less dependable for sustaining physiological pH levels between 7.3 and 7.4 for prolonged periods of time, particularly when there was no CO_2 incubation gas present. In conclusion, physiological temperature and pH is critical to maintain the motility/viability of TS. HEPES medium must be equilibrated in 6%CO_2 in air to maintain pH.

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A Novel Cortisol Biosensor Employing Antibody Functionalised Gold Nanoparticles for Integration into Point-Of-Care and Wearable Platforms

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Biosensors are emerging as essential tools in medical diagnostics due to their ability to rapidly and accurately detect biomarkers. A biosensor typically consists of a bioreceptor that recognises a target molecule, a transducer that converts this interaction into a measurable signal, and a display system for interpretation (1). Cortisol is a critical biomarker involved in stress regulation, metabolism, immune function, and cardiovascular health (2). It follows a circadian rhythm, peaking in the early morning and reaching its lowest levels around midnight (3). Dysregulation of cortisol levels is implicated in conditions such as Cushing's syndrome, Addison's disease, and metabolic syndrome (4-6).

Despite the clinical significance of cortisol, existing methods for its quantification are significantly limited, requiring laboratory infrastructure, long turnaround times, and a lack of portability (7-8). Currently, no commercially available point-of-care or wearable biosensor exists for cortisol detection. Electrochemical biosensors represent a promising alternative due to their portability, affordability, and potential for miniaturisation (9). Sensitivity can be further enhanced by incorporating nanomaterials (10-11). Antibody-based sensors also offer high specificity for cortisol recognition (12).

This project proposes the development of a novel electrochemical cortisol biosensor employing antibody-functionalised gold nanoparticles. Propargyl-PEG_4-thiol will be used to functionalise the gold nanoparticle surface, while azido-PEG_{12}-NHS ester will modify the anti-cortisol antibody. The azide-antibody conjugate will react with the propargyl-modified nanoparticles, forming a stable triazole linkage. Conjugation will be verified using ultraviolet-visible spectrophotometry, and commercially available hydrocortisone will serve as a positive control. The functionalised nanoparticle will be incorporated into an electrochemical transducer platform designed for use with human saliva samples.

This biosensor is intended for integration into wearable and point-of-care systems, offering a sensitive, specific, and non-invasive method for real-time cortisol monitoring. Such technology could enable improved diagnosis and management of endocrine and stress-related disorders in both clinical and remote settings.

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Maternal Antibiotic use while Breastfeeding and Infant Growth in the First 10 Months.

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The discovery of antibiotics has had a tremendous influence on the treatment of infectious diseases leading to increased life expectancy (1). However, antibiotics given to an infant also influence the development of the infant gut microbiome and has been associated with growth development (3). In mice exposed to antibiotic, elevated levels of *Firmicutes* were associated with increased energy harvest (4-5). Maternal antibiotic exposure could reach the infant through breastfeeding leading to enhanced growth (6-8).

To investigate the association between antibiotic exposure through breastfeeding and infant growth in the first 10 months. Also, to examine if effects of antibiotics on growth were sex dependent.

The PANDORA-study used data from the Danish birth and prescription registries. In total 79,179 infants born 2004-20 were included. Exposure: any antibiotic prescribed to the mother while she was breastfeeding. Outcome: change in weight-for-length z-score between a baseline measurement and month 10 using WHO's growth standards. Linear regression analysis was used to examine associations.

Infants exposed to antibiotics through breastfeeding had 0.14 SD units higher change in weight-for-length z-score than unexposed infants after adjustment for covariates ($p<0.001$), corresponding to a difference of 100 grams between exposed and unexposed infants at month 10. There was no evidence for an interaction between sex and antibiotics on growth ($p=0.65$). When stratified by breastfeeding duration, antibiotic exposure was associated with a significantly higher change in weight-for-length z-score among infants breastfed and exposed to antibiotics between 1-2 months (beta=0.20, $p=0.04$) and 1-4 months (beta=0.15, $p=0.007$), compared to unexposed infants. No significant differences were observed for exposures among infants breastfed between 3-4 months (beta=0.07, $p=0.49$) or 5-6 months (beta=0.04, $p=0.67$).

The results of this study show that exposure to antibiotics through breastfeeding during the first six months of life enhance growth in the first 10 months of life.

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Not all mineralocorticoid receptor antagonists are equal: differential transcriptomic effects in an MR-expressing cell line

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Mineralocorticoid receptor antagonists (MRA) have a central role in treating MR-mediated cardiovascular and renal conditions, including primary aldosteronism, resistant hypertension, heart failure and nephropathy. Steroidal MRA, spironolactone and eplerenone, are widely used, while non-steroidal MRA including finerenone, esaxerenone and balcinrenone are in early clinical use. It remains unclear whether these MRA exert equivalent effects on aldosterone-mediated gene expression.

This study aims to compare the transcriptomic effects of five MRAs on aldosterone-induced gene expression in an MR-expressing cell line.

MCF7 cells with doxycycline-inducible MR expression were treated with vehicle or aldosterone (3nM), with or without spironolactone (1μM), eplerenone (5μM), esaxerenone (1μM), finerenone (1μM) or balcinrenone (5μM) for 4 hours. RNA sequencing identified differentially expressed genes (DEG) with >2.0-fold change and <0.05 false discovery rate. Real-time quantitative polymerase chain reaction (RT-qPCR) was performed to validate selected DEGs, and dose-response studies were performed across five concentrations of each MRA.

DEGs were grouped as: 1) MRA-reversed aldosterone-induced upregulation (103 genes), 2) MRA-reversed aldosterone-induced downregulation (14 genes) and 3) MRA-regulated. Some genes were similarly modulated by all MRAs, while others showed divergent responses. For example, non-steroidal MRAs (finerenone and esaxerenone) fully reversed aldosterone-mediated downregulation of AMIGO2 and TNFRSF11B, whereas steroidal MRAs did not achieve full reversal, even at maximal doses.

Although MRAs are often considered interchangeable, our transcriptomic analysis reveals distinct gene regulatory profiles between the different MRAs. These findings suggest that not all MRAs are equal in their molecular actions, which may underlie differences in clinical efficacy and adverse effect profiles.

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Characterising primordial germ cell migration in the fat-tailed dunnart (*Sminthopsis crassicaudata).*

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As the precursors to gametes, primordial germ cells (PGCs) hold the unique and important role of carrying genetic information into the next generation. These cells are therefore essential to species' reproduction and survival, and in mammals they are one of the first cell types specified within the developing embryo. PGC specification and migration has been studied across numerous eutherian mammals, birds and fish, allowing subsequent manipulation including isolation, transplantation, and gene editing. However, research in marsupials is far more limited, with in-depth investigation largely restricted to one species, the tammar wallaby. Marsupials offer an ideal system for studying PGC development due to their altricial birth, where many development processes occur postnatally, including PGC migration.

In this study, we used the fat-tailed dunnart (*Sminthopsis crassicaudata)* as a laboratory-based model to investigate the characteristics and migration of PGCs in perinatal young through histological and immunofluorescent staining. We found that dunnart PGCs can be detected within gonadal ridges by approximately 2 days postpartum (pp) and could be identified by the pluripotency marker POU5F1. The germ cells retained POU5F1 expression in all stages examined, and other markers are currently being characterised. Preliminary results suggest that PGC migration occurs through the hindgut in the fat-tailed dunnart, similar to many eutherian mammals, and some marsupials. However this is in contrast to the described migratory path of PGCs in the tammar wallaby, where they are reported to move primarily through the dorsal mesentery.

This work lays foundations for a deeper understanding of PGC development and migration in marsupials, and the diversity that may exist between clades. It will also provide the basis for future isolation, transcriptomic analysis and manipulation of PGCs in dunnarts and marsupials more broadly for application in conservation initiatives.

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Impact of an autocrine modulator of the calcium-sensing receptor on its amino acid sensitivity

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The calcium-sensing receptor (CaSR) is critical for calcium homeostasis and also mediates amino acid (AA) release of hormones including the GI hormones GLP-1 and PYY, with impacts on macronutrient digestion and energy intake. Solved CaSR structures demonstrate binding sites for both AAs and Ca^{2+}.

The CaSR is sensitive to extracellular Ca^{2+} (Ca^{2+}_o) and AAs in various endocrine cells (e.g., parathyroid), in which AAs promote Ca^{2+}_i mobilization and modulate hormone secretion. However, CaSR-expressing HEK-293 cells have yielded conflicting results. Thus, fura-2 loaded and perifused HEK-293 cells exhibit AA-stimulated increases in Ca^{2+}_i but in static cultures Ca^{2+}_o, but not AAs, induce $G_{q/11}$-mediated inositol phosphate (IP) turnover.

We asked: '*What underlies failure of CaSR-mediated AA responses in some models?'* hypothesising that under some conditions, the CaSR's AA binding site is loaded via an autocrine mechanism rendering the receptor insensitive to AAs but hypersensitive to Ca^{2+}_o.

We investigated this hypothesis in HEK-293 cells stably expressing the CaSR, using an adherent format to facilitate washing. In unwashed cells, Ca^{2+}_o-induced IP_1 and pERK responses were not enhanced by the CaSR-active AA, L-Phe (10 mM), whereas in washed cells, we observed reduced Ca^{2+}_o sensitivity enhanced by L-Phe ($p < 0.05$). Increasing the interval between washing and activation (from 5-60 min), enhanced Ca^{2+}_o-stimulated pERK but decreased L-Phe sensitivity, suggesting accumulation of an endogenous ligand. Mass spectrometry led us to identify reduced glutathione (GSH) as a candidate endogenous ligand of the AA site. GSH accumulated in conditioned medium over 30-60 min and inhibition of GSH synthesis with 100μM buthionine sulfoximine suppressed receptor Ca^{2+}_o sensitivity and exaggerated L-Phe responsiveness.

Our results support autocrine modulation of the CaSR's AA binding site by glutathione and provide a novel mechanism by which CaSR-expressing cells tune their responsiveness to Ca^{2+} and/or AAs.

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Angiotensin II receptor type 1 (AT1) and the lectin-like oxidised low-density lipoprotein receptor-1 (LOX-1) form a heteromer with altered downstream pharmacology

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Angiotensin II (Ang II) is a regulatory hormone that acts upon its type 1 and 2 receptors (AT_1;AT_2) in the renin-angiotensin system (RAS). The Ang II-AT_1 axis is directly linked to the development of atherosclerosis – the formation of plaques in the arteries – which underpins many cardiovascular diseases.[1] The lectin-like oxidized low-density lipoprotein (OxLDL) receptor-1 (LOX-1) is a key receptor that mediates the uptake of modified lipoproteins leading to plaque formation.[2] The AT_1 receptor is a G protein-coupled receptor (GPCR), while LOX-1 is a scavenger receptor; despite this difference, the receptors share significant signalling interplay. Interestingly, GPCRs may form heteromers with non-GPCR partner receptors to induce changes to their pharmacology, signalling and intracellular trafficking.[3,4]. Studies suggest the AT_1 receptor heteromerises with LOX-1, leading to changes in their receptor biology with implications for atherosclerosis, including the action of Ang II.[4]

The present study aimed to demonstrate evidence of heteromerisation between the AT_1 receptor and LOX-1, and investigate novel signalling using the Receptor-Heteromer Investigation Technology (Receptor-HIT) assay.[5] Receptor-HIT detects heteromers through ligand-induced recruitment of interacting proteins to the heteromer complex. In the present study, bioluminescence resonance energy transfer (BRET) techniques were employed to measure such recruitment.[6] By co-expressing one luciferase-labelled receptor and one unlabelled receptor, in addition to a fluorophore-labelled interacting protein, Receptor-HIT detects a BRET signal upon treatment with a ligand specific for the unlabelled receptor. This indicates recruitment of the interacting protein to the receptor heteromer, providing insights into pharmacological changes such as altered G protein signalling.

It was found that AT_1 produced Receptor-HIT signals indicative of heteromerisation when co-transfected with LOX-1, and various signalling proteins. Additionally, AT_1 and LOX-1 co-transfection selectively altered some of the downstream signalling properties of the receptors. These findings demonstrate the existence of the AT_1-LOX-1 heteromer, and support novel signalling changes related to atherogenesis.

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The effect of depletion of oocyte dynamin-related protein 1 (Drp1) on follicle development.

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Dynamin-related protein 1 (Drp1) is essential for mitochondrial fission and maintaining mitochondrial dynamics. Deletion of Drp1 from oocytes leads to defective follicular development and negatively affects embryo development and fertility. It is not understood how manipulating oocyte mitochondrial function leads to compromised development of ovarian follicles.

we have performed an extensive analysis of ovaries from Drp1 conditional knock-out mice (Drp1 cKO), in which Drp1 was deleted in primordial oocytes by crossing $Drp1^{fl/fl}$ female mice with Gdf9-*Cre* males. Follicle counts were performed on ovaries from 4-, 5-, and 7-week-old Drp1 cKO and control mice, while immunofluorescence on ovaries of 5-week-old mice was used to analyse properties of developing follicles. This analysis included granulosa cell proliferation (Ki67 antibody), apoptosis (cleaved Caspase 3 (CC3) antibody), and lysosomal activity (Lamp1 antibody).

Follicle counts revealed no difference in follicle numbers between the ovaries of 4-week-old DRP1 cKO and control mice. However, in 5- and 7-week-old Drp1 cKO mice, there was a significant increase in primary follicle numbers and a decrease in antral follicles compared to controls. These findings suggest that oocyte-specific deletion of Drp1 leads to an arrest of follicle development at the secondary follicle stage. Immunofluorescence analysis revealed a significant decrease in Ki67-positive granulosa cells/follicle, indicating that granulosa cell proliferation was inhibited. This was accompanied by a significant increase in CC3-positive cells, suggesting apoptosis was increased, while LAMP1 labelling was present in a greater proportion of follicles from Drp1 cKO mice compared to controls.

These findings show that manipulating mitochondrial function in the growing oocyte has dramatic effects on the function and viability of the accompanying granulosa cells, suggesting oocyte mitochondrial function may be a critical component of oocyte-granulosa cell metabolic cooperativity necessary for follicle development and fertility.

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Unravelling the role of glycogen in diabetic kidney disease (DKD)

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Diabetes is characterised by impaired glucose homeostasis and storage. This dysregulation significantly alters glycogen levels in various tissues, including the kidneys. Clinical and preclinical studies consistently report renal glycogen accumulation in diabetes, likely due to impaired glucose reabsorption from hyperglycemia. Given the kidneys' key role in glucose handling, understanding kidney glycogen's role, distribution, and significance in diabetes is essential. With over one-third of diabetic patients developing Diabetic Kidney Disease (DKD), insights into kidney glycogen metabolism may reveal novel therapeutic targets.

To investigate this, male kidney-specific Gys1 homozygous knockout (KO) mice (n=3–8/group), generated via the Cre-Flox system, were used alongside wildtype (WT) controls. Type 1 diabetes was induced using five daily intraperitoneal injections of low-dose streptozotocin (STZ, 55 mg/kg/day). Mice were provided standard chow and water ad libitum for 22 weeks before euthanasia.

The Gys1 KO model was validated by significantly reduced glycogen levels in KO diabetic mice compared to WT diabetic controls. WT diabetic mice exhibited significantly lower body weight, impaired blood glucose control (measured by glycated hemoglobin and oral glucose tolerance test), and increased Glomerular Filtration Rate (GFR, via Medibeacon FITC-sinistrin assay) and Glomerular Sclerosis Index (GSI) relative to WT non-diabetic mice. These parameters align with diabetic symptoms and early kidney damage.

There were no significant differences between KO and WT diabetic groups in body weight, glucose control, or GFR. However, the KO diabetic group showed a trend toward better glomerular health (lower GSI) compared to WT diabetic mice. This suggests that excess glycogen storage in diabetic kidneys may not directly affect glycemic control or filtration rate, but may influence glomerular structure. Further investigation is needed to determine whether kidney glycogen plays a protective, harmful, or neutral role in diabetes.

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Effectiveness and safety of sodium-glucose co-transporter-2 Inhibitors in patients with diabetes of the exocrine pancreas: A nationwide population-based study

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Objective: This study evaluates the real-world effectiveness and safety of sodium-glucose cotransporter 2 (SGLT2) inhibitors in individuals with diabetes of the exocrine pancreas (DEP), given the limited research on effective pharmacological treatments for this condition.

Research Design and Methods: A retrospective cohort study was conducted on 66,120 individuals with DEP who initiated glucose-lowering drugs (GLDs) between September 2014 and December 2022, using data from the Korean National Health Insurance Service database. Propensity scores were developed for 1:1 matching between patients initiating SGLT2 inhibitors and those initiating other GLDs. Effectiveness outcomes included major adverse cardiovascular events (MACEs), heart failure, end-stage kidney disease (ESKD), and all-cause mortality. Safety outcomes included hypoglycemia, diabetic ketoacidosis, genital infections, urinary tract infections, fractures, and pancreatitis.

Results: After matching, 4,128 pairs of SGLT2 inhibitor and other GLD users were included, with a mean follow-up of 2.3 years. Compared to other GLDs, use of SGLT2 inhibitors was associated with a significantly lower risk of MACE (hazard ratio [HR] 0.69; 95% confidence interval [CI] 0.51–0.93), hospitalization for heart failure (0.70; 0.51–0.95), ESKD (0.19; 0.06–0.61), and all-cause mortality (HR 0.38; 95% CI 0.27–0.53). For safety outcomes, SGLT2 inhibitor use was associated with a reduced risk of urinary tract infections (HR 0.87; 95% CI 0.78–0.96) and pancreatitis (HR 0.71; 95% CI 0.58–0.87).

Conclusions: We found that SGLT2 inhibitors were associated with reduced cardiorenal outcomes and all-cause mortality risk and were safely used in patients with DEP.

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The impact of testosterone treatment on inflammatory markers in adult males a systematic review and meta-analysis

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Abstract

Background and objectives: Although data suggest a bidirectional relationship between serum testosterone and inflammation, studies on treatment with exogenous testosterone report inconsistent effects on markers of inflammation. We performed a systematic review and meta-analysis to synthesize evidence on how testosterone therapy affects circulating inflammatory biomarkers in adult males.

Materials and methods: PubMed (MEDLINE), Scopus, Embase, and Web of Science were searched from inception to May 2024 for trials in which testosterone was administered for any indication and inflammatory cytokine concentrations were measured. Methodological quality was assessed with the modified Joanna Briggs Institute critical appraisal checklist.

Results: From 6,502 records, 17 studies (n = 1,765) met inclusion criteria; 955 participants received testosterone therapy and 871 served as controls. Testosterone had no significant effect on IL-6 (SMD = –0.04, 95% CI = [–0.09, 0.16]; p = 0.56), TNF-α (SMD = –0.17, 95% CI = [–0.47, 0.14]; p = 0.29), hs-CRP (SMD = –0.19, 95% CI = [–0.41, 0.04]; p = 0.10) or adiponectin (SMD = –0.07, 95% CI = [–0.70, 0.56]; p = 0.82). It produced a marked reduction in IL-1β (SMD = –0.66, 95% CI = [–1.01, –0.32]; p < 0.0001). Leptin fell significantly (SMD = –0.87, 95% CI = [–1.36, –0.38]; p = 0.0005), all studies consistently reporting decrement. Two trials also reported an increase in IL-10 relative to placebo.

Conclusions: Testosterone therapy exerts selective anti-inflammatory effects, particularly lowering IL-1β and leptin, while leaving several other cytokines unchanged. These findings highlight the complex, context-dependent nature of testosterone's immunomodulatory actions and support further mechanistic research.

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Men borderline low serum total testosterone concentration and low sexual desire – does the calculation of free testosterone add value?

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Background:
Guidelines recommend diagnosing androgen deficiency by symptoms e.g. sexual desire plus low serum total testosterone (TT). Studies vary as to whether calculated free testosterone (cFT) adds diagnostic accuracy when TT is borderline low.

Aim:
To determine whether, in men with borderline low TT, cFT improves the ability to infer that insufficient testosterone exposure is related to low sexual desire (SD).

Methods:
A cross-sectional analysis was conducted in 1,195 community-dwelling men aged ≥35 years. TT (via LCMS), cFT (Vermeulen equation), and sexual desire using the Sexual Desire Inventory (SDI) were assessed. Men were classified as having borderline low TT if 6.1-12 nmol/L, low cFT if <0.20 pmol/L and low SDI if <19. Data were analysed by linear regression, with and without age and fat mass adjustment. Exact binomial confidence intervals for the diagnostic accuracy measures were generated.

Results:
Among the 1,169 men with complete data, the mean age was 55 years and BMI 28.6 kg/m². 12 had low TT and 207 had borderline low TT. Men with TT<12 were older (p=0.02), more obese (p<0.001), and had lower SDI scores (p<0.001). In men with borderline TT, a linear association between sexual desire and cFT was explained by age and fat mass. Prevalence of low sexual desire was 23.3% in men with borderline low TT. In men with a low cFT (<0.2), this was 41.9% compared to 18.3% in men with normal/high cFT (positive predictive value 41.9%, negative predictive value 81.7%, false positive 58.1%, and false negative 18.3%).

Conclusion:
In men with borderline low TT, low cFT is weakly predictive of low sexual desire; the effect is better explained by age. Normal cFT is of greater value to exclude low sexual desire in younger but not older men with borderline low TT.

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Bone health in phenylketonuria

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Aims: Phenylketonuria (PKU) is the most common inborn error of amino acid metabolism. With improved life expectancy due to early diagnosis and dietary management, attention has turned to long-term outcomes, including bone health. Adults with PKU may be at risk of compromised bone health, though contributing factors and utility of routine screening remain uncertain.[1-3]

Methods: We retrospectively reviewed 59 adults with PKU attending Western Australia's Inborn Errors of Metabolism clinic. Data included demographics, body mass index (BMI), adherence to dietary protein restriction, plasma phenylalanine (Phe) levels, bone turnover markers and bone mineral density (BMD) via dual-energy X-ray absorptiometry.

Results: The cohort (57.6% female) had a mean age of 40.2 ± 16.5 years (range: 18-78 years) and BMI of 27.7 ± 7.4 kg/m². Of these, 40.7% were always adherent to diet, 50.8% were partially adherent, and 8.5% were non-adherent. Mean 12-month plasma Phe level was 851.7 ± 371.8 µmol/L. Among 36 patients with BMD data, 27.7% had Z-scores >-2 to <–1 and 11.1% had Z-scores ≤–2. Among patients over 50 years of age (n=12), osteopaenia (T-score >-2.5 to <–1) and osteoporosis (T-score ≤–2.5) were present in 50% and 17%, respectively. Most were vitamin D replete and normocalcaemic (mean 25-OH vitamin D: 91.8 ± 36 nmol/L; adjusted calcium: 2.28 ± 0.08 mmol/L).

There was no association between BMD Z-scores and BMI, Phe level, or dietary adherence. No correlation was observed between Phe levels and bone turnover markers (serum CTX or ALP).

Conclusion: Consistent with previous studies, a substantial proportion of adults with PKU have low BMD. However, most BMD values remain within the expected range for age. These findings support the need for regular bone health assessment in this population. Further research assessing risk factors for low BMD and in examining future fracture risk is required to identify patients with PKU requiring earlier screening.
GEKO:52996

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Hyperosmolar hyperglycaemic state: A systematic review of management guidelines and their evidence

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Hyperosmolar hyperglycaemic state (HHS) is a life-threatening endocrine emergency. HHS occurs less frequently than diabetic ketoacidosis (DKA) (1), but has a higher mortality (2), with reported mortality rates of 10-50% (3-7). HHS management is largely varied in clinical practice due to a lack of high-quality evidence. This systematic review aims to compare international guidelines and their underlying evidence base in HHS management. MEDLINE, Embase and Emcare databases were searched, and references of relevant papers were reviewed, identifying 363 papers, of which 7 met the inclusion criteria.

The hallmark features of HHS include profound hypovolaemia, extreme hyperglycaemia, and hyperosmolality (7, 8), although specific diagnostic criteria vary among guidelines from glucose ≥33.3mmol/L and osmolality ≥320mOsm/kg (American Diabetes Association [ADA] and Diabetes Canada [DC]) (7, 9) to glucose ≥30.0mmol/L with osmolality ≥320mOsm/kg (Joint British Diabetes Society [JBDS]) (10) (Table 1). There is also significant heterogeneity in HHS management (Figure 1). The ADA and DC guidelines recommend correction of serum osmolality <3mOsm/kg/hr (7, 9), whereas the JBDS accept osmolality change of 3-8mOsm/kg/hr (10). ADA guidelines suggest 0.9% normal saline at 15-20mL/kg/hr or 1-1.5L/hr (7), whereas JBDS guidelines suggest replacing ~50% of the estimated fluid loss within the first 12 hours (10). The ADA and DC guidelines recommend a fixed rate insulin infusion of 0.1units/kg/hr (7, 9). The JBDS guidelines recommend 0.05units/kg/hr, increasing by 1.0units/hr as required (10).

Current HHS guidelines are consensus-based rather than evidence-based because no randomised controlled trials exist. HHS management is largely driven by evidence derived from small studies in patients with DKA, rather than specific HHS trials. Further high-quality prospective studies specific to HHS are required to standardise diagnosis and optimise management.

Criteria	ADA	JBDS
Serum glucose	≥33.3 mmol/L	≥30.0 r
Osmolality	≥320 mOsm/kg	≥320 m
pH	>7.3	>7.3
Serum bicarbonate	>18 mmol/L	>15 mr
Ketones	Absent to low ketonaemia	<3 mm

Table 1: Comparison of HHS diagnostic criteria.

Abbreviations: ADA = American Diabetes Association

DC = Diabetes Canada

HYPERG

- Serum
- Effect
- Keton
- pH >7

1. HYDRATION

Fluid deficit 100-200mL/kg (7-14L in 70kg person)

- Replace 50% of fluid deficit in first 12-24 hours

Hypovolaemia

Time	Recommended Rates
Hour 1	1000-2000mL/hr
Hours 2-5	500-1000mL/hr
Hours 6-9	250-500mL/hr
Hour 10+	Assess: • Haemodynamic stability • Fluid status • Comorbidities (i.e. cardiac/renal failure)

Shock

Discuss with ICU

2. OSMOLA

VBG 1-2 ho

Osmolality:

- Calculate eff hourly
- Aim to reduc osmolality by

Serum glucose:

- Aim to reduc <5-6.7 mmol

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Impact of pre-pregnancy bariatric surgery on maternal glucose profiles in pregnancy

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Maternal pre-pregnancy bariatric surgery is associated with fewer obesity-related pregnancy complications but increased risk of small for gestational age infants and challenges in glucose assessment.[1] This prospective observational cohort study compared mid-pregnancy glycaemic patterns using continuous glucose monitoring (CGM) between women with and without prior bariatric surgery.

We recruited n=20 women with a history of bariatric surgery and n=16 age-matched controls before 24 weeks' gestation. Participants wore blinded CGM devices for 14 days between 24–29 weeks' gestation. Key CGM metrics included time in range (pTIR, 3.5–7.8 mmol/L), time below range (pTBR, <3.5 mmol/L), time above range (pTAR, >7.8 mmol/L), mean glucose, and glycaemic variability (coefficient of variation, CV). Descriptive statistics were reported using medians with interquartile ranges, and group comparisons were made using independent t-tests or Wilcoxon rank-sum tests.

CGM data were available for n=18 women with pre-pregnancy bariatric surgery and n=13 controls. The bariatric group had a median age of 32.0 (27.5, 36.0) years and BMI of 31.6 (28.5, 34.4) kg/m² versus 33.0 (30.5, 34.5) years and 23.7 (21.5, 25.8) kg/m² in controls. There were no significant differences in pTIR, pTBR, pTAR, mean glucose, or CV between groups (all $p > 0.05$). However, a trend toward increased glycaemic variability was observed in the bariatric group.

In conclusion, although CGM metrics did not differ significantly, the observed trend could suggest greater glucose variability in women with prior bariatric surgery. Further comparisons in BMI-matched groups are warranted to explore CGM's potential as an alternative glucose assessment method in this population.

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Breastfeeding is associated with cancer prevalence: A nationwide population study

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Publish consent withheld

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Measuring Sarcopenia Via Psoas Muscle Volume Changes In Patients With Thyroid Cancer Receiving Lenvatinib

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Background: Lenvatinib is a multikinase inhibitor used for patients with advanced thyroid cancer. Sarcopenia is common in patients receiving Lenvatinib despite reasonable baseline performance status. We utilised a deep learning artificial intelligence tool, the TotalSegmentator which employs an automatic convolutional neural network (CNN) to analyse computed tomography (CT) scans of psoas muscles in people with thyroid cancer receiving Lenvatinib.

Aims: To assess if there is a reduction in muscle volume after administration of Lenvatinib treatment in patients treated for thyroid cancer.

Methods: Patients with advanced thyroid cancer who received Lenvatinib through our centre between 2008 – 2023 were identified. Baseline CT scans and repeat staging scans were analysed before and after commencing Lenvatinib. CT scans were converted to DICOM images and analysed through the Total Segmentator software.

Results: 21 patients were identified, 12 excluded and 9 included (5 female, 4 male). Median age was 56 years (range 38-76). Starting dose Lenvatinib was 24mg in eight patients and 20mg in one patient. Median observation period was 16.9 months (range 3.8 – 27.1). Median baseline psoas muscle volume prior to commencing Lenvatinib was 488585.78 mm3 and at first follow-up imaging was 452975.82mm3 with median time to first follow up imaging 3.05 months (2 – 6.3). Median psoas muscle volume at end of Lenvatinib administration period was 468902.84mm3, representing a mean -8.8% loss of psoas muscle volume (p= 0.01).

Conclusion: We have validated a novel analysis pipeline to quantify sarcopenia on Lenvatinib therapy for patients with thyroid cancer, using the TotalSegmentator software. Patients who received Lenvatinib for thyroid cancer demonstrated reduction in psoas muscle volume during the treatment period. Limitations of this study are the retrospective nature and small sample size. Larger prospective studies are required with a control group to help quantify sarcopenia in patients receiving Lenvatinib and to investigate potential mechanisms.

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Comparison of Cardiovascular Outcomes and Mortality in Diabetic Foot Disease with Non-Diabetic Myocardial Infarction: Cohort Study

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Aims:

We aimed to evaluate cardiovascular outcomes and mortality between patients with diabetic foot disease (DFD) and non-diabetic individuals with myocardial infarction (MI).

Methods:

In a nationwide cohort in South Korea, patients with DFD (n=43,288), and non-diabetic individuals with MI (n=26,873) between 2012 and 2015 were followed until 2021. The primary outcome was a composite of non-fatal MI, non-fatal ischemic stroke (IS), and cardiovascular death. Cox proportional hazard models were used.

Results:

Over a median follow-up of 7.0 years, the primary outcome event rate was 31.5 and 18.1 per 1000 person-years in the DFD and MI groups, respectively (adjusted hazard ratio [HR], 1.60; 95% confidence interval [CI], 1.53–1.66). The risk of non-fatal MI (adjusted HR, 0.94; 95% CI, 0.85–1.04) was comparable between the groups, but the DFD group had significantly higher risks of non-fatal IS (adjusted HR, 2.38; 95% CI, 2.24–2.53) and cardiovascular death (adjusted HR, 1.33; 95% CI, 1.26–1.41). They also exhibited increased risks of heart failure hospitalization (adjusted HR, 1.35; 95% CI, 1.31–1.40) and all-cause death (adjusted HR, 2.09; 95% CI, 2.02–2.15).

Conclusion:

Patients with DFD have a significantly higher risk of major cardiovascular events and mortality than non-diabetic patients with MI.

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Prevalence of cardio-metabolic risk factors among women in early pregnancy

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Background

Pregnancy provides an opportunity to identify young women at risk of future cardio-metabolic diseases. We aimed to determine the prevalence of cardio-metabolic risk factors including metabolic syndrome (MetS) and its components among women in early pregnancy.

Methods

Pregnant women attending antenatal clinics at the Lyell McEwin Hospital prior to 16 weeks' gestation were invited to take part in the study. Those who were willing to attend all four study visits were recruited. Data collected at the first visit included demographic information, medical history, previous obstetric history, family history, exercise, diet, smoking and alcohol intake. Height and weight were measured, and the haemodynamic profile was assessed non-invasively using USCOM BP+ machine. Blood glucose and lipids were assessed.

Results:

Data from 264 women were included in the analyses. The participants were aged between 18 – 46 years. Using the Harmonizing criteria to diagnose MetS, the prevalence of MetS in early pregnancy was 16%, (n = 41). The prevalences of individual MetS components were: high waist circumference, 97% (n = 255); high systolic blood pressure, 3.8% (n=10), high diastolic blood pressure, 1.1% (n=3), high triglycerides, 42.4% (n=112), low HDL 18.1% (n=48) and high random blood glucose level, 1.9% (n=5). The prevalences of other risk factors were: obesity, 38.3% (n=101), smoking, 4.5% (n=12), pre-existing hypertension, 3.4% (n=9), pre-existing type 2 diabetes, 1.5% (n=4), family history of hypertension, 23.9% (n= 63), family history of type 2 diabetes, 22% (n=58).

Conclusions: Metabolic syndrome was diagnosed among 16% of women prior to 16 weeks' gestation. Screening in early pregnancy may help identify young women at risk of future cardio-metabolic diseases.

Keywords: Metabolic Syndrome, cardio-metabolic risk factors, pregnancy

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Progressive Delays in Adrenal Venous Sampling for Regional Patients: A Single-Centre Experience in Far North Queensland

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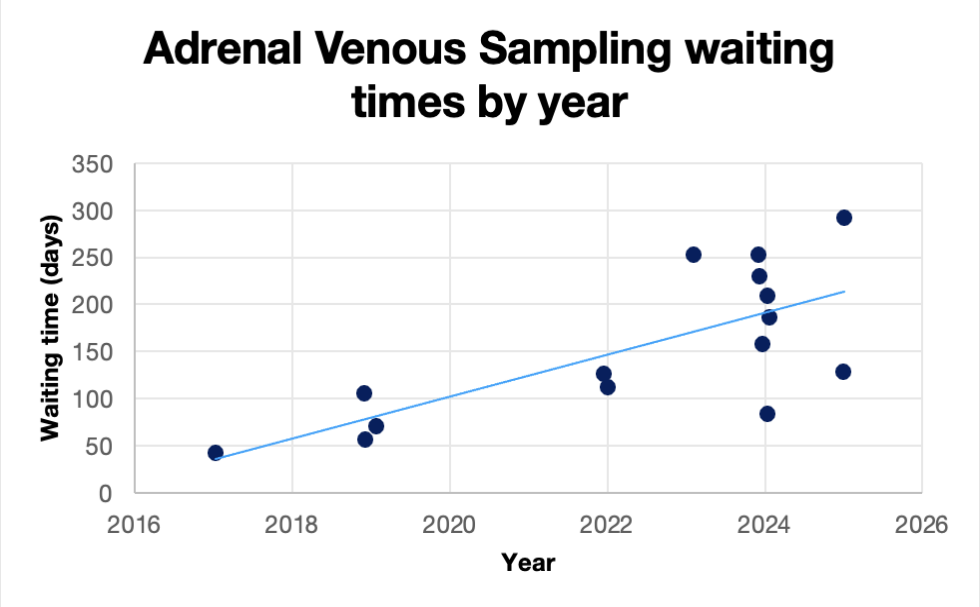
Adrenal Venous Sampling (AVS) is the definitive diagnostic modality for subtyping primary aldosteronism, enabling targeted surgical intervention in unilateral disease.[1] However, in regional centres such as Cairns Base Hospital, patients must be referred to tertiary facilities in Brisbane or the Gold Coast, introducing significant logistical and temporal barriers.

This study evaluated trends in AVS wait times and potential clinical implications of delayed access in a regional cohort.

A retrospective audit was conducted on patients referred for investigation of primary aldosteronism at Cairns Base Hospital between 2017 and 2024. Patients were identified via CaseMix coding and referrals for Seated Saline Suppression Testing (SSST). Exclusion criteria included normotensive results, alternative diagnoses, mortality, refusal, medical management, or incomplete investigations. Data were collected on demographics, biochemistry, comorbidities, antihypertensive burden, and AVS timelines.



Of 63 identified patients, 16 underwent AVS and were included in the final analysis. The mean age was 55.4 years, and the mean aldosterone-to-renin ratio was 191.6. AVS wait times increased significantly over the audit period, from a mean of 68.75 days in 2017–2019 to 175.17 days from 2020 onward. Two patients developed hypokalaemia while awaiting AVS, requiring oral replacement. No macrovascular events were recorded. Common comorbidities included dyslipidaemia and smoking. Most patients (n=10) required three or more antihypertensive agents. While no association was observed between antihypertensive burden and AVS wait time, the majority had suboptimally controlled blood pressure—a well-established risk factor for cardiovascular disease, stroke, and metabolic complications including obstructive sleep apnea.[2]

AVS access delays are increasing for regional patients, with potential negative implications for clinical outcomes and healthcare resource utilisation. These findings support consideration of a locally delivered AVS service in Far North Queensland. In parallel, emerging evidence supporting non-invasive PET-based subtyping techniques warrants investigation in the Australian context to improve diagnostic equity and reduce reliance on tertiary AVS capacity.[3]

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High Incidence of Eating Disorders in Type 2 Diabetes and Their Association with Cardiovascular and Mortality Risks

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Aims: We examined the incidence of eating disorders (ED) in patients with type 2 diabetes and their impact on all-cause mortality, composite cardiovascular disease (CVD), cardiovascular (CV)-related mortality, and CV-related hospitalization. Methods: This nationwide retrospective cohort study included 1,896,493 adults aged 20 years or older who underwent health examinations between 2013 and 2014. Time-varying Cox analyses were utilized to evaluate the effects of ED on all-cause mortality, composite CVD, CV-related mortality, and CV-related hospitalization in patients with type 2 diabetes. Results: The type 2 diabetes group demonstrated an increased incidence of ED (adjusted hazard ratio [aHR], 1.20; 95% confidence interval [CI], 1.12–1.28) compared with the general population. Furthermore, the incidence of ED was higher among insulin users (aHR, 1.30; 95% CI, 1.09–1.54) than among non-insulin users (aHR, 1.18; 95% CI, 1.11–1.27). The type 2 diabetes with ED group showed an increased risk of all-cause mortality (aHR, 2.57; 95% CI, 2.30–2.87), composite CVD (aHR, 1.68; 95% CI, 1.44–1.96), CV-related mortality (aHR, 2.68; 95% CI, 1.94–3.70), and CV-related hospitalization (aHR, 1.61; 95% CI, 1.37–1.89). Conclusion: Type 2 diabetes mellitus and ED increased all-cause mortality, composite CVD, CV-related mortality, and CV-related hospitalization. ED incidence was higher among insulin users with type 2 diabetes. Therefore, early diagnosis and personalized interventions are crucial to improve outcomes in this high-risk population.

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Diffusion tensor imaging of the tibial nerve can detect nerve damage in type 2 diabetes

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Magnetic resonance imaging (MRI) has played little role for the study of peripheral nerve disease. However, recent technological advances in MRI have provided us more information about neural microstructure and higher resolution in peripheral nerves. The aim of this study is to evaluate whether diffusion tensor imaging (DTI) in MRI can detect peripheral nerve abnormalities in patients with type 2 diabetes (T2D). In this prospective, single-center study, 33 T2D patients (mean age, 60.5 ± 7.0 yr; 16 M/ 17F) and 12 healthy controls (61.8 ± 5.3 yr, 5M / 7 F) were included. All T2D patients underwent Michigan Neuropathy Screening Instrument questionnaire and quantitative sensory testing. MRI including DTI and axial T2-weight Dixon sequence was performed for each participant. DTI parameters of the tibial nerves such as fractional anisotropy (FA) and diffusivity (mean (MD), axial (AD), and radial (RD)) were calculated. FA of the tibial nerves was significantly lower in T2D patients than healthy controls at both level 1 (0.42 ± 0.07 vs. 0.57 ± 0.09, P<0.001) and level 2 (0.44 ± 0.07 vs. 0.55 ± 0.08, P<0.001). AD was also significantly lower in T2D patients than controls at both level 1 (1.97 ± 0.43 vs. 2.40 ± 0.63, P<0.05) and level 2 (2.18 ± 0.37 vs. 2.59 ± 0.47, P<0.05). RD was significantly higher in T2D patients than controls at level 1 (0.97 ± 0.21 vs. 0.83 ± 0.13, P<0.05). However, there were no differences in DTI parameters between T2D patients with peripheral neuropathy (PN) and those without PN. In summary, we have demonstrated that DTI can detect microstructural alterations of peripheral nerves in T2D patients with PN as well as those without PN, suggesting that the structural nerve damage can occur before the development of PN in T2D patients.

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Overall and site-specific cancer risk in patients with type 1 and type 2 diabetes: A nationwide population-based cohort study in Korea

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Background: Epidemiologic evidence suggests that diabetes increases the risk of various cancers. This study aims to evaluate the incidence of cancer among Korean individuals with and without diabetes and compare the risk between Type 1 and Type 2 diabetes patients.

Methods: This nationwide cohort study of adults aged ≥ 20 years utilized data from the Korean National Health Insurance Service covering preventive health check-ups from 2009 to 2016. A Cox regression model was applied to estimate the risk of overall and site-specific cancers in diabetes patients.

Results: The cohort included 164,434 non-diabetic individuals and 165,822 diabetic patients (1,604 with type 1 diabetes and 164,218 with type 2 diabetes). Over 3,125,427 person-years of follow-up, a total of 39,132 cancer cases were observed in non-diabetic individuals (incidence rate [IR]: 26.86 per 1,000 person-years), 443 cases in patients with type 1 diabetes (IR: 25.30 per 1,000 person-years), and 42,162 cases in patients with type 2 diabetes (IR: 25.51 per 1,000 person-years). The incidence rate of cancer was significantly higher in diabetic patients compared to non-diabetic individuals; however, there was no statistically significant difference between type 1 and type 2 diabetes. The liver, pancreatic, and bile duct cancers have significantly increased risks in both Type 1 and Type 2 diabetes. Stomach, colorectal, and lung cancers are significantly elevated only in Type 2 diabetes. Thyroid cancer shows a significantly lower risk in both Type 1 and Type 2 diabetes. Additionally, ovarian, uterine, breast cancers and kidney, bladder, prostate cancer exhibit a significantly lower risk only in Type 2 diabetes.

Conclusions: Both Type 1 and Type 2 diabetes patients demonstrated a higher overall cancer risk than non-diabetic individuals. However, the nature of the association varied by diabetes type and cancer site. These findings underscore the importance of tailored cancer screening and preventive strategies for diabetic patients.

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Adherence to HEDTA guidelines in the use of insulin tolerance tests: a retrospective audit at a tertiary hospital.

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Background/aims: Insulin tolerance tests (ITT) are considered gold standard to investigate patients for suspected secondary adrenal insufficiency or growth hormone deficiency. In 2021, the Harmonisation of Endocrine Dynamic Testing – Adult (HEDTA) guidelines were published to assist clinicians in conducting endocrine dynamic tests including ITT. Our aim is to describe testing procedures and adherence to HEDTA guidelines at a tertiary hospital over a three-year testing period.

Methods: We included all non-pregnant patients ≥18 years of age who underwent ITT from 2022 to 2024 at Concord Repatriation General Hospital. Data was collected on patient demographics, testing procedures, indications for testing, and outcomes.

Results: Six patients underwent testing with a median age of 44 years (36 – 54) and 67.7% were female. The indication for testing was secondary adrenal insufficiency in 66.7% (4 of 6) of patients, growth hormone deficiency in 16.7% (1 of 6) and both conditions in 16.7% (1 of 6). Adequate hypoglycaemia of ≤2.2mmol/L, was achieved in 83.3% (5 of 6) of patients with 16.7% (1 of 6) requiring a second dose of insulin to achieve this. Median time to blood glucose nadir, cortisol peak, and growth hormone peak was 32.5, 60 and 60 minutes respectively. Inadequate cortisol or growth hormone responses were seen in 66.7% of tests. Deviations from protocol included variations in timing of blood collection and missing ACTH measurements. There were no adverse events. Hypoglycaemia was treated with both oral glucose solution and intravenous dextrose in 83.3% (5 of 6) of patients and the treatment not documented in the remaining 16.7% (1 of 6).

Conclusion: Despite ITT being gold standard, it is infrequently ordered suggesting potential underutilisation for the assessment of secondary adrenal insufficiency and growth hormone deficiency. Adherence to HEDTA guidelines, particularly regarding the timing of specimen collection, may enhance the clinical utility of ITT.

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Opportunistic Measurement of Sagittal Abdominal Diameter with Bone Densitometry Predicts Abdominal Aortic Calcification and Major Cardiovascular Events

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Abstract

Background: Visceral adiposity has a crucial Pathophysiological role in the development and progression of cardiovascular disease, the major cause of death globally. Sagittal abdominal diameter (SAD) has been proposed as a simple measure for determining visceral adiposity and has previously shown to predict major cardiovascular events (MACE). However, it remains unclear whether SAD is associated with abdominal aortic calcification (AAC), a marker of subclinical cardiovascular disease, or whether it predicts MACE independent of AAC.

Aims: We sought to investigate the association between SAD adjusted for weight with validated machine learning AAC 24-point score (ML-AAC24), and their joint association with MACE.

Methods: SAD and ML-AAC24 were obtained using Dual-energy X-ray Absorptiometry (DXA) during routine vertebral fracture assessment in the Manitoba BMD Registry. Incident MACE (composite of all-cause mortality, acute myocardial infarction [MI], non-hemorrhagic stroke) was ascertained from linked healthcare databases. Cox proportional hazards models examined the simultaneous relationships of SAD/weight and ML-AAC24 with incident MACE.

Results: The study population comprised 8806 individuals (mean age ± SD 75.1 ± 6.6 years, 93.9% women). ML-AAC24 scores were categorised (low <2, moderate 2<6 and high ≥6). Compared to low, those with moderate and high ML-AAC24 had 1.5% and 3.3% higher mean SAD/weight, respectively. Over follow-up of 3.8 (SD 2.2) years, 993 people (11.3%) experienced a MACE. Each increase in SD of SAD/weight was associated higher relative hazard for incident MACE (HR 1.14, 95%CI 1.07-1.21). The hazard ration (HR) of highest compared with lowest tertile of SAD/weight was 1.37 (95%CI 1.16-1.61). Compared to low ML-AAC24 the hazard ratio for moderate and high ML-AAC24 was 1.45 (95% CI 1.24-1.71) and 1.98 (95CI 1.67-2.35), respectively.

Conclusion: SAD/weight is positively associated with ML-AAC24 in older adults attending routine osteoporosis screening. Both measures were associated with incident MACE independent of each other and multiple cardiovascular risk factors.

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Improving Primary Aldosteronism diagnosis and treatment: outcomes from an endocrine hypertension service

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***Background*:** Primary aldosteronism (PA) is a prevalent yet underdiagnosed cause of secondary hypertension, associated with increased cardiovascular, renal and metabolic risk. Limited awareness, resources and expertise contribute to delays in diagnosis and treatment. A dedicated Endocrine Hypertension Service previously improved PA screening and increased primary care referrals in the first three years of operation (2016 – 2019).

***Aims*:** To evaluate the sustained impact of the Endocrine Hypertension Service on PA diagnosis and management over a subsequent three-year period.

***Methods*:** We conducted a retrospective analysis of consecutive new patients seen at a tertiary Endocrine Hypertension Service in Victoria, Australia, from 1 July 2019 to 30 June 2022, a period that included significant COVID-19 related healthcare disruptions. Clinical data were extracted and analysed by referral year (Y1: July 2019 – June 2020, Y2: July 2020 – June 2021, Y3: July 2021 – June 2022) to assess changes over time.

Results: A total of 457 new patients were assessed, with annual referrals increasing over time (Y1: 115; Y2:156; Y3:186). Most referrals originated from primary care (50%), followed by cardiology (23%). At presentation, 20% were treatment-naïve, the median hypertension duration was four years, and 22% had end-organ damage. PA was confirmed in 213 patients (47%), excluded in 171 (37%), and undetermined in 73 (16%) due to incomplete work-up. Among 171 patients treated medically, 78% achieved complete biochemical response and 46% complete clinical response on MRA monotherapy. Among 34 patients who underwent unilateral adrenalectomy, 86% achieved complete biochemical response and 39% complete clinical response.

***Conclusion*:** Growth in referrals, earlier disease detection, and high treatment response rates highlight the sustained effectiveness of a dedicated, structured pathway for timely PA diagnosis and management, even despite COVID-19 disruptions.

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Improvement in metabolic dysfunction-associated steatotic liver disease in overweight and obese adults with incretin analogue pharmacotherapy

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Metabolic dysfunction-associated steatotic liver disease (MASLD) is the most common chronic liver disease and the leading cause of liver-related morbidity and mortality. Its burden lies in the risk of progression to decompensated cirrhosis and hepatocellular carcinoma. While GLP-1 receptor agonists show promising metabolic and hepatoprotective effects in clinical trials, real-world data in overweight and obese populations remain limited. The aim of this study is to evaluate the effect of incretin analogues (semaglutide, liraglutide, tirzepatide) on hepatic steatosis in overweight or obese adults with a diagnosis of MASLD established by ultrasonography +/- elastography.

In this retrospective cohort study, we reviewed serial ultrasonography reports from overweight or obese patients (BMI ≥ 25 kg/m^2) with MASLD obtained before and after pharmacotherapy with semaglutide (n = 18), liraglutide (n = 3), or tirzepatide (n = 7) for an average of 18 months, under the care of an endocrinologist. The primary outcome was the change in hepatic steatosis severity, graded on a semi-quantitative ordinal scale (mild = 1, moderate = 2, severe = 3). Secondary outcomes included changes in fasting lipid profile, and HbA1c.

The mean hepatic steatosis grade improved from 2.03 to 1.48 following pharmacotherapy, with a statistically significant mean reduction of 0.55 (95% CI [0.19 to 0.93], p = 0.004). In addition, a significant reduction in body weight was observed, with a mean loss of 9.97 kg (95% CI [6.03 to 13.92], p < 0.001). Among cardiometabolic parameters, HbA1c showed a mean reduction of 0.8% (95% CI: 0.1 to 1.5; p = 0.009), while changes in the fasting lipid profile were not statistically significant.

These real-world findings suggest that GLP-1 receptor agonists and dual GLP-1/GIP receptor agonists are associated with improvements in hepatic steatosis and weight-loss in overweight and obese adults with MASLD, supporting their potential role in the pharmacological management of MASLD.

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Primary hyperparathyroidism in pregnancy: an evolving paradigm in endocrine and obstetric care

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A 32-year-old primigravida at 8 weeks gestation presented with severe hyperemesis gravidarum, marked weight loss and dehydration. Biochemistry revealed hypercalcemia (corrected calcium 2.82mmol/L) and elevated parathyroid hormone (10.7pmol/L), leading to a diagnosis of primary hyperparathyroidism. 24-hour urine calcium excluded familial hypocalciuric hypercalcemia. The patient received supportive care including intravenous fluids and fortnightly calcium levels. While her hyperemesis improved by 15 weeks, her corrected calcium remained elevated (2.79mmol/L), prompting consideration for parathyroidectomy in the second trimester. Neck ultrasound suggested a possible enlarged right inferior parathyroid gland. 4DCT was suspicious for one right mid posterior 7mm parathyroid. A right unilateral parathyroid exploration is planned for 23 weeks gestation.

PHPT is the leading cause of hypercalcaemia in pregnancy, yet its prevalence is low and presentation often subtle. (1) Untreated maternal hypercalcaemia confers substantial maternal and foetal risks including pre-eclampsia, prematurity, growth restriction, and post-natal hypocalcaemia or tetany. Adverse outcomes correlate with the degree of maternal calcium elevation, with miscarriage rates rising when corrected calcium exceeds 2.85mmol/L. (2,3)

Management hinges on timely surgical intervention. Localisation imaging is limited to ultrasound due to concerns regarding radiation and contrast exposure. 4DCT with foetal shielding, and limiting radiation and contrast has been used successfully in our centre for localisation. Acute stabilisation comprises aggressive hydration, electrolyte correction and vitamin D optimisation. Loop diuretics, bisphosphonates and calcimimetics are generally avoided given limited safety data. Definitive cure is parathyroidectomy, optimally performed in the second trimester (12–24 weeks), when organogenesis is complete and the risk of preterm labour remains low. Postpartum, careful monitoring is essential as the loss of placental calcium transfer can lead to an exacerbation of maternal hypercalcemia. Genetic testing is advisable in specific clinical contexts. (1,4)

Early recognition and coordinated surgical management are critical to safeguarding both maternal and foetal outcomes in pregnancies complicated by PHPT.

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Saline Suppression Tests: Safety, Tolerability, and Blood Pressure Response

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Background:

The saline suppression test (SST) is widely used to confirm a diagnosis of primary aldosteronism (PA), but concerns remain about its acute haemodynamic effects, particularly in patients with elevated blood pressure. Limited data is available on its safety, tolerability, and predictors of blood pressure (BP) changes during testing.

Aim:

To assess the safety and tolerability of the SST, evaluate BP changes during the test, and identify patient characteristics associated with BP changes.

Methods:
We conducted a retrospective audit of 419 patients who underwent SST at a tertiary centre between 2019 and 2025. Patients were classified into PA, low-renin hypertension (LRH), or normal-renin hypertension (NRH). PA was defined by post-seated SST aldosterone (immunoassay) >170 pmol/L; LRH by renin <10 mU/L without meeting PA criteria; NRH comprised the remainder. Clinical, biochemical, and BP data were extracted from records. Multiple linear regression identified variables associated with BP changes at 4 hours post-SST.

Results:
The SST was generally safe and well tolerated. Most patients completed the test without adverse events; only one discontinued early, and five required antihypertensives. Mean BP changes did not differ significantly across diagnostic groups. However, PA and LRH patients showed upward systolic BP trends, with 16% and 13% experiencing ≥20 mmHg increases at 4 hours, respectively. In contrast, NRH patients had minimal BP changes. Regression analysis showed higher baseline BP was associated with smaller BP rises ($p < 0.001$). Older age, higher BMI, and male sex were linked to greater systolic BP increases ($p < 0.05$).

Conclusion:
The SST appears safe and well tolerated in a referred hypertensive population. BP increases during SST, particularly among PA and LRH patients, may reflect salt sensitivity. Patient factors such as age, sex, BMI, and baseline BP influence haemodynamic responses and may guide patient selection and monitoring.

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Diabetes status and in-hospital glycaemic control on COVID-19 related outcomes: A Sri Lankan cohort study

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The aim of this study was to assess the impact of glycaemic control with and without pre-existing diabetes on outcomes in patients with severe COVID-19. This was a prospective observational study of 109 patients with severe COVID-19 treated in either intensive care or high dependency care units at National Hospital Kandy, Sri-Lanka. The most prevalent co-morbidity in severely ill COVID-19 patients was diabetes (66%). hose with HbA1c >/=10% had non-significantly longer duration of hospitalization (median 21 vs. 13 days; p=0.073) than those with HbA1c <10%. Individuals treated with steroids for COVID-19 had higher average capillary blood glucose (CBG) during hospitalization (mean 182.9 mg/dL; SD 47.47 vs. 157.28 mg/dL; SD 34.01; p=0.006), but there was no significant difference before and after commencing steroids (p = 0.593). Daily glycaemic variation showed peak at mid-day. Among 76 who required insulin in-hospital, 46 had non-insulin-dependent diabetes, 15 had no pre-existing diabetes, and 14 were not commenced on steroids. Average daily insulin requirement was higher in those who required oxygen (median 24U vs. 0U; p=0.029). Higher proportion of those who required insulin required intubation-and-ventilation (53.3% vs. 29.2%; p=0.012). Higher proportions of those who developed hypoglycaemia required inotropes (72.4% vs. 37.5%; p=0.001), haemodialysis (24.1% vs. 7.55; p=0.018) and developed high D-dimer (>750ng/mL) (94.7% vs. 70.5%; p=0.033) than those without hypoglycaemia. They had a longer duration of hospital stay (median 16 vs. 11.5 days; p=0.047). Fungal sinusitis developed in 4, of which all had pre-existing diabetes; 2 of whom had HbA1c >10% and were previously insulin dependent. 3 individuals developed persistence of new onset diabetes at 3 months post-COVID-19, of which 1 was not treated with steroids for COVID-19. Pre-existing diabetes status, as well as glycaemic control and fluctuations during the acute COVID-19 infection are associated with acute and long-term COVID-19 related adverse outcomes.

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The impact of blood lipid levels on the performance of percutaneous coronary intervention

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Background and objectives: Dyslipidemia is an accepted cardiovascular risk factor. However, the effect of blood lipid levels on the performance of percutaneous coronary intervention (PCI) is not well known. The aim of this study was to evaluate the impact of blood lipid levels on acute gain after PCI.

Subjects and Methods: Data from 141 consecutive patients (240 lesions) who underwent PCI using drug eluting stents were analyzed.

Results: Before Procedure, the minimal lumen diameter (MLD) was 0.87 ± 0.49 mm. After procedure, MLD was 2.34 ± 0.40 mm. As a result, acute gain was 1.48± 0.55mm. There was positive correlation between LDL cholesterol and acute gain. (correlation coefficient = 0.147; p=0.039) However, there was no correlation between HDL cholesterol and acute gain. (correlation coefficient = -0.103; p=0.148) Also, there was no correlation between triglyceride and acute gain. (correlation coefficient = 0.052; p=0.470)

Conclusions: Increased LDL cholesterol is favorable for acute gain. However, HDL cholesterol and triglyceride were not associated with acute gain. Therefore, we should make more effort to get sufficient acute gain when faced low LDL cholesterol during PCI.

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Data from patients with lactose intolerance and levothyroxine malabsorption in treatment with liquid L-T4 without lactose

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Aims: The prevalence of intolerance to lactose-containing foods is present at birth in humans and gradually declines with age. In hypothyroid patients requiring high doses of levothyroxine (L-T4) to achieve euthyroidism, lactose intolerance (LI) should be excluded due to its high prevalence in the general population. The absorption of oral T4 may be affected in patients with LI, by following a diet containing lactose, while it improves with a lactose-free diet. Lactose is often present in many commercially available drugs, as L-T4 preparations. We aimed at investigating patients with LI and hypothyroidism, who were initially treated with "L-T4 in tablet form containing lactose" (L-T4-Tab+Lactose), and then switched to the same dose of "liquid L-T4 oral solution (lactose-free)" (L-T4-Liq).

Methods: We have enrolled 20 patients treated with L-T4-Tab+Lactose, with stable TSH value in the normal range in the last 2 years. Because of a new diagnosis of LI, patients were switched from L-T4-Tab+Lactose to L-T4-Liq. All patients were diagnosed to be affected by LI, and were taking a low lactose diet. L-T4 was then supplied again at the same dosage in tablets in 8 patients who wished to switch back to the tablet form.

Results: The L-T4-Liq formulation showed a better control of TSH levels, all patients (included those who had been switched back to tablets) were lastly treated with the L-T4-Liq, and TSH, FT3, FT4 were tested again two months after the initial evaluation, and after 12, and 24 months, resulting in the normal range in all subjects.

Conclusion: The L-T4-Liq formulation is able to bypass the issue of LI malabsorption, and can lead to the normalization of TSH, and long term stable TSH levels, in patients with subclinical hypothyroidism. Additional researches are necessary to evaluate the liquid L-T4 formulation in larger numbers of patients with hypothyroidism and lactose intolerance.

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Optimizing screening for metabolic dysfunction-associated steatotic liver disease (MASLD) in diabetes: a clinical audit of current practices

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Aims

Metabolic dysfunction-associated steatotic liver disease (MASLD) commonly co-exists in most people with type 2 diabetes mellitus (DM), with a 65.3% pooled prevalence.[1] It is increasingly recognised in type 1 DM with a prevalence of 22.2%.[2] Furthermore, MASLD has a bidirectional relationship with DM and its metabolic cofactors.[3,4]We aim to evaluate MASLD screening practices within DM at Monash Health diabetes clinics, with sub-analysis of MASLD risk factors, treatments, and referral pathways.

Methods

We conducted a retrospective cross-sectional study of all patients with DM who attended Monash Health Chronic Diabetes Management Clinics between 1 January and 9 May 2024.

Results

There were 416 individual attendees (mean age 62±15 years, 42.5% female), of whom 55.2% had type 2 DM, 19.6% type 1 DM, and 25.3% other forms. Most patients with the relevant data had longstanding DM >10 years 73.1% (277/379), and were either obese 40.0% (68/170) or overweight 37.1% (63/170). Diabetes complications were common (77.2%), including macrovascular (36.7%) and microvascular (69.0%) disease. Approximately 75.5% of patients were on insulin therapy, 31.0% on SGLT2 inhibitors, and 24.5% used GLP-1 receptor agonists.

Less than half of patients 38.0% (158/416) had liver imaging within 5-years of clinic attendance, of whom 64.0% (101/158) had imaging evidence of MASLD. An additional 7.5% (31/416) of attendees had a documented history of MASLD but no available imaging.

Of the 132 attendees with MASLD, 35.3% (47/132) had a calculable Fibrosis-4 (Fib-4) index, and 59.6% (28/47) demonstrated intermediate-to-high fibrosis risk. In this high risk subgroup, 50% (14/28) had transient elastography evaluation within the past five years, and 61% (17/28) had liver clinic follow-up.

Conclusions

MASLD is common in patients with DM, but screening, documentation, and referral practices are suboptimal. Systematic MASLD screening protocols should be integrated into diabetes care pathways, with a focus on identifying patients with progressive liver fibrosis.

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A Single Centre Review of Surgical Outcomes of Rathke's Cleft Cysts

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Background: Rathke's cleft cysts (RCC) are benign sellar lesions comprising 6-10% of symptomatic pituitary lesions.[1] Long-term outcome data in Australia is limited.

Aim: To characterise long-term outcomes of surgically treated RCCs at a single Australian tertiary centre and identify predictors of recurrence requiring operation.

Methods: A retrospective review of RCC patients treated at The Royal Melbourne Hospital and Melbourne Private Hospital from 1993–2025. Clinical data were obtained from medical records.

Results: Forty patients (65% female) with median age of 49 years at diagnosis (IQR 34.8-59.5) were included. The median follow-up was 4.1 years (IQR 2.16-9.04). Compressive symptoms (87.5%) including headache and visual disturbance were common. Pituitary dysfunction was present in 12 patients (28%), most commonly, hypogonadotrophic hypogonadism (20%), hypocortisolism (17.5%). Five patients (12.5%) had hyperprolactinaemia secondary to stalk effect. Median RCC size was 18mm (IQR 16-23). Targeted MRI identified suprasellar extension in 34 lesions (87.5%). Thirty-eight patients (95%) underwent transsphenoidal surgery (14 gross total, 26 subtotal) and 2 patients (5%) had pterional craniotomies. CSF leak occurred in 7.5%. New pituitary hormone deficiency occurred in 8 patients (20%) post operatively: 7 patients (17.5%) developed hypocortisolism, 5 patients developed vasopressin deficiency (12.5%) of which 3 were permanent. Compressive symptoms resolved in 27 patients (77.1%) post-operatively. Pituitary function recovered in 6 patients (50%). Nine patients (22.5%) had RCC recurrence or regrowth requiring re-operation. The median time to first radiological recurrence was 10.6 months (IQR 5.2-26.6), and re-operation was 24.7 months (IQR 6.7-36.8). There was no mortality within the follow-up period. Regrowth rate was higher in the group that required reoperation (13.5mm/year versus 2.3mm/year, $p<0.05$).

Conclusion: Surgery effectively alleviates compressive symptoms of RCCs, but anterior pituitary dysfunction often persists. Rapid regrowth may be a predictor of recurrence requiring intervention. Further studies are needed to validate these findings.

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Silent Macrocorticotrophinomas – Whispering Trouble or Just Background Noise?

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Silent corticotroph adenomas (SCAs) are considered an aggressive subtype of pituitary neuroendocrine tumour and are thought to differ from other non-functioning pituitary neuroendocrine tumours (pitNET), with reports of higher recurrence rates following surgical resection. Our aim was to compare long-term surgical outcomes in patients with SCAs and other pitNETs requiring resection.

We conducted a retrospective cohort study of patients who underwent surgical resection of pitNETs at a tertiary hospital in metropolitan Sydney between June 2010 and June 2025. All participants were managed through a multidisciplinary service and had histopathological confirmation of pitNET. Surgery was indicated for tumour growth or mass effect, including optic apparatus involvement and/or cavernous sinus invasion.

Fifty-seven patients were included, with a mean follow-up of 82.7±48.5months. Nine experienced tumour recurrence (mean time to recurrence 42.8±34.7 months). Age at surgery was similar between recurrence and non-recurrence groups (50.9±15.4 vs. 54.0±13.6 years; p=0.59). Tumour size trended larger in the recurrence group (28.0±9.8mm vs. 24.2±7.0mm; p=0.29).

Gross total resection was significantly associated with long-term remission (75% vs. 11%; p<0.003), while subtotal resection predicted recurrence (88% vs. 25%; p<0.003), despite more frequent use of postoperative radiotherapy in those with recurrence (56% vs. 8%; p<0.003). SCAs were not overrepresented in the recurrence group (1/9 vs. 10/48; p=0.49). Presentation with visual disturbance was significantly more common in those with recurrence (78% vs. 23%; p=0.0012), although there were no significant differences in formal

perimetry or ganglion nerve fibre layer analyses. There was no significant difference in Knosp grades between recurrent and non-recurrent tumours. Rates of optic chiasm compression, cavernous sinus , sphenoid sinus and/or clival invasion were similar across groups.

Tumour recurrence after pitNET resection was strongly associated with subtotal resection and initial visual symptoms. Tumour size, subtype (including SCA), and invasive features did not significantly differ between those with and without recurrence.

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Local community and social media advertisement may be an efficient and cost-effective strategy to recruit postmenopausal women into clinical trials: insights from the ROLEX-DUO study

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Recruiting a sufficient sample size is a major barrier in conducting investigator-initiated clinical trials (1). Despite this, there is scarce literature on success and costs of various recruitment strategies, including use of social media in recruiting older community cohorts, which can add to challenges in planning and budgeting for clinical trials. Hence, we present a preliminary analysis of recruitment for an ongoing clinical trial in postmenopausal women.

ROLEX-DUO is a placebo-controlled randomised controlled trial (RCT) conducted at RNSH/Westmead Hospitals, Sydney (2, 3). The primary aim is to assess whether high-intensity resistance/impact exercise can enhance effects of romosozumab on bone mineral density in postmenopausal women over 8-months (n=75). Eligible women are 50-80yrs with osteoporosis/osteopenia and able to commit to a twice-weekly local exercise program. Women are excluded if any recent fragility fracture, or current/recent osteoporosis pharmacotherapy. Recruitment data is collected prospectively and efficiency of recruitment strategies based on enrolment conversion rates (% expressions-of-interest (EOIs) converted to participant enrolment).

Between March 2024-May 2025, out of 450 EOIs, n=64 women underwent screening assessments of which n=43 participants were enrolled (conversion rate 9.6%) (Table 1). Clinician referrals were the most efficient recruitment source (40%), followed by community/council newsletters (12.7%), hospital/university advertisement (11.4%), word-of-mouth (9.3%) and social media (9.1%). Most frequent reasons for exclusion were other osteoporosis/hormonal pharmacotherapy (n=107), no longer interested (n=89), already participating in resistance exercise (n=48), age out of range/perimenopausal (n=40) or unable to be contacted (n=38). A total $1,070 AUD has been spent on recruitment.

In this preliminary recruitment analysis of an RCT, local community-based and geo-targeted social media advertisement have been efficient strategies in recruiting an older postmenopausal cohort. Recruitment at this scale may be performed with minimal costs. Greater transparency and reporting of recruitment data may better inform future clinical trial research.

Table 1: Efficiency of various recruitment strategies

EOI source	Total EOIs (n)	Screening conversion rate (n/n, %)	Enrolment conversion rate (n/n, %)
Clinician referral	20	8/20 (40%)	8/20 (**40%**)
DXA referral	21	1/21 (4.8%)	1/21 (**4.8%**)
Hospital flyer	53	4/53 (7.5%)	2/53 (**3.8%**)
Hospital/university advertisement	35	5/35 (14.3%)	4/35 (**11.4%**)
Community/council newsletter	71	12/71 (16.9%)	9/71 (**12.7%**)
Community noticeboard	29	4/29 (13.8%)	2/29 (**6.9%**)
Social media	99	18/99 (18.2%)	9/99 (**9.1%**)
Word-of-mouth	86	12/86 (14.0%)	8/86 (**9.3%**)
Other	1	0/1 (0%)	0/1 (**0%**)
Unknown	35	-	-
All	450	64/450 (14.2%)	43/450 (**9.6%**)

EOI = expression of interest. DXA = dual-energy Xray absorptiometry.
Screening conversion rate (%) = screening visits/EOIs x 100.
Enrolment conversion rate (%) = participants enrolled/EOIs x 100.

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The effect of prednisolone ingestion and acute exercise on lipocalin-2 and its variants in young males

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Lipocalin-2 (LCN2) has three main variants; polyaminated (hLCN2) and non-polyaminated (C87A and R81E). The polyaminated form is proposed to positively influence energy control, whereas the non-polyaminated forms negatively impact energy control in mice. Glucocorticoids negatively affect glucose regulation and exercise has a positive effect. We hypothesise that glucocorticoids will suppress, while exercise will increase hLCN2, and decrease C87A and R81E, which will be associated with improved insulin sensitivity.

In a randomised crossover design, nine young healthy men (aged 27.8 ± 4.9 years; BMI 24.4 ± 2.4 kg/m^2) completed 30 min of high-intensity aerobic exercise (90-95% heart rate reserve) after glucocorticoid or placebo ingestion. Blood was collected and analyzed for LCN2 and its variants levels at baseline, immediately, 60 min and 180 min post-exercise. Insulin sensitivity was assessed using hyperinsulinemic-euglycemic clamp.

A main effect, increase in LCN2 was detected for prednisolone ingestion (overall treatment effect $p = 0.001$), but not LCN2 variants (all $p > 0.05$). Main effects for time were observed for exercise for LCN2 and all variants (overall time effect all $p < 0.02$). Regardless of treatment, LCN2, C87A, R81E, and hLCN2 increased immediately after exercise compared with baseline (all $p < 0.04$). C87A, but not LCN2 or its other variants, remained elevated at 180 min post-ex ($p = 0.007$). LCN2, but not its variants, was elevated in response to prednisolone ingestion. LCN2 and its variants are transiently increased by acute exercise, but this increase was not related to insulin sensitivity. The clinical implication of elevated LCN2 and its variants post-exercise on satiety and energy regulation, as well as the mechanisms involved warrant further investigation.

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Participant satisfaction and perceived impacts of a community-based diabetes prevention program among Chinese adults with pre-diabetes

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4. The United Christian Nethersole Community Health Services, Hong Kong

5. Hong Kong Red Cross, Hong Kong

6. Health In Action, Hong Kong

Background:

Type 2 diabetes is a major public health concern, especially among Chinese adults with obesity and pre-diabetes. Lifestyle modifications, including diet and physical activity, are the first line strategies for diabetes prevention. Culturally tailored, community-based lifestyle interventions are essential to effectively engage this population and promote sustainable behavioral change for diabetes prevention.

Aims:

This study aims to evaluate participant satisfaction and perceived impacts of a community-based diabetes prevention program among Chinese adults with obesity and pre-diabetes.

Methods:

The research team trained five local NGOs to deliver an evidence-based, culturally adapted diabetes prevention program. Chinese adults with obesity (BMI≥25kg/m^2) and pre-diabetes were recruited from community settings. Participants engaged in structured lifestyle interventions over six months. The program included six monthly group sessions (15–20 participants, two hours each), emphasizing diet, physical activity, and goal setting, along with two individual diet counseling sessions. An anonymous evaluation form was completed by participants after 6-month intervention, assessing satisfaction with the group-based intervention and individual diet counseling, as well as perceived improvements in health knowledge and behaviors.

Results:

676 participants enrolled (72.8% female, mean age = 53.5 years, mean BMI =28.4 kg/m^2), with 450 evaluation forms were received (66.6% response rate). Nearly all participants (98%) reported increased knowledge about diabetes prevention and increased awareness of their health status (98%), along with improved dietary habits (97%) and exercise habits (93%). 98% agreed/ strongly agreed that individual diet counseling sessions provided personalized guidance addressing their individual dietary needs. Participants rated the nutrition class and individual diet counseling as the most useful intervention components. Furthermore, 96% agreed/strongly agreed that this program helped them manage their weight and prevent diabetes.

Conclusion:

The group-based lifestyle interventions achieved high satisfaction and promoted behavioral change among participants. Future research should assess the long-term effectiveness of these programs in diabetes prevention.

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Experience of Vasomotor Symptoms in Men Undergoing Androgen Deprivation Therapy for Prostate Cancer (VASOPRO)

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Aims: To prospectively audit a dedicated androgen deprivation (ADT) clinic at a single tertiary centre, focusing on men undergoing ADT for prostate cancer. The audit encompasses treatment duration, prevalence and severity of vasomotor symptoms (VMS), current treatment patterns for symptom management, demographic data, serum testosterone levels, prostate-specific antigen, and liver function tests in patients receiving fezolinetant. Among those receiving pharmacologic therapy for VMS, the use of a written survey to evaluate patient-reported outcomes assessing VMS severity, impact on quality of life, treatment effectiveness, and any adverse effects experienced.

Methods: VASOPRO is an ongoing prospective, observational audit conducted at a dedicated ADT clinic within a single tertiary centre. Men receiving ADT are systematically reviewed for the presence and severity of VMS. For those reporting symptoms warranting treatment, pharmacologic interventions—such as selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, and off-label use of the neurokinin-3 receptor antagonist fezolinetant—are documented. In addition, consenting patients undergoing treatment for VMS complete serial patient-reported outcome surveys to assess symptom burden and therapeutic response over time.

Results: Preliminary data reveal that 61.1% (22 of 36) of men on ADT attending our dedicated clinic report VMS of any severity. Among this symptomatic cohort, 27.3% (6 of 22) are receiving pharmacotherapy for symptom relief. 22.7% (5 of 22) of those receiving treatment are using off-label fezolinetant, reflecting early clinical adoption and potential interest in novel therapeutic options.

Conclusion: VMS are a common and often undertreated adverse effect of ADT in men with prostate cancer. A substantial proportion of affected individuals remain untreated despite symptomatic burden. Off-label use of fezolinetant, although limited, highlights the need for further research into targeted therapies for male VMS. Ongoing data collection from this audit will inform future clinical management strategies and support the development of evidence-based guidelines for this underappreciated aspect of prostate cancer care.

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Bone health in heart transplantation: a Melbourne perspective revealed a higher rate of post-transplant fractures in females which occurred earlier than in males despite antiresorptive therapy and preserving bone density those who received it.

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To evaluate bone health outcomes of cardiac transplant recipients given the known bone density loss and fragility fractures in this cohort (1). The primary outcome was effect of antiresorptive therapy (treatment) on incidence of post-transplant fragility fractures. Secondary outcomes included the treatment impact on bone mineral density (BMD) and adverse events.

This retrospective cohort study included 196 adult patients (mean age 48 ± 12.9 years; 30.1% female) who underwent heart transplantation between 2012 and 2021 at the Alfred Hospital in Melbourne. Patient data were extracted from medical records.

Fragility fractures occurred in, 21 patients (10.7%) with a post-transplant fracture rate of 9.2% (18 patients).

Those treated had significantly lower baseline BMD (Table 1a). Treatment attenuated BMD loss at 12- and 24-months post-transplant at all sites (Table 1b) but fracture rates were equal in both treatment-naïve (9.2%, 7/76) and treatment-exposed (9.4%, 11/117) groups. Treatment naïve patients lost BMD most significantly in the first 12 months after transplant, with 4% BMD loss in the spine (figure 1), 7% in total hip (figure 2) and 5% in femoral neck (figure 3) compared with those treated (95% CI 0.26 range, $p<0.001$).

Females fractured significantly more often and earlier than males (19.0% vs 5.2%, $p = 0.006$) (mean fracture-free survival 3,295 vs 3,918 days, $p=0.001$) even after adjusting for age, rejection rates and treatment.

In this real-world cohort, antiresorptive therapy attenuated BMD loss but did not reduce fracture incidence in adult heart transplant recipients, likely due to selection bias where high risk patients were preferentially treated. Female recipients had a higher and earlier risk of fractures.

These findings support a need for proactive bone health management in cardiac transplant recipients, particularly for female patients who represent a vulnerable and high-risk group. This is in line with international guidelines' recommendations for an individualised approach (2).

Table 1a	Mean ± Standard Deviation	
	Antiresorptive therapy naïve	Antiresorptive exposed
Baseline BMD Spine (g/cm2)	1.09 ± 0.172	0.88 ± 0.187
Baseline BMD Femoral Neck (g/cm2)	0.911 ± 0.183	0.722 ± 0.140
Baseline BMD Hip (g/cm2)	0.994 ± 0.148	0.829 ± 0.157
Table 1b		
Change in lumbar spine BMD at 12 months	-0.044 ± 0.078	0.007 ± 0.082
Change in lumbar spine at 24 months	-0.055 ± 0.111	0.024 ± 0.096
Change in femoral neck at 12 months	-0.722 ± 0.083	-0.031 ± 0.067
Change in femoral neck at 24 months	-0.087 ± 0.092	-0.027 ± 0.074

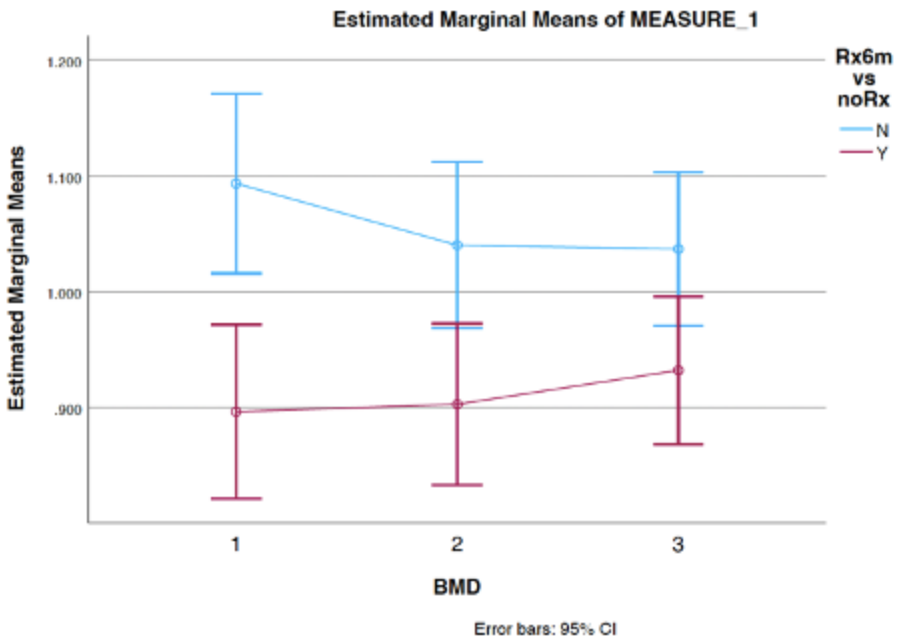


Figure 1: BMD Spine a

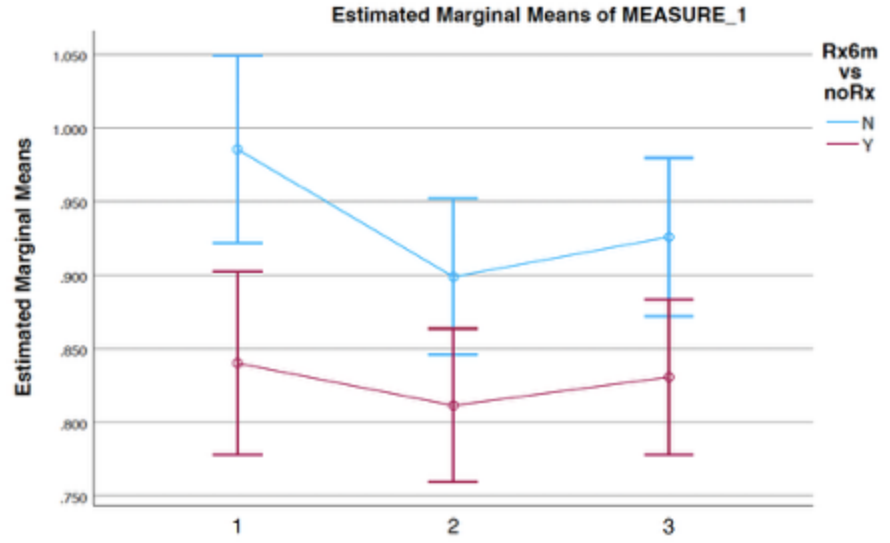
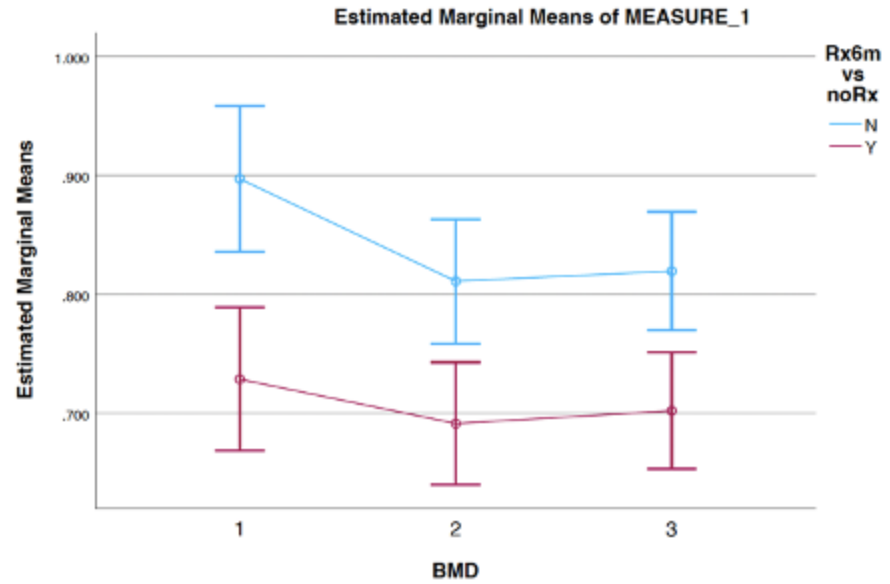


Figure 2: BMD total hip



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Low-renin hypertension in the era of expanded screening for primary aldosteronism: a cohort study

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Publish consent withheld

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The prevalence of low-renin hypertension worldwide: a systematic review and meta-analysis.

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Publish consent withheld

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In vitro antineoplastic effects of the kinase inhibitor CLM24 in aggressive dedifferentiated thyroid cancer

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Aims Thyroid cancer is the most frequently diagnosed cancer among endocrine tumors. Surgery is the standard therapeutic strategy for patients with differentiated thyroid carcinomas (DTC). After thyroidectomy radioactive iodine (RAI) treatment is used to ablate residual thyroidal tissues. When DTC progresses, cells can develop refractoriness to RAI, impacting negatively the prognosis. The available therapeutical strategies (i.e., surgery, chemotherapy and external beam radiation therapy) can cause significant side effects with no prolongation of survival. Thus, it may be worthy to delineate an effective systemic therapy in patients with dedifferentiated DTC (De-DTC) to ameliorate their quality of life. In the next future, the success of treatments may be increased by novel and more effective antineoplastic compounds. Testing the sensitivity of human primary DeDTC cells obtained from each subject, to different drugs, could determinate an increase in the effectiveness of the treatment avoiding the administration of inactive therapeutics.

Methods In this study we planned to evaluate *in vitro* the antineoplastic effects of CLM24, a compound with pyrazolo[3,4-d]pyrimidine nucleus, in human primary De-DTC cell cultures and in the AF cell line, derived from primary anaplastic TC cells.

Results CLM24 demonstrated a significant antiproliferative action on the AF cell line (with BRAF V600E mutation), and a significant pro-apoptotic effect. In primary De-DTC cells with/without V600EBRAF mutation, CLM24 reduced significantly the proliferation (vs. control), while did not in primary normal thyroid follicular cells. In De-DTC cells with/without V600EBRAF mutation, the ratio of apoptotic cells increased in a dose dependent manner after treatment with CLM24, which also significantly inhibited cell migration and invasion.

Conclusion The pyrazolo[3,4-d]pyrimidine derivative CLM24 demonstrated a potent antineoplastic effect *in vitro* in primary De-DTC cells, and this effect did not depend on the presence/absence of the V600EBRAF mutation. These promising results make CLM24 worthy of further investigation for a possible clinical trial.

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Co-Design, implementation and evaluation of a nested diabetes model-of-care for adults living with cystic fibrosis

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Aim

Cystic fibrosis (CF) life expectancy is increasing and this is leading to new health challenges, especially diabetes. Nearly 25% of adults with CF develop diabetes, but only a minority receive endocrinology care (1). This study aimed to co-design, implement, and evaluate a nested diabetes model of care (MOC) within a single tertiary adult CF centre in Queensland (2).

Methods

We utilised the Consolidated Framework for Implementation Research to design surveys and workshops for consumer and healthcare provider end-users. We then implemented the co-designed diabetes MOC and used database-driven analytics to evaluate change in primary clinical outcome of HbA1c pre and 12-months post, comparing those who were engaged versus disengaged. A mixed-methods approach was used to evaluate secondary clinical and non-clinical outcomes.

Results

The co-designed diabetes MOC was nested within the pre-existing adult CF services. It promoted multidisciplinary collaboration specifically co-consultations with an endocrinologist, dual credentialed diabetes educator and dietitian. Case conferencing with psychology, social work and other disciplines was also supported. Co-designed referral pathways, flexible diabetes care delivery integrating diabetes technology that supported intensive insulin titration, and co-scheduling of appointments enabled streamlined patient journeys. Our diabetes MOC had high engagement, with 76.7% of our entire CF cohort with confirmed diabetes reviewed within the first year of operationalisation. Engagement with the MOC was associated with a statistically significant decline in HbA1c (-0.54% vs +0.33%, P-value 0.004) and a 0.22% [95% CI 0.19 -0.32] per month increment in percent predicted forced expiratory volume (ppFEV1). End-user satisfaction with the MOC was high.

Conclusion

Our co-designed MOC demonstrated high engagement, improved glycaemic management and lung function in adults with CF living with diabetes. Our approach to CF diabetes care may assist with reducing treatment burden in the order of initiating a new diabetes medication while concurrently enhancing end-user experiences of healthcare.

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Infrastructural imp

Address gaps in se

Monitor MOC outcome

Evaluation

Action: Gather clinical, non-clinical & end-user satisfaction outcomes

Outcome: Iteratively refine MOC to facilitate sustainability

Enable innovative design el

Assist providers with i

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Ethnic Variations and the Influence of BMI on Blood Glucose Levels in Gestational Diabetes Patients at Westmead Hospital: An Analysis Using Health2Sync

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Gestational diabetes mellitus (GDM) is associated with adverse maternal and fetal outcomes. Emerging evidence indicates that ethnicity and BMI may influence glycemic control, hence understanding these relationships can improve management.
This study assesses how ethnicity and BMI(Body Mass Index) affect fasting and post-prandial blood glucose levels in GDM patients at Westmead Hospital. This is with the aim to identify any potential disparities that could inform targeted interventions.
A retrospective analysis of GDM patients recording their blood glucose levels via Health2Sync (a mobile application) was conducted. Participants included East and Southeast Asian, European, Indian, Middle Eastern, and Other ethnicities. Blood glucose readings were analyzed alongside BMI data to examine associations with statistical comparisons to identify significant differences across groups.
There was no significant difference found in fasting blood glucose levels across the different ethnicities. However, BMI was positively correlated with both fasting and post-prandial glucose levels despite no statistical significance, with higher BMI associated with worse glycemic control. Post-prandial glucose was significantly elevated in Indian, Middle Eastern, and East/Southeast Asian populations compared to Europeans. These findings indicate that BMI influences glycemic levels universally, and that certain ethnic groups experience higher post-meal glucose responses.
In summary, BMI substantially impacts fasting and post-prandial glucose levels, with variations influenced by ethnicity. Culturally tailored dietary guidance and weight management are essential components of effective GDM care. Recognising these differences allows for more personalised and effective interventions to improve outcomes. Future research should prioritise integrated, culturally tailored, multidisciplinary models of GDM care that account for both BMI and ethnic diversity.

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Understanding the Biopsychosocial Impact of Thyroid Cancer: Real-World Patient-Reported Outcomes from an Australian Cohort

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Thyroid cancer is increasingly diagnosed in Australia and, while typically associated with a favourable prognosis, the diagnostic and therapeutic journey can impose a substantial burden on patients. Despite this, limited real-world, patient-centred outcome data exist—particularly in the context of evolving therapies and clinical care models. The biopsychosocial impact of thyroid cancer was evaluated primarily examining how cancer subtype (DTC vs MTC), sex, age, and time since diagnosis influence patient experience and symptom burden.

Data were sourced from a web-based patient-reported outcomes (PROMs) questionnaire distributed to patients at Royal North Shore Hospital and from the Australian and New Zealand Thyroid Cancer Registry (ANZTCR). Quantitative analyses included descriptive statistics on demographics, clinical characteristics, and quality of life metrics. Qualitative responses were analysed using thematic coding.

A total of 156 patients met inclusion criteria, with the majority having DTC (90.4%; n=141). The mean age was 52.0 years (range 18–90), and 64.7% were female (n=101). Sex was the most variable factor, with female respondents reporting higher rates of nearly all assessed symptoms. Time since diagnosis showed minimal variation and did not correlate linearly with symptom burden. A dominant theme in qualitative data was a strong desire for complete cure or disease stability, highlighting a gap in patient education around treatment expectations.

These findings point to the need for improved communication regarding treatment aims and prognosis, alongside broader supportive care strategies. Female patients may benefit from targeted interventions, and fatigue and mental health support remain common needs across the cohort.

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Composite Phaeochromocytoma-Ganglioneuroma – A Rare Diagnosis 20 Years in the Making

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Case:A 59-year-old female, with no history of endocrine tumours or familial cancer syndromes, had a laparoscopic partial left adrenalectomy for a left adrenal nodule concerning for lung squamous cell carcinoma oligometastasis. The surgery was complicated by acute pulmonary oedema and severe cardiomyopathy, which required stabilisation with an intra-aortic balloon pump. The Intensivist and Cardiologist diagnosed catecholamine surge as the most likely cause. Histology from the surgery demonstrated a ganglioneuroma.

20 years later, the patient was referred to our Endocrinology Clinic for a 2.6 cm left adrenal nodule. Clinically, the patient was hypertensive and reported headaches, sweating, and palpitations; biochemically, plasma normetanephrine 2970 (<1560) and metadrenaline 1280 (<447) were elevated. The adrenal lesion was avid on F-DOPA PET. As such, suspicions were raised for a phaeochromocytoma. The patient subsequently underwent an uncomplicated left re-do retroperitoneoscopic completion adrenalectomy, with histology confirming a low-risk phaeochromocytoma.

The two adrenal specimens, from the first stage partial adrenalectomy and second stage completion adrenalectomy, were reviewed at our MDT meeting. The histologies were unequivocally different, with no phaeochromocytoma tissue evident on the first specimen, and no residual ganglioneuroma evident on the second specimen. We postulate that, based on her complications during the first surgery, she must have had a phaeochromocytoma present – in addition to the ganglioneuroma – which was left behind and has grown over the intervening years.

Discussion: Composite phaeochromocytomas are rare neuroendocrine tumours, comprising phaeochromocytoma and neurogenic components[1]. There are 110 published cases[2]. They may present heterogeneously like ordinary phaeochromocytomas and are ideally managed surgically with a multidisciplinary approach[3]. Our case required curative surgical resection 20 years after the initial surgery, which appears to be the first case of its kind. Clinicians should maintain a high index of suspicion for this condition, as more research is vital to fully understand its behaviour and outcomes.

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1,25-Vitamin D-mediated hypercalcaemia in the setting of immune therapy-related sarcoid-like reaction

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Introduction: Immune checkpoint inhibitors (ICIs) have recently become a crucial component of cancer therapy, subsequently triggering a range of immunotherapy-related adverse effects (IRAEs), including hypercalcaemia due to drug-induced sarcoid-like reactions (DISRs). DISRs are defined as systemic granulomatous reactions that occur in relation to the initiation of offending agents. Clinically, DISRs and sarcoidosis both present with bilateral hilar lymphadenopathy, cutaneous lesions, uveitis and hypercalcaemia, thereby posing difficulty in distinguishing one from another. Unlike sarcoidosis, the resolution of symptoms with cessation of the offending drug can favour a diagnosis of DISRs.

Case Summary: We presented a case of a 72-year-old male with severe hypercalcaemia of 3.84 mmol/L following the second cycle of immunotherapy with ipilimumab and nivolumab in the setting of metastatic melanoma with bone metastases. Further investigations demonstrated hilar lymphadenopathy, which was not present in previous imaging, and subsequent hypercalcaemia work-up demonstrated a significantly elevated serum calcitriol level as high as 429 pmol/L. A diagnosis of drug-induced sarcoid-like reactions or DISRs was made on the basis of hypercalcaemia and hilar lymphadenopathy following immunotherapy. Hypercalcaemia was effectively treated with intravenous fluids and medical therapy including a short course of subcutaneous calcitonin, a total of 120 mg of denosumab and oral prednisolone.

Conclusion: DISRs are a rare complication of immunotherapy and may mimic metastases. A temporal relationship between commencement of therapy and progression on clinical imaging is important in making an accurate diagnosis.Calcitriol-mediated hypercalcaemia secondary to DISRs is an important differential diagnosis to hypercalcaemia of malignancy and should be considered in patients who have undergone immunotherapy.Prednisolone should be considered as the next line of treatment after fluid therapy in patients with calcitriol-mediated hypercalcaemia. Prednisolone and denosumab both reach maximum clinical efficacy between 7 and 10 days. Therefore, treatment administration should be spaced out by at least five days to avoid iatrogenic hypocalcaemia.

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Hypercalcemia with methotrexate pneumonitis: a rare phenomenon

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Methotrexate is commonly prescribed for autoimmune conditions but can rarely cause serious adverse effects [1]. Methotrexate toxicity is a rare cause of hypercalcaemia, particularly in patients with impaired renal function.

We present a case of severe hypercalcaemia secondary to methotrexate-induced granulomatous pneumonitis, a rare but significant adverse event. A 67-year-old man with rheumatoid arthritis and stage IV chronic kidney disease, on methotrexate therapy, presented with respiratory symptoms, cyclical fevers, and mood changes including mania. Investigations revealed severe PTH-independent hypercalcaemia (adjusted calcium 3.47 mmol/L), suppressed parathyroid hormone, and markedly elevated 1,25-dihydroxyvitamin D. Chest imaging showed bilateral pulmonary infiltrates. Extensive evaluation excluded malignancy, infection, and vasculitis. The diagnosis of methotrexate-induced granulomatous pneumonitis was made based on the modified Searles and McKendry criteria, including clinical, radiologic, and biochemical features.

Hypercalcaemia did not respond to initial treatment with intravenous rehydration, pamidronate, and calcitonin. Given the diagnostic uncertainty and the patient's psychiatric comorbidities, corticosteroid use was initially deferred. Ultimately, a cautious trial of oral prednisolone 25 mg daily was initiated in conjunction with methotrexate cessation, resulting in rapid and sustained resolution of both hypercalcaemia and pneumonitis. The patient was transitioned to leflunomide for his rheumatoid arthritis and later recommenced on lithium with psychiatric support.

This case highlights the diagnostic complexity of unexplained hypercalcaemia in patients on methotrexate, particularly in the setting of chronic kidney disease. While rare, methotrexate-induced granulomatous pneumonitis should be considered in patients presenting with hypercalcemia, pulmonary infiltrates, and elevated 1,25-dihydroxyvitamin D [2]. Literature on this phenomenon remains limited, though similar clinical features and outcomes have been reported [3].

Clinicians should maintain a high index of suspicion for this under-recognised adverse drug reaction. Prompt recognition and treatment with corticosteroids – such as prednisolone – and methotrexate cessation are essential for recovery.

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Effective Use of Pasireotide in Non-Insulinoma Pancreatogenous Hypoglycaemia Syndrome

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A 25-year-old woman was referred for investigation of symptomatic hypoglycaemia. She described episodes of tremor, confusion, and dizziness, occasionally progressing to seizures, which resolved with oral carbohydrates.

A mixed meal test was non-diagnostic, but a supervised 72-hour fast confirmed hyperinsulinaemic hypoglycaemia (table 1). Endoscopic ultrasound and CT abdomen/pelvis were unremarkable. Ga-68 GLP-1 receptor PET/CT demonstrated diffuse uptake throughout the pancreas without discrete mass, consistent with nesidioblastosis (figure 1). Genetic testing did not reveal a monogenic cause.

Medical therapy with diazoxide was ineffective. A calcium channel blocker was ceased due to postural hypotension and lack of efficacy. Octreotide produced transient benefit only. Surgical resection was not pursued due to high operative risk and uncertain benefit.

In 2024, Pasireotide—a second-generation somatostatin analogue—was commenced, resulting in complete resolution of hypoglycaemia and restoration of quality of life. Symptom recurrence during a treatment break supported its clinical efficacy (figure 2).

Discussion:

Non-insulinoma pancreatogenous hypoglycaemia syndrome (NIPHS) is a rare cause of hyperinsulinaemic hypoglycaemia in adults and can be congenital, idiopathic or occur post gastric bypass. Surgical resection may be ineffective and carries substantial risk. Dietary interventions and medical therapies such as diazoxide, calcium channel blockers, and glucocorticoids are variably effective and frequently limited by adverse effects.

Somatostatin exerts its effects via five receptor subtypes. SSTR2 and SSTR5 are particularly relevant to glucose homeostasis: both inhibit insulin secretion from pancreatic beta cells, while SSTR2 also suppresses glucagon activity. First-generation analogues (e.g. Octreotide) predominantly bind SSTR2, reducing insulin but potentially worsening hypoglycaemia via glucagon suppression.

Pasireotide has markedly higher affinity for SSTR5 and relatively lower affinity for SSTR2, thereby more selectively inhibiting insulin secretion. Although hyperglycaemia is a common side effect, this pharmacologic profile offers a therapeutic advantage in NIPHS. Our case illustrates successful use of Pasireotide in refractory NIPHS, supporting its role in select cases.

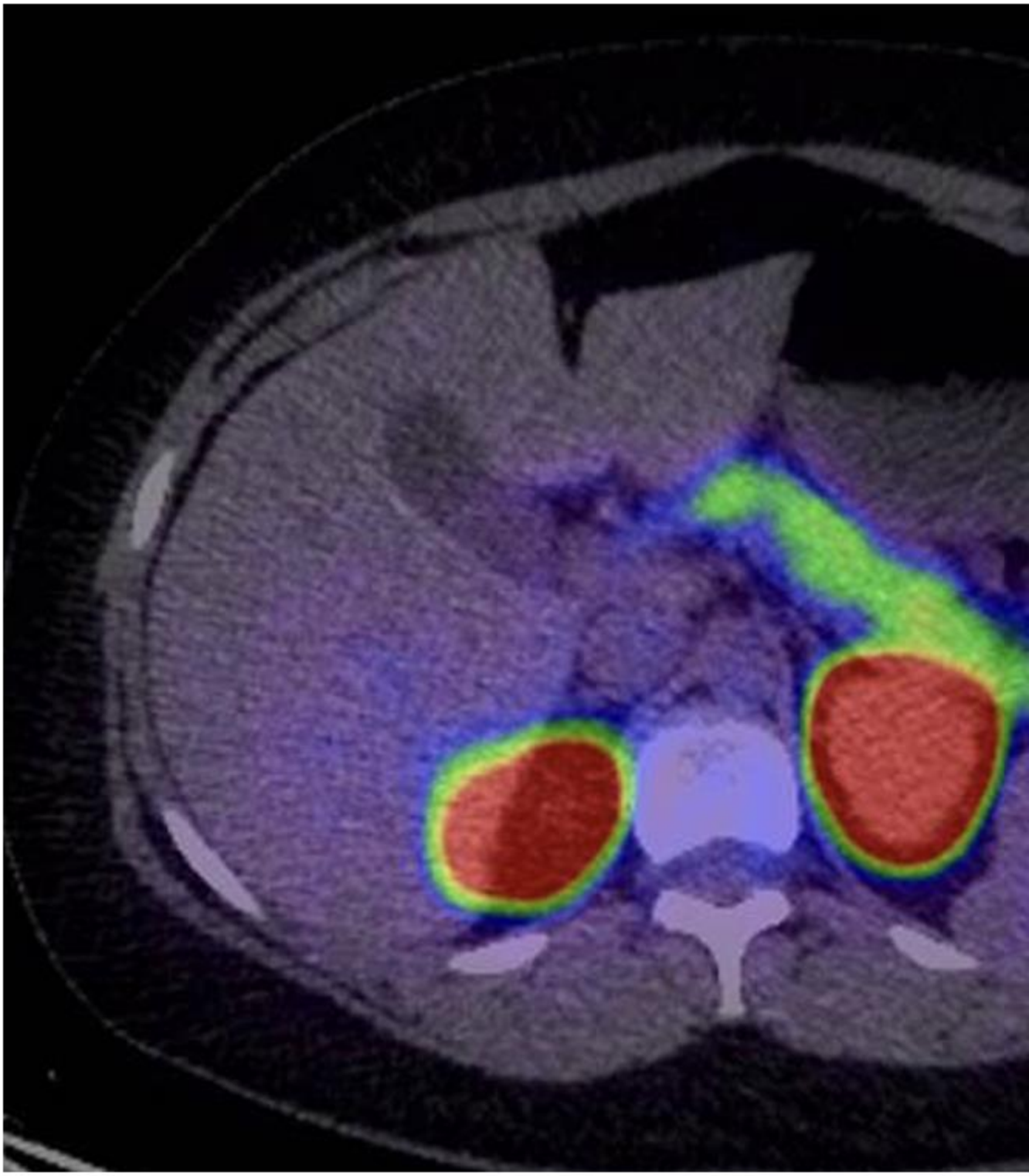

Figure 1: Diffuse 68-Ga-exendin-4 uptake throughout the panc

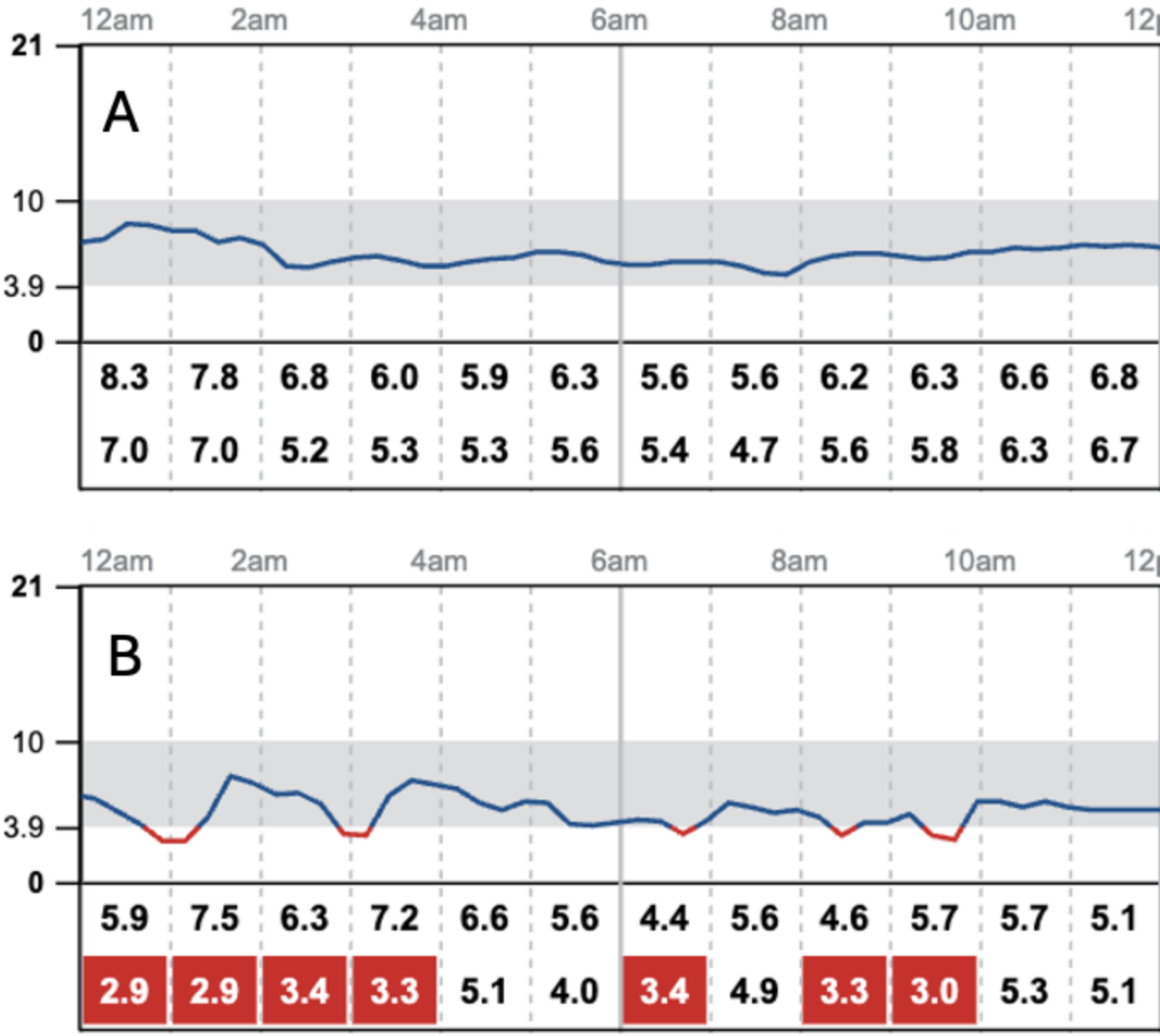

Figure 2: 24-hour CGM data
A: CGM data captured whilst on Pasireotide; B: CGM data wh

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Osilodrostat in ectopic ACTH syndrome: a case series using a block and replace strategy and literature review

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Case 1: PF, a 78-year-old female was admitted with treatment-resistant hypertension on a background of metastatic lung neuroendocrine tumour (NET). Ectopic ACTH syndrome (EAS) was diagnosed in the setting of raised late-night salivary cortisol (LNSC) 16×ULN, 24-hour urinary free cortisol (24hrUFC) 4.2×ULN, ACTH 4×ULN(**Table 1**) and rapid onset of complications of hypercortisolism(**Table 2)**. PF was commenced on osilodrostat block and replace strategy with 10mg BD and dexamethasone 0.75mg daily(**Table 2**). 24hrUFC normalised after 6 days of treatment(**Figure 1A**). After 52 days of osilodrostat, an expected increase in precursors (11-deoxycorticosterone and 11-deoxycortisol) without hyperandrogenism was observed(**Figure 2**).

Case 2: MC, a 58-year-old female was admitted for epigastric pain on a background of recently diagnosed metastatic pancreatic/duodenal neuroendocrine carcinoma. Due to refractory hypokalaemia, EAS was suspected and confirmed on biochemistry including 24hrUFC 139×ULN(**Table 1**). Osilodrostat block and replace strategy with 10mg bd and dexamethasone 1mg daily was commenced(**Table 2**) and 24hrUFC normalised after 21 days(**Figure 1B**).

Discussion: We described two cases of EAS successfully treated with osilodrostat block and replace strategy without major adverse effects.

EAS is associated with rapid onset of life-threatening complications from severe hypercortisolism. Definitive management is NET resection, however, NETs are often metastatic or occult/unresectable(1). Steroidogenesis inhibitors, rather than bilateral adrenalectomy, are frequently used in this setting, although some cases are refractory or intolerant of combination therapy of ketoconazole and metyrapone(1). Osilodrostat, a novel, potent oral reversible steroidogenesis inhibitor of 11β-hydroxylase and aldosterone synthase, is effective in treating Cushing's disease(2, 3), but has limited data in EAS(4, 5) which may require higher doses and faster dose titrations. Dormoy and colleagues demonstrated that in 33 patients with EAS, osilodrostat significantly reduced 24hrUFC and improved clinical features including cases refractory to other steroidogenesis inhibitors, however 24% developed adrenal insufficiency(6). An algorithm to treat EAS with osilodrostat was proposed(**Figure 3**)(6).

	Initial biochemistry		
	Case 1 - PF	Case 2 - MC	Reference ranges
Sodium	141	144	135-145
Potassium	3.2	2.3	3.5-5.2
Bicarbonate	34	30	22-32
Urea	10.5	5	3.0-8.0
Creatinine	50	47	45-90
eGFR	89	>90	>60
Morning cortisol (nmol/L)	1200, 800	2500	150-700
ACTH (pmol/L)	40, 36.2	35.1	2-10
LNSC (nmol/L)	93.0, 59.3, 45.2 (8-16x)	-	<5.7
24h UFC LCMS (nmol/24h)	711 (4.2x)	23580 (139x)	<170
1mg dexamethasone suppression test cortisol (nmol/L)	-	2400	< 50
8mg high dose dexamethasone suppression test cortisol (nmol/L)	-	2400	
Aldosterone (pmol/L)	76	142	<650
Renin (mU/L)	3	11.6	3-40
TSH (mU/L)	<0.01	0.27	0.40-4.00
fT4 (pmol/L)	11	6	9-19
fT3 (pmol/L)	2.9	2	3.0-5.5
Venous glucose (mmol/L)	24.2	11.5	3.0-5.4
HbA1c (%)	8.3	5.3	<6.0

Table 1. Initial biochemistry for case 1 (PF) and case 2 (MC). Red values indicate values outside of reference range.

	Case 1 - PF	Case 2 - MC
Age	78 yrs	58 yrs
Oncological diagnosis	Metastatic lung NET	Metastatic pancreatic/duodenal NEC
24hr UFC at diagnosis of EAS	711 nmol/24hr (4.2x ULN)	23,580 nmol/24hr (139x ULN)
Clinical complications of hypercortisolism	Refractive hypertension, myopathy, significant hyperglycaemia, fluid overload, hypokalaemia, labile mood, urosepsis	Severe refractive hypokalaemia, peripheral oedema, hyperglycaemia, behavioural disturbances, pericardial effusion
Initial therapy for EAS (block and replace)	Osilodrostat 10mg BD Dexamethasone 0.75mg OD	Osilodrostat 10mg BD Dexamethasone 1mg OD
Oncology treatment for NET	Octreotide 30mg IM monthly (since 2017) Everolimus (new)	Carboplatin + etoposide (new) Palliative radiotherapy (new)
Post Osilodrostat initiation		
Time to normalise 24hr UFC	6 days	21 days
Clinical improvement	Yes	Yes
Complications from osilodrostat	Possible transient mineralocorticoid deficiency (aldosterone 75, renin 1800)	Nil
Current therapy for EAS	Osilodrostat 5mg BD Dexamethasone 0.75mg OD	Osilodrostat 5mg BD Dexamethasone 0.5mg OD
Recent 24hr UFC	<10 nmol/24hr (56 days of osilodrostat)	10 nmol/24hr (52 days of osilodrostat)

Table 2. Clinical summary of the two cases.

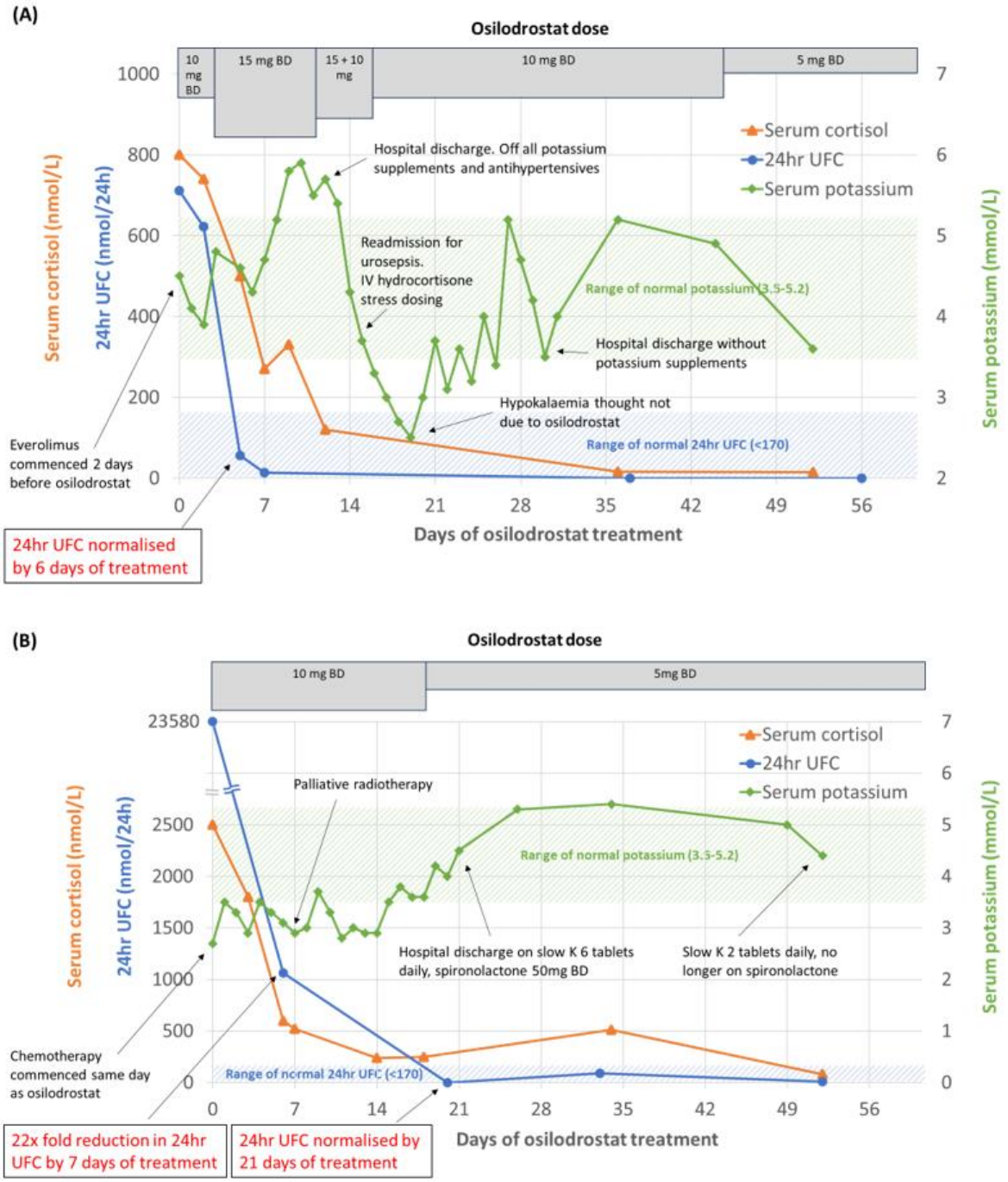

Figure 1. Trends of serum cortisol, 24hr-UFC and serum potassium after commencing osilodrostat for patient 1 PF (**A**) and patient 2 MC (**B**). Dose of osilodrostat shown on the top of each graph. 24hrUFC normalised by 6 days of osilodrostat treatment for PF and 21 days of treatment for MC.

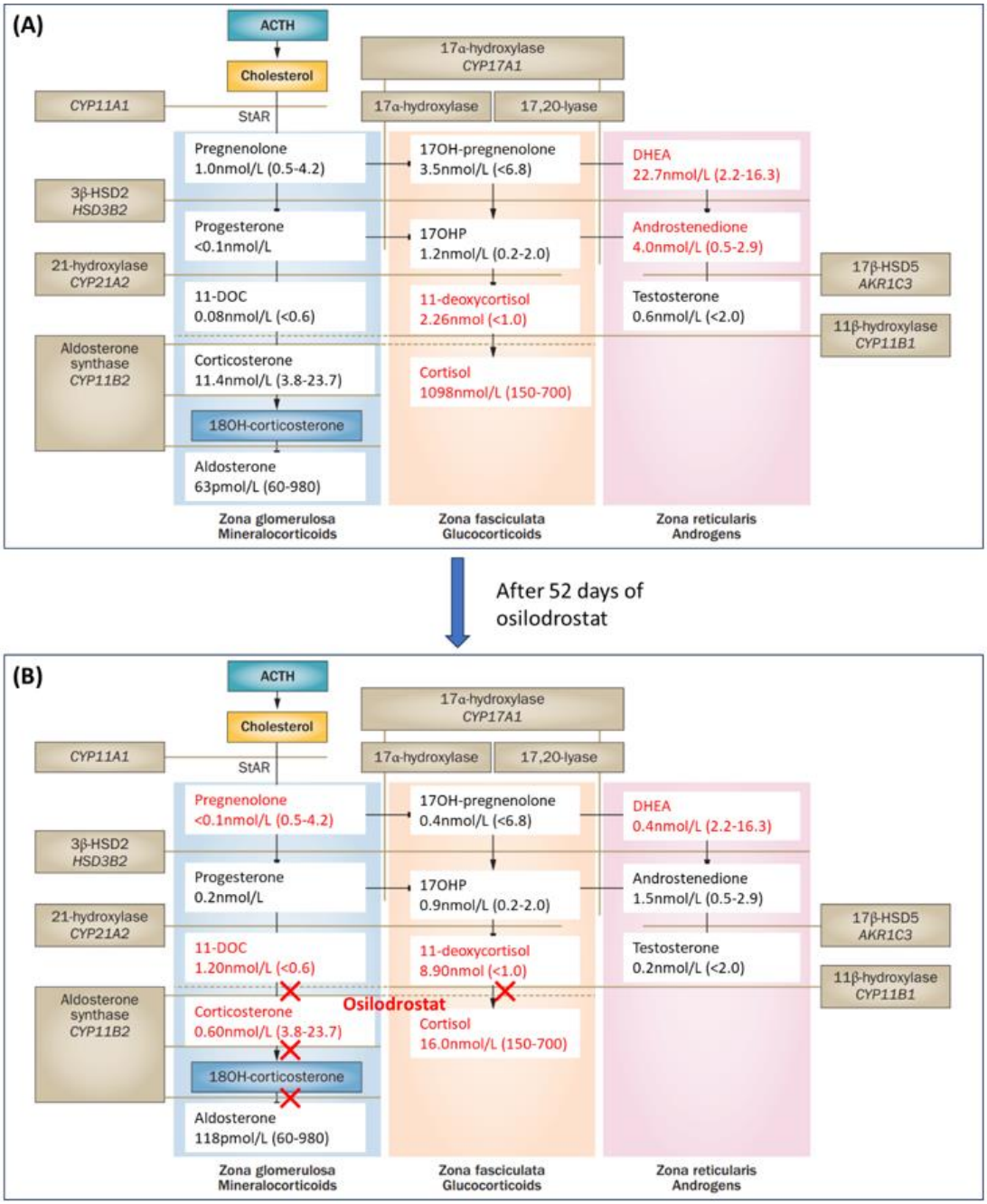

Figure 2. Serum LCMS 18-analyte steroid panel results for PF before osilodrostat was commenced (**A**) and after 52 days of osilodrostat (**B**) overlaid on the adrenal steroidogenic pathway. After 52 days of osilodrostat, the precursors 11-deoxycorticosterone (DOC) and 11-deoxycortisol expectedly increased. Hyperandrogenism, which is a known side effect of osilodrostat, was not observed. Enzymatic inhibitory action of osilodrostat shown in **B** with red crosses**.** Red values indicate values outside of reference range. Adapted from Han et al., Nat. Rev. Endocrinol. 2014.

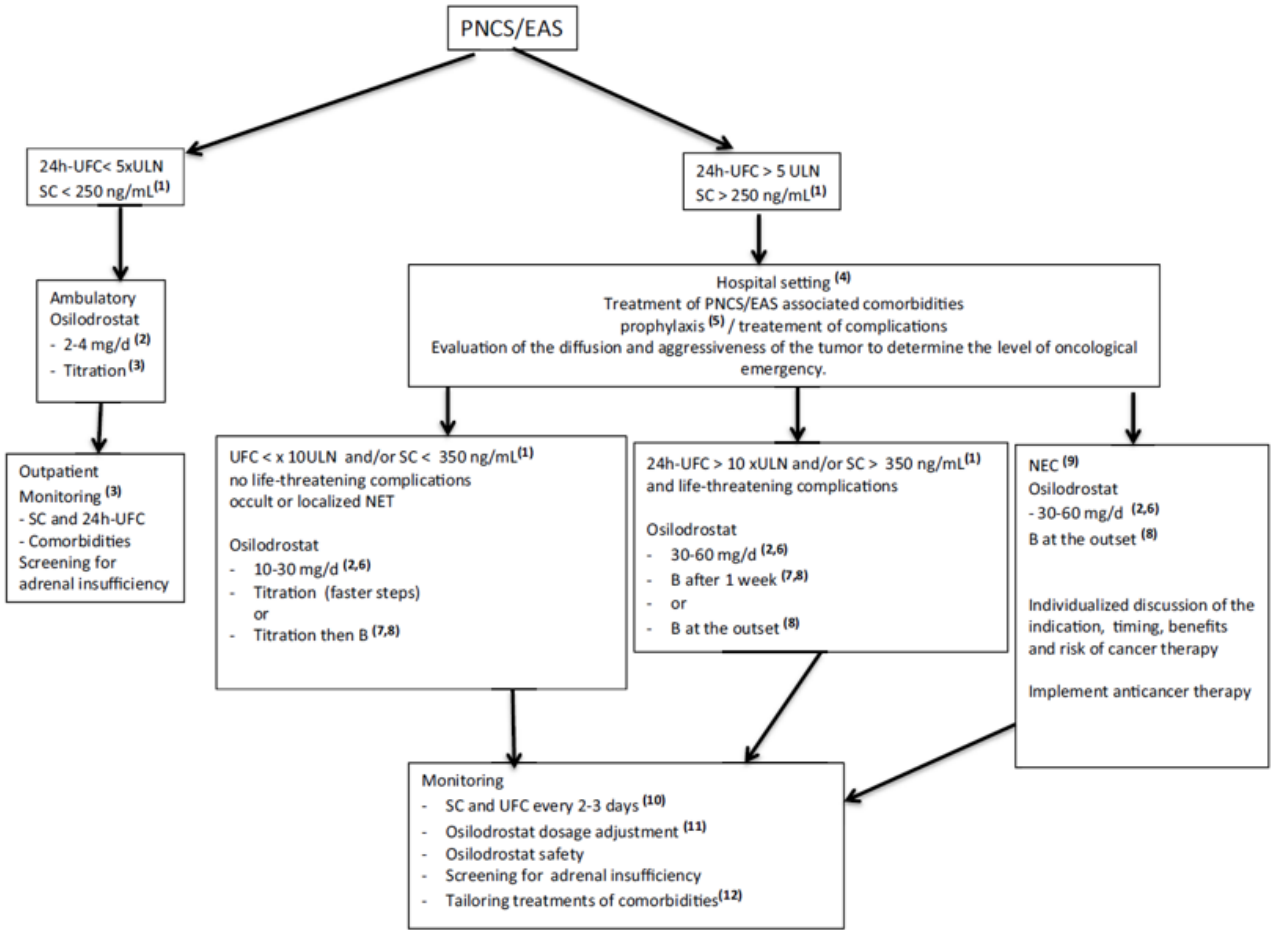

Figure 3. Proposed algorithm for the practical use of osilodrostat in patients with EAS based on scenarios depending on the intensity of hypercortisolism, associated complications and oncological status. To convert serum cortisol ng/mL to nmol/L x 2.759 (1ng/mL = 2.759nmol/L). For block and replace, recommended glucocorticoid replacement is hydrocortisone 20 to 30mg/day or prednisolone 4 to 7mg/day or dexamethasone 0.5mg/day. Adapted from Dormoy et al (6). B: block and replace strategy; PNCS: paraneoplastic Cushing's syndrome; SC: serum cortisol.

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Thyrotoxic periodic paralysis – an uncommon presentation of Graves' Disease

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Thyrotoxic periodic paralysis (TPP) is a rare, potentially life-threatening complication of hyperthyroidism characterized by recurrent muscle weakness and hypokalaemia. We report a case of a 33-year-old male presenting to the emergency department with sudden generalized weakness following prolonged sitting, preceded by nonbilious vomiting. A similar self-limiting episode occurred one month prior. The patient, a fruit picker with no significant medical history, exhibited blood pressure of 143/77 mmHg, heart rate of 69 bpm, and respiratory rate of 26 breaths/min. Neurological examination revealed bilateral lower limb power of 2/5, absent deep tendon reflexes, and upper limb power of 3/5. No overt hyperthyroid signs were noted. Biochemistry showed severe hypokalaemia (potassium 1.7 mmol/L) and overt hyperthyroidism (TSH <0.01 mU/L, free T4 27.73 pmol/L). ECG displayed prolonged PR interval and U waves, consistent with hypokalaemia. TSH receptor antibodies and a thyroid uptake scan confirmed Graves' disease. Intravenous potassium chloride (60 mmol) normalized serum potassium within 6 hours, with clinical improvement. The patient was started on carbimazole (10 mg TDS) and propranolol (10 mg BD) and monitored in the ICU. Discharged after three days, he remains asymptomatic with improving thyroid function on a weaning dose of carbimazole. TPP, more common in males and East Asian populations, results from thyroid hormone-induced sodium-potassium ATPase hyperactivity, driving potassium into cells. Treatment involves cautious potassium replacement, beta-blockers, and definitive hyperthyroidism management. This case underscores the importance of considering TPP in young males with sudden weakness and hypokalaemia, emphasizing multidisciplinary management to prevent complications like arrhythmias. Awareness of TPP is critical, particularly in non-Asian populations where it may be underdiagnosed.

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Plasmapheresis as a treatment for type 2 amiodarone-induced thyrotoxicosis in a cardiac transplant recipient – case report.

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Thyrotoxicosis is a challenging endocrine complication associated with amiodarone treatment in cardiac patients. We present a case of a 51-year-old man with type 2 amiodarone-induced thyrotoxicosis (AIT) occurring five months after cardiac transplantation. His medical background was significant for hypertrophic cardiomyopathy requiring left ventricular assist device prior to transplant and paroxysmal atrial fibrillation requiring amiodarone for greater than 12 months.

He presented to hospital acutely with deterioration in cardiac graft function. On examination, he was tachycardic (heart rate ~110 bpm) and hyperthermic. Laboratory evaluation on admission demonstrated thyrotoxicosis with fully suppressed TSH (< 0.02 mIU/L) and elevated FT4 (46.2 pmol/L) and FT3 (6.1 pmol/L). TRAB was not elevated. Thyroid ultrasound demonstrated diffuse heterogeneous echotexture with reduced vascularity, suggesting destructive type 2 amiodarone-induced thyrotoxicosis. Treatment with anti-thyroid medication and glucocorticoids was commenced empirically to cover both type 1 and type 2 AIT. Concurrently, he was admitted to hospital and treated with plasmapheresis for presumed antibody-mediated cardiac graft rejection.

Within days, there was marked biochemical resolution of thyrotoxicosis as well as improvement in cardiac ejection fraction from 15% to 50%. However, thyrotoxicosis rapidly recurred after plasmapheresis was ceased requiring re-initiation of high dose thionamide and glucocorticoid treatment with a slow wean over the ensuing 3 months. He remains euthyroid at follow up.

Our case highlights plasmapheresis as a highly effective therapy to rapidly remove circulating free thyroxine in emergent cases of AIT, however the effect is short term and transient.

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Type 1B pseudohypoparathyroidism presenting with bilateral avascular necrosis of the femoral heads

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Pseudohypoparathyroidism (PHP) is a group of endocrine disorders characterised by resistance to parathyroid hormone (PTH), resulting in hypocalcaemia and hypophosphatemia (1-3). Subtypes of pseudohypoparathyroidism include 1a and 1b (1-4). Clinical features may include early growth plate closure, ectopic ossification, brachydactyly, early obesity, respiratory disorders, and short stature, with variable resistance to other hormones (FSH, TSH, LH, and GHRH) (1-4). Type 1a is associated with Albright's hereditary osteodystrophy (AHO) (1,2). Type 1b, the rarer form, is characterised by renal resistance to PTH (1,2). This case review examines the diagnosis and management of type 1b PHP, highlighting key similarities and differences between the PHP subtypes.

Mrs X is a 55-year-old female who presented with bilateral hip pain and was diagnosed with bilateral femoral head avascular necrosis. Routine biochemistry revealed a calcium of 2.16 mmol/L, a phosphate of 1.0 mmol/L, a vitamin D of 70nmol/L, and an increased PTH of 120 pmol/L. Past medical history included severe asthma, hypertension, hypercholesterolemia, hypothyroidism, Type 2 Diabetes mellitus, sleeve gastrectomy, dental decay, recurrent sinusitis, and renal impairment (atrophic left kidney). CTx, ALP, and P1NP were

increased (1678 ng/L, 194 U/L, and 235 U/L, respectively) with mild renal impairment (Cr 98). There was no brachydactyly, and a bone scan showed widespread increased uptake. A diagnosis of probable PHP was made, and genetics confirmed type 1b PHP (methylation at the GNAS locus). She was commenced on calcitriol with the goal of maintaining PTH near the upper limit of normal, with ongoing input from orthopaedics and genetic services.

This case illustrates a relatively rare endocrine bone disorder, which carries a significant burden for patients and can be challenging to diagnose. It highlights the differences between type 1a and b pseudohypoparathyroidism and emphasises the importance of a multidisciplinary approach to care.

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Brown tumours secondary to tertiary hyperparathyroidism mimicking lytic bone metastases in the evaluation of back pain

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Brown tumours are rare, non-neoplastic, osteolytic bone lesions that arise in the setting of prolonged hyperparathyroidism. The lesions represent a manifestation of longstanding abnormal bone metabolism driven by persistently high parathyroid hormone (PTH) levels, often requiring both medical and surgical management. Brown tumours can be solitary or multiple, found in any part of the skeleton and the appearance can mimic skeletal metastasis. We present the rare case of multifocal brown tumours secondary to tertiary hyperparathyroidism and discuss relevant diagnostic and therapeutic considerations.

A 69-year-old female patient with end stage kidney disease secondary to focal sclerosing glomerulonephritis, requiring regular hemodialysis, reported symptoms of lower back and right hip pain. She had postmenopausal osteoporosis and tertiary hyperparathyroidism which required a partial parathyroidectomy 10 years prior. An initial CT scan of the spine revealed widespread skeletal lesions, which were evaluated in favor of metastasis and she was referred to an oncologist. A subsequent whole body PET scan showed bony lytic lesions throughout the spine, pelvis, all ribs, scapulae, skull, femur, distal humeri and distal left ulna. With no primary neoplastic focus, the PET scan findings were highly suggestive of brown tumors secondary to tertiary hyperparathyroidism. This was confirmed with a left sacral bone biopsy. The results of her laboratory tests showed calcium 2.27mmol/L (ref: 2.10-2.60), phosphate 1.27 mmol/L (ref: 0.75-1.50) and parathyroid hormone (PTH) 209.7 (ref: 1.6-7.2). She was reviewed by her endocrinologist and commenced on more aggressive medical treatment for tertiary hyperparathyroidism with increased cinacalcet dosage and commencing bisphosphonates to prevent bone resorption. She was urgently referred to an endocrine surgeon for a complete parathyroidectomy.

We present an unusual case of multifocal brown tumours secondary to tertiary hyperparathyroidism. This case was initially suspected as widespread metastases and highlights the importance of a comprehensive diagnostic approach, particularly in patients with chronic kidney disease.

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Case report: The role of plasma metanephrine in adrenal vein sampling for assessing primary hyperaldosteronism with cortisol co-secretion

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67-year-old man presented with long-standing hypertension and osteoporosis with recurrent vertebral fractures.

Initial investigation revealed an elevated aldosterone renin ratio of 97 (aldosterone 680pmol/L, renin 7mU/L) with spontaneous hypokalaemia 3.3mmol/L. Dedicated CT adrenal found 19x19x13mm right adrenal adenoma with Hounsfield unit 1.0. Further biochemical assessment showed normal plasma metanephrines, and a non-suppressed 1mg dexamethasone suppression test (basal cortisol 602nmol/L, ACTH 6.6pmol/L and post cortisol 69nmol/L). 24hour urine free cortisol was normal at 171nmol/24hr, and serum DHEAS low at 1.0umol/L. A 2mg low dose dexamethasone suppression test found basal cortisol 581nmol/L and post cortisol 66nmol/L. Seated saline suppression test found baseline potassium 3.7mmol/L, cortisol 312 nmol/L and aldosterone 578pmol/L with 4-hour results showing potassium 3.1mmol/L, cortisol 707nmol/L and aldosterone 779pmol/L. He has been referred for adrenal vein sampling (AVS). Given the possibility that the adrenal adenoma may be coproducing aldosterone and cortisol, the use of plasma metanephrine to determine cannulation and lateralisation is planned.

It is becoming increasingly recognised that adrenal aldosterone-producing adenomas can co-secrete cortisol, with prevalence of 5-26% (1-4). In this group there are higher rates of cardiovascular complications, dysglycaemia and osteoporosis when compared to aldosterone-producing adenomas (1,5). The presence of hormonal co-secretion raises challenges with standard AVS interpretation, which relies on cortisol results for assessment of cannulation and lateralisation (6,7). Use of plasma metanephrine has been proposed as an alternative parameter to cortisol, and has been shown to be more reliable in cases of cortisol and aldosterone co-secretion (8-10). Adrenalectomy is recommended in cases where lateralisation is confirmed on AVS, however in patients with co-secretion of aldosterone and cortisol there are increased postoperative rates of glucocorticoid deficiency, which is typically transient (3).

We report on a case of a man with hyperaldosteronism with possible mild autonomous cortisol secretion (MACS), and discuss the diagnostic challenges.

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A Clinical Approach to *MEN1* Variants of Uncertain Significance: Application of In Silico Tools to Upgrade Variants

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Aims

Multiple Endocrine Neoplasia Type 1 (MEN1) is an autosomal dominant hereditary tumour syndrome characterised by high penetrance and phenotypic heterogeneity (1). Variants of uncertain significance (VUS) in the *MEN1* gene, encoding menin, present a significant challenge for clinical diagnosis, risk stratification, and genetic counselling. This study aimed to assess the potential utility of advanced

in silico prediction tools, AlphaMissense and REVEL, in supporting the reclassification of *MEN1* VUS in individuals with a clinical MEN1 phenotype.

Methods

A retrospective review was conducted across three Australian tertiary centres, identifying six individuals with clinical features of MEN1 and *MEN1* VUS. Detailed clinical, familial, and genetic data were analysed. Variant pathogenicity was reassessed using the ACMG/AMP framework (2), incorporating in silico predictions from AlphaMissense (3) and REVEL scores (4). Structural implications were evaluated through AlphaFold-based protein modelling and visualised with PyMOL to assess variant localisation within conserved and functionally critical menin domains (5).

Results

The cohort of six individuals comprised four missense, one frameshift, and one in-frame deletion variant. All missense variants demonstrated strong pathogenic predictions via AlphaMissense (score >0.99), supported by high REVEL scores (>0.89) and localisation to structurally constrained or functionally essential regions of the menin protein. Structural modelling indicated disruptions affecting domains integral to menin's tumour suppressor activity.

Conclusion

This study highlights the clinical applicability of computational predictive tools such as AlphaMissense and REVEL in the interpretation of *MEN1* VUS. When integrated with protein structural modelling and clinical phenotyping, these tools offer a practical and scalable strategy for variant reclassification. This has meaningful clinical implications, including more precise risk assessment, tailored surveillance protocols, informed reproductive decision-making, and appropriate cascade genetic testing for affected families.

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Lessons from a case series of diabetic ketoacidosis in dialysis patients

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Diabetic ketoacidosis (DKA) is a life-threatening complication of diabetes mellitus, and while it is relatively uncommon in patients with end-stage renal disease (ESRD), its diagnosis and management in this population poses distinct challenges. (1) This case series aims to highlight the atypical presentation, and describe the altered pathophysiology, and complications from DKA treatment in individuals with diabetes undergoing dialysis.

The cases are summarised in the table below. The hospital uses a fixed rate insulin infusion (0.1 units/kg/hr) DKA protocol, and all patients had some modification during their treatment (table 1). We noted that complications such as iatrogenic hypoglycaemia appeared higher in our case series participants compared to the general population treated with the same dose fixed rate insulin infusion protocol. (2)

The clinical features and biochemical presentation differ in our patient cohort due to altered pathophysiology. The key differences include (i) reduced and variable baseline urine output and absence of polyuria limiting the dehydration at presentation, (ii) potential correction of acidosis (but not insulin deficiency) at dialysis sessions and (iii) glucose-based dialysate contributing to hyperglycaemia in patients on peritoneal dialysis and (iv) significantly decreased insulin clearance, which protects against development of DKA in first place but also can lead to protracted hypoglycaemia during treatment. (3,4)

Despite the altered pathophysiology in development of DKA in dialysis patients, there is a lack of larger studies and most DKA guidelines do not address or provide specific guidance in this regard. With the small case series and brief review, we highlight the challenges in managing these patients and provide suggestions for an individualised approach including considerations of reduced intravenous fluid administration, judicious potassium replacement and lower insulin infusion rates which may help clinicians in managing such patients.

Table 1 – Summary of patient cases

Case	Patient details	Methods of dialysis	Background	Symptoms
1	31-year-old female with type one diabetes diagnosed at 26-years-old admitted with moderate severity DKA.	Haemodialysis via arteriovenous fistula	Cannabinoid dependency. Diabetic nephropathy and retinopathy. Borderline personality disorder.	Nausea, vomit, abdominal pain
2	33-year-old male diagnosed with type one diabetes at 12-years-old admitted with severe DKA.	Continuous ambulatory peritoneal dialysis.	Diabetic nephropathy, retinopathy and neuropathy. Hypertension	Fever, nausea, vomit, dyspnoea, reduced consciousness
3	47-year-old female with type one diabetes diagnosed at 26-years-old admitted with moderate severity DKA.	Haemodialysis via arteriovenous fistula.	Diabetic nephropathy, diabetic foot ulcers. Hypertension. Atrial septal defect. Recurrent urinary tract infections.	Headache, malaise, nausea, vomit

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A "K"-ritical Situation: Unmasking Primary Hyperaldosteronism After Cardiac Arrest

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Background: Primary hyperaldosteronism (PHA) is a common cause of secondary hypertension, typically presenting with hypertension and hypokalaemia. Excess aldosterone causes direct cardiovascular toxicity through structural and functional cardiac changes, increasing arrhythmia risk [1]. However, sudden cardiac arrest as the initial presentation is exceptionally rare [2].

Case Presentation: A 71-year-old male with well-controlled hypertension, atrial fibrillation, and dyslipidaemia presented with sudden cardiac arrest due to ventricular fibrillation requiring extensive resuscitation. Post-resuscitation investigations revealed profound hypokalaemia (initial K 7.8 mmol/L, rapidly dropping to 1.9 mmol/L), necessitating aggressive potassium replacement (up to 550 mmol/24 hours). Cardiac catheterisation showed unobstructed coronaries. Renal workup demonstrated potassium wasting (TTKG 9), prompting PHA investigation despite reasonably controlled blood pressure. Biochemical testing revealed elevated aldosterone (720 pmol/L), suppressed renin (<2 mIU/L), and ARR >360. Saline suppression test was positive. CT imaging identified a 15mm left adrenal adenoma, with adrenal venous sampling confirming lateralised aldosterone production. The patient underwent successful left adrenalectomy.

Clinical Significance: This case demonstrates the critical importance of investigating secondary causes of hypokalaemia in life-threatening arrhythmias. While hypokalaemia is a recognised PHA complication, its severity and presentation with sudden cardiac arrest were unusual. The patient's underlying chronic hypokalaemia (historical outpatient K 3.0-3.2 mmol/L) likely predisposed to acute

decompensation. Post-adrenalectomy, complete normalisation of blood pressure occurred, allowing cessation of all antihypertensive medications.

Conclusion: PHA should be considered in patients with profound, refractory hypokalaemia presenting with life-threatening arrhythmias, even without severe hypertension. Early diagnosis and targeted surgical intervention can achieve complete resolution of biochemical abnormalities and hypertension [3], emphasising the importance of recognising this potentially curable cause of secondary hypertension.

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Opioid-induced hypopituitarism in a young woman: case report

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Opioids inhibit hypothalamic-pituitary function, commonly causing opioid-induced hypogonadotrophic hypogonadism and adrenal insufficiency(1,2). Chronic opioids suppress hypothalamic CRH and GnRH secretion via mu-opioid receptor inhibition(3,4).

We report a case of a 29-year-old woman with long-standing type 1 diabetes and autoimmune thyroiditis who has been on high dose opioids (up to 400-600mg/day tapentadol and 60mg/day oxycodone) for over four years for chronic abdominal pain.

Patient presented with hypotension unresponsive to fluid resuscitation in 2024. Initial investigations revealed adrenal insufficiency with low morning cortisol (20 nmol/L) and low-normal ACTH (2.1 pmol/L). Serum sodium (141 mmol/L) and potassium (3.9 mmol/L) were within normal limits. Short Synacthen test demonstrated robust adrenal response (cortisol: baseline 28 nmol/L, rising to 413 nmol/L at 30 minutes, 1378 nmol/L at 60 minutes). Pituitary MRI showed no evidence of a structural abnormality related to the pituitary, and imaging showed normal adrenals. Hydrocortisone 10mg twice-daily was commenced with resolution of hypotension.

One year later the patient represented with secondary amenorrhea. Her BMI was 27.5 kg/m², with no signs of undernutrition. Investigations showed hypogonadotropic hypogonadism (LH<1 IU/L, FSH 2 IU/L, oestradiol<89 pmol/L), alongside persistent cortisol deficiency (54 nmol/L) with a suppressed ACTH (1.2 pmol/L). Metyrapone testing confirmed inadequate ACTH response (3.1 pmol/L) with low 11-deoxycortisol (12 pmol/L) with adequate adrenal cortisol suppression (<28 nmol/L). Pituitary functional screening was otherwise unremarkable. Repeat pituitary MRI was normal. No cause of pituitary axis suppression was identified other than chronic opioid use. The patient was commenced on a combined oral contraceptive pill and referred to an outpatient chronic pain clinic.

This case demonstrates opioid-induced concurrent hypothalamic-pituitary-adrenal and gonadotropin axis suppression. Given increasing chronic opioid use, clinicians should screen for multi-axis pituitary dysfunction in patients on high-dose opioids, particularly young women, to ensure that appropriate and timely management of possible multiple suppressed hypothalamic-pituitary axes occurs.

Table 1. Investigation Results – Initial presentatio

Test	Patient's
Sodium (mmol/L)	14
Potassium (mmol/L)	3.
LH (IU/L)	4
FSH (IU/L)	6
Oestradiol (pmol/L)	15
8AM serum cortisol (nmol/L)	2(
ACTH (pmol/L)	2.
Short Synacthen Test	
Serum cortisol baseline (nmol/L)	2
Serum cortisol 30 mins (nmol/L)	41
Serum cortisol 60 mins (nmol/L)	13

Table 2. Investigation Results – Later presentatio

Test	Patient's
LH (IU/L)	<
FSH (IU/L)	2

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Non-functioning adrenocortical carcinoma presenting as acute spontaneous retroperitoneal haemorrhage

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This report has the objective of highlighting adrenal haemorrhage as a presenting feature of adrenocortical carcinoma (ACC) and stressing the importance of close follow-up and thorough initial investigation of adrenal nodules to ascertain their underlying aetiology and ultimately prevent delay to appropriate management.

Adrenocortical carcinomas (ACC) are a very rare entity with an incidence of approximately 0.5 to 2 cases per million per year (1). They are often difficult to diagnose clinically, attributing to non-specific signs and symptoms especially with non-functioning tumours, with histopathology required for confirmatory diagnosis. Atraumatic adrenal haemorrhage has been described in the literature as a rare presentation of ACC.

We describe a case of a gentleman in his 50s presenting with acute spontaneous unilateral adrenal haemorrhage on a background of a pre-existing known incidental adrenal nodule that was lost to follow-up. The patient underwent angio-embolisation and subsequent laparoscopic adrenalectomy, with histopathology demonstrating ACC.

Our case mirrors that of existing studies with high attrition rates and stresses the need for judicious follow-up of adrenal incidentalomas. All adrenal nodules require exclusion of hormonal excess and dedicated adrenal imaging, with provision of clear plans to primary health practitioners if investigations are not completed in the inpatient setting.

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STIMULA(N)ting Hypercalcaemia – an uncommon case of hypercalcaemia following orthopaedic surgery

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Bioabsorbable bone substitutes have been used in orthopaedic surgery for the last century, providing a low cost and readily available osteoconductive alternative to autografting. Calcium sulfate beads, such as Stimulan, offer the additional benefit of delivering local antibiotic therapy in deep bone infections.(1) This is especially important with increasing incidence of periprosthetic joint infections (PJI) and the global increase in infections caused by antibiotic-resistant bacteria.(2) With increasing use of Stimulan, a few cases are emerging of subsequent hypercalcaemia.(3-11) (Table 1)

We present a case of a 71-year-old Caucasian male who had a stage 1 revision procedure for an acute, delayed right knee PJI. He developed PTH-independent hypercalcaemia to 2.92 mmol/L on day 3 post-operatively, with associated acute kidney injury. He was otherwise asymptomatic. He had no known history of calcium, endocrine, kidney or malignant disorders. He was not on any medications that cause hypercalcaemia. Notably, his pre-operative calcium and kidney function had been in the normal range. Four boxes of Stimulan were used intra-operatively.

Initial bloods investigating the cause of hypercalcaemia are outlined in Table 2, excluding primary hyperparathyroidism, thyroid disease, myeloma and granulomatous disease as causes. He was treated with aggressive intravenous fluids with good response. Bisphosphonate therapy was avoided due to the likely transient nature of the cause. Intravenous fluids were weaned at day 13 (after failing initial wean on day 7). His hypercalcaemia resolved 2 weeks post-operatively.

This case illustrates the potential for transient PTH-independent hypercalcaemia following the use of Stimulan, with onset 3 days post-operatively and resolution 2 weeks post-operatively. This is the first report of hypercalcaemia following Stimulan in Australia, with only limited literature in the US, UK and Europe. Recognition of Stimulan as a potential cause will allow for appropriate timely intervention in severe cases and provide reassurance given the time-limiting natural history.

Table 1: Existing case reports and case series of hypercalcaemia following
sulfate beads in surgical management of PJIs

Study	Cases	Peak Ca(c)* (mmol/L)	Duration (days post-op)	Management
Carlson et al USA 2015[3]	1	3.62	8	IV fluids, calcit
Kallala et al UK 2015[4]	3/15	3.54	Unknown	IV fluids, zoled
Madaleno et al USA 2019[5]	1	4.34	9	IV fluids, calcit
Vora et al USA 2019[6]	1	3.92	13	IV fluids, calcit
Jung et al US 2020[7]	1	5.29	11	IV fluids, meth furosemide, pa
Kallala et al UK 2018[8]	41/755	2.69 – 3.72	10	IV fluids, bisph
Sandiford et al+ UK 2020[9]	0/29	N/A	N/A	N/A
Epstein et al USA 2022[10]	1	3.59	16	IV fluids, pami
Dimofte et al+ Europe 2024[11]	0/45	N/A	N/A	N/A

*Ca(c): serum corrected calcium. +Studies with screening for hypercalcae
sulfate beads with no cases identified

Table 2: Initial blood results investigating the cause of hypercalcaemia

Investigation	Result	Ref range
Ca(c) (mmol/L)	2.92	2.10 - 2.60
Creatinine (umol/L)	126	60 - 110
eGFR (mL/min/1.73m2)	49	> 60
PTH (pmol/L)	1.0	1.8 - 7.9
25-hydroxy vitamin D (nmol/L)	39	> 50
1,25-hydroxy vitamin D (pmol/L)	17	48 - 190
TSH (mIU/L)	1.46	0.27 - 4.20
Serum and urine EPG and IEPG	negative	
Serum free light chains	negative	

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Seeing double? Co-existing myasthenia gravis and gonadotroph macroadenoma in a patient presenting with diplopia

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Myasthenia gravis is an autoimmune neuromuscular disorder characterised by muscle weakness and fatiguability including ocular symptoms such as ptosis and diplopia. Conversely, pituitary macroadenomas are benign tumours that may present with visual deficits due to compression of the optic chiasm, most notably bitemporal hemianopia. While both conditions can independently cause visual

symptoms, their concurrent presentation is rare. We present the unique case of a patient with both myasthenia gravis and a gonadotroph macroadenoma, requiring separate simultaneous treatment modalities.

A 55-year-old male from a regional city presented with sudden onset diplopia. Past medical history included psoriatic arthritis (methotrexate). CT imaging showed a pituitary macroadenoma 14 x 20 x 20 mm with effacement of the optic chiasm, in adjunct to an incidental finding of a thymoma; 71 x 40 x 46 mm. Referral followed to a tertiary hospital for further work-up. Clinical examination revealed bilateral ptosis and fatiguable eye movements. Visual field testing confirmed bitemporal hemianopia. Laboratory tests showed **FSH 16.9 IU/L** (Ref: 1-12), LH 3.9 IU/L (Ref: 0.6-12.1), **prolactin 1970 mIU/**L (Ref: 73-410), TSH 2.79 mIU/L (Ref: 0.40-4.00) and **T4 8.3 pmol/L** (Ref: 9.0-19.0). Nerve conduction studies and positive acetylcholine receptor antibodies confirmed the concurrent diagnosis of myasthenia gravis. The patient underwent transsphenoidal resection of the macroadenoma. Histological examination confirmed a gonadotroph adenoma, positive for FSH, SF-1, GATA3 and ER on immunohistochemistry. Thyroxine replacement was initiated as well as prednisone for the treatment of myasthenia gravis. He was referred for consideration of a thymectomy.

This is one of few case reports describing a concurrent gonadotroph secreting macroadenoma and thymoma-associated seropositive myasthenia gravis. While thymomas are known to be associated with autoimmune disorders, a definitive association with pituitary adenomas remains undetermined. This case highlights the importance of collaborative multidisciplinary care and conducting a thorough diagnostic work-up for patients presenting with diplopia.

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Familial Chylomicronaemia Syndrome: A Rare Case of Recurrent Pancreatitis

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Familial Chylomicronemia Syndrome (FCS) is a rare autosomal recessive disorder caused by biallelic loss-of-function mutations in genes involved in chylomicron metabolism, most commonly lipoprotein lipase (LPL). Impaired intravascular lipolysis results in persistent fasting hypertriglyceridaemia, typically >10 mmol/L, and a lifelong risk of recurrent pancreatitis. Unlike multifactorial chylomicronemia, FCS is typically unresponsive to statins, fibrates, niacin, and PCSK9 inhibitors, which act via hepatic lipid pathways rather than chylomicron metabolism.

We present the case of a 60-year-old Indigenous woman with recurrent hypertriglyceridaemia-associated pancreatitis. Despite maximal tolerated medical therapy, including rosuvastatin/ezetimibe, fenofibrate, strict dietary fat restriction, and insulin, her triglycerides remained severely elevated (25.8–64 mmol/L). HDL levels were consistently low (0.5 mmol/L), and LDL levels could not be accurately measured due to lipaemic interference. Glycaemic control was suboptimal (peak HbA1c 13.5%) and likely exacerbated her metabolic dysregulation. A clinical diagnosis of FCS was made in 2023 following review in a specialist lipid clinic.

During a hospital admission in 2025 for severe pancreatitis (TG 49.9 mmol/L, lipase 288 U/L), the patient underwent inpatient plasmapheresis, with consideration of outpatient therapeutic plasma exchange for long-term management. PCSK9 inhibitors were not pursued due to mechanistic ineffectiveness in FCS.

This case highlights the therapeutic challenges of managing FCS. While insulin and plasmapheresis may offer temporary reductions in triglyceride levels, long-term control remains difficult. Novel therapies targeting APOC3, such as volanesorsen, olezarsen and plozasiran, have shown promise in reducing triglycerides and pancreatitis risk but remain largely inaccessible in Australia.

Strict dietary fat restriction remains the foundation of long-term management. Early recognition and referral to lipid clinics are essential to optimise care and facilitate access to emerging treatments in this high-risk population.

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Recurrent pericardial effusions in a young adult with congenital hyperinsulinism: A rare complication of diazoxide?

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The aim of this case report is to present a complex case of recurrent pericardial effusions and cardiac tamponade in a young man with diazoxide-responsive congenital hyperinsulinism (CHI), and to explore the rare but documented association between diazoxide and pericardial effusions.

We describe a 25-year-old Indigenous male from regional New South Wales with CHI diagnosed at birth, who presented with recurrent pericardial effusions requiring pericardiocentesis. He was transferred to a tertiary cardiothoracic unit for definitive management with partial pericardiectomy. His care was coordinated by a multidisciplinary team, including endocrinology, cardiothoracic surgery, clinical pharmacy and diabetes education. The patient had been taking diazoxide 300 mg twice daily since childhood, with no dose adjustment since his late teens. His family had opted not to pursue genetic testing, and he had been lost to follow-up following transition from paediatric to adult services. He experienced frequent hypoglycaemic seizures due to lack of treatment efficacy and/or poor adherence and had hypoglycaemia unawareness. From 2017 to 2025, he developed chronic pericardial effusions and ultimately life-threatening cardiac tamponade.

Diazoxide remains the cornerstone of therapy for diazoxide-responsive CHI but is associated with adverse effects including fluid retention, pulmonary oedema, and congestive heart failure [1,2]. Pericardial effusion is a rare complication, with only six cases reported in the literature, predominantly in paediatric populations [3–5]. In several reports, a temporal relationship between diazoxide use and effusion recurrence was observed [6].

Management included initiation of octreotide, itself complicated by liver dysfunction, addition of hydrochlorothiazide and compassionate continuous glucose monitoring. Functional imaging and genetic testing were pursued, with a view to possible subtotal pancreatectomy.

This case underscores a rare but important potential complication of diazoxide therapy and highlights potential management strategies, particularly in adults with long-standing CHI.

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When imaging fails, the vein prevails: Investigating postmenopausal hyperandrogenism with adrenal and ovarian vein sampling

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Aims

To evaluate the role of selective adrenal and ovarian vein sampling in postmenopausal women with significant hyperandrogenism where conventional imaging fails to localise the source of androgen excess.

Methods

We present two postmenopausal women with virilising symptoms and markedly elevated serum testosterone levels. Both underwent comprehensive biochemical assessment and cross-sectional imaging, which failed to identify a clear source. Adrenal and ovarian vein sampling (AVS/OVS) was subsequently performed to localise androgen production and guide management.

Results

Case 1 was a 67-year-old woman with progressive androgenic alopecia and hirsutism (Ferriman-Gallwey score 30), with testosterone levels rising to 7.8 nmol/L (Table 1). Pelvic imaging was unremarkable, and an 11 mm indeterminate adrenal nodule was identified. OVS demonstrated a significant testosterone gradient in the left ovarian vein (Table 2). She was referred for bilateral oophorectomy, which is pending.

Table 1. Baseline androgen profile and comparison over the followi

Date Pathology Provider	**07/10/2022 Monash Pathology**		**24/04/2023 Dorevitch Pathology**		**12/ Mo**
Hormone (units)	**Measured level**	**Reference Range**	**Measured level**	**Reference Range**	**Me lev**
Testosterone LCMS (nmol/l)	4.6	0.1-1.7	5.6	0.3-1.1	7.8
SHBG (nmol/l)	19	17-125	27	18-114	28
FAI	24.4	0.2-5.4			27
Calculated Free Testosterone (pmol/l)			118	4-20	
Androstenedione LCMS (nmol/l)	3.3	0.5-2.9			
DHEAS (mcmol/l)	0.9	0.3-3.6			
FSH (IU/l)	46.4	16.8-114*			
LH (IU/l)	34.0	11.0-58.0*			
Oestradiol (pmol/l)	90	<175*			
17-OH Progesterone LCMS (nmol/l)	1.3	0.6-2.0			
Cortisol after 1mg DST (nmol/l)	50	185-625			

*Reference ranges for post-menopausal women

[+] Greyed out if not measured or collected for that date

[$]Highlighted if result above the reference range

Table 2. Adrenal vein and ovarian vein sampling results (04/07/2024)

Type of vein sampling		Side	17OH-Progesterone LCMS (nmol/l)	Androstene-dione LCMS (nmol/l)	Cortisol (nmol/l)
		Reference range	0.6-2.0	0.5-2.9	185-625
AVS	Sample 1	Right	54.5	269.8	5039
		Left	47.4	194.8	4567
	Sample 2	Right	43.8	232.5	4886
		Left	38.9	181.8	4340
	Peripheral		1.2	4.7	234
OVS	Sample 1	Left	322.8	1091.2	
	Sample 2		154.8	477.2	
	Peripheral		1.3	5.3	

Case 2 was a 54-year-old woman with deepening of the voice and worsening hirsutism (Ferriman-Gallwey score 19), with persistently elevated serial serum testosterone, androstenedione, and free androgen index levels (Table 3). Imaging revealed a non-functioning adrenal adenoma but no ovarian abnormality. A urinary steroid profile (Table 4) was largely normal, with no evidence of congenital adrenal hyperplasia. Subsequent AVS/OVS results are outlined in Table 5, with biochemistry suggestive of a testosterone gradient consistent with an ovarian source. She was referred for bilateral oophorectomy, and histopathology confirmed bilateral ovarian stromal hyperthecosis.

Table 3. Selected hormone levels over time (Monash Pathology)

Date	17 OH Progesterone (nmol/L)	Androstenedione (nmol/L)	Cortisol (nmol/L)
Reference range	0.6-2.0	0.5-2.9	185-625
01/11/2023			
06/12/2023			412
07/02/2024		4.2	
18/03/2024	3.7	5.4	
20/05/2024	3.2	5.2	273
12/06/2024			
19/06/2024			
04/08/2024	4.7	4.6	377

*Reference ranges for post-menopausal women

+ Greyed out if not measured or collected for that date

$Highlighted if hormone was above the reference range

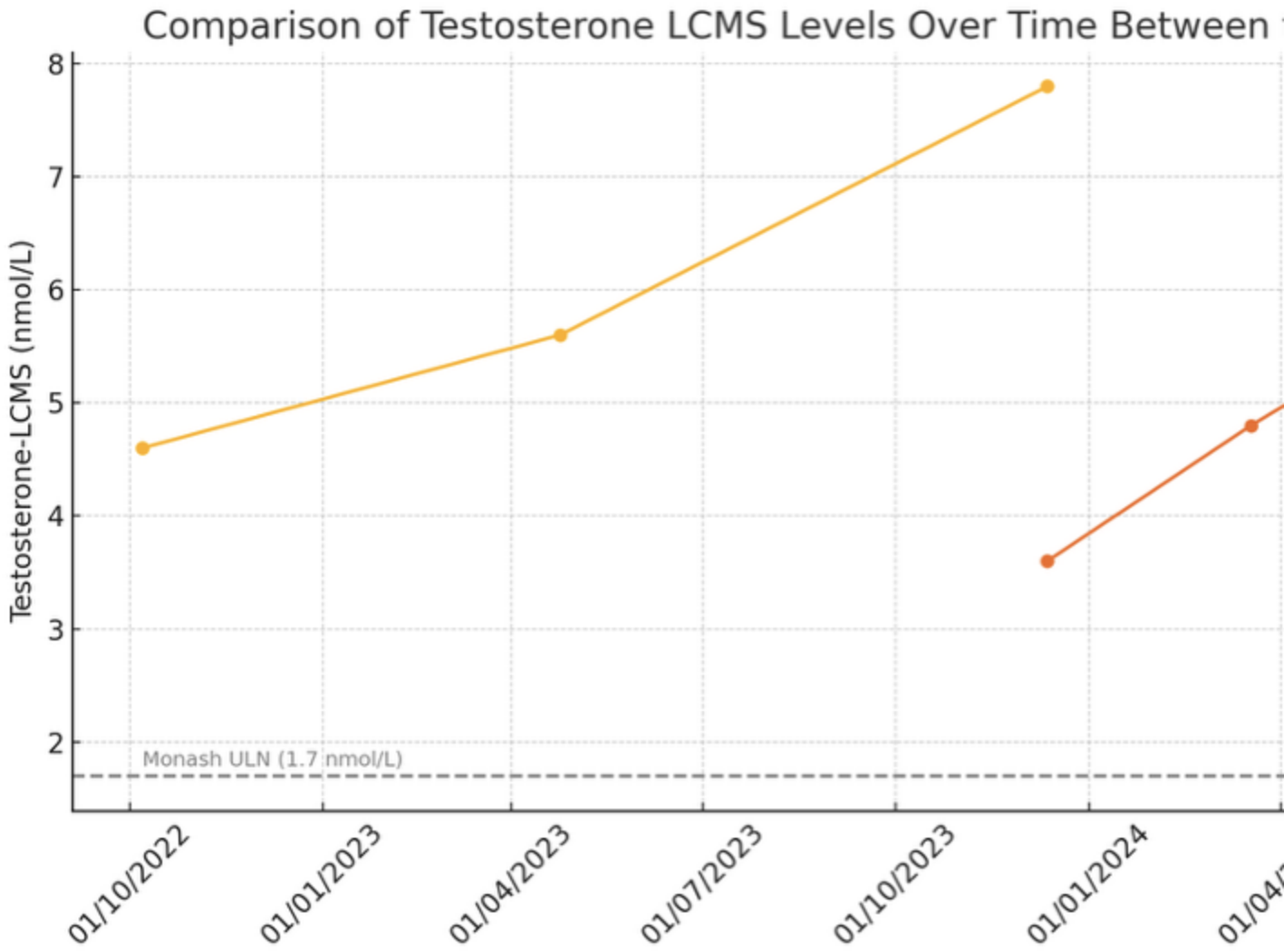
Table 4. Urinary steroid profile of Case 2 (Monash Pathology 19/06/2

Steroid	Concentration (µmol/L)	Concentration (µmol/24hrs)	Ref (µ
Androsterone	3.6	5.9	1.5 – 12
Etiocholanolone	2	3.3	1.5 – 12
5β-17α-OH Pregnanolone	0.5	0.8	< 1.0
Pregnanetriol	1.8	3	0.5 – 3.
TH-11 Deoxycortisol	0.3	0.4	< 0.5
Pregnanetriolone	<0.1	<0.2	< 0.5
TH Cortisone	8.1	13.3	2.5 – 12
TH Cortisol	4.7	7.7	0.7 – 6.
Allo TH Cortisol	2.2		

Table 5. Adrenal vein and ovarian vein sampling results (15/08/2024)

Type of vein sampling		Side	Cortisol (nmol/l)	DHEAS (micromol/)	Oestradiol LCMS (pmol/l)	Te (n
		Reference range	185-625	0.2-.5.1	10-80	0.1
AVS	Sample 1	Right	1412	1.7		3.5
		Left	1749	1.5		3.6
	Sample 2	Right	1282	1.9		3.8
		Left	1852	1.5		3.6
	Peripheral		154	1.2		4.3
OVS	Sample 1	Right			11528	73
	Sample 1	Left			3273	21
	Peripheral				150	4.1

Figure 1. Graphical representation of measured testosterone levels i compared with the upper limit of normal leading up to adrenal and o sampling



Conclusion

Both cases demonstrate the utility of adrenal and ovarian vein sampling in the diagnostic algorithm of investigating imaging-negative causes of hyperandrogenism in post-menopausal women (1). Both patients had biochemical profiles concerning for androgen-secreting pathology despite inconclusive imaging. Testosterone levels significantly above the upper limit for postmenopausal women are highly suggestive of an androgen-secreting tumour or ovarian hyperthecosis (2).Selective venous sampling provided diagnostic clarity and influenced clinical decision-making.

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Resist Jumping to Conclusion

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Central hyperthyroidism, elevation in T3 and T4 concentration with an unsuppressed TSH can be seen in TSH-secreting pituitary adenomas (TSH-oma), thyroid hormone resistance (RTH) and heterophile antibody interference. We present a case of 35-year-old male with central hyperthyroidism and large pituitary macroadenoma measuring 24.7 × 18.8 × 26.7 mm initially suggestive of TSH-oma. However, subtle clinical features including childhood hearing impairment and speech delay, along with biochemical testing with borderline alpha subunit level of 0.7 U/L (< 0.7 U/L), SHBG of 19 nmol/L (10-50 nmol/L) prompted further dynamic testing with TRH stimulation test. The TRH stimulation showed a six-fold increase TSH consistent with receptor resistance and confirmatory genetic testing was done which showed an autosomal dominant heterozygous missense mutation in the THRB gene (Val458Ala) and therefore avoided unnecessary pituitary surgery. Adults with THRβ resistance develop a unique metabolic profile due to heterogeneous tissue sensitivity to thyroid hormone. Tissues expressing predominantly WT THRα, such as bone, vascular smooth muscle, and skeletal muscle, are exposed to a relative state of thyrotoxicosis. Over time, this can increase the risk of developing osteoporosis, systolic hypertension, and sarcopenia. In contrast, tissues predominantly expressing mutant THRβ, particularly the liver, exhibit a hypothyroid state despite elevated circulating thyroid hormone which causes dyslipidaemia and risk of fatty liver disease. Retrospective cohort studies of individuals with heterozygous THRβ mutations reported an increased incidence of earlier-onset major adverse cardiovascular events, occurring on average 11 years earlier. The challenge in this case is he may need to undergo pituitary surgery at some stage if the macroadenoma were to further grow and threaten his vision, post operative hormone replacement will be challenge as TSH and free T4 are unreliable markers of treatment adequacy in this patient cohort.

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I CAHn't believe that sodium

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CB, a 45-year-old woman presented as an ambulatory patient to the Emergency department with intractable vomiting that escalated over two weeks, having coincided with escitalopram commencement. On examination she was haemodynamically stable and initial biochemistry revealed profound hyponatraemia (serum sodium 97 mmol/L), hyperkalaemia (serum potassium 6.1 mmol/L), bicarbonate 16 mmol/L, urea 4.1 mmol/L and creatinine 71 umol/L.

CB was diagnosed with simple virilizing congenital adrenal hyperplasia at birth with ambiguous genitalia and usually maintained on fludrocortisone 100 mcg and prednisolone 1mg daily. However, she had omitted these for three months, with intermittent compliance for 5 years. She reported longstanding secondary amenorrhea and hirsutism. Deranged androgen profile was documented during her admission (table 1).

CB was managed with intravenous hydrocortisone 100mg, 3% sodium chloride (NaCl) 3mg/kg, 0.9% NaCl infusion and reactive desmopressin use. She was admitted to the Intensive Care Unit for three days.

CB had hypovolaemic hyponatraemia which reflects a true sodium and water deficit. This was multi-factorial, including chronic aldosterone and cortisol deficiency; elevated ACTH; escitalopram commencement; and vomiting(1-3).

CB was at high risk of osmotic demyelination syndrome to very low initial serum sodium (≤105mmol/L) and several reversible cause of hyponatraemia(4). Guidelines recommend a serum sodium increase of 5mmol/L in the first hour, not exceeding 10mmol/L in 24 hours(1). There is no randomised controlled trial data regarding severe, chronic, hypovolaemic hyponatraemia so recommendations to replenish salt and water with isotonic saline are based on pathophysiology(1). Evidence on proactive vs reactive desmopressin use is conflicting(4-6).

CB's post-discharge bloodwork reflects remarkable improvements of the androgen synthesis biomarkers and normalisation of serum sodium and potassium. She made a full recovery and reports strict adherence with medications.

An outpatient CT abdomen revealed bilateral macronodular and heterogeneously low-density adrenal glands (Images 1, 2). Genetic studies are underway to confirm compound heterozygosity.

Table 1	Results on admission (22/03/25)	Results during admission (27/03/25)	Results following discharge (30/05/25)	Reference range (units)
Sodium	97	123	137	135-145 (mmol/L)
Potassium	6.1	4.8	3.8	3.5-5.2 (mmol/L)
Creatinine	71	70	65	45-90 (umol/L)
Cortisol	131.6	43.5	349.1	150-700 (nmol/L)
11-Deoxycortisol	6.8	0.9	<0.7	<1.0 (nmol/L)
17-Hydroxy progesterone	1549.1	919.0	1.5	0.2-7.0 (nmol/L)
21-Deoxycortisol	143.10	4.40	2.94	<0.15 (nmol/L)
Androstenedione	258.0	104.2	0.4	0.9-7.5 (nmol/L)
Testosterone	59.0	23.3	<0.1	<2.0 (nmol/L)
11-Deoxycorticosterone	3.10	0.80	<0.06	<0.6 (nmol/L)
Aldosterone	283.4	-	-	Supine: <650, Erect: 60-980 (pmol/L)
Renin	13690	-	-	<50 (mU/L)
ACTH	>165*	-	-	2-10 (pmol/L)

**ACTH added on to EDTA sample, not collected on ice*

Image 1: CT abdomen, sagittal view

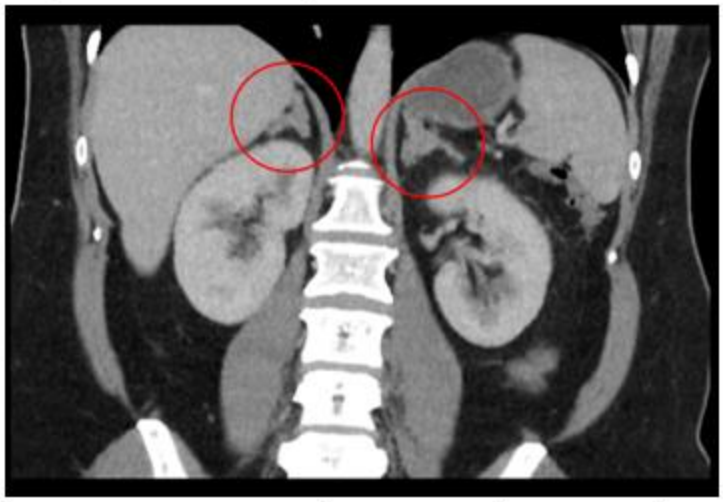
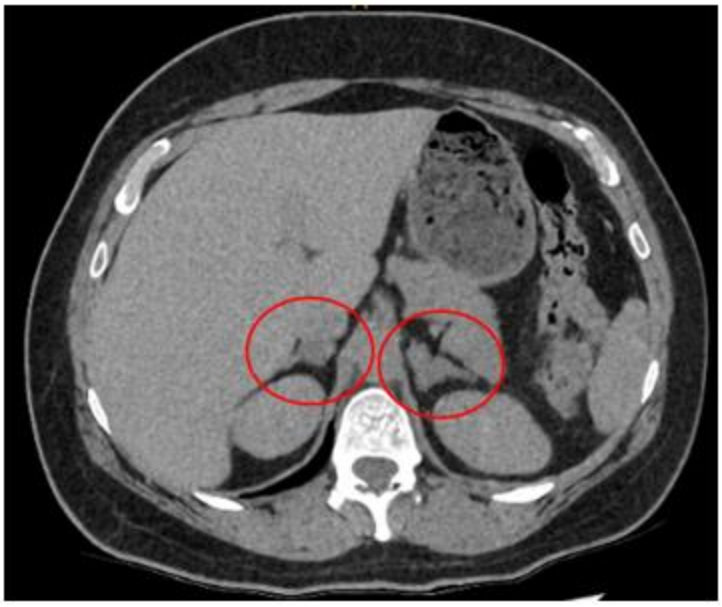


Image 2: CT abdomen, axial view



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Multisystem Sarcoidosis with Vertebral Involvement: Diagnostic and Therapeutic Challenges

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We describe a diagnostically complex case of multisystem sarcoidosis presenting with PTH-independent hypercalcaemia, diagnosed on vertebral biopsy.

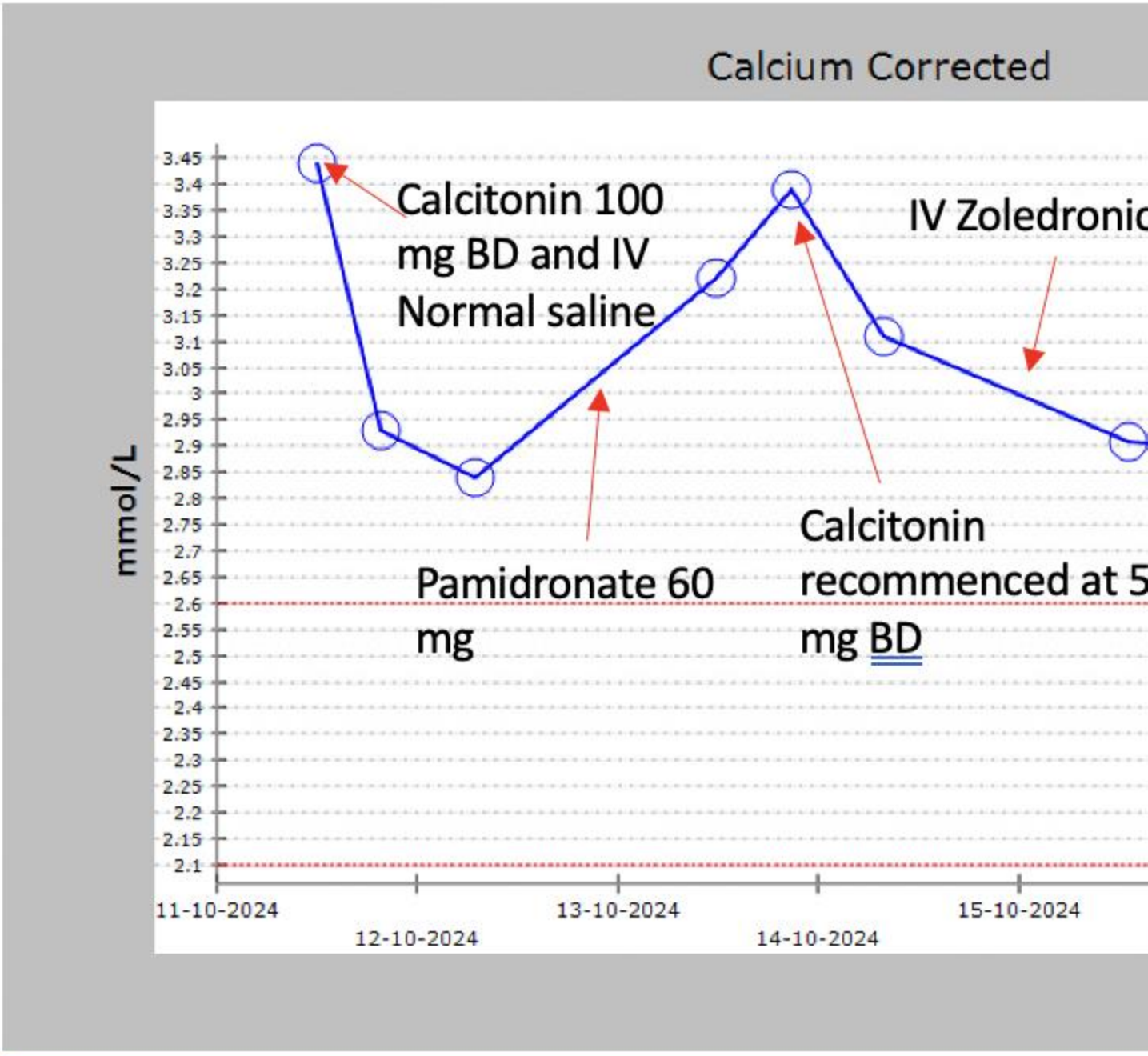
A previously well 60-year-old woman was referred with six weeks of fatigue. Initial examination revealed only dehydration. Investigations demonstrated a corrected calcium 3.44 mmol/L (2.1–2.60), iPTH 1.3 pmol/L (1.6–6.9), creatinine 116 µmol/L (45–90), urine calcium/creatinine ratio 2.64 (0.1–0.58), and 25-OH vitamin D 42 nmol/L. Myeloma screening and tumour markers were negative. CT identified bilateral mediastinal lymphadenopathy with lung nodules. Serum ACE was 138 U/L (20–70), and 1,25-dihydroxy vitamin D was >480 pmol/L (48–190).

Initial management included calcitonin, intravenous 0.9% saline, intravenous bisphosphonate and 40 mg prednisone daily. EBUS-guided lymph node sampling was non-diagnostic, possibly due to partial treatment response. FDG-PET demonstrated uptake in multiple hilar and perihilar lymph nodes, right axillary lymph node and L5 and S1 vertebrae. Right axillary node biopsy was inconclusive. Quantiferon gold was negative.

Infiltrative changes in C5, L5, and S1 vertebrae were subsequently noted on MRI spine, prompting a CT-guided L5 vertebral biopsy which confirmed non-necrotising granulomatous inflammation consistent with sarcoidosis.

Hypercalcaemia resolved (2.39 mmol/L) and ACE level normalised with corticosteroids and bisphosphonate. Given acute kidney injury, methotrexate was avoided, and she was transitioned to adalimumab following histopathological confirmation. Constitutional symptoms improved and prednisone was weaned.

Vertebral sarcoidosis is rare, with fewer than 50 published cases[1,2]. Diagnosis is often delayed due to nonspecific symptoms and inconclusive investigations. This case highlights the value of vertebral biopsy when FDG-PET uptake is present and conventional lymph node sampling is non-diagnostic. It also underscores the role of targeted immunosuppression. The successful use of adalimumab reinforces its emerging role as a steroid-sparing agent in extrapulmonary sarcoidosis[3-5]. Heightened awareness of vertebral sarcoidosis may facilitate earlier diagnosis and treatment.


Calcium Corrected
mmol/L
3.45
3.4
3.35
3.3
3.25
3.2
3.15
3.1
3.05
3
2.95
2.9
2.85
2.8
2.75
2.7
2.65
2.6
2.55
2.5
2.45
2.4
2.35
2.3
2.25
2.2
2.15
2.1
Calcitonin 100 mg BD and IV Normal saline
IV Zoledronic
Pamidronate 60 mg
Calcitonin recommenced at 5 mg BD
11-10-2024
12-10-2024
13-10-2024
14-10-2024
15-10-2024


Calcium Corrected
3.45
3.4
3.35
3.3
3.25
3.2
3.15
3.1

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An unusual sella lesion expressing TTF-1

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Background

Lesions expressing Thyroid-Transcription-Factor-1(TTF-1) are a rare subset of suprasella lesions. TTF-1 is a tissue-specific transcription factor expressed in differentiated cells derived from the foregut endoderm and neuroectoderm including thyroid follicular cells and type-II alveolar epithelial cells. We describe an atypical lesion with strong TTF-1 expression, and atypical morphology.

Case

A 48-year-old woman with minimal past medical history presented following a finding of a pituitary fossa lesion on CT investigation of chronic headaches. MRI demonstrated a 22x21x21mm mixed cystic and solid pituitary lesion with partial enhancement, favouring a cystic pituitary adenoma over a Rathke's cleft cyst. There were no pituitary axis hormonal deficits on biochemical evaluation, nor suggestive clinical symptoms. During surgery, a heterogenous tumour was found with a large component described as a yellow, waxy, and cheese like in consistency.

Histopathological examination described tumour cells comprising cuboidal and columnar epithelioid cells within cohesive glandular/rosette-like structures, papillary-like structures and solid areas. There were some pleomorphic nuclei, with occasional atypical mitoses. Immunohistochemistry demonstrated TTF-1, cytokeratin 7 and Cam 5.2 positivity. Synaptophysin and all anterior pituitary hormone stains were negative. The Ki67 was estimated at 20%.

Considering the tumour morphology, atypical mitoses and TTF-1 positivity, differential diagnoses of metastatic thyroid carcinoma[1] or lung adenocarcinoma[2] were considered, however PET/CT and thyroid ultrasound studies did not reveal avid extracranial disease. TTF-1 expression is also strongly found in pituicytes[3], raising differentials of rarer sella tumours including pituicytomas, although the morphology was not suggestive. Primary papillary epithelial tumour of the sella[4] has been considered, however elevated Ki67 and mitoses and have not been described in these exceedingly rare cases.

Conclusion

Thus far we have described a suprasella mass without a clear histopathological diagnosis. Our patient is well post-operatively, will undergo serial MRI with consideration of repeat PET/CT to continue to investigate the origins of this lesion.

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AVP-D's salty unseen opponents

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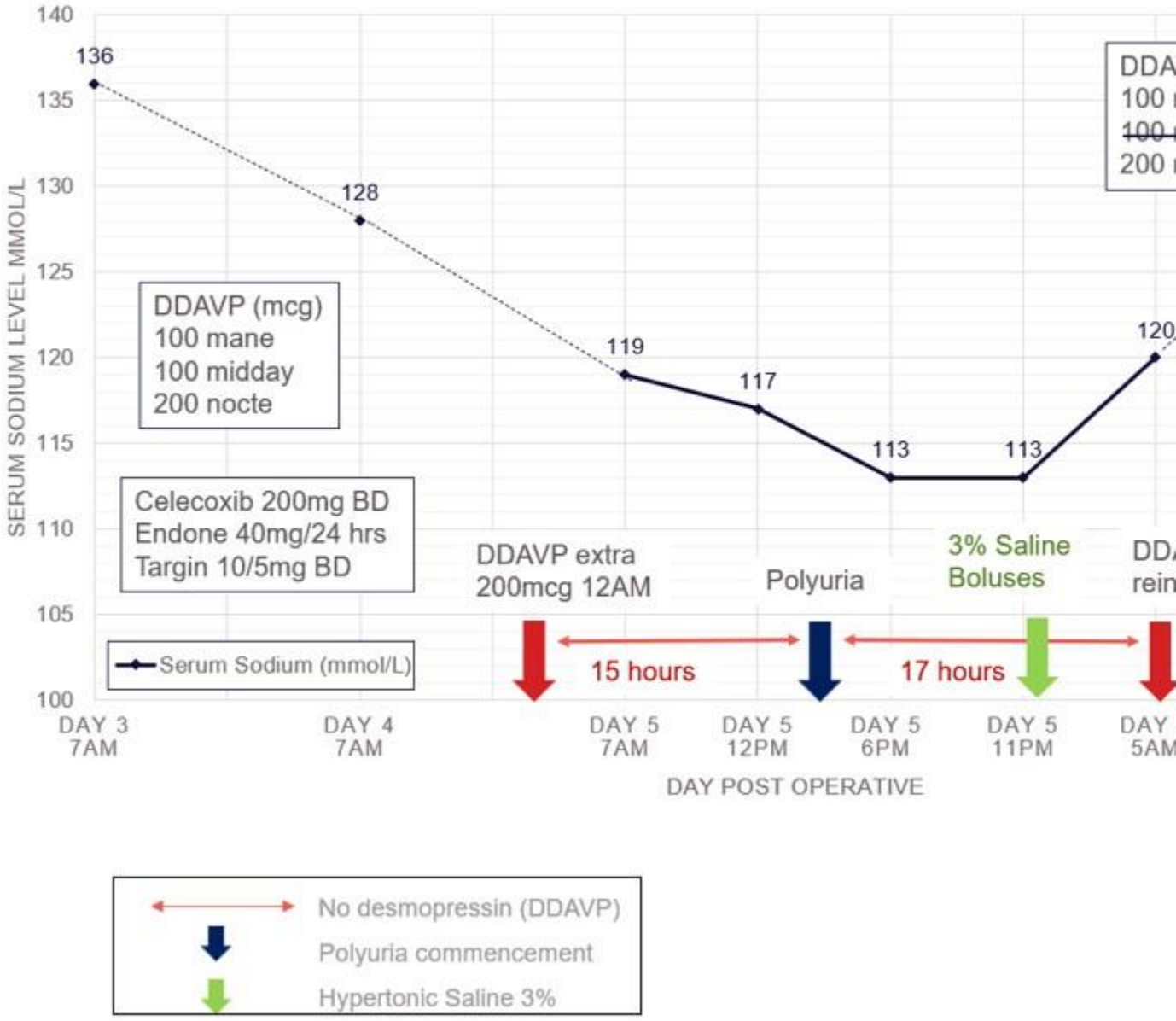
Figure 1 Serum Sodium levels and management with desmopressin (DDAVP) rein



A 59-year-old woman with idiopathic arginine vasopressin deficiency (AVP-D) presented for knee replacement and developed severe hyponatraemia due to opioid and NSAIDs use with her desmopressin (100 mcg mane/midi, 200 mcg nocte). Post operative analgesia was celecoxib, oxycodone and oxycodone/naloxone.

On day 4 her sodium was 128 mmol/L [135-145], despite being 136mmol/l the day prior. The patient continued desmopressin.

Sodium was 119 mmol/L the next morning. Her weight had increased by 6kg. Examination was unremarkable. Immediate management was withholding desmopressin, fluid restriction of 500 ml/day, and monitoring electrolytes thrice daily. Her sodium level was 117 mmol/L by midday that day. 15 hours after her last desmopressin dose, she became polyuric. Sodium dropped to 113 mmol/L by 6 pm. She received 500 millilitres of 3% saline over several hours correcting her serum sodium to 120 mmol/L in 8 hours. Oral 100mcg desmopressin was given to prevent further rapid sodium correction. Over the next 24 hours, her sodium level increased from 120 mmol/L to 134 mmol/L. Desmopressin continued to be administered based on polyuria onset BD (figure 1). There were no neurological sequalae. Dosing was regularly reviewed with urine output, daily weights, electrolytes. Oxycodone was used cautiously. NSAIDs were not restarted. On discharge her weight had returned to baseline and sodium had been stable on desmopressin 100mcg morning and night.

There are 14 case reports of severe hyponatraemia when desmopressin is combined with NSAIDs and/or opioid medications. To improve outcomes and reduce mortality in AVP-D patients, future guidelines should recognise the risk of hyponatremia from commonly used medications. Mechanisms of actions for hyponatraemia due to NSAIDs/opiods are via AVP independent pathways that attenuate diuresis, enhance water permeability and so promote water retention.

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Corticotrophin-independent hypercortisolism in a patient with bilateral adrenal adenoma: Diagnostic and therapeutic conundrum

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Hypercortisolism due to bilateral adrenal disease is an uncommon but challenging entity in endocrine practice. Despite the absence of overt clinical phenotypes, consequences of prolonged mild hypercortisolism can be profound. These include higher risk of diabetes, hypertension, osteoporosis and cardiovascular mortality; however, distinguishing these from general population risk is often difficult.

A 55-year-old male with diabetes and poorly controlled hypertension, was found to have bilateral adrenal masses (right: 34x30mm, left:11mm, both with attenuation <-10 Hounsfield units) incidentally detected five years ago on abdominal imaging done for diverticulitis, with normal hormonal profile. Recent repeat imaging showed a 11mm increase in size of the left adenoma albeit retaining lipid-rich morphology. Clinically there was no weight gain, easy bruising, low trauma fractures, headaches or visual disturbances. Repeat biochemistry revealed normal Aldosterone-renin-ratio and plasma metanephrines, however had non-suppressed Overnight Dexamethasone Suppression Test (ODST) of 62 mmol/L raising the possibility of mild autonomous cortisol secretion. Subsequent biochemistry showed evidence of ACTH-independent cortisol hypersecretion (LDDST 58 nmol/L, late night salivary cortisol 9.5 and 10.1nmol/L, 24-hour Urinary-free-cortisol 176 nmol/day, ACTH 6pg/mL). He had worsening blood pressure control and was osteopenic on bone densitometry. Adrenal venous sampling was conducted to localize origin of cortisol secretion, using metanephrines for selectivity index. This showed bilateral cortisol hypersecretion (lateralization index <2).

Given the patient's relatively young age and established complications likely exacerbated by hypercortisolism, intervention was considered. However, management decisions were constrained by the risks of bilateral adrenalectomy, limited access to cortisol-lowering medications via Pharmaceutical Benefits Scheme (PBS) and the relative toxicity of available therapies. Thus decision was made for aggressive management of complications with close monitoring, with a plan to consider medical or surgical intervention if worsening hypercortisolism.

This case highlights the diagnostic complexity and therapeutic ambiguity posed by bilateral adrenal adenoma with hypercortisolism and importance of individualized treatment decisions.

Time	Site	Cortisol nmol/L	Metanephrin pmol/L
0925	R/adrenal 1	3251	7169
	Peripheral	236	167
0927	R/adrenal 2	3730	13232
	Peripheral	232	166
0929	R/adrenal 3	4234	10034
	Peripheral	241	167
Selectivity index >12 in RA1-3 and LA 1-3: Suc			
Lateralization index 1.9 (RA3 /LA3): consisten			
No clear evidence of lateralization.			

Table 1: Adrenal Venous Sampling Study for

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Severe Prolonged Hypercalcaemia Due to Vitamin D Toxicity: A Case Report

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Introduction

Vitamin D toxicity (VDT) is an uncommon but important cause of hypercalcaemia, increasingly reported due to unregulated supplement use. Management is challenging because of the long half-life and storage of vitamin D in adipose tissue, resulting in prolonged toxicity.

Case Presentation

A 68-year-old female presented with two-week history of nausea, fatigue, polyuria, constipation, and confusion. She had been taking herbal vitamin D drops of unknown dose for many years. Investigations revealed severe hypercalcaemia (adjusted calcium 4.74 mmol/L), suppressed PTH (0.8 pmol/L), hypokalaemia (2.9 mmol/L). Serum vitamin D levels were markedly elevated (25(OH)D >1100 nmol/L and $1,25(OH)_2D$ >480 pmol/L). Extensive work-up excluded malignancy and granulomatous disease (Table 1). The patient

received intravenous hydration, potassium replacement, calcitonin, pamidronate, denosumab, and glucocorticoids. Despite these measures, hypercalcaemia persisted for four months, and vitamin D levels normalised only after nine months (Graph 1, Table 2). Hypokalaemia resolved in parallel with declining serum calcium.

Discussion

VTD is defined as 25(OH)D levels greater than 375 nmol/L,[1] in this case, levels were over three times higher. VDT primarily increases intestinal calcium absorption, leading to hypercalcaemia.[2] The lipophilic nature of Vitamin D causes slow release from hepatic and adipose stores, prolonging hypercalcaemia despite standard therapies.[3] Hypokalaemia, likely due to increased distal tubular calcium delivery and potassium wasting was a notable feature.[4] Glucocorticoids play a critical role by reducing $1,25(OH)_2D$ synthesis and intestinal calcium absorption, yet clearance ultimately depends on time.[2,5]

Conclusion

This case highlights the severe and prolonged nature of hypercalcaemia in VDT, which is often refractory to conventional treatments. Clinicians should counsel patients on the risks of non-prescribed vitamin D use and ensure regular biochemical monitoring. Extended glucocorticoid therapy may be required, and patients should be counselled for a prolonged course. Interdisciplinary collaboration between endocrinology and primary care is essential for long-term management of VDT.

Table 1. Summary of investigations

Initial biochemistry (serum/plasma unless stated otherwise)	
Ionised Ca	2.28 mmol/L (Reference, 1.11-1.28
Serum calcium	4.74 mmol/L (Reference, 2.10-2.60
Adjusted Calcium	4.85 mmol/L (Reference, 2.10-2.60
PTH	0.8 pmol/L (Reference, 2.0-9.9)
Vitamin D	1147 nmol/L
Magnesium	0.50 mmol/L (Reference, 0.70-1.10
Phosphate	1.20 (Reference, 0.75-1.50)
Albumin	34 (Reference, 33-46)
Bilirubin	12 (Reference, <21)
ALT	37 (Reference, <40)
AST	37 (Reference, <30)
ALP	62 (Reference, 30-110)
GGT	23 (Reference, <38)
PTH independent hypercalcaemia investigation	
PTHrP	<1.0 (Reference, <1.40)
CA-19-9	48 kU/L (Reference, <38)
CEA	3 µg/L (Reference, <6)
1,25 (OH)D	>480 pmol/L (Reference, 50-190)
ACE	64 U/L (Reference, 20-70)
Myeloma screen	Kappa/Lambda ratio= 1.39 (Referen Serum protein electrophoresis: mo detected.
24-hour urine calcium	Volume 2261ml 15.13 mmol/day (Reference, 2.50-7
Imaging	
CT chest/ abdomen/ pelvis	No malignancy identified. CBD is mildly dilated (8mm), with v of the intrahepatic ducts of equivo Multiple calcified uterine fibroids.

Graph 1. Adjusted calcium level over time during the course inpatient tr

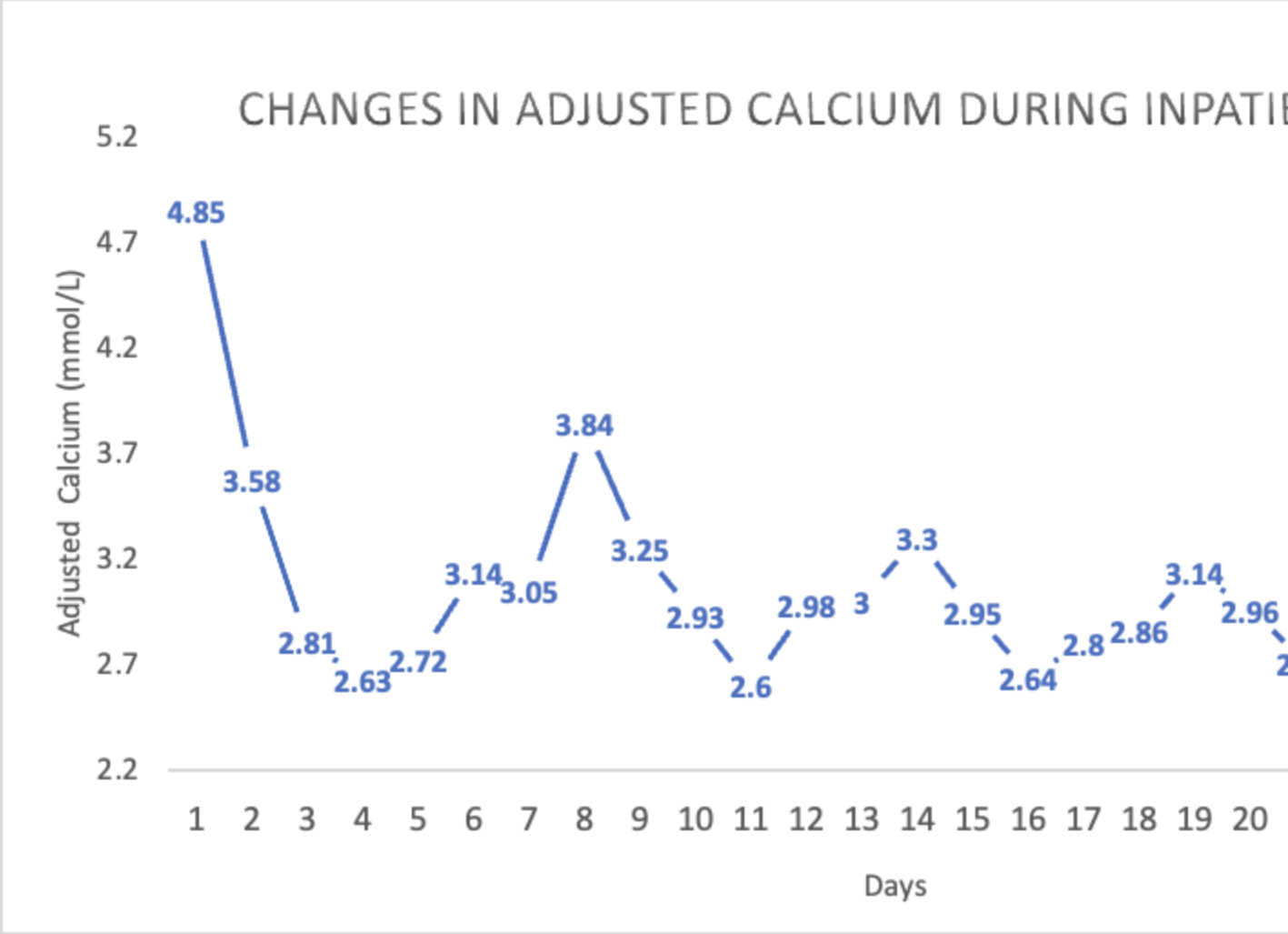

Table 2. Investigations of vitamin D metabolites and calcium over time

Date	12/9/24	15/9/24	23/9/24	11/10/24	21/10/24
Adjusted Calcium, mmol/L				3.1	2.86
25(OH)D, nmol/L	>1380	1147		652	384
$1,25(OH)_2D$, pmol/L			>480	364	

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Initial experience with Somatostatin receptor scintigraphy in evaluating patients with Neuroendocrine neoplasms in a resource-limited setting

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Neuroendocrine neoplasms (NENs) are rare tumors that frequently express somatostatin receptors (SSTR), making them amenable to functional imaging with somatostatin receptor scintigraphy (SRS). Although advanced SRS are now available, lack of access to functional imaging remains a major obstacle in the effective management of NEN in developing countries. We present the initial experience with Octreotide scan in Sri Lanka.

Case 1: 44-year-old male with suspected MEN-1 syndrome had a pancreatic lesion, liver metastases and elevated gastrin levels with gastric hyperplasia. SRS helped to localize the gastrinoma.

Case 2: 41-year-old male with suspected MEN-1 syndrome had pancreatic lesions, elevated gastrin levels. SRS demonstrated NEN in 2nd part of duodenum and uncinate process of pancreas.

Case 3: 53-year-old male with cervical, mediastinal lymphadenopathy was found to have NEN on biopsy. Anterior mediastinal mass, pericardial effusion with a cardiac free-wall mass, suggested metastasis. SRS aided the diagnosis of a metastatic NEN.

Case 4: 50-year-old male with prior hemicolectomy, presented with carcinoid syndrome and was found to have SSTR-positive hepatic metastases on SRS.

Case 5: 47-year-old male with MEN-1 syndrome had prior insulinoma resection with positive LN. He underwent SRS for suspected pancreatic tumor recurrence; scan was negative guiding conservative follow-up.

Case 6: 42-year-old female with a history of distal pancreatectomy for NEN, presented with Zollinger-Ellison syndrome. Biochemistry suggested NEN recurrence. Although CECT was negative, SRS demonstrated SSTR positive focus in liver.

Case 7: 68-year-old male with diarrhoea, mesenteric mass, liver metastases had biochemistry suggesting NEN. However, SRS was negative suggesting poorly differentiated NEN.

Patients with SRS demonstrating SSTR positivity, were commenced on Octreotide treatment.

These highlight the clinical utility of Octreotide scan in management of NEN, where conventional imaging is inconclusive in a resource-limited setting. However, financial constraints and lack of international collaborations continue to hinder the sustainability of this service.

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Low K leads the way … but time is short

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Background

Ectopic ACTH syndrome(EAS) is an infrequent but often severe form of ACTH-dependent Cushing's syndrome. It frequently poses significant diagnostic and management challenges due to atypical presentation and intensity of hypercortisolism.

Case Presentation

A 74-year-old, previously-well Chinese male presented with fatigue. He was found to have hyperglycaemia, hypokalaemic metabolic alkalosis, thrombocytopenia, and deranged liver function tests(Table 1). He had no Cushingoid features but reported substantial consumption of licorice-containing beverage, raising suspicion for pseudoaldosteronism.

However, further inpatient investigations identified bilateral adrenal hyperplasia and significant ACTH-dependent cortisol excess, which did not suppress with dexamethasone 1mg or 8mg(Table 2). A presumptive diagnosis of EAS was made based on biochemical profile and absence of a pituitary lesion. CT chest revealed rapidly growing pulmonary nodules, raising suspicion for lung malignancy as possible ectopic source of ACTH.

The patient developed progressive myopathy, bruising, and skin thinning. Osilodrostat was commenced as cortisol-lowering therapy. Lung biopsy revealed pulmonary aspergillosis with no malignancy. Pulmonary aspergillosis was compounded by MSSA bacteraemia, leading to septic shock and rapid clinical demise(Figure 1). He died before PET imaging or IPSS could be performed to identify source of presumed EAS.

Discussion

EAS often causes intense hypercortisolism due to unregulated ACTH production by a neuroendocrine tumour.[1,2] The intensity of hypercortisolism leads to rapidly accelerated disease course with significant morbidity.[1,3] However, EAS diagnosis is often delayed due to atypical presentation with hypokalaemic alkalosis, hypertension and hyperglycaemia, rather than classic Cushingoid appearance.[1,4]

Osilodrostat is a recently developed steroidogenesis inhibitor which has shown to be effective in rapidly reducing cortisol levels in EAS, though it requires close monitoring of electrolytes, QT-interval and for development of adrenal insufficiency.[1,5]

Conclusion

EAS should be considered in patients with hypokalaemic metabolic alkalosis, even in the absence of overt Cushingoid signs. Early recognition and aggressive cortisol-lowering therapy are essential to improve outcomes.

Test		Normal values
Venous pH	7.54	7.3 - 7.4
Sodium (mmol/L)	148	135 - 145
Potassium (mmol/L)	2.6	3.5 - 5.2
Chloride (mmol/L)	102	95 - 110
Bicarbonate (mmol/L)	34	22 - 32
Creatinine (µmol/L)	61	60 - 110
eGFR (mL/min/1.73m²)	> 90	> 60
Venous glucose (mmol/L)	35.1	3.5 - 7.7
ALT (U/L)	146	10 - 50
AST (U/L)	77	10 - 35
GGT (U/L)	62	5 - 50
ALP (U/L)	90	30 - 110
Bilirubin (µmol/L)	31	<= 20
Albumin	26	30 - 44
CRP (mg/L)	<0.3	<= 5.0
Hb (g/L)	134	130-170
WCC (x10^9/L)	6.7	4.0 - 11.0
PLT (x10^9/L)	58	150-400
TSH (mIU/L)	0.27	0.27-4
HbA1c	13.6%	< 5.5%

Table 1. Initial (day 0) pathology results

Test	1st week of admission	1 mg DST (Day 12)	8 mg DST (Day 18)
Sodium (mmol/L)	146	146	145
Potassium (mmol/L)	4.1	3.6	4.1
Chloride (mmol/L)	107	104	104
Bicarbonate (mmol/L)	31	31	29
Creatinine (µmol/L)	68	58	58
eGFR (mL/min/1.73m²)	89	> 90	> 90
ALT (U/L)	132	136	84
AST (U/L)	50	59	27
GGT (U/L)	45	43	29
ALP (U/L)	113	99	92
Bilirubin (µmol/L)	19	18	25
Albumin	18	19	21
CRP (mg/L)	24.9	3.4	4.7
Hb (g/L)	120	118	102
WCC (x10^9/L)	11.6	10	9.1
Neutrophils	10.9	9.3	8.7
Lymphocytes	0.2	0.2	0.2
PLT (x10^9/L)	97	104	90
Aldosterone (pmol/L)	73		
Renin (mIU/L)	<1		
ACTH (pmol/L)	13.76	16.86	
Cortisol level (nmol/L)	872	1,082	1,393
24-hour urine cortisol (nmol/24 hr)	>7270		
TSH (mIU/L)	0.4		
Free T4 (pmol/L)	8.8		
Free T3 (pmol/L)	1.8		
Luteinising hormone (IU/L)	< 0.3		

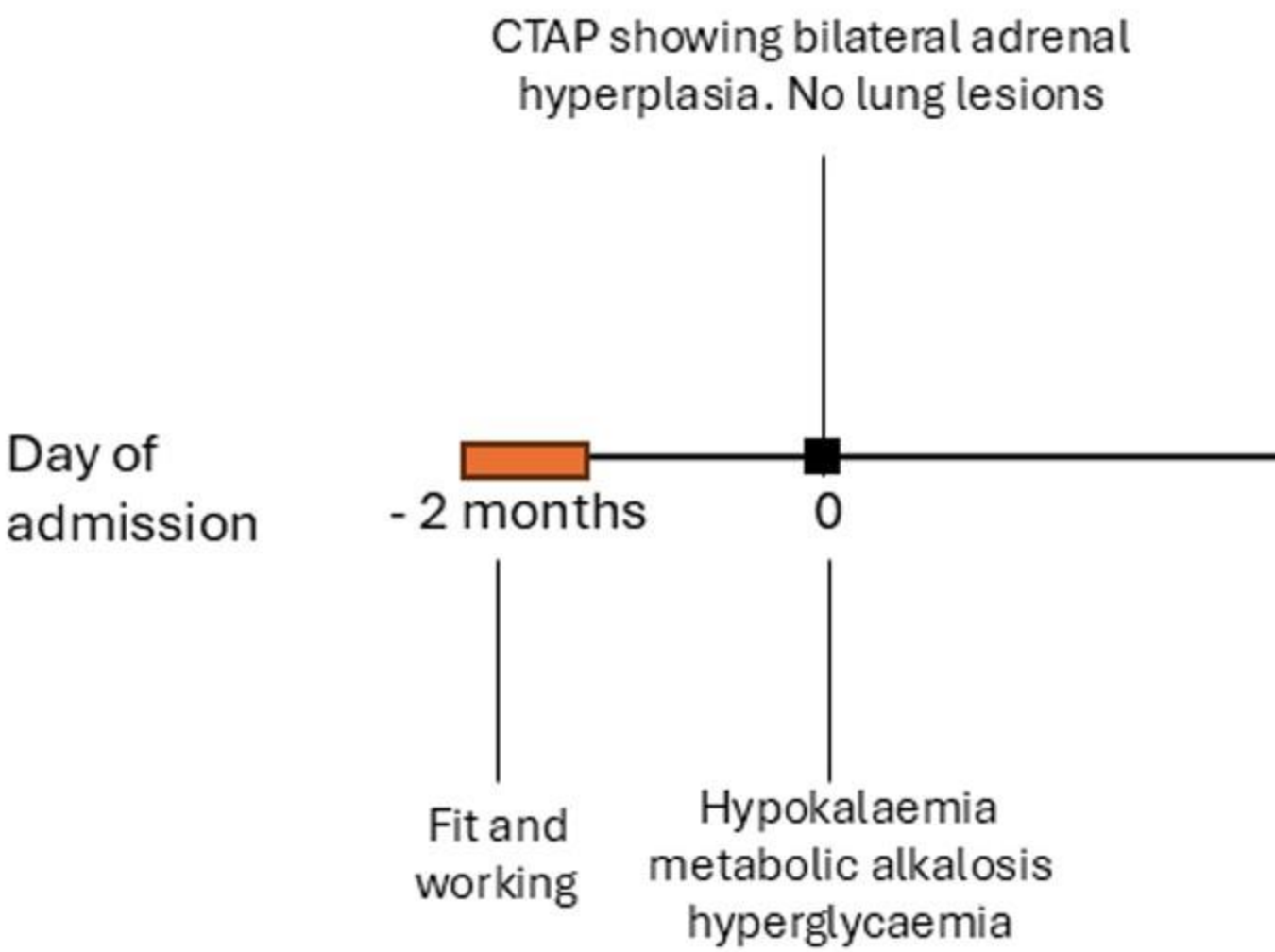

Figure 1. Timeline of admissio
baseline

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Hypoglycaemia with a Twist: Not Your Typical Beta Cell Story

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Hypoglycaemia in adults without diabetes mellitus is uncommon and requires systematic evaluation. While insulin-mediated causes are most prevalent, non-insulin-mediated mechanisms—particularly inborn errors of metabolism (IEMs)—are diagnostically challenging. Although IEMs are classically paediatric, adult-onset presentations are increasingly recognised, especially during catabolic stress (1,2).

A 59-year-old woman presented with recurrent symptomatic hypoglycaemia (blood glucose ~2.8–3.0 mmol/L) in both fasting and post-prandial states, worsening after a COVID-19 infection in 2024. She had no known history of diabetes mellitus, no insulin or sulfonylurea exposure, and a stable BMI of 20.3 kg/m². Continuous glucose monitoring revealed 40% time in the low range (BGL 3.0–3.8 mmol/L) and 5% time in the very low range (BGL <3.0 mmol/L). A supervised 72-hour fast was terminated at 29 hours due to symptomatic hypoglycaemia (glucose 2.3 mmol/L), with undetectable insulin, proinsulin, and low C-peptide, and elevated beta-hydroxybutyrate (3.0 mmol/L), consistent with preserved ketogenesis. Imaging (MRI pancreas, FDG-PET, DOTATATE-PET) showed no evidence of an insulinoma or neuroendocrine tumour. IGF-2–mediated hypoglycaemia was excluded based on the preserved ketotic response and absence of malignancy.

Metabolic testing between episodes, including acylcarnitine profile, lactate, urate and creatine kinase, was normal. Given her mixed fasting and post-prandial symptoms and the absence of insulin excess, rare metabolic disorders such as fatty acid oxidation defects or partial glycogen storage disorders were considered. She is awaiting review by a tertiary metabolic genetics service for further evaluation.

This case underscores the value of a structured approach to unexplained hypoglycaemia. Suppressed insulin markers and preserved ketogenesis effectively exclude insulin-mediated causes. Adult-onset inborn errors of metabolism, though often subtle, may be unmasked by stressors such as illness or fasting (2). Normal metabolic markers between episodes do not rule out partial defects (2). In such cases, early referral for genetic evaluation is key to diagnosis and management.

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Do all good things come in pairs? An atypical case of bilateral adrenal masses with cosecretion

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Case summary: A 50-year-old male with a background of familial adenomatous polyposis (FAP), colectomy and loop ileostomy 2002 with high stoma output, presented with large bilateral adrenal lesions (right 57mm, left 59mm) with benign characteristics on CT in 2024(**figure 1**). Lesions were absent in 2006 and present on CT 2022 (10mm smaller). Malignancy could not be excluded on FDG-PET/CT(**figure 2**)

Cosecretion of aldosterone and cortisol was confirmed(**table 1**). Plasma aldosterone was markedly elevated (50,700, 136,000pmol/L) by immunoassay and confirmed by LCMS(**table 1**), with unsuppressed renin, elevated ARR and unremarkable sodium and potassium(**table 1**). An LCMS 18-analyte-steroid-panel measured on a stored serum sample from 2009 demonstrated an isolated elevated aldosterone 7,710pmol/L (an order of magnitude less to 2024)(**table 2**). The same assay in 2024 demonstrated elevated aldosterone precursors 11-deoxycorticosterone and corticosterone(**figure 3**). ACTH was undetectable, presumedly suppressed by adrenal metabolites. He had no clinical manifestations of primary aldosteronism or Cushing's syndrome (besides obesity). Plasma metanephrines were unremarkable

His markedly elevated aldosterone with unsuppressed renin were considered a homeostatic response to decades of unattended high stoma output i.e. longstanding compensatory secondary aldosteronism(**1**). This process, with his genetic predisposition(**2**), presumedly lead to the development of large bilateral adenomas and increased secretion of aldosterone precursors. Aldosterone resistance via downregulation of (or defective) intestinal mineralocorticoid receptor (MR) and epithelial sodium channels (ENaC) may be contributory(**3,4**). MACS was present which is associated with bilateral lesions (**5**). He was referred to the stoma nurse and is undergoing surveillance for malignant transformation and clinical features of MACS.

Discussion: The physiology of mucosal adaptation and sodium resorption post bowel surgery, mediated by hyperaldosteronism and upregulation of ENaC, will be outlined(**1,6,7**). Aldosterone resistance in the context of excessive gastrointestinal fluid loss will be explored(**3,4**). Finally, the associations between FAP and adrenal masses, malignancy and hormone excess will be reviewed(**2,8,9,10**).

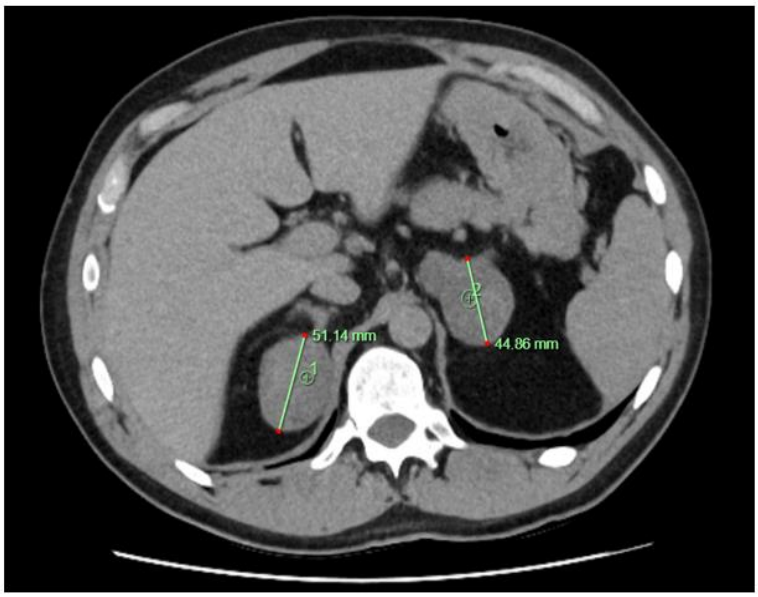

Figure 1. Adrenal CT (February 2024) demonstrating the large bilateral adrenal lesions.

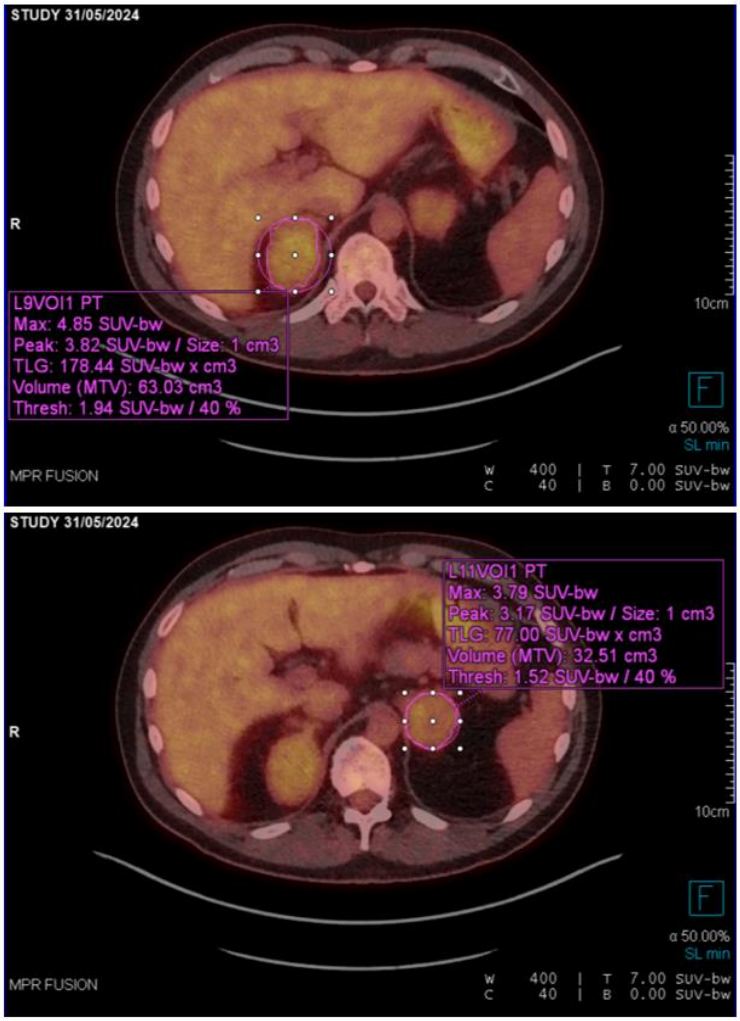

Figure 2. FDG-PET/CT (May 2024) demonstrating low to moderate uptake involving bilateral adrenal masses.

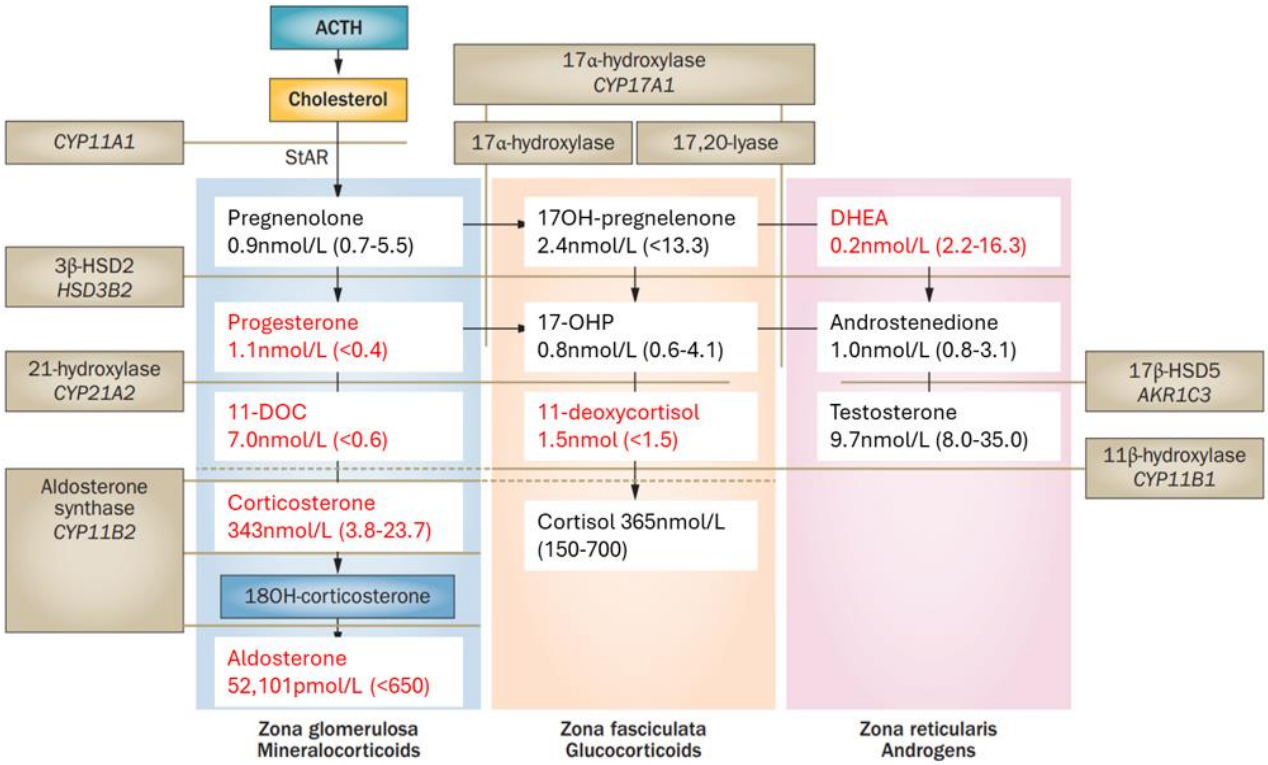

Figure 3. Plasma C18-oxygenated steroid panel results from 2024 for patient DD overlaid on the adrenal steroidogenic pathway suggesting predominantly hyperfunction of the Zona Glomerulosa. Red values indicate values outside of reference range. Adapted from Han et al., Nat. Rev. Endocrinol. 2014.

	May 2025	Jun 2024	Aug 2024	Reference range
24hr urine free cortisol LCMS (nmol/24hr)	889			**< 170**
1mg dexamethasone suppression test cortisol (nmol/L)	260			**< 50**
Late night salivary cortisol (nmol/L)	33.2, 17.7	27.2, 46.9		**< 5.7**
ACTH (pmol/L)		< 1.1		**2.0 - 10.0**
Morning serum cortisol (nmol/L)		450		**150 - 700**
Aldosterone (pmol/L)	50,700	136,000		**< 650**
Aldosterone LCMS (pmol/L)	43,800			
Renin (mU/L)	34.3	206.3		**3 - 40**
ARR (pmol/mU)	1,478	659		**< 50**
Normetadrenaline (pmol/L)	80			**< 750**
Metadrenaline (pmol/L)	100			**< 300**
3-Methoxytyramine (pmol/L)	< 20			**< 100**
Sodium (mmol/L)	138	140	140	**135 - 145**
Potassium (mmol/L)	4.3	4.7	4.4	**3.5 - 5.2**
Bicarbonate (mmol/L)	22	18	21	**22 - 32**
Creatinine (umol/L)	105	114	108	**60 - 110**
eGFR (mL/min/1.73m2)	71	64	68	**> 60**
HbA1c (%)	5.4		5.4	**< 6.0**
LDL-C (mmol/L)	2.8			**< 3.0**
Triglycerides (mmol/L)	1.2			**< 2.0**
Urine ACR (mg/mmol)			0.5	**< 2.5**
17-OHP (nmol/L)			1.6	**0.6-4.1**
Progesterone (nmol/L)			3	**< 4**

Table 1. Biochemical investigations. Red values indicate values outside of reference range.

LCMS 18 STEROIDS PANEL RESULTS

Age		Years		Collection Date
Sex	Male (M)	35		3/08/2009

Order No. / UMRN		P09-1523937L (B4267176)			
	Analyte	Result	Units	Reference Ranges	
1	Aldosterone	7712.0	pmol/L	Erect: 60—980	Supine: <650
2	Cortisone	46.7	nmol/L	33—97	
3	Cortisol	167.0	nmol/L	150—700	
4	21-Deoxycortisol	<0.07	nmol/L	<0.15	
5	Corticosterone	5.30	nmol/L	3.8—23.7	
6	11-Deoxycortisol	0.20	nmol/L	<1.5	
7	Androstenedione	1.2	nmol/L	1.2—4.7	
8	11-Deoxycorticosterone	0.09	nmol/L	<0.6	
9	21-Deoxycorticosterone	<0.06	nmol/L	<0.15	
10	Testosterone	11.5	nmol/L	8.0—35.0	
11	Androstenediol	3.5	nmol/L	<12	
12	17-Hydroxyprogesterone	2.0	nmol/L	0.6—4.1	
13	Dehydroepiandrosterone	7.8	nmol/L	4.6—27.0	
14	17-Hydroxypregnenolone	3.0	nmol/L	<13.3	
15	Dihydrotestosterone	0.77	nmol/L	0.35—2.5	
16	Androsterone	0.5	nmol/L	<1.0	
17	Pregnenolone	3.6	nmol/L	0.7—5.5	
18	Progesterone	0.1	nmol/L	<0.4	

** Pregnenolone value may be significantly low if the sample is not stored frozen*

Table 2. Plasma LCMS 18 steroid panel from 2009. Only aldosterone (in red) was elevated.

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Turner by chromosome, not by gender: a case of clinical exclusion

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A 22-year-old male was referred for management of 45,X/46,XY mosaicism, diagnosed prenatally on amniocentesis (96% 45,X, 4% 46,XY). He had male genitalia at birth and short stature (3rd centile). Bilateral orchidopexy at age 4 revealed markedly reduced germ cells and ovarian-type stroma in the left testis.

He was initiated on testosterone at 14 for delayed puberty (Tanner stage II, testes 3–5 mL), progressing to Tanner stage IV by 17 (testes 12–15 mL). Adult height was 160 cm, below mid-parental height (172 cm).

At age 24, semen analysis showed azoospermia. Sperm extraction was offered but declined. He currently has no partner or fertility plans.

Surveillance followed adapted Turner syndrome guidelines. Cardiac imaging identified a bicuspid aortic valve with mild regurgitation but stable aortic dimensions. Renal and testicular ultrasounds were normal. Bone density scan revealed osteopaenia (lumbar Z-score -1.1; femoral neck -1.9). Secondary osteoporosis screen was negative.

He attends annual endocrinology review.

Discussion Summary

45,X/46,XY mosaicism is a rare sex chromosome disorder affecting both males and females. Despite male phenotype, affected individuals share comorbidity profiles with Turner syndrome—including increased mortality risk, cardiac anomalies, thyroid disease, metabolic syndrome, and osteoporosis. Most males undergo spontaneous puberty but are infertile due to Sertoli-cell-only histology and elevated gonadotropins.

Tumour risk remains elevated, even with normal male genitalia, due to Y chromosome-linked oncogenes (e.g., TSPY) and dysgenetic gonads. Up to 36% may have histologically detected gonadal neoplasia. Surveillance should include annual ultrasound and consider post-pubertal gonadal biopsy.

These individuals are often under-investigated and under-recognised. Coordinated multidisciplinary care is essential to address endocrine, cardiac, fertility, and psychosocial health.

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Hypertension, Hormones, and Aortic Rupture: A Complicated Triad

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Introduction

Primary aldosteronism (PA) is the most common cause of secondary hypertension[1] and has rarely been reported in combination with aortic dissection[2]. Whilst optimal investigation of PA requires discontinuation of interfering medications, this is not always possible.

Case Presentation

A 57-year-old man presented to the emergency department with chest and abdominal pain. Blood pressure was 224/130mmHg and he was hypokalaemic (potassium 2.5mmol/L). A computed tomography (CT) scan revealed a type B aortic dissection, initially managed conservatively, followed by an endovascular repair.

Whilst on metoprolol, perindopril and hydrochlorothiazide, aldosterone was 699pmol/L with suppressed renin <2.0mIU/L and ARR 349. Cortisol was mildly elevated on multiple 1mg dexamethasone suppression tests, without Cushingoid features. An adrenal CT reported bulky adrenal glands bilaterally and a right-sided 8mm arterially-enhancing nodule.

After further presentations with hypertensive crisis, antihypertensives were up-titrated to spironolactone, amlodipine, metoprolol, perindopril and hydralazine. The patient will be referred for adrenal vein sampling (AVS) on his current medications using metanephrines instead of cortisol due to cortisol co-secretion.

Discussion

This case highlights the challenges in PA workup and management where interfering medications cannot be withdrawn. There have been few reported cases aortic dissection associated with PA[2]. The main risk factor for aortic dissection is hypertension, mainly resistant hypertension[3]. PA is the most common form of secondary hypertension and is associated with greater end-organ damage compared with essential hypertension[2,4].

To screen for PA, guidelines recommend washout of interfering medications[5], however, if not safe, testing can be performed if renin remains suppressed despite the use of interfering agents[1]. Once PA is confirmed biochemically, AVS determines the laterality and subtype[5]. Co-secretion of aldosterone and cortisol (5-27% of cases[1]) can confound AVS results due to suppressed cortisol production from the contralateral gland. In this instance, it has been shown that plasma metanephrines can be successfully used instead[6].

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Unravelling the mystery of idiopathic hypoparathyroidism

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We present the case of Mr JJ, 46-year-old gentleman who initially presented with a 3-week history of muscle cramps, malaise and paraesthesia correlating with severe hypocalcaemia, hypomagnesaemia and hypoparathyroidism, requiring high doses of oral supplementation. There was no history of neck surgery, nor a personal or family history of autoimmunity. He was diagnosed with idiopathic hypoparathyroidism. He required frequent dose titrations and the addition of a thiazide to reduce urine calcium excretion. Despite his normalising calcium levels, he still experienced significant symptoms and his condition became increasingly debilitating. Given his circumstances, he was unable to afford PTH analogues.

He was referred to rheumatology for review of inflammatory arthritis as he developed bilateral ankle and wrist pain associated with increased inflammatory markers. Around this time, his renal function worsened, prompting a renal biopsy which revealed interstitial nephritis without granulomata. The unifying diagnosis was not apparent, however extra-pulmonary sarcoidosis was a differential, and

he was trialled on prednisone among other immunosuppressive therapies. This controlled his arthropathy and over the course of months, also resulted in significantly reduced calcium supplementation and normalising PTH levels.

Surgical hypoparathyroidism accounts for 70-80% of patients with hypoparathyroidism (1). Non- surgical hypoparathyroidism is often labelled idiopathic, however this describes a heterogenous group of conditions which have an underlying genetic or autoimmune basis (2). Autoimmune hypoparathyroidism can occur as an isolated condition or part of a larger autoimmune syndrome such as APS1, with case reports supporting the use of immunosuppressive agents which target calcium sensing receptor (CaSR)-activating antibodies (3,4,5) thereby increasing PTH secretion.

This case highlights 'idiopathic' hypoparathyroidism having an underlying autoimmune component, responding well to immunosuppression. This modality of treatment is useful to consider in patients who have suspected autoimmune hypoparathyroidism and are intolerant of calcium supplementation or who suffer adverse effects associated with excessive calcium supplementation.

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Too big to ignore: a hidden cause of hypoglycaemia

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We present a previously well 49-year-old female referred for evaluation for recent-onset seizure-like episodes occurring over one month. Symptoms included eye-rolling, jerking movements, confusion, and agitation lasting up to 45 minutes. MRI Brain and EEG were normal. She was diagnosed with focal impaired awareness seizures and commenced levetiracetam, but symptoms persisted despite dose escalation. During her second admission, hypoglycaemia (capillary glucose 1.3 mmol/L) was detected, with resolution following intravenous dextrose. She reported progressive abdominal bloating and 4 kg weight gain over 9 months. There was no history of diabetes mellitus, insulin/sulphonylurea use, or relevant family history.

A mixed-meal test and supervised 72-hour fast, which confirmed hypoglycaemia within 4 hours of fasting (Table 1). Biochemistry suggested a non-insulin-mediated cause (suppressed insulin, proinsulin, C-peptide). Persistent hypoglycaemia necessitated intravenous dextrose and glucocorticoids. CT imaging revealed a 156 x 114 x 125 mm left renal mass with central necrosis and normal pancreas, raising suspicion for non-islet cell tumour hypoglycaemia secondary to insulin-like growth factor 2 (IGF-2). She was referred for surgical management.

Table 1: Biochemical investigation summary.

Time	72 Hour Fast							Pre-op
	19:41 (Baseline)	22:12	23:36	Glucagon Given	23:45	23:55	00:05	
Glucose (mmol/L)	9.2	2.2	1.2		3.9	5.3	5.5	
C-peptide (nmol/L)	0.50	< 0.03	< 0.03					
Insulin (mU/L)	9.1	< 1.6	<1.6					
Proinsulin (pmol/L)			<3.1					
3-Hydroxybutyrate (mmol/L)	<0.1	<0.1	<0.1		<0.1	<0.1	<0.1	
IGF-1 (Reference range: 7.41 – 30.68 nmol/L)								1.91
IGF-1 (ug/L)								14.6
IGF-2 (ug/L)*								85.5
IGF-2/IGF-1 ratio								5.9
IGF-BP3 (Reference range: 93.5 – 216.6 nmol/L)								

* Reference range not available for IGF-2.

The patient underwent left renal artery embolization followed by radical nephrectomy (Figure 1). Histopathology confirmed a 130 mm encapsulated solitary fibrous tumour (SFT) confined to the kidney, with adverse-risk features including large tumour size, high mitotic activity, and necrosis. RNA sequencing identified a NAB2-STAT6 fusion, consistent with SFT of intermediate/high-risk (93% 5-year disease-specific survival). Hypoglycaemia resolved immediately post-operatively. At 3-month follow-up, she remains asymptomatic with no evidence of recurrence.

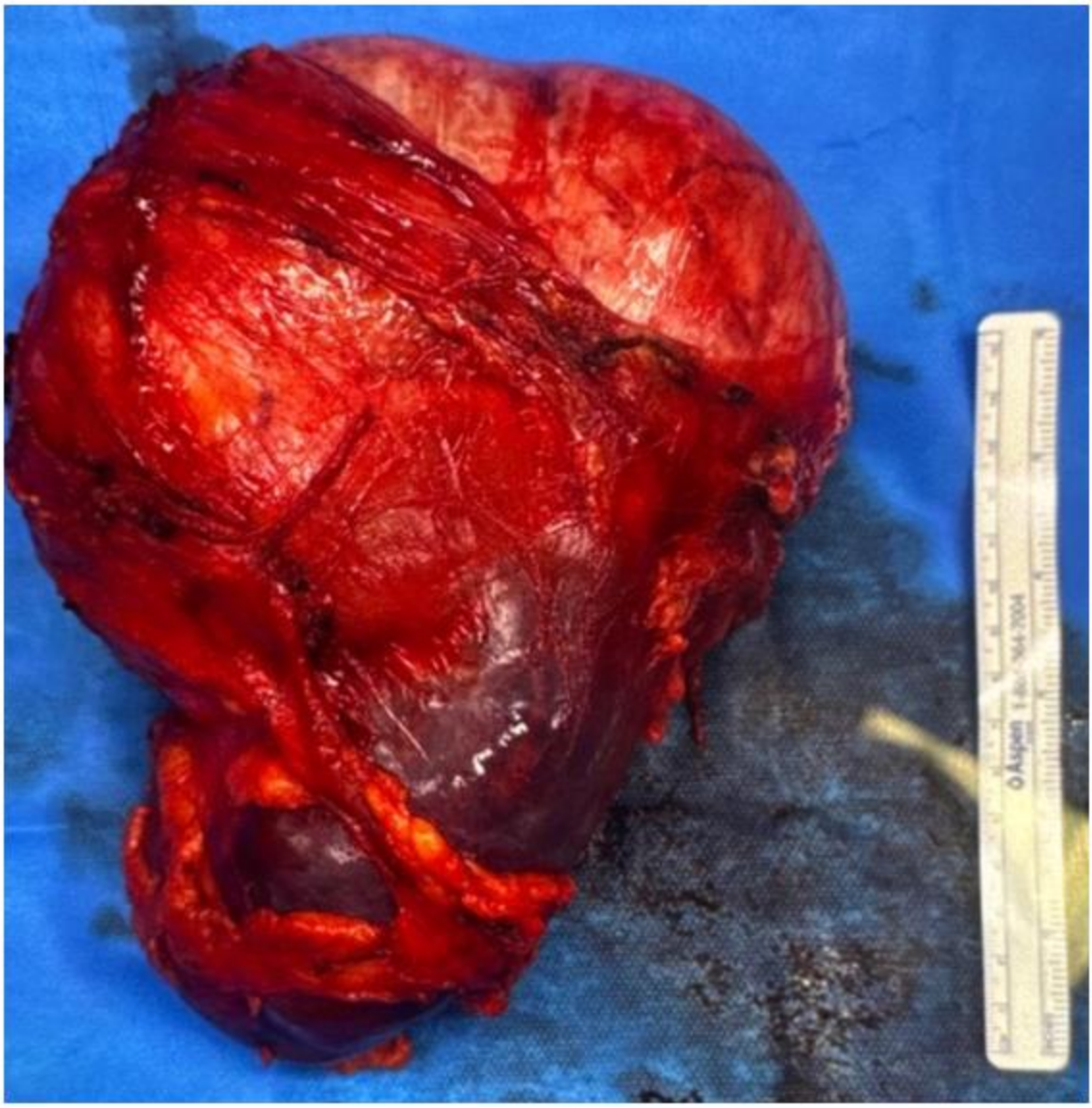

Figure 1: Left radial nephrectomy surgical spe

NITCH is rare (1 case/million annually). Diagnosis is based on Whipple's triad, characteristic biochemistry, tumour identification and resection. SFT-related hypoglycaemia (Doege-Potter syndrome) occurs via high levels of immature IGF-2 secretion (1), which activates insulin receptors, suppresses hepatic glucose production and increases peripheral glucose utilisation. An IGF-2:IGF-1 ratio >10 (normal <3) is suggestive of NICTH (2). Surgical resection remains the only curative treatment.

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A decade of discordant thyroglobulin elevation – a case of malignant struma ovarii with thyrotoxic related heart failure

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Malignant struma ovarii is a rare ovarian germ cell tumour containing >50% thyroid tissue, with malignant transformation reported in 5–15% of cases (1). Follicular carcinoma is the most common thyroid-type carcinoma arising in struma ovarii. As in primary differentiated thyroid carcinoma, serum thyroglobulin (Tg), in the absence of anti-Tg antibodies, serves as a reliable tumour marker (2). However, diagnostic and therapeutic challenges arise when Tg remains elevated without localisable structural disease.

We present a 51-year-old female with metastatic malignant struma ovarii, initially diagnosed in 1999 following right oophorectomy for an ovarian teratoma. In 2000, she underwent surgical decompression of a T8 vertebral lesion, revealing metastatic follicular thyroid carcinoma. This prompted total thyroidectomy and radioactive iodine therapy. Histopathology showed entirely benign thyroid tissue, suggesting the struma ovarii as the sole site of malignancy.

Over the following decade, she developed skeletal metastases, including thoracic spine, pubis, jugular foramen and cervical vertebrae, identified on FDG-PET and treated with external beam radiotherapy, most recently in 2015. Tg levels remained chronically elevated (Table 1) with undetectable anti-Tg antibodies, prompting long-term TSH-suppressive thyroxine therapy while she remained asymptomatic.

Table 1: Thyroglobulin with corresponding TSH levels across time.

Year	2013	2017	2018	2019	2020	2021	2022	2023	20
Tg (ug/L)	1600	531	484	501	466	467	509	526	74
TSH (mIU/L)	-	0.01	<0.01	0.02	0.02	<0.01	0.02	0.31	1.(

In 2022, she developed atrial flutter and cardiomyopathy with severely-reduced ejection fraction, which resolved post down-titration of thyroxine and normalisation of TSH (heart rate 63 bpm, LVEF 55%). Re-staging scans revealed stable iodine-avid right-sided pulmonary nodules (4mm, 6mm) and osseous metastases (base of skull, C5 transverse process, T8). Given the stability of residual disease, suppressive thyroxine therapy was de-escalated to achieve euthyroidism, correlated with a rise in Tg level (Table 1). Thyroglobulin was sent for mass spectroscopy to confirm rising thyroglobulin concentration despite anatomical and functional scan stability. Bone density was normal.

This case highlights the challenge of rising thyroglobulin despite stable imaging and no symptoms, emphasising the need for personalised decisions about prolonged TSH suppression.

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A case of life-threatening licorice-induced pseudohyperaldosteronism

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Introduction: Licorice-induced pseudohyperaldosteronism is a crucial differential for hypokalaemia. We report a case of a life-threatening presentation to highlight the diagnostic and management considerations, and the need for public awareness measures.

Case presentation: A 71-year-old man with a history of hypertension on hydrochlorothiazide was admitted to the Intensive Care Unit (ICU) for severe hypokalaemia and hypertension. A thorough history revealed he had consumed approximately 800g of licorice confectionary over the preceding six weeks. Investigations revealed a potassium nadir of 1.9 mmol/L and metabolic alkalosis. The endocrine workup was consistent with pseudohyperaldosteronism, with suppressed plasma renin (<2.0 mU/L) and aldosterone (50 pmol/L) levels, and metabolic alkalosis.

Management and outcome: Management involved immediate cessation of licorice and hydrochlorothiazide. He required ICU admission with aggressive intravenous potassium replacement (approx. 800 mmol) and spironolactone. His potassium level normalised, and he was discharged safely.

Discussion: This case highlights the risk of life-threatening complication from excess licorice consumption. Though recognized as generally safe, toxicity becomes more likely above recommended levels and the public health concern of licorice in food items in food remains topical. A history of licorice intake should be considered in anyone presenting with hypokalaemia. There is a need for greater public awareness and clearer product labelling to mitigate the risk of severe adverse events.

A Rare Case of Pituitary Macroadenoma - Tuberculous Granulomatous Hypophysitis

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A previously well, 57-year-old male, presented with acute worsening of longstanding headaches, with new onset nausea and vomiting in the setting of Influenza A. Past medical history was significant for investigations into chronic headaches five months prior with magnetic resonance imaging (MRI) demonstrating an enlarged pituitary gland measuring 11mm (**Figure 1A**). Serum cortisol measured at 10:00 am was 32nmol/L, prompting glucocorticoid replacement. Urgent repeat MRI revealed interval growth in the pituitary lesion to 14mm with contact of the optic chiasm and new central non-enhancement (**Figure 1B**). On examination, he remained normotensive and afebrile. There were no signs of pituitary hormone excess or visual compromise. Chest examination was normal. Pituitary panel results are summarised in **Table 1**.

Our patient underwent endoscopic endonasal resection of the pituitary lesion with an uncomplicated recovery (including no AVP-deficiency). Day 8: TSH 0.14 IU/L, FT4 11.4 and FT3 4.5 pmol/L. Testosterone levels are being monitored. Histopathology revealed granulomatous hypophysitis (GRH). A secondary screen for GRH was positive for QuantiFeron-TB (tuberculosis) gold assay (**Table 2**). Pan computed tomography (CT) studies did not demonstrate other sites of granulomatous disease. Whilst mycobacterium tuberculosis polymerase chain reaction (PCR) is still pending, he has been empirically commenced on anti-microbial therapy, including dexamethasone.

The frequency of pituitary incidentalomas detected on MRI varies from 0.3 to 3% with >80% being adenomatous (1). Of non-adenomatous lesions, the majority represent Rathke's cleft cysts with hypophysitis accounting for <1% of incidentalomas (1). GRH is therefore extremely rare (2). As its clinical presentation and imaging can mimic adenomas, histological confirmation is crucial (2). GRH can be idiopathic or due to secondary causes including tuberculosis, sarcoidosis, syphilis and vasculitis (2).

In a recent case-series, 60% of patients with tuberculous hypophysitis had evidence of disease elsewhere (3). Our patient is being empirically managed for solitary pituitary involvement.

Table 1: Pre- and Post-operative Pituitary Panel Investigations

Pituitary panel	Preoperative results	Postoperative results (Day 3)	Results reference ranges
ACTH, pmol/L	4		(<10)
Cortisol, nmol/L	**32** (10:00)	**36** (08:00)	(185-625)
TSH[a], mIU/L	**0.06**	**0.14**	(0.40-4.80)
T4, pmol/L	13.4	11.3	(8.0-16.0)
T3, pmol/L	4.3	4.5	(3.2-6.1)
LH, IU/L	2.9	Pending	(2-8)
FSH, IU/L	5.9	Pending	(1.2-5.2)
Testosterone, nmol/L	**3.5**	Pending	(10-27.6)
Prolactin, mIU/L	67	Pending	(60-280)
GH, IU/L	2.0	Pending	(0-3.0)
IGF-1, nmol/L	25.6	Pending	(15.2-46.9)
Plasma Na, mmol/L	145	144	(135-145)
Serum osmolality mOSm/kg	**307**	298	(280-300)
Urine osmolality mOsm/kg	320	504	(50-1200)

a, TRABs: negative, TPO Ab: <1.0 IU/mL (0-9)

Table 2: Secondary

Test
Ionized Calcium, mmol/L
Serum ACE, U/L
IgG4, g/L
ANA
ANCA
HIV serology

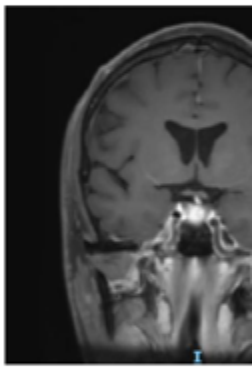

Figure 1A – MRI Pituita measuring 11mm cran

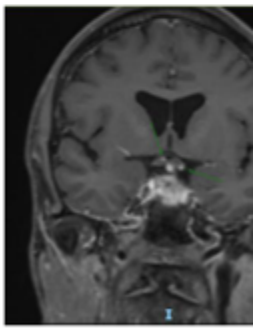

Figure 1B – MRI Pituita image on right. Enlarge developed central non- hyperintensity of optic

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Calcium malabsorption in autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy

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Background: Autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED) is an autosomal recessive disease caused by mutations in the autoimmune regulatory (AIRE) gene. The classic triad comprises of chronic mucocutaneous candidiasis, hypoparathyroidism and Addison's disease, however other autoimmune manifestations may occur. Autoimmune metaplastic atrophic gastritis (AMAG) and pernicious anaemia occurs in approximately 16% of patients with APECED (1), which may cause impaired calcium absorption (2,3).

Clinical Case: A 23-year-old female with APECED had known clinical manifestations of hypoparathyroidism, adrenal insufficiency, chronic mucocutaneous candidiasis, and premature ovarian failure. In terms of calcium supplementation, she was taking in total six tablets of calcium carbonate and eight tablets of calcitriol daily. She presented to emergency with symptomatic hypocalcaemia with QT prolongation. She had been mostly adherent with her calcium supplements and had no increased gastrointestinal losses. Initial ionised calcium was 0.89 mmol/L (1.13-1.33 mmol/L), corrected calcium was 1.95 mmol/L (2.10-2.60 mmol/L), magnesium was 0.73 mmol/L (0.7-1.10 mmol/L), phosphate was 2.21 mmol/L (0.75-1.50 mmol/L), parathyroid hormone was <0.01 pmol/L (1.5-7.0 pmol/L), 25-OH vitamin D was 100 nmol/L (50-250 nmol/L), and haemoglobin was 131 g/L (120-160 g/L). She had previous multiple similar presentations with symptomatic hypocalcaemia. It was noted that she had vitamin B12 deficiency two years prior despite non-vegetarian diet and had replacement with injections previously. Retesting revealed low vitamin B12 again with holotranscobalamin level of 24.3 pmol/L (>35.0 pmol/L). Consequently, co-existing AMAG was further investigated for and showed positive intrinsic factor antibodies with a level of >480.0 U/mL (>7 U/mL). Alternative calcium supplementation was explored including calcium citrate, which may have superior absorption than calcium carbonate in patients with achlorhydria and atrophic gastric mucosa (3).

Conclusion: Calcium malabsorption should be considered in APECED patients with hypoparathyroidism presenting with recurrent hypocalcaemia. This case highlights AMAG as an important comorbidity to screen for in this population.

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Idiopathic hypercalciuria as a treatable cause of secondary osteoporosis in men

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Background: Osteoporosis is under-recognized in men and the incidence of secondary osteoporosis in men is high, between 50% and 80%. Idiopathic hypercalciuria (IH) is defined by excessive renal calcium excretion and is an important secondary cause of osteoporosis. Treatment of IH-associated osteoporosis with antiresorptive agents does not relieve the underlying pathology and treatment should instead focus on increasing calcium reabsorption via the distal convoluted tubule.

Aim: To increase awareness of IH as a highly treatable cause of secondary osteoporosis.

Methods: Retrospective analysis of three male patients with IH-associated osteoporosis treated with chlorthalidone, a thiazide-like diuretic, over 12-months.

Results: Three men (median age 59, range 48-60) were referred independently to an endocrinology clinic for assessment of osteoporosis and minimal trauma fracture. On baseline DEXA, median lumbar spine and femoral neck BMD were reduced, measuring 0.94 g/cm2 (T-score –2.3 SD) and 0.79 g/cm2 (T-score –2.2 SD) respectively. Baseline bone turnover was elevated based on plasma markers, with median P1NP 60 ug/L (range 45-105) and CTX 660 ng/L (range 504-678). Urine collection over 24-hours on two occasions confirmed hypercalciuria with median calcium excretion 9.2 mmol/day (normal range 2.5-7.5). Chlorthalidone 25 mg daily was prescribed with repeat urine collection performed after 6-weeks of treatment demonstrating normalization of 24-hour urine calcium excretion. On repeat DEXA following 12-months of chlorthalidone treatment, median lumbar spine and femoral neck BMD increased a median 8% (range 6-14) and 3% (range 2-9), respectively with concomitant median reduction in bone turnover marker P1NP by 50% (range 16-53) and CTX by 62% (range 19-68).

Conclusion: All men with unexplained osteoporosis should be screened for IH with a 24-hour urine calcium collection. Treatment of IH-associated osteoporosis with chlorthalidone results in marked improvement in bone density and may avert the need for treatment with potent antiresorptive agents like bisphosphonates or RANKL inhibitors.

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Comparison of the gut microbiome composition of pregnant women with Type 2 Diabetes, gestational diabetes and normoglycaemic controls

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Pregnancy, diabetes, and diabetes medications have been associated with changes to the composition of the gut microbiome. However, it is unclear if pre-existing Type 2 Diabetes (T2D) differentially affects the composition and function of the gut microbiome, in comparison to women with gestational diabetes (GDM) and normoglycaemia in pregnancy. In addition, the effect of metformin treatment on the gut microbiome during pregnancy is unclear.

Faecal samples were collected from women with T2DM (n = 9, metformin: n = 7), GDM (n = 29, metformin: n = 8) and normoglycaemic women (n=58) between 24-36 weeks' gestation as part of three studies conducted in Brisbane, Australia. Metagenomic shotgun sequencing was performed, and the taxonomic and functional profiles were analysed using MetaPhlAn4.0 and HUMAnN3.6. Compositional changes were assessed through alpha and beta diversity, and differential abundance (DA) analysis was conducted using a consensus approach of ALDEx2, ANCOM-BC2, MaAsLin2, LinDA, ZicoSeq and DESeq2 with taxa/pathways only considered significant if 50% of tools identified a significant association. Results were adjusted for study, BMI and ethnicity.

Due to a high proportion of women with T2DM being treated with metformin, the effect of metformin is assessed in women with GDM only. Examining the richness of the microbiome by diabetes status, women with T2DM but not GDM have a borderline significant decrease in richness ($p = 0.05$) compared to normoglycaemic women. Neither diabetes status nor metformin use affected beta diversity. DA analysis using the consensus approach identified increases in pathway PWY-8190: 'L-glutamate degradation XI,' in association with T2DM. There were no DA taxa or pathways associated with GDM or metformin use.

Overall, there were minimal differences in the microbiome associated with T2DM or GDM, or metformin use in pregnancy. Further research in a larger cohort is required to confirm this finding.

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Integrating imaging-based machine learning analyses in high-content screening of prostate cancer organoids

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Background: New treatments are urgently needed for advanced prostate cancer, with organoids established from patient-derived xenografts (PDX; human cancer samples grown in mice), emerging as a promising preclinical model system. While high-throughput drug screening using these 3D cultures can accelerate therapeutic discovery, accurately interpreting organoid responses remains challenging due to their complex morphology and diverse phenotypes. Furthermore, traditional endpoint viability assays provide limited insight into drug effects on organoid structure and behaviour. Machine learning approaches offer new possibilities for extracting and analysing multidimensional features from microscopic images of treated organoids.

Objective: Here, we aimed to develop an image-based high-content screening assay integrated with machine learning methods to enable more sophisticated analyses of drug responses in prostate cancer organoids.

Study design and results: We screened 882 compounds, selected from phase I-IV clinical trials or approved cancer therapeutics, on organoid cultures established from six PDXs of diverse phenotypes of prostate cancer, as well as two cell line-derived spheroid models. Using an automated high-throughput platform, we captured brightfield and Hoechst-stained fluorescent images of treated

organoids at the end of the assay. Our machine learning pipeline extracted morphological and textural features to discriminate between viable and non-viable organoids. This approach successfully identified previously reported drug sensitivities, validating our screening platform, while also revealing novel therapeutic vulnerabilities specific to different prostate cancer phenotypes.

Conclusion: This approach demonstrates the power of combining automated high-content imaging with machine learning analyses in preclinical studies. Our platform presents a valuable advancement for drug screening and discovery, offering enhanced capability to analyse complex organoid phenotypes and drug responses.

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Understanding diabetic kidney disease (DKD), COVID-19 infection, and mitochondrial dysfunction

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The comorbidities of diabetes and COVID-19 have been strongly associated with increased morbidity and mortality. Previous studies have linked both diseases with kidney damage and mitochondrial dysfunction. Considering the importance of mitochondrial dysfunction in both diabetes and COVID-19, we hypothesized that improving mitochondrial function would be an effective treatment strategy for preventing kidney damage when these diseases are present.

To investigate this, male C57Bl6/J mice (n=12-16/group) were assigned to 5 groups: 1) non-diabetic,non-treated,and non-infected; 2) non-diabetic,non-treated,and infected; 3) non-diabetic,treated,and infected; 4) diabetic,non-treated,and infected; and 5) diabetic,treated,and infected. MitoA is an antioxidant compound that has demonstrated potency and efficacy in ameliorating mitochondrial dysfunction in other mitochondrial diseases. Type1 Diabetes was induced in the diabetic groups by 5 daily intraperitoneal injections of low-dose streptozotocin (STZ, 55 mg/kg/day) at 5 weeks of age. Groups that received MitoA treatment were given a daily dose via oral gavage, with control groups receiving saline. At 18 weeks of age, the COVID-infected groups were infected with mouse-adapted strains of the SARS-CoV-2 virus via respiratory injection and monitored daily. When the average body weight of one group decreased by over 20% of the pre-infection body weight, mice from all groups were euthanised.

Post-infection body weight measurements showed that COVID-19 infection significantly decreased body weight, with the group that was diabetic, untreated, and infected being affected most severely. The body weight decrease was significantly reduced in groups receiving MitoA treatment, with or without diabetes.

The infected diabetic group that received daily MitoA treatment showed significantly less overall kidney damage (measured by Glomerular Sclerosis Index) and qualitatively less fibrosis (measured by Sirius Red staining) when compared to the untreated group. MitoA treatment had no noticeable effect on blood glucose control. These results suggest that MitoA may ameliorate some of the effects of diabetes and COVID-19 infection on kidney health.

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Unique pharmacology of a novel G protein-coupled receptor heteromer revealed with bioluminescence resonance energy transfer biosensors.

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Aims: This ongoing PhD project aims to identify and characterise potential preclinical G protein-coupled receptor heteromer candidates as therapeutic targets for chronic inflammation and fibrosis. Chronic inflammation and organ fibrosis underpins much of the morbidity of many common diseases, such as chronic-obstructive pulmonary disease, diabetes, stroke, cirrhosis, heart disease and chronic kidney disease. These diseases cause 18% of all mortality worldwide (1). There is clearly an unmet need in controlling the pathophysiological inflammatory axes of these diseases effectively. G protein-coupled receptors (GPCRs) are prominent targets of existing therapeutics, owing to their cell membrane expression, and profound potential for modulating physiology. Some GPCRs are shown to influence the function of other GPCRs through heteromerisation, presenting new opportunities for pharmacological intervention.

Methods: Our objective is to identify novel GPCR heteromers with Receptor-Heteromer Identification Technology (HIT) and profile their unique pharmacology using a suite of bioluminescence resonance energy transfer (BRET)-based biosensors. Receptor-HIT is a proprietary assay format to identify receptor-receptor proximity. The β-arrestin2 recruitment BRET HIT assay was conducted to screen combinations of GPCRs with relevance to chronic inflammation and fibrosis. From this screen, heteromer candidates proceeded toward pharmacological characterisation using BRET-based biosensors. These include sensors for GPCR intracellular trafficking, G protein activation and second-messenger generation.

Results: The heteromer candidate identified demonstrate unique pharmacology dependent on protomer co-stimulation with endogenous agonists. An asymmetrical perturbance to internalisation was observed upon co-stimulation of protomers with the BRET trafficking sensor. The G protein activation BRET sensor reveals a similar effect on upon co-stimulation, with this effect extending to a complimentary second-messenger BRET sensor.

Conclusions: This project has identified a novel candidate with pharmacology consistent with the criteria to classify it as a putative GPCR heteromer. This candidate will undergo further scientific and commercial validation.

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CLINICAL SIGNIFICANCE OF GPR68 EXPRESSION IN CUTANEOUS MELANOMA

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GPR68 is a proton-sensing G-protein coupled receptor implicated in tumour biology, but its role in human melanoma remains poorly understood. This study aimed to evaluate the clinical significance, prognostic value, and potential functional role of GPR68 expression in cutaneous melanoma. A secondary analysis was conducted using publicly available RNA sequencing and clinical data from 439 melanoma tumours (TCGA-SKCM) and 76 unrelated melanoma cell lines (Sequence Read Archive). GPR68 expression was compared between tumours and cell lines, and assessed for associations with patient demographics, sample type, disease-specific survival, $CD8^+$ T cell abundance, and gene set enrichment pathways. GPR68 expression was significantly higher in melanoma tumours than in melanoma cell lines ($p < 0.001$). Within tumours, expression did not differ significantly by sex, age group, or sample type. Higher GPR68 expression was associated with prolonged disease-specific survival ($p = 0.040$) and increased $CD8^+$ T cell abundance ($p < 0.001$), which remained the only significant predictor in a general linear model including other clinical variables ($p < 0.001$). Gene set enrichment analysis showed that tumours with high GPR68 expression were enriched for immune signalling pathways, while those with low expression were enriched for proliferative and metabolic pathways (FDR $q < 0.05$). These findings suggest that GPR68 expression in melanoma is associated with favourable prognostic features, including tumour immunogenicity and improved survival. Further studies are needed to determine GPR68 cell-type expression and function in melanoma tumours, before its therapeutic relevance can be evaluated.

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Treatment of Endometrial Cancer Cell Lines with Telmisartan and VTP-27999 Reduces Cellular Proliferation and Viability

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Current treatments for endometrial cancer are not always effective, particularly for advanced or recurrent cases, and can have significant side effects. Our *in silico* analysis utilising The Broad Institute Drug Repurposing Hub database identified telmisartan, an angiotensin II type I receptor antagonist, and VTP-27999, a renin inhibitor, as medications that could be repurposed to reduce endometrial cancer cell viability *in vitro*. This study aimed to further examine the effect of telmisartan and VTP-27999 on endometrial cancer cell growth *in vitro*.

Endometrial cancer cell lines Ishikawa (Grade I), HEC1A (Grade II), and AN3CA (Grade III) were treated with 100uM of telmisartan or VTP-27999 (n=3/per cell line) for 48hrs *in vitro*. The SX5 Incucyte Live Cell Imager was used to measure cellular proliferation, cell viability was measured using the MTT assay. Scratch assays and trans-well invasion assays, alongside proteomic investigation, will also be performed.

Ishikawa cell proliferation was significantly reduced by 100uM telmisartan or VTP-27999 after 12hrs (p=0.027 and 0.009, respectively), persisting to 48 hrs of treatment (both p<0.0001). Treatment with 100uM VTP-27999 significantly decreased HEC1A proliferation after 36hrs (p<0.0001), persisting to 48hrs (p<0.0001). Proliferation of HEC1A cells was also decreased at 48hrs with 100uM telmisartan (p=0.003, and p=0.0135, respectively). AN3CA cellular proliferation was significantly decreased with 100uM telmisartan or VTP-27999 treatment for 12hrs (p=0.017, and p=0.005, respectively), continuing to 48hrs (p=0.005 and p=0.011, respectively). Cell viability was significantly decreased in Ishikawa and AN3CA cell lines after 48hr treatment with 100uM telmisartan or VTP-27999 (Ishikawa: p=0.006 and p=0.017, AN3CA: both p<0.0001). HEC1A cell viability did not change with either treatment.

Both telmisartan and VTP-27999 slowed the proliferation of all endometrial cancer cell lines and decreased the cellular viability of Ishikawa and AN3CA cells. Therefore, telmisartan and VTP-27999 show strong potential to be repurposed for endometrial cancer treatment and to improve clinical outcomes.

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Associations of cognition and incident dementia with sex hormone concentrations in men: individual participant data meta-analyses

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Background

Previous cohort studies have associated lower testosterone concentrations with poorer cognitive function, and higher dementia risk, with clinical trials of testosterone providing inconclusive results.

Aims

To clarify whether endogenous concentrations of testosterone, and of other sex hormones, were associated with cognition and incident dementia in men.

Methods

A systematic review was conducted, identifying suitable studies from which individual participant data (IPD) were requested (PROSPERO registration: CRD42019139668). Eligible studies were prospective cohort studies measuring testosterone using mass spectrometry, with at least five years of follow-up data. IPD meta-analysis (IPDMA) models were fitted. Datasets that included both the outcome (baseline cognitive function or time to dementia diagnosis) and exposure (total testosterone [T] or sex hormone-binding globulin [SHBG] concentration) were analysed.

Results

The cross-sectional analysis included 9,741 men, median age 74 years, from 7 cohorts; the longitudinal analysis had IPD for 8,852 men from 5 cohorts (114,168 participant-years follow-up) plus aggregate statistics for an additional study (n=1,463). Harmonised z-scores of global cognition were not associated with T but were non-linearly with SHBG (estimated mean difference [MD] at medians of quintile 1, 26.5 [Q1] vs. quintile 5, 76.9 [Q5] nmol/L; MD, 0.088 [CI, 0.002 to 0.174]). Incident dementia was nonlinearly associated with T (adjusted hazard ratio, HR for Q1 vs Q3, 1.17, [CI 1.02 to 1.34] and with lower SHBG (Q2 vs Q5; adjusted HR, 0.82 [CI 0.70 to 0.96]).

Conclusions

Constraining study eligibility to those that assayed testosterone using mass spectrometry facilitated analyses of high-quality datasets, using multivariable non-linear models. Lower T is a potential biomarker for higher risk, and lower SHBG a potential biomarker for reduced risk of incident dementia in men, warranting further studies to explore potential mechanisms.

Clinical audit of the polycystic ovary syndrome service at Monash Health

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Objective: Polycystic ovary syndrome (PCOS) is the most common endocrinopathy in women of reproductive age (1). This complex disorder presents multisystemic health implications including reproductive, metabolic and mental health disorders. Monash Health established a comprehensive statewide PCOS service in November 2017. This study aims to examine the patients' demographics, PCOS subgroup distribution, and prevalence of metabolic and mental health disorders among women attending the Monash Health PCOS service.

Methods: A retrospective audit was conducted of all patients (n=143) attending the Monash Health PCOS service between January 2024 to June 2024.

Results: 67.4% (n=95) of patients were born in Australia. Mean age was 29.1 (standard deviation [SD] 8.0) years. PCOS subgroup distribution revealed ovulatory dysfunction with hyperandrogenism as most prevalent at 42.9% (n=60). Obesity prevalence was 65.7% (n=92), with mean body mass index of 34.5 (SD 9.8) kg/m^2. 9.8% (n=14) of patients have known history of type 2 diabetes mellitus (T2DM). Screening for T2DM within two years occurred in 77.3% (n=99) of patients without pre-existing T2DM, identifying new onset diabetes in 5.1% (n=5). 9.8% (n=14) of patients have known hypertension. Blood pressure measurement within the past year was documented in 66.2% (n=47) of in-person appointments (n=71), detecting new hypertension in 19.1% (n=9). The prevalence rates of mental health comorbidities were 30.2% (n=43) for anxiety, 28.7% (n=41) for depression and 4.2% (n=6) for eating disorders. General mood screening was documented in 37.9% (n=33) of patients without prior history of anxiety or depression (n=87).

Conclusion: This clinical audit confirms elevated metabolic and mental health comorbidity burden in women with PCOS attending specialised care. Despite established service provision, gaps remain in cardiovascular risk factor and mental health screening. Enhanced systematic screening protocols aligned with evidence-based guidelines are essential to optimise patient outcomes and reduce long-term complications in this high-risk population.

Table 1. Demographics of patients

Demographic	n (%)
Age (n=143)	
Mean ± SD (years)	29.1 ± 8.0
Country of birth (n=141)	
Australia	95 (67.4)
India	12 (8.5)
Philippines	6 (4.3)
Sri Lanka	4 (2.8)
Other	24 (17.0)
Preferred language (n=141)	
English	133 (94.3)
Other	8 (5.7)
SD, standard deviation.	

Table 2. Number (%) of patients with different characteristics of PCOS

PCOS feature	n (%)
Irregular menstrual cycles (n=142)	122 (85.9)
Clinical HA (n=143)	136 (95.1)
Hirsutism (n=140)	119 (85.0)
Acne (n=135)	94 (69.6)
Alopecia (n=128)	59 (46.1)
Biochemical HA (n=136)	60 (44.1)
PCOM (n=115)	70 (60.9)
PCOS subgroups (n=140)	
OD + HA + PCOM	59 (42.1)
OD + HA	60 (42.9)
HA + PCOM	8 (5.7)
OD + PCOM	2 (1.4)
Not meeting diagnostic criteria	11 (7.9)

Table 3. Metabolic complications associated with PCOS

Metabolic complication	n (%)
BMI (n=140)	
Mean ± SD (kg/m^2)	34.5 ± 9
BMI category[a] (n=140)	
Underweight	1 (0.7)
Healthy weight	25 (17.9
Overweight	22 (15.7
Class I obesity	30 (21.4
Class II obesity	26 (18.6
Class III obesity	36 (25.7
Glycaemic status	
History of T2DM[b] (n=143)	14 (9.8)
T2DM screening performed within 2 years[c] (n=128[d])	99 (77.3
New diagnosis of T2DM on screening within 2 years (n=99)	5 (5.1)
Blood pressure	
History of hypertension (n=143)	14 (9.8)
Blood pressure measured within 12 months of in-person appointments (n=71[e])	47 (66.2
New hypertension detected (n=47)	9 (19.1)

BMI, body mass index; PCOS, polycystic ovary syndrome; SD, s
type 2 diabetes mellitus.
[a]BMI category: underweight = BMI <18.5, healthy weight = BMI
BMI 25-29.9, class I obesity = BMI 30-34.9, class II obesity = BM
obesity = BMI ≥40.
[b]Known history of T2DM prior to 2 years before PCOS clinic app
[c]T2DM screening with Hba1c or oral glucose tolerance test perfo

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Does exercise augment the effects of vitamin D supplementation on blood pressure and arterial stiffness? Results from a randomised controlled trial

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Background: We report on the vascular outcomes of a vitamin D and exercise pilot trial in overweight/obese older adults with vitamin D deficiency.

Methods: Fifty individuals {19 (38%) men (median [95%CI] age: 58 [55 to 63] years; BMI 28. 5 [26.9 to 33.4] kg/m2)} with 25-hydroxyvitamin D < 50 nmol/L were randomly allocated to receive either vitamin D3 (4,000 IU/day) or placebo for 24 weeks. Between weeks 12 - 24, all participants completed multimodal exercise while continuing with treatment. Mean changes in systolic (SBP), central SBP (cSBP), diastolic (DBP), central DBP (cDBP) and mean arterial (MAP) blood pressures (in mmHg)), heart rate (HR) as well as pulse wave velocity (PWV) and augmentation index (Aix) at weeks 12 and 24 were compared between groups. Analyses were conducted in the full cohort and in those with good adherence to the programme; and with outliers excluded. Registration: ACTRN12616000563460.

Results: Vitamin D- and exercise-related changes in vascular outcomes did not differ between groups at 12 or 24 weeks. However, vitamin D supplementation alone appeared to (non-significantly) improve SBP [-7.03mmHg (-19.8 to 5.8)], cSBP [-7.38 mmHg (-17.2 to 2.4)], PP [-6.18 mmHg (-15 to 2.7)], HR [-3.84bpm (- 12 to 4.3)] and Aix [-7.02% (-15.3 to 1.3)] but these changes were attenuated with the addition of exercise.

Interpretation: Vitamin D supplementation alone had potentially favourable but small effects on some vascular markers in overweight/obese older adults with vitamin D deficiency, but the addition of exercise appeared to add no further benefit.

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What are the risk factors for diabetic ketoacidosis at first presentation of type 1 diabetes?: an eight-year (2015-2022) audit at an Australian regional hospital

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Background: Few studies have studied risk factors of diabetic ketoacidosis (DKA) at first presentation of type 1 diabetes (T1DM), with inconsistent findings requiring further studies. Family history of T1DM was protective, whilst the effect of pancreatic autoimmunity is uncertain.

Aims: This retrospective study was conducted at Townsville University Hospital to determine whether incidence of DKA at first presentation of T1DM was associated with a) family history of T1DM, b) number or titre of pancreatic autoantibodies.

Method: All patients diagnosed with T1DM between January 2015 and December 2022 were included. Medical data were retrospectively collected, and analysed using SPSS.

Results: 146 patients were studied. Median age was 13 years. 64 patients (43.8%) were female. 78 (53.4%) patients presented with DKA. Median HbA1c for DKA-patients was higher (12.90%) compared to non-DKA-patients (10.80%) (P < 0.001). Among patients with at least 1 relative with T1DM, 19 (36.5%) had DKA (OR: 0.35, CI: 0.17-0.72, P = 0.004). Among those with 1st degree relative with T1DM, 4 (18.2%) had DKA (OR: 0.16, CI: 0.05-0.49, P <0.001). There was no significant difference in DKA risk with number or titre of antibodies.

Conclusion: Our study found that having a first degree relative with T1DM was protective against DKA at first presentation of T1DM. This may be from increased awareness of diabetes symptoms and readily available glucose test kits in the family. Higher HbA1c seen in DKA presentations may reflect longer duration of undiagnosed hyperglycaemia which may relate to familial and health provider awareness of diabetes. Pancreatic autoantibodies were non-contributory. Our study was the first of its kind covering both adult and paediatric cohorts in regional Queensland, Australia.

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Genetic and Clinical Characterisation of Maturity-Onset Diabetes in Young (MODY) in a South Asian Cohort: Findings from a Resource-Limited Setting

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Unlike in Western countries, diagnosis of MODY has been limited in the South Asian region. It is uncertain if this reflects a genuine low prevalence of diagnostic limitations. This study aims to determine the prevalence, clinical characteristics, and genetic profile of individuals with young-onset diabetes in a resource-poor setup.

This cross-sectional study was conducted by recruiting patients with young-onset diabetes with a family history and clinical suspicions of MODY. A targeted next-generation sequencing-based diagnostic test for MODY, including a selected set of syndromic diabetes-associated genes, was designed.

Among 51 patients recruited, 29 (56.9%) were females. These non-obese patients (mean BMI 21.2 ± 4.06 kg/m²) were diagnosed young (mean age 17 ± 5.49 years) with hyperglycemia (mean HbA1C 9.7% ± 3.28). Aligning with diagnostic criteria, the majority of the participants had detectable C-peptide levels (median: 1.97 ng/mL), indicating preserved insulin production. Most had a strong family history, no history of diabetic ketoacidosis, and absent pancreatic autoantibodies. Currently, participants are predominantly on oral medication or a combination of insulin and oral medication, with some achieving glycemic control without any medication. Mutations were detected in 51% (n=26), with the most common being HNF1A, associated with MODY 3 (15.7%), followed by KLF11 (5.9%). GCK, NEUROD1, and PAX4 were detected in 3.4% each. 2 patients had mutations identified as WFS1 (c.1967G>A). 11 patients with an Exeter probability score below 20% had a genetic change associated with MODY, suggesting the tool may have limited predictive value in South Asians.

High incidence of variant detection, including variants of uncertain significance, emphasizes the importance of identification and characterization of genetic heterogeneity in improving treatment outcome and quality of life. Larger population-based studies are warranted to understand the MODY burden in Sri Lanka and the South Asian region.

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Trabecular Bone Score in Lung Transplant Recipients

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Background

Lung transplant recipients are at an increased risk of osteoporosis due to prolonged steroid regimens, and risk factors including smoking, sarcopenia, and chronic inflammation(1,2,3). The poor correlation between fracture risk and bone mineral density (BMD) is particularly evident in steroid associated osteoporosis(4). Trabecular bone score (TBS) is a validated measure of bone microarchitecture that enhances fracture risk prediction when combined with BMD(5,6). TBS was introduced in June 2021 to Alfred Health, the state-wide lung transplant service in Victoria.

Aims

To evaluate the utility of TBS in lung transplant recipients by examining its correlation with BMD, its association with post-transplant fracture incidence, and its impact on fracture risk prediction through TBS-adjusted Fracture Risk Assessment (FRAX).

Methods

This was a retrospective study of patients aged >50 years who underwent lung transplantation from June 2021 to June 2024 at Alfred Health. Data collected from medical records included BMD, TBS, cumulative steroid use, lung function, and osteoporotic fractures.

Results

In our pilot study (n = 54), spine BMD and corresponding T-score improved following transplantation, with the T-score increasing from –1.2 ± 1.7 to –0.95 ± 1.5—shifting from the osteopaenic to the normal bone density range. However, the TBS was unchanged post-transplant, varying only slightly from 1.27 ± 0.1 to 1.24 ± 0.1, remaining within the partially degraded bone category (TBS 1.2–1.35). We aim to further investigate this observed divergence between BMD and TBS in our ongoing expanded study of 104 participants (64 ± 6 years, 67% male). We will present these findings including correlation of baseline TBS and post lung transplant fractures, and correlation between FRAX, TBS-adjusted FRAX and post lung transplant fractures.

Conclusion

This study will provide insights into the utility of TBS and its clinical implications for managing osteoporosis in the lung transplant population.

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Effects of myocyte-specific deletion of vitamin D receptor on muscle function and structure in notexin-injected mice

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Aim: This research explores how myocyte-specific deletion of the vitamin D receptor (mVDR) affects skeletal muscle function, structure, and regenerative capacity following induced injury.

Methods: Male mVDR mice (n = 15) were generated by crossing floxed vitamin D receptor (VDR) mice with human skeletal actin-Cre mice, and their male floxed littermates were used as controls (n = 13). Muscle injury was induced by intramuscular injection of 25 µg/kg Notexin into the right tibialis anterior (TA), with saline injected contralaterally as control. Body weight, grip strength, treadmill endurance, and voluntary wheel-running were assessed. TA and quadriceps were collected for histological analysis.

Results: Body weight, endurance capacity, and voluntary running activity did not differ significantly between mVDR and floxed controls (FC). Grip strength was significantly reduced in mVDR mice 26 days post-notexin injury (~6.5% decrease; $p < 0.01$) compared to FC. TA weight was 25% lower following injury in mVDR relative to their own saline-treated limb ($p = 0.045$), but remained 18% heavier than injured FC. Hematoxylin & eosin staining of mVDR notexin-treated muscles revealed a marked increase in centralised nuclei (43.4% mVDR vs. 20.7% FC) and slightly greater cross-sectional diameter of myofibres (27.49 µm mVDR vs 26.18 µm FC), as well as prominent signs of inflammation, angulated fibres, and adipocyte infiltration. Sirius Red staining demonstrated enhanced collagen deposition in mVDR muscles (7.7% mVDR vs. 4.8% FC), indicating increased fibrosis.

Conclusion: Myocyte VDR deletion alters skeletal muscle regeneration following injury. Further investigation of gene expression profiles and muscle fibre-type composition is needed to elucidate the underlying molecular mechanisms.

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Metformin exposure during pregnancy and lactation affects milk lipid composition in a healthy nondiabetic mouse model

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Lactation is a critical window for offspring development. Changes in milk composition, particularly milk lipids, can have short- and long-term effects on infant growth and development. Metformin, a commonly prescribed medication used in the treatment of gestational diabetes and other pregnancy complications, is known to affect plasma lipid metabolism. However, its possible effect on breastmilk lipids is unknown. Therefore, this study aimed to examine the effect of metformin on milk lipid composition and mammary gland lipid-related gene expression, using a mouse model.

From embryonic day 0.5 until postnatal day (PND) 13, healthy, non-diabetic C57Bl/6 mice received drinking water containing 5 g/L of metformin or control (untreated) drinking water. Milk was collected at PND13 to perform targeted lipidomics using liquid chromatography-mass spectrometry. Mammary glands were also collected from subsets of dams at PND0 and PND13 to determine the expression of genes involved in lipid synthesis and metabolism.

Lipidomics analysis quantified 583 lipid species, from 32 lipid classes. Compared to the control group, there were 282 lipids significantly altered in the metformin group, with 29.4% of lipids increased and 70.6% of lipids decreased (p-value<0.05). Lipid set enrichment analysis showed that the metformin-treated mice had decreased sphingolipids, glycerophospholipids, ether lipids, plasmalogens, and alkyl lipids in their milk, compared to the control mice. Additionally, mammary gland expressions of *Srebf1*, *Elovl1*, *Fasn*, *Scd1*, and *Fads1* were lower in metformin-treated dams at PND0 but not PND13.

Metformin exposure during pregnancy and lactation in a healthy mouse significantly affects milk lipid composition and related mammary gland gene expression. These altered lipids and lipid-regulating genes have known functions in brain and immune system

development, cell membrane function, and serve as a source of energy. Further research is required to determine how these changes in milk composition and mammary gland gene expression affect offspring development.

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Antenatal exposure to intraamniotic ciclesonide matures the preterm sheep lung

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Background: Antenatal corticosteroids (ACS) stimulate lung maturation, reducing risks of respiratory diseases and death for preterm babies, but also impact brain development and later function. We are therefore investigating whether ciclesonide, a glucocorticoid prodrug with tissue-specific activation, can stimulate lung maturation without impacting the preterm sheep brain. As the placenta also expresses activating enzymes, we have evaluated functional and molecular outcomes after intraamniotic administration of ciclesonide to bypass placental activation.

Methods: Twin-bearing pregnant ewes were randomised to antenatal treatment with ciclesonide (0.5, 1 or 2 mg/kg estimated fetal weight) 48 h before delivery. Maternal and fetal plasma samples were collected at pre, 1, 2, 4, 24 and 48 h after intraamniotic ciclesonide administration and concentrations of the active form, des-ciclesonide, were measured using established LC-MS/MS assays. Lambs (4-5/group) were delivered preterm by C-section at ~130 gestational days (term ~150d), ventilated for 60 minutes with volume guarantee (target volume 7 ml/kg, $ETCO_2$ 45-50 mmHg), then humanely killed for tissue collection. Expression of glucocorticoid responsive genes was measured in the lung (lower right lobe) and brain (prefrontal cortex and hippocampus); molecular and structural indices of lung maturation were also determined. Data was analysed by two-way repeated measures ANOVA with $P<0.05$ considered statistically significant.

Results: Following intraamniotic ciclesonide administration, des-ciclesonide was rapidly detected in plasma of treated lambs, with limited transfer to maternal circulation, and no transfer to the untreated twin except at 2mg/kg. Dynamic lung compliance was higher in treated than untreated twins ($P=0.033$), which coincided with lower *PER1* and *SCNN1G* expression ($P=0.019$ and $P=0.018$, respectively), and higher *AQP5* expression ($P=0.031$). Expression of glucocorticoid responsive genes in the prefrontal cortex and hippocampus was similar in treated and untreated twins.

Conclusions: Intrauterine des-ciclesonide exposure matures the preterm lung without activating glucocorticoid-mediated signalling in the brain in this clinically-relevant sheep model of preterm birth.

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Native corticosteroid-binding globulin to treat life-threatening sepsis and septic shock.

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Septic shock carries high mortality, with one-third of patients exhibiting depletion of the corticosteroid carrier, corticosteroid-binding globulin (CBG), which predicts a threefold increase in mortality. We investigated CBG replacement therapy in a precision murine model of polymicrobial sepsis, addressing the urgent need for novel ICU interventions

Male C57BL/6 mice (N=106, 8-10 weeks old) were pre-fitted with wireless arterial telemetry and then underwent cecal ligation and puncture (CLP) with dual 21g puncture and 18mm cecal ligation. Mice were randomised to postoperative support with or without intravenous CBG therapy (3.5 mg/kg at 6 hrs, 2.5 mg/kg at 30 hrs) and monitored every 8 hrs. Terminal bloods were collected at humane endpoints or 4 days.

CLP induced circulatory shock in all mice, progressing to septic shock by 39 hrs with 58% mortality at 4 days; marked increases in immune and organ damage biomarkers indicated multiple organ failure. Intravenous CBG therapy shortened circulatory shock duration

by 75%, improved survival threefold (to 17% mortality), suppressed the pro-inflammatory cytokine peak (45-59%), reduced systemic and organ damage biomarkers, and augmented anti-inflammatory IL-10 and IFN-β1 responses to 4 days.
We have mapped the progression of septic shock in a precise murine model, demonstrating significant benefits of CBG therapy on disease, morbidity, and mortality. Our findings advocate for a Phase I trial of CBG therapy in septic shock patients.

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SIRT1 overexpression in female mice results in an increase in blastocyst cell numbers following IVF

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Aims: Sirtuins are a class of NAD-dependent deacetylases that have been implicated in regulating longevity and oxidative stress, with SIRT1 being of interest in regulating oocyte quality[1, 2]. The success of IVF treatment is correlated with female age and related oxidative stress. This study aimed to (1) investigate the ability for SIRT1 overexpression in mice to protect oocytes against oxidative stress and (2) evaluate the impact of SIRT1 overexpression on IVF embryo development.

Methods: Oocytes were collected from 4–7 week-old $SIRT1^{super}$ hemizygous overexpression ($SIRT1^{super}$) and wild type mice following superovulation. Total oocyte numbers and stages were recorded in response to superovulation. IVF was conducted with wild type sperm and resulting embryos were cultured for 4.5 days. The impact of SIRT1 overexpression on embryo development and quality was analysed using H_2DCFDA to measure reactive oxygen species (ROS) production in untreated and 25μM hydrogen peroxide (H_2O_2) treated embryos at 8-cell/morula stage. Differential nuclear staining was performed to assess cell allocation in blastocysts.

Results: Blastocysts derived from $SIRT1^{super}$ mice had significantly more cells in their trophectoderm (87.87±3.0 vs 97.69±2.5, $P<0.05$; $n>60$) and total blastocyst cell number (112.4±3.0 vs 123.6±2.7, $P<0.01$; $n>60$) compared to wild type embryos. No difference in fertilisation, 2-cell or blastocyst rates and in the total number of oocytes ovulated per mouse was determined, however $SIRT1^{super}$ mice ovulated fewer mature MII oocytes (78.12±3.9 vs 67.85±3.5, $P<0.05$; $n=8$ biological replicates). There was no significant difference in intracellular ROS between $SIRT1^{super}$ and wildtype embryos. However, a trend towards decreased sensitivity to H_2O_2 was observed for $SIRT1^{super}$ embryos, suggesting further experiments are needed to understand this response.

Conclusion: $SIRT1^{super}$ mice produce blastocysts with significantly higher cell numbers compared to wild type. They do however, ovulate fewer mature oocytes following superovulation. These data suggest that modulating SIRT1 is beneficial in improving IVF embryo quality.

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A Systematic Review Evaluating the Efficacy of Digital Interventions Versus Standard Care in Enhancing Fertility Outcomes for Individuals Trying to Conceive

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Poor fertility-related outcomes are a severe challenge facing every healthcare system in the world. There is a growing pool of specialised digital health interventions aimed at helping individuals or couples to digest obstetric information and maintain a healthy pregnancy. However, the relationship between these digital health interventions and key reproductive outcomes, including improved conception rates, greater glycaemic and weight control and access to obstetric care, has not been systematically reviewed. Therefore, we aimed to clarify relationships between digital interventions and improving fertility outcomes through a systematic review.

A systematic review of all studies investigating associations between digital health interventions (smartphone applications, telehealth and menstruation tracking devices) and fertility outcomes (live births, conception time) in adults was conducted. Relevant randomised controlled trials (RCT) published before 3 March 2025 were identified by searching six databases (MEDLINE®, Embase, CINAHL®, Scopus and PsycInfo), and citation and reference list checking. Cochrane Risk of Bias tool for RCT assessed the risk of bias of included studies.

Twenty studies were included. The most frequently evaluated digital intervention was telehealth, followed by social and online media, and menstruation tracking applications. Telehealth demonstrated the greatest impact on improving glycaemic control among women with gestational diabetes (n=11). Social and online media interventions enhanced utilisation of local obstetric services and were associated with a higher probability of live birth compared to non-users (n=7). The use of menstruation tracking applications was positively associated with an increased likelihood of achieving pregnancy relative to non-use (n=2).

Digital interventions, particularly telehealth, show promise in improving glycaemic control in gestational diabetes, while social media and menstruation tracking applications may enhance reproductive outcomes. Future studies should examine the degree digital interventions improve fertility outcomes alone or combined with individualised coaching. These findings support the integration of digital health strategies in reproductive care to optimise patient-centred outcomes.

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Association between Menstrual Cycle Irregularity and Cancer Prevalence in Young Women

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Publish consent withheld

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FSH receptor targeting for selective liposomal delivery to ovarian cancer cells

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Advancing advocacy in reproductive health through education and industry partnership

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Social media is a powerful platform for the dissemination and distortion of scientific information, making the ability to communicate evidence-based knowledge clearly and responsibly a critical graduate capability in the health and biomedical sciences. Through a 4-year-long partnership, advocacy group Reproductive Health Australia (RHA) and the Graduate Diploma of Reproductive Sciences aimed to develop students' capacity to engage meaningfully with the public and advocate for reproductive health through the production of online campaigns.

The initiative challenged students to design public-facing social media campaigns on topical issues in reproductive health, including plastics and fertility, preconception wellbeing, men's health and unpacking the scientific basis of popular fertility aids or apps. Campaigns demonstrating clear, evidence-based messaging had the opportunity to be published on RHA's platforms, offering real-world visibility and engagement with the community.

The collaboration has produced measurable outcomes for both students and RHA. Students reported increased confidence in communicating complex concepts, a greater understanding of scientists' roles in public discourse, and a motivation to pursue advocacy in future careers. Student-led campaigns resulted in increased engagement across RHA's online platforms while generating diverse, on-brand content that would otherwise require significant time and resources. Beyond the assessment task itself, several course alumni have since volunteered with or are employed by RHA. The enduring engagement between course alumni and RHA has

enabled ongoing mentorship for junior reproductive scientists, as well as strengthening connections within a national network of like-minded advocates for reproductive research.

This model of collaboration offers a practical and scalable approach to embedding industry partnerships into teaching and learning. By connecting students with real-world issues and audiences, we have supported the development of essential graduate capabilities in science communication and advocacy, while creating meaningful public engagement with reproductive health and research.

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An evaluation of the quality of recommendations for polycystic ovarian syndrome provided by generative artificial intelligence

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Polycystic Ovarian Syndrome (PCOS) is an endocrine disorder affecting 5-15% females (1). It is a heterogeneous disease, with each woman's symptomology being vastly different. (2-5). Consequently, diagnosis is delayed and treatment difficult to find, so women self-manage their condition, seeking information from sources such as ChatGPT (2-3). There is, however, little data on the accuracy of evidence about PCOS (6-7). This study, therefore aims to assess the quality of recommendations provided by ChatGPT for PCOS management.

Common PCOS questions were gathered from various social media platforms. Meetings with PCOS and fertility experts were conducted where questions were verified. The questions were then categorised into groups using NVivo. The questions were typed into ChatGPT using a non-institutional email in a new conversation each time. After 14-21 days, questions were re-queried by another reviewer. The accuracy of the answers was then analysed by comparing its recommendations to PCOS guidelines. 6-point and 3-point likert scales were used to assess the accuracy and completeness of answers, respectively.

Across all questions (n=36), the mean accuracy score was 4.2 and the mean completeness score was 1.8. All questions were re-queried and re-graded approximately 14-21 days later with a mean accuracy score of 4.4 and mean completeness score of 2.5. The scores differed between reviewers because ChatGPT is constantly evolving to provide more accurate information. However, there were limitations, including providing outdated and wrong advice and not using clinical guidelines as an information source. Answers to many of the questions were also the same, highlighting the lack of creativity of ChatGPT.

ChatGPT generated mostly accurate and complete answers to a range of questions regarding PCOS, although with some limitations. ChatGPT may be improved by including its references in its responses. It would also benefit from more robust training where it utilises information from credible, evidence-based sources.

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Dysbiosis and antimicrobial peptide/protein dysregulation in reproductive biofluids of endometriosis patients

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Endometriosis is a debilitating, incurable disease that significantly impacts quality of life, yet the cause remains unknown[1]. Emerging research has provided evidence of an association between endometriosis and uterine dysbiosis[2-4]. Endogenous antimicrobial peptides and proteins (AMPs) within the female reproductive tract (FTR) act as a first line of defence against pathogens[5]. In this study, we aim to assess the presence of three pathogens associated with endometriosis and the dysregulation of AMPs in reproductive biofluids.

Uterine (UF) and peritoneal (PF) fluids were collected using sterile technique from women diagnosed with (n=25) and without endometriosis (n=14). Biofluids were centrifuged to isolate the pellet and supernatant. Genomic DNA was extracted from the pellet, and levels of *Fusobacterium nucleatum*, *Mycoplasma genitalium* and *Erysipelothrix* were quantified and normalised against Eubacteria 16S rRNA, via RT-PCR. The PCR product was visualised using gel electrophoresis. The concentration of AMPs; α-defensin 1, hepcidin and Trappin-2 was quantified using ELISA. Mann-Whitney test was used to determine statistical differences between the groups.

Bacteria were detected in all UF and PF from the control and endo groups, supporting the presence of microbes in the FRT. *F. nucleatum was* identified in UF in 44% (11/25) of endometriosis patients but was also detected in 21% (3/14) of control participants who had symptoms associated with endometriosis (infertility and dysmenorrhea), although not diagnosed with endometriosis. *F. nucleatum* was not detected in PF of either group. α-defensin 1 and hepcidin were abundant in the uterine fluid, with increased concentration in the menstrual phase. Although not significant, they were less abundant in the endometriosis group compared to the control group. Trappin-2 also showed a similar pattern among the two groups over different phases of the menstrual cycle.

Our data supports the association of microbes in endometriosis and that uterine dysbiosis may be associated with dysregulation of AMPs.

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Comparative development of human 1PN and 3PN day 5 blastocysts cultured in Global® and synthetic SafeIVF® media

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The aim of this study is to elucidate the impact of the presence or absence of serum proteins in two embryo culture media (ECM) on the quality of blastocysts generated from 1PN and 3PN human embryos.

The media used were the synthetic protein-free SafeIVF® (SM, Malaysia) and Global® protein-containing (GM, USA) media. The proportions and qualities of day 5 blastocysts generated were statistically compared using the modified statistics-enabled blastocyst grading method (1).

The blastocysts generated from 1PN and 3PN embryos in both media were statistically similar (Table 1).

Table 1: Comparison of development of 1PNand 3PN blastocysts in Global® and SafeIVF® media

Description	Global medium (%)	SafeIVF medium (%)	Significance
% Development of total blastulation (i.e: Cavitated Morula/Early Blasts/Blastocysts)	72/110 (65.6%)	72/110 (65.6%)	p=1.000; NS
% Development of day 5 blastocysts only	46/110 (41.8%)	45/110 (40.9%)	p=1.000; NS
% Development of Early blastocysts only	26/110 (23.6%)	27/110 (24.5%)	p=1.000; NS

Cumulative score for total blastulation (Blastocoel expansion (or Volume)+ICM+Trophectoderm) Key: 12=Excellent; 9=Good; 6=average; 3=poor	9.6	9.8	p=0.2649; NS
Summarized grade score (V+ICM+Trophect) (Grading:4=Excellent; 3=good; 2+ average; 1=poor)	3.2	3.3	p=0.2601;NS

The present study has demonstrated that the synthetic SafeIVF® protein-free medium is comparable in efficacy to contemporary protein-containing ECM (GM®) with reference to proportions and qualities of blastocysts generated. Previous studies with cleavage stage embryos generated in synthetic safeIVF medium has resulted in clinical pregnancy rates of about 50% with live births (2) similar to or better than protein-containing medium. The use of synthetic medium in therapeutic human IVF procedures will eliminate the potential for transmission of disease and harmful donor proteins, prevent batch-to-batch variation in ECM quality, allow longer shelf life and preserve the genetic constitution of the embryo.

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Nuclear dimensions correlate with developmental stage and cell lineage in early mouse embryos

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Nuclear dimensions have been proven to be an important indicator of cellular health and nuclear shape-changes are often associated with pathological processes. However, there is still little known about the typical development of nuclear morphology over early mammalian embryonic stages. Here, we have investigated changes in the shape and size of mouse embryo nuclei from 8 cell stage to the developmental day E5.5. We concluded that nuclear size generally decreases until the 128-cell stage, before increasing at E5.5, and the nuclei also follow a general trend of increasing ellipticity over this period. We also found that there were significant differences in nuclear dimensions between nuclei of different lineages from the 32-cell stage onwards, opening the possibility to use nuclear shape and size as non-invasive assessment of lineage formation in mammalian embryos.

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Investigating the effects of hyperthermia on male germ cell precursors

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RepeatSeeker – A tool for characterising transposable element-driven transcripts with long-read sequencing.

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Transposable elements (TEs), including LINEs, SINEs, and long terminal repeats (LTRs), constitute a substantial portion of the eukaryotic genome. TEs can function as cis-regulatory elements, serving as alternative promoters to regulate tissue-specific gene expression. However, comprehensive characterisation of TE-driven transcripts remains a major challenge due to the repetitive and complex nature of these elements, especially when using short-read sequencing technologies. To overcome these limitations, we developed RepeatSeeker, a Python-based tool designed to identify and annotate TE-driven transcripts using long-read sequencing platforms. RepeatSeeker integrates aligned reads, gene annotations, and repeat element annotations to detect repeat-exon overlaps at single-transcript resolution. To further explore the biological insights into TE-driven transcripts, we also developed downstream analytical pipelines: (i) to assign epigenetic states such as DNA methylation to individual TE-driven transcripts, and (ii) to perform CDS

analysis to assess the coding potential of TE-driven transcripts. As a benchmark, we first analysed published PacBio mouse oocyte data [1]. RepeatSeeker successfully verified that the majority of TE-driven transcription in mouse oocytes originates from MaLR-ERVL-type LTRs. By integrating DNA methylation data, we further characterised their methylation profiles at single-transcript resolution and confirmed that these LTRs are predominantly unmethylated in mouse oocytes. This demonstrates the accuracy and utility of RepeatSeeker in analysing TE-driven transcripts. We then hypothesised that TE-driven transcripts contribute to both transcriptomic and proteomic diversity. To address this hypothesis, we applied the CDS analysis pipeline to our Oxford nanopore datasets of the mouse placental transcriptome. The results indicated that most LTR-derived transcripts in mouse placenta encode proteins with peptide sequences different from those of their associated (host) genes. This suggests that TE-driven transcription not only increases transcriptomic diversity but may also expand diversity of the proteome.

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The marsupial imprinted gene *MLH1* has several marsupial retrocopies

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The mut-L homologue 1 gene (*MLH1*) is a DNA repair gene and has a key role in tumour-suppression in mammals. Genomic imprinting results in parent-of-origin-specific gene expression and has been identified in marsupials and eutherians. *MLH1* is imprinted in the brushtail possum [1] and koala [2] and appears to be a marsupial-specific imprinted gene. Allele-specific methylation in the tammar wallaby indicated that *MLH1* was maternally methylated in pouch young tissue. In kidney, liver, spleen and brain, the maternal *MLH1* allele was completely silenced. In late term yolk sac placenta, the maternal *MLH1* allele was methylated but incompletely silenced.

Expression analysis of the chromosome 3 *MLH1* identified a second *MLH1* site on chromosome 6. Alignment of the *MLH1* transcript sequence indicated this second site was an intronless retrocopy, formed through the *MLH1* mRNA incorporating into the genome. Assessment of marsupial reference genomes identified an orthologous *MLH1* retrocopy in two macropodids and an additional two non-orthologous *MLH1* retrocopies in the bilby and marsupial mole. Partial *MLH1* retrocopies were identified in 9 out of 23 other marsupial genomes examined. The tammar, bilby and marsupial mole *MLH1* retrocopy loci had an intact open reading frame. Analysis of transcriptomes and cDNA indicated transcripts were expressed from both the tammar and bilby retrocopy loci. Aligning the predicted protein sequences from the parental and retrocopy MLH1 indicated the retrocopy protein may have a comparable function to the parental MLH1 protein.

A transcriptionally active *MLH1* retrocopy has previously been identified in the common marmoset [3], indicating there are at least four functional *MLH1* retrocopies across mammalian lineages. This second site of *MLH1* expression may introduce a redundancy to *MLH1* expression and in marsupials, compensate for the reduced gene expression which results from silencing of the maternal allele of the parental *MLH1*.

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Within-individual variation in peripheral blood regulatory T cells number and phenotypes across menstrual cycles in women

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Regulatory T (Treg) cells play a critical role in orchestrating maternal immune tolerance, allowing pregnancy success. Deficiency in Treg cell abundance and/or function is implicated in reproductive and pregnancy complications, including recurrent pregnancy loss (RPL). No definitive diagnostic exists to identify and characterise immune dysfunction in RPL patients, consequently treatment interventions including immunotherapies cannot be matched to patient subtypes.

We are developing a flow cytometry-based diagnostic test to identify T cell-based immune dysregulation in RPL patients using peripheral blood immune cells. A key knowledge gap is to quantify the temporal within-individual variation in abundance and phenotype of peripheral blood T cells in women. Hence, this pilot study aims to determine within-individual variation in T cell populations collected from healthy reproductive-aged women (n=15) during the mid-luteal phase of the menstrual cycle.

Medical and reproductive history were recorded, and blood samples collected over three menstrual cycles within a 3-6 month period. Leukocytes were isolated by density gradient centrifugation and analysed by 15-colour multi-parameter flow cytometry to identify T

cells subsets and characterise Treg cell phenotype. The mean coefficient of variation (CV) was calculated for each T cell parameter to determine the degree of within-individual variability.

Treg cell abundance and expression of key phenotypic markers, including CTLA4 (CV=2.4%), Helios (CV=1.3%) and FOXP3 MFI (CV=10.1%) varied little within an individual over time. Within memory Treg cell subsets, there was little variation in central memory Treg cells (CV=11.8%) and naïve Treg cells (CV=8.9%). However, RORγt and Tbet expression varied moderately (CV=31.3% and 21.6% respectively).

These results indicate low within-individual variation in Treg cell abundance and phenotype over time, raising the prospect that a single blood draw will be broadly informative for T cell parameters relevant to RPL risk. The findings of this study will govern the development of protocols for immune-phenotyping diagnostics in RPL.

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Impact of temperature and incubation in 6%CO_2 in air on testicular sperm motility. Part 1: TESA sperm

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This work aims to ascertain the usefulness of incubating overnight TESA spermatozoa (TS) in HEPES-buffered flushing medium (FM) at 37°C in the gaseous phase (6% CO_2 in air).

After maceration in FM, the testicular tissue was divided into four equal portions for individual treatments (Tx). The suspensions are held overnight at either room temperature (RT) or 37°C with or without incubation gas (6% CO_2 in air) as follows: (i) without CO_2@RT; (ii) without CO_2@37°C; (iii) with CO_2@RT; with CO_2@37°C. The tubes are capped tightly with incubation gases sealed within the tube, and kept at RT or 37°C (in the incubator) overnight. Statistical analyses performed were Chi-square, Pearson's correlation studies, paired-T test, and two-by-two tables.

A significant proportion of TS (21.4% vs 5.3%, $p<0.001$) became motile after Tx's, indicating that physiological temperature (37 °C) and physiological pH (attained by overnight incubation in 6%CO_2 in air) induced motility in and retained the viability of the TS. The differences between Tx's were statistically highly significant ($p<0.001$), indicating the critical impact of both physiological temperature and physiological pH on TS viability and motility induction. There was a significant strong interaction ($p=0.0000$) between Tx's and positive correlations between the Tx's ($p<0.001$; highly significant).

Physiological temperature and pH appear critical for retaining the viability of and for initiating motility in TS. It is safer to induce motility with physiological temperature and pH than with embryotoxic pentoxyfylline or theophylline. When exposed to ambient temperature and air, the HEPES medium drifted toward the alkaline phase, making it less dependable for sustaining physiological pH levels between 7.3 and 7.4 for prolonged periods of time, particularly when there was no CO_2 incubation gas present. In conclusion, physiological temperature and pH is critical to maintain the motility/viability of TS. HEPES medium must be equilibrated in 6%CO_2 in air to maintain pH.

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Potential Role of Guayusa to Alleviate Inflammation in Mouse Leydig Cells

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Male factors are estimated to account for about 50% of infertility cases, and testicular inflammation is considered one of the main issues. Reducing inflammation in the testis can restore testis/sperm function. Based on this, we considered whether a safe, plant-based compound could be applied to reduce inflammation and related infertility. We focused on guayusa (*Ilex guayusa* Loes;), a tea leaf native to South America, which has anti-inflammatory properties. This study investigated its effects on the secretion of pro-inflammatory cytokines on a testis-derived Leydig cell line.

Mouse Leydig tumour cells (I-10) were treated with guayusa extracts, followed 1 h later by nigericin to induce inflammatory response. After 3 h, supernatants were collected, and levels of inflammatory cytokines such as interleukin-1β (IL-1β) and interleukin-6 (IL-6) were measured. Lactate dehydrogenase (LDH), a cell death marker, was measured. Treating with nigericin increased IL-1β, IL-6 and LDH secretion, all of which were reduced by guayusa treatment. Since nigericin is known as an activator of the NLRP3 inflammasome, the inhibitors of NLRP3 inflammasome including glibenclamide (ATP-sensitive potassium channel), MCC950 (NLRP3 inhibitor) and AC-YVAD-cmk (caspase-1 inhibitor), were treated simultaneously with guayusa. While no significant changes were observed with MCC950 and AC-YVAD-cmk, treatment with glibenclamide tended to decrease IL-1β secretion and significantly reduced IL-6 secretion. To investigate the cytokine-suppressive mechanism of guayusa, we measured the protein expression of Gasdermin D

(GSDMD), which controlling cell death by creating holes in the cell membrane. Treatment with guayusa significantly reduced GSDMD protein compared to treatment with nigericin alone. Consistently, treatment with necrosulfonamide (NSA), a GSDMD and MLKL phosphorylation inhibitor, resulted in decreased secretion of IL-1β and IL-6.

These findings suggest that the inhibitory effect of guayusa for IL-1β and IL-6 reduction induced by nigericin may be meditated through potassium ion channels and GSDMD rather than via the NLRP3 inflammasome system.

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Urogenital defects in live births to women dispensed clomiphene citrate: A study within a whole of population birth cohort.

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Abstract

The impact of environmental endocrine disruptors on urogenital anomalies has been reported in numerous species. However, quantifying robust models in humans is difficult due to the lack of precision on exposures and time precedence.

We address these issues by reporting on the therapeutic administration of a selective estrogen receptor modulator (SERM), clomiphene citrate, for the treatment of sub-fertility and the subsequent occurrence of urogenital defects in children born after a defined periconceptional exposure window.

We employed a population-based cohort study of South Australia by linking all records from the state-wide perinatal registry for births between July 2003 and December 2011, including defects coded to ICD9 and BPA, with Commonwealth government data on pharmaceutical dispensing in the national Pharmaceutical Benefits Scheme (PBS), which includes individual level prescribing and dispensing of drugs for ovulation induction, including clomiphene citrate (CC).

De-identified pregnancy outcome data for all births in South Australia were linked to individual level national prescription data to examine the prevalence of urogenital birth defects (>20 weeks gestation) for births occurring between July 2003 and December 2011 following clomiphene citrate dispensing, with 5-years follow-up for defect notifications. Multivariate analysis in STATA within a Secure Unified Research Environment (SURE) was used to calculate odds ratios, adjusted for maternal confounders and socioeconomic circumstance. The analysis was restricted to singleton births.

Following CC exposure proximal to conception, the risk of urogenital defects was elevated in singletons (OR = **1.66, CI=1.28 -, 2.15)** and approximately doubled in male babies **1.92 (1.47, 2.52)**, with no substantial effect in females.

The sex-specific effect is consistent with a causal role for clomiphene citrate. The apparent absence of effect in females is not reassuring as clomiphene citrate is known to cause reproductive anomalies in females, which may may need decades for their full expression.

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Backgrounds on miRNA synthesis and secretion in bovine follicular fluid

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Aims: MicroRNAs(miRNAs) are present extracellular vesicles (EV) in the follicular fluid (FF) and play a role in oocyte and early embryonic development. We identified several miRNAs in the FFs (miR-148a, miR-151-5p, miR-199a-3p, miR-29b, and miR-425-5p) that play essential roles in proper embryonic development and DNA demethylation. However, the molecular mechanism underlying miRNA synthesis in granulosa cells (GCs) and miRNA secretion from GCs into FFs remain unclear.

Methods: FFs and GCs were collected from small antral follicles (3-5 mm in diameter) of ovaries derived from 10 individual cows. The frequency of miRNAs in FFs and GCs was determined using small RNAseq. In addition, the mRNAs in the corresponding GCs were subjected to RNAseq. Frequency of miRNAs compared between FFs and the corresponding GCs. Correlations between pairs of miRNAs within 10 FFs or 10 GCs samples were calculated. Ten FFs and GCs samples were rated based on the frequency of each miRNA and divided into the top 3 rich and bottom 3 poor samples to obtain differentially expressed genes (DEGs) using RNAseq data. The top upstream regulators and Kyoto Encyclopedia Genes and Gnome pathways of the DEGs for each miRNA were predicted using Ingenuity Pathway Analysis and DAVID functional annotation, respectively.

Results and conclusion: A total of 352 miRNAs were detected in FF samples and 304 miRNAs in GCs samples. Only nine miRNAs were correlated between GCs and FFs, indicating a selective secretion mechanism. In addition, we found that groups of miRNAs were significantly correlated in both FFs and GCs. The FF data is useful for predicting the miRNA secretion mechanism, and those of GCs are useful for exploring miRNA synthesis mechanisms. In addition, upstream regulators and KEGG pathways associated with high expression levels of each miRNA were predicted, which could help determine key factors regulating follicular conditions.

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Effect of treatment with ursodeoxycholic acid *vs.* rifampicin on the composition of the gut microbiota in women with intrahepatic cholestasis of pregnancy

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Intrahepatic cholestasis of pregnancy (ICP) is characterised by increased maternal serum total bile acids (TBA) and symptoms, including pruritus, in women without known active liver disease. In severe ICP with TBA ≥100 mmol/L, risks of stillbirth are increased. The gut microbiome is an important regulator of BA metabolism through the conversion of primary BA into secondary BA, which can signal through the TGR5 receptor. Standard treatment for ICP is ursodeoxycholic acid (UCDA) but this is not always effective. The TURRIFIC trial is an RCT comparing the effects of UCDA with rifampicin (RIF), an antibiotic with capacity to reduce TBA outside of pregnancy. In TURRIFIC, stool samples are collected throughout pregnancy for analysis of the gut microbiome.

We compared the effect of treatment with UCDA against RIF on the composition of the gut microbiome in 13 women with ICP, 5 of whom were treated with UCDA and 8 with RIF. We conducted metagenomic sequencing at 3 GB depth. Sequencing data was analysed with the MetaPhlAn pipeline for taxonomy and HuMaN3 for function. Differential abundance was determined using MaAsLin2 and adjusted for multiple testing.

Interindividual variability was extensive. Treatment with RIF significantly reduced alpha diversity in both taxonomic and functional analyses, whereas beta diversity was altered only at the taxonomic level. RIF treatment decreased the abundance of *Ruminococcus bromii, Romboutsia* and *Candidatus_Cibionibacter* compared with that of UCDA-treated or untreated ICP. There were, however, no significant changes to the functional pathways or to antibiotic-resistance gene abundance in the microbiomes between the groups.

The results of this study show that, in this small cohort, there was no major effect on the composition of the gut microbiome or on antibiotic-resistance gene carriage in response to treatment of women with ICP with RIF rather than UCDA. Larger studies may be required to detect any significant differences.

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Metabolic syndrome in pregnancy and the risk of adverse pregnancy outcomes: a systematic review and meta-analysis

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Background: Women who experience adverse outcomes of pregnancy including preeclampsia, gestational diabetes mellitus (GDM), small for gestational age (SGA) and spontaneous preterm birth (sPTB) are known to be at increased risk of coronary artery disease (CAD) in later life. However, it is not known whether these women have pre-existing risk factors that contribute to both increased risk of adverse pregnancy outcomes and CAD. Metabolic syndrome (MetS) is a collection of CAD risk factors. We conducted a systematic review and meta-analysis to assess the risk for adverse pregnancy outcomes among women with MetS in pregnancy.

Methods: The PubMed, EMBASE, CINAHL, Web of Science and Scopus databases were searched. The review protocol is registered in PROSPERO (CRD42023460729). The risk for adverse pregnancy outcomes was measured using a fixed effects model using the JBI SUMARI software. Quality assessment was performed using the JBI critical appraisal checklist. The study selection, data extraction and data analyses were performed in accordance with the MOOSE guidelines.

Results: Seven studies met the inclusion criteria and were included in the meta-analysis, providing data on 4,446 pregnant women with metabolic syndrome and 43,095 pregnant women without metabolic syndrome. Women with MetS in pregnancy are at 2.72 (95% CI 1.80- 4.12) times increased risk of adverse pregnancy outcomes compared to women without MetS in pregnancy.

Conclusion: Screening for MetS in early pregnancy may help identify women at risk of adverse pregnancy outcomes and later life CAD.

Keywords: metabolic syndrome, prevalence, preeclampsia, gestational diabetes mellitus, small for gestational age, spontaneous preterm birth

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Myometrium Quiescence Maintained by Histone Deacetylases Inhibitors

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Publish consent withheld

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Pantry to placenta: natural compounds for the treatment of preeclampsia

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Preeclampsia remains a leading cause of maternal and perinatal morbidity worldwide, with no effective treatments. Emerging evidence suggests that bioactive compounds derived from plants and plant compounds (used as traditonal Japanese medicine) offer therapeutic potential through anti-inflammatory, antioxidant, and vasomodulatory actions. In this study, we investigated extracts from *Cinnamomum cassia* and *Zingiber officinale*, alongside key phytochemicals including cinnamaldehyde, trans-cinnamic acid, and allyl isothiocyanate. These compounds were evaluated for their ability to modulate disease-relevant pathways highly implicated in preeclampsia pathogenesis. By bridging traditional botanical sources with mechanistic screening, this project explores the therapeutic potential of selected fundamental plant-derived compounds for intervention.

Primary human cytotrophoblast cells and placental villous explants were isolated from term uncomplicated pregnancies (delivered via elective caesarean section) and treated for 24 hours with a concentration range of 0.15–1.25 mg/mL for plant extracts (*C. cassia*, *Z. officinale*) and 10–100 µM for individual phytochemicals. Conditioned media and RNA were collected for analysis of angiogenic markers. Both *C. cassia* and *Z. officinale* extracts significantly reduced secretion of the anti-angiogenic factor sFlt-1 and increased production of the pro-angiogenic molecule PlGF. In parallel, expression of the pathogenic splice variant sFlt-1-e15a was markedly decreased. These changes were consistent across both isolated individual cytotrophoblast and whole tissue villous explants. In contrast, the individual phytochemicals (cinnamaldehyde, trans-cinnamic acid, allyl isothiocyanate) had no significant effect on angiogenic mRNA expression or secretion at any concentration tested. Ongoing studies are examining the effects of these compounds on pro-inflammatory cytokines and key signalling pathways to further elucidate their potential mechanism of action.

These findings support the potential of whole plant extracts, rather than isolated components, to restore angiogenic balance in the placenta. This work contributes to the growing field of pregnancy-safe therapeutics derived from natural products and highlights the promise of plant-based interventions for preeclampsia.

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Proteomic insights into pregnancy and maternal recognition in the koala (*Phascolarctos cinereus*)

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In order to investigate maternal recognition in the koala, this study used a combination of endocrinology and proteomics to identify potential pregnancy biomarkers. Plasma progesterone levels and the proteome of the koala luteal phase were investigated in pregnant (n = 4), mated but non-pregnant (n = 4), and GnRH ovulation induced (non-mated) females (n = 7). Plasma samples were collected on the day of mating or GnRH injection (D0) and multiple days (D) post mating/GnRH injection for the duration of the luteal phase. Progesterone was measured by enzyme-linked immunosorbent assay. While AUC analysis revealed no significant difference in overall progesterone concentration profiles across the treatment groups over the course of the luteal phase, the mean progesterone concentration of pregnant females on D2 was significantly higher than GnRH treated females (40.7 ± 3.33 ng/ml vs 15.71 ± 1.83 ng/ml). Plasma also underwent FASP digestion and analysis by LC-MS/MS with SWATH acquisition. Overall, 158 proteins were identified across the treatment groups. At D2, circulating LRG1 (an acute phase-like protein) was significantly more abundant in mated females compared to GnRH treated females. LRG1 was also elevated at D2 in the plasma of pregnant koalas and then significantly declined on D9 and D19. At the expected time of maternal recognition (D9), 5 additional proteins were detected in pregnant females when compared to those that ovulated but failed to produce pouch young and those only treated with GnRH; one such protein was an albumin isoform. As progesterone rose (D20), an inter-a-trypsin heavy chain 4 (ITIH4) like molecule was only detected in pregnant females. Biomarkers of interest will be further profiled by ELISA to determine their value for early pregnancy detection and embryonic loss. The outcomes of this projects will aid in understanding maternal recognition in koalas and assist management of captive koala breeding programs.

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Mandatory folic acid fortification and supplementation alters one-carbon metabolites in pregnant women: implications for gestational diabetes mellitus

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Background: Folate is essential in pregnancy. Australia has implemented folic acid (FA; synthetic folate) food fortification policies and supplementation guidelines. Many pregnant women now exceed recommended FA intake, which is increasingly associated with gestational diabetes mellitus (GDM). Both folate and FA act in one-carbon metabolism (1CM) though FA has limited capacity to be

metabolised. We hypothesise fortification and supplementation increase folate status beyond metabolism thresholds, increasing unmetabolised FA (UMFA), with downstream implications for related one-carbon metabolites, and pregnancy outcomes.

Objective: Characterise maternal folate and related one-carbon biomarkers with respect to FA-fortification, supplementation dose and GDM.

Methods: Maternal serum (12-15 weeks' gestation) was collected from women pre- (2005-2008, n=861) and post-FA fortification (2015-2018, n=1216). Folate, UMFA, B12, homocysteine, cysteine and methionine were measured using HPLC (BeVital, Norway). Relative GDM risk was adjusted for age, BMI, ethnicity, smoking and socioeconomic index.

Results: Folate (25%), B12 (7%) and UMFA (72%) increased post-fortification (all p<0.001). UMFA also increased with high-dose FA supplementation (≥800 µg; 63.1% p=0.01). Homocysteine and cysteine (both 10% p<0.001) increased post-fortification but homocysteine:cysteine ratio was unchanged and methionine (4% p<0.001) decreased.

GDM increased from 5% (pre-fortification) to 15% (post-fortification). One-carbon metabolites associated with GDM in SCOPE only. UMFA was not associated with GDM. Folate (13% p=0.003) increased GDM risk. Homocysteine (17%, p=0.04) and homocysteine:cysteine ratio (68%, p=0.01) decreased risk. Methionine was not associated with GDM.

Interpretation: FA intake now exceeds metabolic capacity, resulting in detectable circulating UMFA. Post-fortification, homocysteine is shunted to the transsulphuration pathway, seemingly at the expense of the methionine pathway. In GDM, homocysteine:cysteine ratio is reduced, which may be a compensatory response, increasing antioxidant capacity to reduce GDM-associated oxidative stress. No metabolites associated with GDM post-fortification, but incidence tripled. High and chronic FA exposure impacts 1CM in individual women differently placing some at increased risk for GDM.

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The association between antibiotic exposure before and during pregnancy and the risk of ADHD in children: A cohort-based study of trimester-specific effects

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Antibiotic use during pregnancy is common [1,2], yet its potential impact on the neurodevelopment of the offspring remains uncertain [3–6]. This cohort study investigated whether maternal antibiotic exposure before and during pregnancy is associated with the risk of Attention Deficit Hyperactivity Disorder (ADHD) in children.

Data was derived from the Danish PANDORA cohort, linking national registries on births, prescriptions, and patient diagnoses for 787,035 singletons born 1997–2023. Maternal antibiotic exposure was defined as redemption of antibiotics three months preconception or during any pregnancy trimester. Cox proportional hazards regression estimated crude and adjusted hazard ratios (HR) for ADHD diagnosed between age 2-18 years, adjusting for maternal age, education, origin, and ADHD diagnosis.

Results showed that any antibiotic exposure was associated with a 40% increased ADHD risk in offspring (adjusted HR: 1.40 [95% CI: 1.36-1.45]). Secondary analyses indicated that risk increased with among individuals with >1 prescriptions and varied slightly by timing with the risk being highest in the preconception period and second trimester (adjusted HR: 1.43 [1.36-1.50] and 1.44 [1.37; 1.52], respectively). Specific antibiotic subgroups also showed differing associations, with the highest risks observed for certain beta-lactam, penicillins and quinolone compounds. Sensitivity analyses adjusting for maternal smoking and pre-pregnancy BMI yielded similar effect estimates (adjusted HR: 1.25 [1.20-1.30]).

These findings add to the growing concern over the rising prevalence of mental disorders in children [7,8] and underline that maternal antibiotic use before and during pregnancy may modestly increase ADHD risk, reinforcing the importance of carefully weighing indication, timing, and necessity when prescribing antibiotics to women of childbearing age.

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Prenatal ambient heat exposure and neurodevelopment: a scoping review of human and animal research

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Ambient heat exposure during pregnancy is associated with adverse outcomes, with emerging evidence suggesting potential impacts on neurodevelopment. This scoping review synthesises human and animal evidence on the association between prenatal ambient heat exposure and adverse neurodevelopmental outcomes. A search was conducted across MEDLINE, Global Health, Web of Science, PsycINFO, and CINAHL. Studies published up to May 2025 examining prenatal ambient heat exposure and neurodevelopmental outcomes, including congenital malformations and mental health conditions, were included. Two reviewers independently screened and extracted in duplicate using Covidence. Studies were categorised based on short-term (congenital anomalies, early brain metrics) or long-term outcomes (childhood behaviour and psychiatric diagnoses). The search yielded 8,189 studies, with 60 meeting the inclusion criteria (18 human, 42 animal). Most animal experimental studies (n = 32) used rodents and imposed extreme, hyperthermia-inducing temperatures. Epidemiological human studies were heterogeneous in terms of exposures and methodological approaches. For short-term outcomes, such as malformations and brain parameters, animal studies reported adverse effects of prenatal heat on neurodevelopment, whereas human findings were conflicting. Minimal human and animal studies focused on long-term outcomes, such as mental health, but those that did generally reported adverse outcomes. Overall, the evidence suggests a potential link between prenatal heat exposure, CNS malformations and altered brain size in animal models; however, the implications for humans remain uncertain. Animal studies often employed unrealistic heat exposures, limiting their applicability to humans. In contrast, human studies are limited in number and yield inconsistent findings. This review identifies three key priorities to strengthen the evidence: (1) designing animal experiments with realistic heat exposures to improve translational evidence, (2) prioritising large-animal models over rodents to better approximate human physiology and (3) standardising outcome and exposure metrics in human studies to improve comparability and reproducibility.

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A systematic review and bibliometric analysis of the impacts of extreme heat exposure on pregnancy outcomes

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Heatwaves pose significant health risks during pregnancy due to physiological changes that impair the body's ability to regulate temperature. With growing interest in the effects of heat on pregnancy, numerous studies have been published. However, the expanding evidence base remains fragmented, making it difficult to identify major patterns and gaps. This study combined bibliometric analysis and systematic review to map the existing literature and summarise key findings. A total of 259 articles published between 2000 and 2024 were retrieved from the Web of Science Core Collection. Most studies were conducted in high-income countries. Keyword analysis identified four major themes: preterm birth, methodological approaches, co-exposure to heat and air pollution, and physiological or mechanistic pathways. Most studies used cohort designs, and the distributed lag non-linear model, in combination with other methods, was the most common analytic approach. Preterm birth was the most frequently studied outcome, with strong evidence linking both acute and chronic heat exposure to increased risk. Several studies examined co-exposure to heat and air pollutants (e.g., $PM_{2.5}$, PM_{10}) in relation to various pregnancy outcomes, reporting synergistic effects, such as up to 48% of preterm birth risk attributed to combined exposure. Antagonistic effects were also observed, such as between ozone and heat on pregnancy loss. Our review also identified pathways linking heat exposure to adverse outcomes. Maternal hypertension, placental weight, and fetal heart rate changes were reported as mediators, with effects ranging from 3.7% to over 50%. Other pathways included reduced uterine artery pulsatility index and impaired placental function. Some studies reported outcomes indicative of physiological stress and strain, such as increased heart rate, core temperature, white blood cell counts, and changes in newborn respiratory function. This review highlights the scarcity of studies from developing countries, the narrow focus on outcomes, methodological inconsistencies, and uncertainty surrounding the underlying mechanisms

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The novel NPSR1 G42C point mutation in endometriosis

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Introduction/Background

Variants of the neuropeptide S receptor 1 (NPSR1) gene like the G42C NPSR1 variant are linked to endometriosis, particularly advanced stages[1]. Its ligand NPS enhances actin cytoskeletal remodeling and cell invasion in endometrial cells via sphingosine signalling, indicating a role in disease progression[2]. Here, we investigated the effect of the G42C NPSR1 variant on NPS/NPSR1-mediated sphingosine signalling in endometriosis.

Materials and Methods

G42C-carrying SH-SY5Y cells and WT controls were stimulated with 100 nM NPS for 45 minutes alongside endometrial ECC-1 and 12Z cell lines. Expression of sphingosine signalling genes *CIB1*, *SPHK1*, *SPHK2*, and *SPGL1* was measured by qRT-PCR (n=2 repeats). For cytoskeletal remodelling, cells were treated with 100, 300, and 900 nM NPS for 45 minutes and stained with TRITC-phalloidin/Hoechst 33258. Experiments were performed in duplicates and two repeats. Imaging was done by confocal microscope (Olympus FV1000), data were analysed using GraphPad Prism v10.

Results

The sphingosine signalling genes were significantly upregulated in ECC-1 (> 2 fold, $p<0.05$). *SPHK1* and *SPHK2* showed similarly high expression in ECC-1, with *SPHK2* being particularly elevated in ECC-1 compared to the other lines. *SPHK1* displayed moderate expression in both ECC-1 and 12Z, while *SPGL1* was detectable only in ECC-1. Interestingly, *SPHK2* was highly expressed. Surprisingly, *SPHK1*, *SPHK2*, or *SPGL1* were not detected in the G42C-carrying SH-SY5Y clone following NPS stimulation (100 nM). Interestingly, cytoskeletal actin staining revealed no marked differences between NPS-treated and untreated cells.

Conclusion

qRT-PCR results highlight the importance of genetic background in cellular responses to NPS and suggest that NPSR1 variants, such as the G42C-carrying SH-SY5Y, may significantly influence gene regulation preventing activation of downstream transcriptional responses, which might explain their involvement in endometriosis pathophysiology.

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Seminal extracellular vesicle mediated nfκb signalling in the female reproductive tract

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Seminal fluid exposure at coitus activates immune responses in the epithelial cells lining the female reproductive tract, promoting molecular and cellular changes that support successful pregnancy. In addition to soluble signalling mediators present in the fluid portion of the ejaculate, the seminal plasma, and seminal extracellular vesicles (SEVs) may also contribute. However, the identity of SEV signalling mediators remains unknown. In this study, we used bioinformatics analysis of transcriptomic data from SEV co-cultured with ectocervical cells (Ect1 cells) to predict SEV signalling mediators. Immunoblotting and qPCR were then employed to provide evidence of the role of these mediators in SEV signalling. Prominent among the upstream regulators predicted by bioinformatics analysis was the Nuclear factor kappa-light-chain-enhancer of activated B cells (NFκB) complex (Z-score=5.78, $p<0.05$) with other NFκB associated molecules including Interleukin-1A (Z-score=5.14, $p<0.05$), RELA proto-oncogene, NF-kB subunit (Z-score=4.79, $p<0.05$), Toll-Like Receptor 4 (Z-score=4.61, $p<0.05$) and Tumour Necrosis Factor (TNF, Z-score=7.15, $p<0.05$). Immunoblotting further characterised NFkB complex molecules in SEVs showing the presence of NFκB inhibitor epsilon (NFκBIE) and nuclear factor kappa B subunit 2 (NFκB2). However, these subunits were also expressed in resting Ect1 cells, and both *NFκB2* and *NFκBIE* were upregulated at the gene expression level following SEV co-incubation, compared to untreated media alone controls. These findings suggest NFκB signalling is activated in female reproductive tract cervical epithelial cells in response to SEV exposure. We are currently exploring whether paternal SEV-derived NFκB signals are driving these inflammatory gene expression changes or whether other SEV signals may be responsible. Overall, this suggest that SEVs may deliver specific NFκB mediators to epithelial cells in the female reproductive tract, potentially priming the local immune environment to support a healthy pregnancy.

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Impact of temperature and incubation in 6%CO2 in air on testicular sperm motility. Part 2: microTESA sperm

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The aim of this study is to determine the usefulness of overnight incubation at 37ºC in gaseous phase (6%CO_2 in air) of microTESA testicular spermatozoa harvested (mTS) in HEPES-buffered flushing medium (FM).

The testicular tissue was macerated in FM and apportioned into 4 equal portions for individual treatments (Tx). The macerated microTESA tissue suspension was incubated with or without incubation gas (6%CO_2 in air) and were held at either room temperature (RT) or 37ºC overnight as follows: (i) Without CO_2@RT; (ii) Without CO_2@37ºC; (iii) With CO_2@RT; With CO_2@37ºC. After exposure to incubation gas for maximum 60 mins in centrifuge tubes, it is sealed airtight with its cap with the gases sealed inside the tube, and placed at RT or at 37ºC. Statistical analyses used were paired-T test, Pearson's correlation studies, Chi-square and 2 by 2 tables.

Significant proportion of TS (11.4% vs 3.3%, p>0.0001) became motile after Tx's indicating both physiological temperature (37ºC) and physiological pH (attained after overnight incubation in 6%CO_2 in air) induced motility in and retained the viability of the mTS. The differences between Tx's (except between control versus RT20; P>0.05) were statistically highly significant (p<0.0005). There was significant interaction between Tx's and highly significant (p=0.0000) positive correlations.

Physiological pH and temperature induces motility in mTS, which is a safer method to initiate motility in mTS than embryotoxic pentoxyfylline or theophylline. The HEPES buffered medium drifted towards alkaline phase which makes this medium less reliable for maintaining the physiological pH of 7.3-7.4 for extended periods of time when exposed to ambient air and temperature especially in absence of CO_2 gas mixture. In conclusion, physiological temperature and pH is critical to retain the viability and to initiate motility in mTS. The HEPES medium must be equilibrated in 6%CO_2 in air to maintain the pH close to physiological level.

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Testicular spermatozoa Part 3: Gross sperm morphological abnormalities in diagnostic TESA and micro TESA, and a case of positive fertilization with abnormal sperm

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The aim of this communication is to present the various forms of abnormality noted in testicular sperm (TS).

The testicular tissue was macerated using two 1ml syringes fitted with 27g needles in FM. The macerated suspension was placed in 15x60mm culture dishes and was observed under inverted microscope at 20x and 40x objectives..

Morphological features of abnormal sperm encountered were oftentimes abnormal with a grossly bizarre range of abnormalities. These were photographed and presented. Grossly abnormal spermatozoa exhibit fertilization potential. We present one case in which 50% fertilization (2 of 4 eggs) was noted after injection with grossly abnormal spermatozoa. One oocyte appeared to have fertilised but the pronucleus fragmented and subsequently did not cleave. Another egg also appeared to have fertilised and undergone syngamy but the video showed one pronucleus fragment and subsequently no cleavage was noted. Two other oocytes did not fertilise.

We perform one of the largest diagnostic testicular biopsies for detection of spermiogenesis / spermatogenesis in the Kingdom of Saudi Arabia with well over 750 cases per year. We have noted fertilizations and oftentimes cleavages in a number of patients but quality of embryos generated do not appear viable. Grossly morphologically abnormal sperm are frequently encountered in testicular tissue. The use of surgically retrieved sperm in ICSI invariably will have to be performed with grossly abnormal sperm for lack of normal sperm, although this is less productive than ICSI with normal sperm, but still allows the generation of transferable embryos for a small proportion of patients and the possibility of treatment cycle completion. PGT must precede ET. In conclusion, in spite of the less than optimal fertilization rates, embryo development potential and pregnancy, there is often no alternative besides the use of such grossly abnormal sperm. The patient must be well counselled to anticipate failure.

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Capacitation Media Matters: Boosting Equine Sperm Function for IVF

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Aims: Improving fertilisation efficiency in equine *in vitro* fertilisation (IVF) depends heavily on effective sperm capacitation. We explored how capacitating agents individually influence stallion sperm function, aiming to identify the most effective doses for IVF regimens. **Methods:** Semen from six normospermic Shetland and miniature crossbred pony stallions were collected via artificial vagina. The samples were immediately diluted with semen extender and processed via single-layer colloidal centrifugation. After centrifugation sperm pellets were resuspended in Biggers, Whitten, and Whittingham (BWW) medium containing different doses of each of the following elements: heparin, bovine serum albumin (BSA), D-penicillamine, epinephrine, hypotaurine, and sodium metabisulfite (SMB); and incubated for 22 h (37˚C, 5% CO_2). Sperm motility was assessed using CASA. Viability and acrosome status were evaluated with LIVE/DEAD™ Far Red and FITC-PNA staining, respectively. Capacitation-associated tyrosine phosphorylation was detected via immunofluorescence using anti-phosphotyrosine antibodies and fluorescent secondary labelling, followed by flowcytometric evaluation. **Results:** Increasing concentrations of epinephrine and D-penicillamine significantly improved sperm viability ($P \leq 0.05$). Treatment with SMB increased the percentage of tyrosine phosphorylated spermatozoa at 20, 100, and 200 µM compared to the control (20 µM 28.06 ± 3.52, 100 µM 32.44 ± 6.15, and 200 µM 29.27 ± 3.01 vs Control µM 17.21 ± 2.22; respectively, $P \leq 0.05$). Hypotaurine and heparin did not affect sperm motility or capacitation. Notably, while BSA enhanced sperm viability, it also caused a significant decline in total and progressive motility. **Conclusion:** These results suggest that epinephrine, D-penicillamine, and SMB can improve specific aspects of stallion sperm fertilising capacity. Further research will be essential to optimise a capacitation protocol that can reliably support successful IVF outcomes in horses.

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Testicular heat stress upregulates lncRNA 4930555K19Rik which interacts with FUBP1 and alters cell cycle signalling

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Male germ cells are uniquely sensitive to thermal stress, which can impair spermatogenesis and compromise fertility. To elucidate the early molecular responses to heat in male germ cells, we previously profiled transcriptomic changes in round spermatids isolated following testicular hyperthermia.

We identified the long non-coding RNA 4930555K19Rik as the most significantly upregulated transcript and confirmed concurrent induction in spermatocytes. Using pull-down assays 4930555K19Rik, was shown to interact with Far upstream element-binding protein 1 (FUBP1), a transcriptional regulator of cell cycle progression. In accordance with this, overexpression of 4930555K19Rik in mouse melanoma cells led to cell cycle inhibition, the same phenotype observed upon FUBP1 disruption. To understand this further, we looked at expression of two genes supressed by FUBP1 activity, namely Cdkn1a (p21) and Trp53 (p53). Overexpression of 4930555K19Rik in somatic cells led to significant upregulation of both genes, suggesting functional impairment of FUBP1. Furthermore, in male germ cells, the FUBP1-regulated gene Ccna1 essential for meiotic progression, was significantly downregulated in spermatocytes 6 hours after heat stress.

These findings implicate a novel role of 4930555K19Rik as a potential inhibitor of FUBP1 function, which has implications in the male germ cell heat stress response, causing cell cycle arrest.

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Proteomic and Phospho-proteomic Profiling of Male Precursor Germ Cells Under Testicular Heat Stress: Insights into Mechanisms of Male Infertility

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Male infertility is an issue of growing global concern, with various environmental, genetic and physiological factors contributing to declining sperm quality and function. Among these, testicular heat stress has emerged as a critical disruptor of spermatogenesis, particularly affecting the thermosensitive precursor germ cells, pachytene spermatocytes and round spermatids, manifesting as low amounts of poor-quality sperm being produced. The aim of this work is to understand the consequence of testicular heat stress and elucidate the initial molecular basis by which hyperthermia leads to poor quality sperm formation.

Herein we show that testicular hyperthermia causes a rapid (<6 hours) loss of structural integrity in the liquid-liquid phase separated (LLPS) chromatoid body (CB), a large ribonucleoprotein granule essential for spermatogenesis. Using transmission electron microscopy, we observed that heat exposure (42^{O}C water bath 30 min) resulted in a significantly less dense chromatoid body compared to anaesthetic control (33^{O}C water bath 30 min). Further visualisation of the CB through poly-dt staining resulted in a significant loss of signal, suggesting a loss of mRNA retention in the chromatoid body.

As a LLPS complex, formation of the CB is influenced by both temperature and post-translational modifications. To examine this further, we have employed a phospho-proteomic approach using two models. Firstly, pachytene spermatocytes and round spermatids

were enriched, and subject to in vitro heat stress (33^{O}C – 38^{O}C) for 30 min. Secondly, individual mice were subject to water bath heating (33^{O}C – 42^{O}C) for 30 min to achieve testicular hyperthermia. Following treatment, phospho-peptides were enriched (TiO_2) and quantitative total and phospho-proteomic analyses (TMT, 16-plex coupled LC-MS/MS) was performed to investigate temperature-induced changes in global protein expression and phosphorylation patterns.

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Investigating the conservation of CLKs and their role in male fertility

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Publish consent withheld

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The impact of obesity and fatty acid profiles on human semen parameters for a western australian cohort

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Male infertility is a significant global health concern, contributing to approximately half of all couple infertility cases[1]. A decline in semen quality has been increasingly linked to obesity and poor dietary patterns[2,3]. In Australia, around 65% of men are classified as overweight or obese, which presents a pressing public health issue[4]. Although interest in the nutritional determinants related to male reproductive health is growing, the specific impact of dietary fat intake is limited. Furthermore, the relationship between obesity and semen quality remains underexplored, particularly for Australian populations.

This project aims to investigate the impact of obesity and spermatozoa fatty acid profiles on semen parameters in a Western Australian male cohort. In addition, examine if lifestyle variables such as weight, BMI, smoking and alcohol consumption correlate with fatty acid lipidomic measures and overall semen quality.

The study will use measures of sperm quality, including standard semen analysis and sperm DNA fragmentation. Fatty acid profiles (saturated fatty acids (SFAs), polyunsaturated fatty acids (PUFAs) and monounsaturated fatty acids (MUFAs) will be objectively measured using liquid chromatography–mass spectrometry (LC-MS), providing a precise alternative to self-reported dietary tools.

This will be the first known Australian study to apply LC-MS-based lipidomic profiling to spermatozoa, addressing a notable methodological gap in male fertility research. Western Australian males remain underrepresented in reproductive health research, and most existing studies are based on populations outside Australia. Given the similarities in dietary patterns and obesity prevalence between Australian and American men, particularly the high intake of saturated fats, this research is both timely and necessary to determine whether existing findings are generalisable[5-7]. Findings are expected to improve our understanding of the biological mechanisms linking diet, obesity, and male fertility. Ultimately, this research may guide the development of targeted dietary and lifestyle interventions to enhance reproductive outcomes.

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Adiponectin and leptin expression in term placenta from a Western Australian cohort

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The prevalence of maternal obesity in Australia has markedly increased and is a public health concern. During pregnancy, the placenta plays a crucial role in the development of the foetus. Adiponectin and leptin are adipokines involved in nutrient transportation in the placenta and examination of these proteins may provide key information related to the mechanisms associated with physiological adaptation to maternal obesity. Research has found that expectant mothers with gestational obesity have perpetually low levels of adiponectin and increased leptin expression. This is proposed to affect placental development which influences foetal development.

This study will explore adipokine RNA expression in human placental tissue samples for a Western Australian cohort. Placental adiponectin and leptin measures will be determined for participants from six subsets based on maternal weight/ BMI at antenatal booking. Statistical analyses will include adipokine expression related to sociodemographic, anthropometric, maternal, placental and natal outcomes.

To achieve the research aims, RNA will be extracted from frozen placental tissue samples and reverse transcribed into cDNA then amplified by real-time PCR. Adiponectin and leptin expression and adipokine ratios will be examined, using TaqMan assays. Immunohistochemistry of select placental tissue samples will allow for localisation of adipokine expression in placental cell lines.

It is vital to understand the relationship between maternal obesity and adverse placental and foetal outcomes. The impact of weight gain during pregnancy needs further exploration as the biological mechanisms that link maternal obesity and foetal overgrowth are contentious. Investigation of adiponectin and leptin expression in the placenta can lead to preventative measures that can be applied pre and post conception. A healthy mum means a healthy baby and the provision of improved outcomes in adulthood. These processes begin even before birth.

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Engineering placentoid cultures to model human placental villi complexity *in vitro*

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Aims

The maternal–fetal interface of the placenta consists of villi containing specialised trophoblast cells. Organoids offer a promising approach to model placental villi *in vitro*; however, current methods fail to replicate key aspects of villous structure and trophoblast cell characteristics[1, 2, 3]. This study aims to validate human stem cell-derived 'placentoids', grown on 3D-printed scaffolds, to better mimic villous architecture and support the differentiation of diverse trophoblast subtypes within a single system.

Methods

Polydimethylsiloxane (PDMS) villi scaffolds were fabricated using moulds printed with a 3D inkjet printer (Agilista, Keyence; 635×400 dpi, 15 µm resolution)[4]. PDMS (1:10) was poured into moulds, degassed under vacuum, and cured overnight at room temperature. Scaffolds were rendered wettable by ozone treatment prior to cell seeding. Human pluripotent stem cells (PSCs) were maintained in mTeSR1 before differentiation. PSCs were disaggregated into colonies (<250 µm) and seeded onto scaffolds. Trophoblast differentiation was induced using StemPro medium supplemented with BMP4 (10 ng/mL), SB431542 (20 µM), and SU5402 (20 µM). Cultures were maintained for up to 14 days and fixed with 4% paraformaldehyde for immunofluorescent staining and imaging using an Olympus FV3000 confocal microscope.

Results

Cells covered scaffold surfaces and lost pluripotency markers (Oct4) by day 3 (n = 3). Gradual expression of syncytiotrophoblast (STB) and extravillous trophoblast (EVT) markers was observed throughout the culture period. By day 12, cytotrophoblast cells (Ki67 and ITGB4 positive) were present alongside STBs (hCGβ and SDC1 positive) and EVTs (HLA-G positive). By day 14, HLA-G positive EVT bridges had formed between scaffold projections.

Conclusion

This placentoid culture system supports the differentiation of multiple trophoblast subtypes within a single culture system. Moreover, as placentoids more closely resemble placental villous structure than existing organoid models, this system provides a valuable tool for studying human placental villi development and dysfunction.

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Early pregnancy is associated with lower daily methane production but no change in metabolic markers in Brahman heifers

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Methane is a major contributor to greenhouse gases. Methane is produced by the ruminal microbiome and eructed by cattle. While there have been some investigations into the determinants of methane emissions, these have mainly been done in dairy cattle, not in grazing beef cattle. Given that the female herd spends most of their life pregnant, the effects of pregnancy on methane emissions are important to investigate.

In a cohort of 20 pregnant and 18 non-pregnant heifers, we measured methane emissions across 5 days at the end of trimester 1 of pregnancy using the SF_6 tracer gas methodology. Methane yield was analysed using GC-MS and levels were averaged across the days of measurement both as g/day and in g/kg live weight and compared between the groups. Methane yield (CH_4 g/DMI) was not measured in this study. Blood was obtained at the same time and glucose, triglycerides, total cholesterol, NEFA and progesterone were measured in the veterinary pathology laboratory.

Pregnant heifers had lower methane emissions than their non-pregnant counterparts both as measured in g/day (pregnant 116 ± 25 g/d *vs.* non-pregnant 195 ± 110 g/day, p=0.005) and as g/kg live weight (pregnant 0.27 ± 0.06 g/kg LW *vs.* non-pregnant 0.48 0.27 g/kg LW, p=0.003). There were no differences in circulating metabolites, but progesterone levels were higher in pregnant (43 ± 14 nmol/L) than in non-pregnant heifers (13 ± 14 nmol/L, p<0.0001), as expected. However, methane emissions were not directly correlated with progesterone or metabolite levels.

In summary, early pregnancy is associated with lower daily methane production. There was no evidence that metabolic markers or progesterone levels in heifers are major determinants of methane levels. It is possible that changes in feed intake or the ruminal microbiome in early pregnancy can explain the lowering of methane emissions.

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Leveraging education theory to enhance endocrine clinical teaching: an illustrative study

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Introduction

Complex clinical decision-making requires more than just knowledge transmission; it involves developing clinical reasoning and comprehension in learners. Using education theories to inform clinical teaching practices can facilitate this process. This applied research study examined the impact of the explicit application of education theories (situated learning theory, cognitive apprenticeship theory, visible thinking and cognitive load theory), in the teaching of blood glucose level (BGL) management to final year medical students.

Methods

Pre-intern medical students (Monash University, Peninsula campus) participated in a two-part interactive lecture series on inpatient BGL management. Ten students volunteered for pre- and post-teaching case-based interviews to assess clinical decision-making strategies. The teaching approach emphasised expert visible thinking, providing students with tools to scaffold information from authentic scenarios and break down decision-making processes into observable steps, while managing cognitive load through provision of a visual reference tool. Student interviews were analysed using template-based thematic analysis.

Results

Pre-teaching interviews revealed varied baseline knowledge, but significant uncertainty in clinical decision-making, with many students relying on observations from senior clinicians without clear understanding. Post-teaching interviews demonstrated increased confidence and a deeper ability to justify decisions, particularly in terms of insulin choice and dosing. Students highlighted that the visible thinking methodology made previously obscure clinical reasoning processes more accessible, and they utilised insulin charts for reference allowing them to manage cognitive load effectively.

Discussion

This study demonstrates that visible thinking can scaffold clinical learning by making expert reasoning explicit and accessible to novice learners. Students exhibited improved decision-making, problem representation and confidence. More broadly, these findings highlight the value of education theory application to the design and delivery of clinical teaching and are pertinent across clinical disciplines.

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Delivering Integrated, Inclusive Sexual and Reproductive Health Services: Insights from SHINE SA's Model of Care

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This study aimed to explore how sexual and reproductive health (SRH) services are integrated and delivered in practice at SHINE SA, a specialist SRH provider in South Australia. Through ten in-depth interviews with clinical and non-clinical staff, the research examined service delivery models, coordination strategies, and the barriers staff encounter. Data were analysed thematically to identify how integration functions in real-world settings.

Findings reveal that integration is operationalised through both clinical and organisational means. Providers routinely combine STI and HIV screening, contraception, gender-affirming care, mental health support, and chronic disease management within a single care pathway. Services are delivered through multidisciplinary collaboration, shared care planning, and inclusive communication practices, with staff often tailoring care to clients' intersecting needs—such as those of LGBTQ+ populations, people living with HIV, and neurodiverse individuals.

Despite a strong internal culture of person-centred care, service delivery is significantly constrained by structural barriers. Chronic underfunding, limited clinic infrastructure, long waiting times, and workforce shortages—particularly in general practice and gender-affirming services—undermine access and equity. High demand has led to closed referral lists and reduced availability of gender-affirming care, forcing staff to triage complex needs while managing resource limitations.

The study concludes that while SHINE SA demonstrates a robust model of integrated SRH care, its sustainability depends on targeted investment in clinical infrastructure, funding for multidisciplinary staffing, and formalised partnerships with external agencies. These findings offer key insights for health systems seeking to implement inclusive, integrated SRH services responsive to community needs.

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Examining current Australian health policies for pregnant people during heat exposure and heatwaves

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The risks associated with extreme heat stress during pregnancy are of growing concern (1), especially in Australia where the frequency and severity of heatwaves is expected to increase in the following decades (2). However, the extent to which Australian legislation and public health policy adequately address heat stress during gestation remains unclear. This gap in knowledge is of concern as health policies and advisories inform what protective mechanisms are implemented by the healthcare system, its providers and pregnant people themselves. Hence, this project aims to identify gaps in public health messaging for pregnant people during heat exposure, and recommend how current Australian policies and frameworks can be improved from a health equity perspective. Keyword searches via Google Advanced Search and targeted websites were conducted to identify grey literature related to heat, pregnant health and general human health. Only documents published between January 2014 to present were included. These documents were imported into Covidence for systematic screening and review. A set list of variables was extracted from each document before being analysed via a "social determinants of health" approach (3). A qualitative thematic analysis was conducted via NVivo software, with identified themes analysed against current literature on pregnant health and heat to develop recommendations. A preliminary keyword search using the Analysis & Policy Observatory website identified 50 documents with the keywords "heat" and "health" in Australia; none of these documents made mention to pregnant health. Given that this website has been identified as a key open-access resource for policy documents, we thus far conclude that there may be a gap in Australian policy which references heat-health impact in the context of pregnant people. It will be crucial to further investigate the extent to which "informal" health messaging is captured in grey literature, and its accessibility to identified priority pregnant populations.

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Estimating alcohol consumption during pregnancy in Western Australia: a multi-source approach

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Publish consent withheld

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Major and minor histocompatibility antigen disparity between parents affects offspring growth trajectory and glucose metabolism in adulthood

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The maternal immune response at conception sets the trajectory for pregnancy success. Tolerance mediated by regulatory T cells (Treg cells) towards paternally-inherited major and minor histocompatibility complex antigens (MHC and MiHC) expressed by placental and fetal cells is essential. However, the relative contributions of MHC and MiHC genes for improved pregnancy outcomes and their significance for offspring phenotype is unknown.

C57BL/6 female mice were mated with C57BL/6 (MHC&MiHC-matched), Balb/b (MHC-matched, MiHC-disparate) and Balb/c (MHC&MiHC-disparate) males, and pregnancy outcomes were evaluated on gestational day (gd) 17.5 (n=15-17 dams/group). In another cohort, offspring growth trajectories were measured and metabolic health was evaluated by glucose tolerance test in adulthood (n=3-7 dams/group).

On gd17.5, pregnancies sired by Balb/b and Balb/c showed reduced fetal loss compared to C57BL/6 males ($p<0.01$). Although fetal and placental weights were higher in Balb/b and Balb/c matings compared to C57BL/6 mating ($p<0.001$), the fetal-to-placental weight ratio was 11% lower after Balb/b than Balb/c mating and histological analysis of mid-sagittal placental sections revealed a larger placental labyrinth zone ($p<0.05$), indicative of reduced placental efficiency, when parental MHC was not disparate.

Postnatally, both male and female offspring of Balb/b and Balb/c sires were heavier than C57BL/6 sires from weaning until week 20 postpartum (pp; $p<0.001$), and exhibited improved glucose tolerance (area under curve, $p<0.0001$). Female offspring from Balb/b sires weighed more after week 5pp and were less glucose tolerant than Balb/c offspring ($p<0.0001$).

Our findings demonstrate that disparity in both MHC and MiHC between parents maximises pregnancy outcomes by inducing robust placentation with long-term benefits for offspring metabolic health, particularly in female offspring. We conclude that disparity between parental MHC and MiHC is critical for efficient female reproductive investment and offspring growth trajectory and metabolic health after birth.

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Stressing the phosphoproteome: Largescale dysregulation of human sperm phospho-signalling quantified in response to lipid stress

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Spermatozoa rely on kinase/phosphatase mediated protein phosphorylation to modulate cellular processes in the absence of *de novo* transcription and translation. In congruence, recent studies have detailed extensive remodelling of the sperm protein phosphorylation signature during post-testicular maturation in the epididymis and subsequent capacitation. However, cellular functions in spermatozoa, including phosphorylation signalling, are intrinsically under threat of disruption by oxidative stress due to the cell's paucity of cytoplasmic antioxidants and enrichment in polyunsaturated fatty acids. This renders the intracellular environment of spermatozoa uniquely susceptible to lipid peroxidation leading to the production of cytotoxic reactive carbonyl species such as 4-hydroxynonenal (4HNE). In turn, increased intracellular 4HNE is associated with a loss of sperm-egg recognition impacting fertilization capacity.

For the first time in human spermatozoa, we have quantified a distinct dysregulation of protein phosphorylation by the exogenous application of low levels of 4HNE (50 μM) using high-resolution tandem mass spectrometry. Specifically, we observed a 4HNE-induced dysregulation of 30.3% of the total phosphopeptides detected in spermatozoa (375 of 1,239), including those within A-kinase anchoring protein 4 (AKAP4), sperm acrosome-associated protein 9 (SPACA9) and sperm flagellar protein 2 (SPEF2). Moreover, application of a lipid-based strategy to protect human sperm function during 4HNE treatment (through the pharmacological inhibition of arachidonate 15-lipoxygenase (ALOX15)), reduced phosphopeptide dysregulation (12.5% of total phosphopeptides) during 4HNE exposure. Proteins protected from 4HNE-induced dysregulation included SPACA9 and SPEF2. However, aberrant phosphorylation of AKAP4 proved refractory to lipoxygenase inhibition. We are now poised to further investigate oxidative stress induced dysregulation of protein

phosphorylation signatures caused by environmental stressors with our *in silico* analyses able to reveal kinases/phosphatases responsible for this dysregulation. Moreover, we have demonstrated a protective but also selective effect of ALOX15 inhibition on phosphorylation signalling in human sperm with potential applications extending to the use of ALOX15 inhibition in medically assisted reproduction.

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The germline proteome undergoes dynamic remodelling in response to in vitro and in vivo proteotoxic stress

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Stringent regulation of the proteome during periods of stress is necessary for the maintenance of cellular homeostasis, function and survival. While proteome regulation has been extensively explored in somatic cells, knowledge of how germ cells respond to proteotoxic stress is lacking. This study aimed to investigate how the proteome of mouse spermatocytes and spermatids are remodelled in response to three proteotoxic stressors; 4HNE (lipid aldehyde; *in vitro*), MG132 (proteosome inhibitor; *in vitro*) and heat stress (8h 35°C/16h 25°C for 14-days; *in vivo*). Here, we adapted a somatic cell protein solubility fractionation protocol[1,2] for germ cells and coupled it to a label-free proteomic workflow[3]. This approach permits the quantification of stress-dependent changes in total protein abundance as well as changes in protein solubility from the same population of cells. Interrogation of total protein abundance revealed that *in vivo* heat exposure elicited the largest response in spermatocytes with 409 proteins downregulated and 437 proteins upregulated in response to heat stress. Comparatively, later stage spermatids had a dampened response with 145 proteins upregulated and 204 proteins downregulated following heat exposure. Functional assessment of these heat-dysregulated proteins revealed an enrichment in membrane remodelling proteins (e.g., MMGT1 and ZDHHC21) and a reduction in proteins involved in lipid metabolism (e.g., CYP2E1 and ALDH1B1). Despite different protein subsets being modulated between spermatocyte and spermatid populations, the modulated proteins appeared to contribute to analogous functions. Finally, dysregulated proteomic signatures across the stress conditions had substantial conservation (e.g. 47% conservation in 4HNE and MG132 in spermatocytes) whilst distinct impacts from the individual stressors could still be observed. Ultimately, this study will provide an increased understanding of proteostasis and stress response pathways in the male germline; a crucial step to inform future strategies to fortify germ cells against environmental stressors with potential implications for fertility and offspring health.

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X chromosome and germ cell meiosis: are two Xs better than one?

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Publish consent withheld

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Evaluating Therapeutic Strategies for Maternal Cardiovascular Dysfunction in a Nanoparticle-Induced Mouse Model of Preeclampsia

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Introduction

Preeclampsia is a dangerous cardiovascular disorder of pregnancy and a leading cause of maternal and neonatal death globally. Although the pathogenesis is poorly understood, angiogenic imbalance is a hallmark feature. We aimed to elucidate the impact of angiogenic imbalance (high sFlt-1/low FKBPL) on the maternal cardiovascular system during pregnancy and to evaluate potential treatments in an established in vivo model1.

Methods

Wild-type (WT) and *fkbpl*$^{+/-}$ C57BL/6N mice were administered RALA-sFlt-1 (5µg) nanoparticles intravenously on embryo day (E)8 and 12 and randomly allocated to i) control (100µl, n=10), ii) exercise (n=5), iii) metformin (200 mg/kg/day via drinking water, n=7) or iv) AD-01 (0.003mg/kg/day, n=8). Blood pressure and heart rate were measured using the tail-cuff method every two days from E8. Echocardiography and placenta/embryo weight were determined, and tissues were harvested on E18 for analysis.

Results

Nanoparticles (sFlt1-RALA) showed satisfactory size (<100 nm), charge (40–60 mV), and excellent uniformity. In WT mice, pregnancy increased cardiac output vs. non-pregnant controls ($p<0.0081$). sFlt-1 overexpression reduced cardiac output vs. vehicle controls ($p<0.044$), while exercise restored it ($p<0.0015$) and metformin showed a trend toward improvement ($p<0.054$). In *fkbpl*$^{+/-}$ mice, exercise showed a trend toward rescuing sFlt-1-induced cardiac output reduction ($p<0.065$). At GD12, *fkbpl*$^{+/-}$ mice with sFlt-1 overexpression in the exercise group showed significant improvements in systolic ($p<0.027$), diastolic ($p<0.031$), and mean ($p<0.028$) arterial pressure, compared to sFlt-1 *fkbpl*$^{+/-}$ controls. ELISA showed a significant reduction in cardiac sFlt-1 protein in metformin-treated sFlt-1 *fkbpl*$^{+/-}$ mice ($p<0.035$). Uterine artery resistance and pulsatility indices were not significantly altered across treatment groups.

Conclusion

Our nanoparticle-induced preeclampsia model of angiogenic imbalance, driven by high sFlt-1 and/or low *fkbpl* expression, adversely impacts the maternal cardiovascular system. Exercise and metformin show therapeutic potential in reversing dysfunction, which is clearly *fkbpl* genotype dependent.

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Dysregulated miR-124-3p in human endometrial epithelial cells reduces endometrial receptivity by altering cell adhesion

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The human endometrium undergoes substantial remodelling in each menstrual cycle to become receptive to an implanting embryo. Abnormal endometrial receptivity is one of the major causes of embryo implantation failure and infertility. MicroRNAs are dysregulated in the endometrial epithelium of women with infertility at the receptive phase. However, there is limited evidence on how individual dysregulated microRNAs lead to endometrial dysfunction. In this study, we aimed to determine the function of microRNA-124-3p on the adhesive capacity of endometrial epithelial cells, which is essential for securing firm embryo attachment to the endometrial surface. qPCR and *in situ* hybridization were used to determine the expression and localisation of microRNA-124-3p in fertile and infertile human endometrium. To test the regulation of microRNA-124-3p on cell adhesion, primary human endometrial epithelial cells and Ishikawa cells (a receptive endometrial epithelial cell line) were subjected to trophoblast spheroid (blastocyst surrogate) adhesion assay and xCELLigence, respectively. We optimized a trypsin “shaving” condition to cleave Ishikawa cell surface-accessible proteins following control or microRNA-124-3p overexpression. Mass spectrometry was applied to determine profile of cleaved proteins. Our results showed that MicroRNA-124-3p was abnormally increased in the endometrial luminal epithelium of women with unexplained infertility during the receptive phase, compared to fertile controls. Functionally, microRNA-124-3p overexpression in primary human endometrial epithelial cells and Ishikawa cells significantly impaired their adhesive capacity compared to respective controls. Incubation of trophoblast spheroids with trypsin shaving media significantly impacted their adhesion to untreated Ishikawa monolayers. Mass spectrometry analysis of the shaved surface proteins from Ishikawa cells (both control and microRNA-124-3p overexpressed) identified a total of 298 proteins, with 17 of them being significantly reduced after microRNA-124-3p overexpression. Overall, our findings suggest that microRNA-124-3p plays a role in blocking endometrial receptivity by reducing epithelial cell adhesion.

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Pregnancy complications leave a proteomic signature of future health risk.

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Epidemiological studies have identified associations between pregnancy complications, fetal growth restriction (FGR) and preeclampsia, and increased risk of maternal chronic disease. However, no blood tests can identify women at risk. Using a novel aptamer-based proteomics platform, machine learning algorithms (SomaSignal tests) have identified protein signatures associated with chronic disease risk[1,2]. We sought to assess whether these algorithms could identify disease risk during pregnancy.

Employing a case cohort design, we measured 7,000 plasma proteins using the aptamer-based proteomics platform. We measured samples collected at 36 weeks' gestation: an Australian study (n=115 <3rd birthweight centile/FGR n=92 preeclampsia, n=177 cohort), and a United Kingdom study (n=80 <3rd birthweight centile/FGR, n=172 cohort). Samples were collected prior to diagnosis of term fetal growth restriction or preeclampsia. SomaSignal test algorithms were applied to assess protein signatures associated with long-term chronic disease risk.

In the Australian study, women who later delivered a fetal growth restricted infant showed protein signatures associated with reduced heart function (within 6 and 12 months, p=0.001), and 33% increased risk of cardiovascular events ($p=7.6x10^{-6}$) compared to the cohort. These protein signatures were also associated with increased risk of mid-life dementia ($p=1.5x10^{-9}$), greater visceral fat ($p=4.06 x10^{-6}$) and body fat percentage (p=0.003). These findings were validated in the United Kingdom cohort.

Women who later developed term preeclampsia showed more pronounced chronic disease-associated protein signatures, supporting existing epidemiological data. This included protein signatures associated with reduced heart function (within 6 and 12 months, p=0.001) and increased cardiovascular ($p=5.54x10^{-6}$), hepatic (p=0.001) and renal (p=0.0007) disease risk relative to the cohort. Protein signatures for these women were also associated with increased mid-life dementia risk ($p=1.61x10^{-8}$), glucose intolerance (p=0.001), and visceral fat ($p=5.35x10^{-10}$).

Here, we demonstrate the potential to identify chronic disease risk during pregnancy. This may aid improved post-partum care, offering an earlier window for intervention strategies.

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PRC2 safeguards granulosa cell identity and promotes proliferation to support ovarian follicle growth

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The development of unique cell types in multicellular organisms is achieved through careful coordination of gene expression, involving signalling, transcription factors and epigenetic modifications. Tight epigenetic regulation is critical for normal cell function and epigenetic modifications are often disrupted in disease, including cancer. Despite substantial influence of epigenetic modifications on cell identity and function, and tissue patterning, the epigenetic regulation of ovarian development or how dysregulation of epigenetic modifications contributes to ovarian dysfunction is poorly understood. Polycomb Repressive Complex 2 (PRC2) is a widely conserved epigenetic modifier which catalyses the repressive modification Histone 3 Lysine 27 trimethylation (H3K27me3). While PRC2 regulates cell function and identity in many developmental contexts, how PRC2 regulates ovarian function is poorly understood. Using genetic and pharmacological mouse models and human granulosa tumour cells (KGN cells), we investigated how reduced PRC2 function impacts ovarian function. Combining immunofluorescence and spatial transcriptomics we demonstrate that PRC2 is essential for granulosa cell proliferation and follicular development in mouse ovaries. Further, *Eed* deletion resulted in aberrant expression of SOX9 in granulosa cells, suggesting PRC2 silences male-promoting genes to maintain granulosa cell identity. Additionally, the PRC2 inhibitor MAK683 reduced both H3K27me3 and proliferation of KGN cells, indicating PRC2 may also regulate proliferation in human granulosa cells and could be a useful target for treatment of specific ovarian cancers. These findings provide functional evidence that PRC2 is an essential regulator of follicle development and female endocrine regulation. Our work generates important insights into epigenetic regulation of ovarian development, with implications for understanding disorders of female reproductive health. This includes conditions in which granulosa cell function and steroid production are abnormal, such as granulosa cell tumours, primary ovarian insufficiency and infertility. Moreover, this work provides insight into potential impacts of emerging PRC2 inhibiting drugs on ovarian function and ovarian cancer cells.

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Unravelling the molecular signature of human endometrial stem/progenitor cells to understand endometrial regeneration and differentiation

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The human endometrium is a highly regenerative tissue undergoing >400 cycles of shedding, regeneration, proliferation and differentiation during a woman's reproductive life. The endometrium has two layers, an upper functionalis (shed during menstruation) and a basalis layer that is retained and is from which the new functionalis forms. Adult stem cells reside in the basalis human endometrium including N-cadherin+ (CDH2) epithelial progenitors and mesenchymal stem cells. Perturbations in these stem/progenitor cells likely leads to endometrial dysfunction, gynaecological disease and infertility. Our aim was to define the molecular signature of human endometrial stem/progenitor cells to better understand their role in endometrial regeneration, differentiation and disease.

Human hysterectomy endometrium (n=5) was digested to single cells for 6-way FACSorting to enrich for stem/progenitor cell subpopulations. The six cell fractions were combined and analysed by single cell RNA sequencing (scRNAseq). Immunofluorescence examined the endometrial localisation of thyrotropin releasing hormone (TRH) and Indian Hedgehog (IHH) co-localisation of SSEA-1, CDH2 and IHH, and BOC and SSEA-1.

scRNAseq identified four populations of endometrial stem/progenitor populations of epithelial and mesenchymal origin from a total of 16 cell populations. Epithelial progenitors transitioned into mature cell states including a novel population in the junctional zone between the glands and luminal epithelium. Epithelial progenitors had high expression of *TRH* and *IHH*. Thyroid signalling pathway featured prominently in epithelial progenitors. TRH and IHH localised to the basalis endometrial glandular epithelia. CDH2, SSEA-1 and IHH co-localised in the basalis endometrial glands. Key interactions were identified between *IHH* in epithelial progenitors and its co-receptors *BOC* and *CDON* in the stroma. BOC and SSEA-1 co-localised in the glandular and luminal epithelia.

Determining novel roles for IHH and TRH signalling in endometrial epithelial progenitors provides fundamental understanding of the regenerating endometrium and the potential pathogenesis of endometrial proliferative disorders such as endometriosis, adenomyosis, and infertility.

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Peri-conceptional viral mimetic poly I:C administration in male mice leads to impaired fetal growth and placental insufficiency associated with altered seminal fluid composition

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Paternal health before conception is critical for pregnancy outcome and infant health, yet the mechanisms remain underexplored. Accumulating evidence shows bioactive factors in seminal fluid are sensitive to environmental cues, and can modulate endometrial receptivity to in turn shape fetal development. Given emerging viral threats, we sought to investigate how peri-conceptional paternal anti-viral immune activation affects seminal fluid components and subsequent pregnancy.

Here, we administered a synthetic viral RNA mimetic (polyinosinic:polycytidylic acid; poly I:C) that induces inflammation through toll-like receptor 3 activation. To assess the acute impact of poly I:C on male reproductive function, C57Bl/6 male mice were treated with 10mg/kg poly I:C or vehicle, followed by sperm motility assessment by computer-assisted semen analysis at 0h, 6h, 12h and 24h post-treatment. Pro-inflammatory cytokine gene expression was measured in seminal vesicles by qPCR at the same timepoints. Poly I:C- or vehicle-treated males were mated with BALB/c females on the night of treatment, and fetal outcome was assessed at late gestation on day 17.5 post-coitum.

Poly I:C increased pro-inflammatory *Ccl2*, *Il6*, *Ifng* and *Tnf* expression in seminal vesicles at 6 hours post-treatment (>6-fold increase, n=4-5/group, $p<0.05$). Although pregnancy rate, implantation rate and fetal viability in late gestation were comparable between groups, fetal weight was reduced by 6.5% in poly I:C-sired pregnancies, accompanied by decreased fetal:placental weight ratio indicating decreased placental efficiency (n=11-15 dams/group, $p<0.05$). Sperm parameters were not affected at 24 hours after poly I:C treatment, suggesting impaired fetal growth may be due to altered seminal plasma composition and effects on endometrial receptivity.

Collectively, these findings indicate that peri-conceptional paternal viral infection may dysregulate seminal fluid molecular composition, with potential to adversely affect fetal growth. Future experiments will examine the underlying mechanisms driving suboptimal pregnancy, which will provide insights into potential therapeutic strategies to mitigate impaired fetal growth caused by paternal infection.

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All of Obesity is genetic or Epigenetic

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All of obesity is genetic or epigenetic. Lifestyle can only cause mild overweight. The reason is as follows: Identical twins have a very high correlation in body weight even when they are reared apart from birth (1). When 12 pairs of identical twins were force fed for 100 days in Canada, there was a range of weight gain but the twins tracked together (2). Individuals that were adopted soon after birth have a statistically significant correlation with the biological parents whom they had never met, but no correlation with the body weight of parents that adopted them(3). At the moment there are 3 known mechanisms for epigenetic obesity. The first, and possibly the most important, occurs before the baby is conceived (4), the second occurs in utero (5) and the third occurs in early life(6). Individuals not carrying a gene for obesity cannot develop obesity because humans have 2 negative feedback systems to prevent it. The first is the hormone leptin, a powerful inhibitor of hunger. It is made mostly in fat cells. There is also a backup negative mechanism that uses Osteocytes in bones to send a message to the brain to eat less (7). The last line of evidence that obesity is genetic is the fact that the body defends weight vigorously by making the individual hungrier and more fuel efficient after modest weight loss (8) in order to go back to the person's original weight. The body would not do that if obesity was caused simply by poor lifestyle. It is very important that organizations like ANZOS accept this fact because individuals with obesity are discriminated by all of society who believe that obesity is self-induced. By stressing to all of the media and to all politicians that obesity is not self-induced, we can make a start to eliminate bias towards these unfortunate individuals.

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Effects of tirzepatide and acute exercise for fatty liver therapy by anti-inflammation

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Objectives: Our objective is to investigate the independent and synergistic effect of acute exercise and the GLP-1/GIP agonist(Tirzepatide) on fatty liver and other metabolic biomarkers in the high-fat diet mice.

Methods: We fed male C57BL/6 mice high-fat diet(HFD) for 12 weeks. We divided the mice into four groups(exercise/Tirzepatide, non-exercise/Tirzepatide, exercise/saline, and non-exercise/Tirzepatide, n=3/group). Then, the mice were observed in metabolic cage to develop a profile of activity and metabolism at both the beginning and end of the study. Also, measures of daily body weight and plasma samples were obtained. At the end of the study, abdominal ultrasound was performed, relevant tissues were harvested, and protein multiplex analysis and metabolite analysis were performed.

Results: Acute exercise for 7 days only doesn't affect weight change, but once injection of Tirzepatide showed significant weight loss in our study. There were no differences in the energy expenditure rate and respiratory exchange ratio(week 2) between the four groups. Our results showed a statistically significant decrease of 65%($p<0.001$) in ALT(60U/L, $p<0.05$) after the once injection of Tirzepatide and 7 days of acute exercise. Analysis of serum inflammatory markers showed a 43% of decrease(3pg/ml) in TNF-α levels in the Tirzepatide/exercise group as compared with the control group($p<0.05$). Tirzepatide/acute exercise group showed a trend of 10% reduction in liver fattiness(measured by brightness), but no statistical significance in the ultrasonography at the end of the study as compared with control group.

Conclusion: In this study, we found that the significant decreased in serum ALT level and serum TNF-α level after the once injection of Tirzepatide and 7 days of acute exercise in the high-fat diet mice. Synergistic intervention with Tirzepatide and acute exercise which may be mediated by their anti-inflammatory effects, appears to be an effective therapy against fatty liver.

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The effect of insulin resistance on 12-month weight outcome in adults with class 3 obesity without diabetes attending a multidisciplinary weight management program.

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This study aims to assess the effect of insulin resistance (IR) on 12-month weight outcome in adults with class 3 obesity without diabetes attending a multidisciplinary weight management program (WMP).

Adults (≥18 years) with body mass index (BMI) ≥40kg/m2 and no diabetes enrolled in a WMP in Sydney, Australia between January 2019 and February 2024, who completed 12 months of the program were included. Demographic details, anthropometric variables and clinical data were collected. IR was calculated using the HOMA-IR formula: (Fasting Plasma Glucose [mmol/L] × Fasting Insulin [pmol/L]) ÷ 135. T-tests were used to assess differences between group means. Univariate and multivariate regression analyses were used to evaluate the association between IR and weight change outcomes using SPSS v29.

A total of 231 patients were included with mean (±standard deviation) age 45.5±13.5 years, weight 154.7±35.2 kg, female (69.7%) and Caucasian (79.3%). At baseline, 89.1% of the cohort had insulin resistance (HOMA-IR >2.71) and the mean baseline HOMA-IR was 8.1±6.1. At 12 months, significant weight loss was observed in this cohort (-4.6±7.4% baseline weight, p<0.001), with no change in HOMA-IR (p=0.628). Patients with no IR at baseline (n=21), compared to patients with IR (n=172), had significantly lower weight at baseline (134.9±24.7 kg vs 160.0±35.9 kg, p<0.001). There was no significant difference in weight change between the two groups over 12 months (no IR: -5.8±11.2% vs IR: -4.5±7.1%; p=0.612). On univariate and multivariate regression analyses, adjusting for age and sex, log-transformed HOMA-IR was significantly associated with baseline weight (univariate p<0.001, multivariate p=0.001) but not weight change over 12 months (univariate p=0.535).

IR is highly prevalent among adults with class 3 obesity without diabetes and is positively associated with weight. These findings suggests that IR did not affect weight outcomes in adults with class 3 obesity without diabetes undergoing a 12-month multidisciplinary WMP.

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Snapshot of inpatient and emergency patient obesity and coding in South Australian public tertiary hospitals

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Background: Prevalence of obesity among inpatients and emergency (I&E) presentations in South Australian (SA) tertiary public hospitals remains unclear. While national data suggest obesity is under-coded in hospitals, this has not been specifically reviewed in SA (1,2,3).

Aims: The primary aim was to determine the prevalence of obesity in I&E presentations across SA's metropolitan tertiary hospitals, comparing different local health networks (LHN) Central (CALHN), Southern SALHN), and Northern Adelaide (NALHN). Secondary aims included evaluating obesity-related clinical coding, its impact on comorbidities, and length of stay (LOS).

Methods: A cross-sectional point prevalence study of obesity in I&E presentations was conducted across major SA tertiary hospitals using electronic health record data over two consecutive days in February 2024. Body Mass Index (BMI) was calculated from height and weight data to classify patients as obese (BMI ≥30kg/m^2) or non-obese (BMI <30kg/m^2). ICD-10 codes were reviewed. Mann-Whitney U and Chi-square tests were used for group comparisons, and obesity prevalence assessed using generalised linear model.

Results: Of the 3914 I&E patient data collected, 3077 (78.6%) had BMI determined. Overall obesity prevalence was 31.8% (n=979), broadly comparable to the Greater Adelaide obesity rates (33.4%) (4). Prevalence differed significantly across LHNs (p=0.048), with NALHN showing the highest rates. Obese patients were younger, more likely female, Australian-born, and had higher rates of type1 and type 2 diabetes (32.8% vs 21.7%, p<0.001), obstructive sleep apnoea (2.4% vs 0.4%, p<0.001) and osteoarthritis (4.0% vs 1.6%, p<0.001). Obesity was coded in only 2.7% of cases. Class III (BMI ≥ 40.00 kg/m^2) obesity was highest in NALHN (8.4%) and exceeded general SA rates (3.9%). LOS was longer in the non-obese group (Median:13 days vs 10 days, p<0.001).

Conclusion: Obesity prevalence among I&E patients in SA tertiary hospitals reflects community levels, but Class III obesity is overrepresented. Clinical coding for obesity remains low.

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Obesity and haemodynamic profile in early pregnancy

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Background: Obesity is known to be associated with haemodynamic alterations that can lead to cardiovascular disease. We investigated the haemodynamic profile of women living with obesity and normal weight women.

Methods: Pregnant women attending antenatal clinics at the Lyell McEwin Hospital prior to 16 weeks' gestation were recruited. Data collected included demographic information, medical history, previous obstetric history, family history, exercise, diet, smoking and alcohol intake. Height and weight were measured, and the haemodynamic profile was assessed non-invasively using USCOM BM+ machine. Haemodynamic parameters of women living with obesity (BMI ≥30, n = 104) were compared with those of normal weight women (BMI 18 – 24.9, n = 104).

Results: Age and gestational age at recruitment were similar in women living with obesity and normal weight women (29.6±5.3 vs 28.6±4.7 p>0.05). Pregnant women living with obesity had significantly higher peripheral systolic blood pressure (115±15 vs 101±11 mmHg, p< 0.001), peripheral diastolic blood pressure (67±8 vs 61±6 mmHg, < 0.001), central systolic blood pressure (103±13 vs 92±11 mmHg, p< 0.001) central diastolic blood pressure (68±9 vs 61±8 mmHg, p< 0.001) and mean arterial pressure (87± 9 vs 77± 8mmHg, p < 0.001) compared to normal weight pregnant women. After adjusting for confounding factors including age, gestational

age at assessment and smoking, the results remained significant. Augmentation index was higher among women living with obesity compared to normal weight women but was not statistically significant (49.8±24 vs 61±22, p=0.8).

Conclusion: The mean blood pressure values observed in the two groups are within the normal reference values. However, the significantly higher values seen in the women who were living with obesity group suggest alterations in young women. Screening these women in the post-partum period after the physiological changes in pregnancy return to normal, will help identify young women who may be at increased risk for cardiovascular disease.

Key words: haemodynamic profile, obesity, pregnancy

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Participant experience of a healthy lifestyle program for children and young people in Boorloo/Perth, Western Australia

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Publish consent withheld

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Comparative weight loss and Type 2 diabetes prevalence in people with clinically severe obesity across different BMI categories in a multidisciplinary weight management program

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Aim: There is a clinical perception that adults with more severe obesity have lower weight loss compared to people with lower grades of obesity. This study aimed to compare weight loss in people with clinically severe obesity (body mass index [BMI] >35kg/m^2 and at least one significant obesity-related complication) following 12 months in a publicly funded multidisciplinary weight management program (WMP) across different BMI categories, and also compared the prevalence of Type 2 diabetes (T2D) in these BMI categories.

Methods: A retrospective review of all adult patients with clinically severe obesity who commenced a publicly funded WMP in Sydney between March 2018 and April 2024 and followed up at 12 months, comparing weight loss and T2D prevalence across BMI groups.

Results: Of 398 participants, 68% female, age 50.2±13.1 years, mean weight 149.6±34.8kg, BMI 53.1±10.1kg/m2, and 70% Caucasian, mean percentage body weight loss (%BWL) at 12 months was 5.4±7.3%. Mean %BWL within the groups was, respectively: 3.2±8.3% (BMI 35-39.9kg/m^2, n=22); 5.7±7.1% (BMI 40-49.9kg/m^2, n=147); 5.4±7.1% (BMI 50-59.9kg/m^2, n=136); 5.5±6.7% (BMI 60-69.9 kg/m^2, n=60) and 5.2 ±8.3 (BMI >70 kg/m^2, n=33). No significant difference in mean %BWL was found between the BMI classes (p=0.67).

The prevalence of T2D across groups was 68.2% (BMI 35-39.9kg/m^2, n=22), 53.7% (BMI 40-49.9kg/m^2, n=147), 42.6% (BMI 50-59.9kg/m^2, n=136), 33.3% (BMI 60-69.9kg/m^2, n=60), and 36.4% (BMI >70kg/m^2, n=33). There was a negative association between BMI group and T2D status with the proportion of T2D decreasing with increasing BMI group (p=0.01) although this was not adjusted for age, sex or race.

Conclusions: Participation in a multidisciplinary weight management program for twelve months facilitated modest weight loss across all BMI categories in people with severe obesity with no significant difference between the BMI categories despite clinical perceptions. Paradoxically the higher BMI groups seemed to have a lower prevalence of T2D.

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Obesity and Pulmonary Hypertension in Pregnancy Requiring Extracorporeal Membrane Oxygenation: Diagnostic Delay and the Role of Tirzepatide in Pre-Transplant Optimisation

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A 37-year-old woman, BMI 56.6 kg/m², presented at 19+6 weeks' gestation with severe respiratory failure. Her progressive dyspnoea and chest discomfort had been attributed to obesity hypoventilation and sleep apnoea for years, delaying appropriate investigations. Obesity may also complicate imaging, further contributing to diagnostic delays[1]. By presentation, she was oxygen-dependent with severely impaired functional capacity.

Imaging and right heart catheterisation confirmed pulmonary veno-occlusive disease with moderate pulmonary hypertension (PH). Despite maximal medical therapy, her condition deteriorated, requiring ICU admission, mechanical ventilation, and initiation of venovenous extracorporeal membrane oxygenation (VV-ECMO) to prioritise fetal survival in line with the patient's wishes. Caesarean delivery was performed at 23+5 weeks, and the neonate required NICU. Postpartum, the patient suffered limb ischaemia, requiring thrombectomy and fasciotomy, further complicating recovery. Her baby has since been discharged and is doing well.

Lung transplantation was considered; however, her BMI exceeded eligibility thresholds (BMI >35 kg/m² being an absolute contraindication[2]). Obesity likely contributed to PH progression through mechanisms such as hypoventilation, obstructive sleep apnoea, chronic inflammation and increased intravascular volume[3]. A very low energy diet and compassionate access to tirzepatide, a dual GLP-1/GIP receptor agonist, were initiated. Over 15 weeks, she achieved a 22% weight reduction (127.4 kg to 99 kg), improving transplant candidacy.

This case underscores the impact of weight bias in delaying PH diagnosis and highlights obesity as both a contributor to PH severity and a barrier to definitive treatment. Tirzepatide demonstrates significant potential in facilitating rapid, medically supervised weight loss, enhancing access to life-saving interventions such as lung transplantation. Wider, equitable access to tirzepatide in Australia, similar to the UK's targeted rollout[4], may improve outcomes for patients with class 3 obesity and severe comorbidities, reduce healthcare costs, and address health inequities.

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Change in eating behaviours and eating disorder risk with GLP-1 receptor agonist medications for treatment of obesity and type 2 diabetes: A rapid review

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Systematic reviews of glucagon-like peptide-1 receptor agonists (GLP-1RAs) demonstrate improvements in weight, and cardiometabolic health, while the effects on psychological outcomes are mixed (1,2). This review aimed to evaluate the effect of GLP-1RAs on eating behaviours and eating disorder risk. MEDLINE and Embase were searched to January 2025. Randomised controlled trials (RCTs) and longitudinal studies evaluating obesity or type 2 diabetes treatment with a GLP-1RA for adolescents or adults were included. Eligible studies reported on adverse events, changes in eating disorder risk scores, or eating behaviours post-intervention or follow-up. Summary data were extracted and synthesised according to Synthesis Without Meta-analysis guidelines. A total of 1597 records were screened and 25 trials (k) were included. Of two adolescent trials, one RCT (n=251) reported development of eating disorders following liraglutide (n=2/125). One retrospective cohort study (n=24 adolescents) reported reduced uncontrolled eating with

no change in other eating behaviours following liraglutide. Twenty-three trials were in adults (n=8,722). One study reported an eating disorder adverse event, and two studies reported no binge eating adverse events. Liraglutide reduced global eating disorder risk scores, with no differences between groups (k=1). Binge eating episodes and prevalence reduced following liraglutide and semaglutide, respectively. Binge eating scores improved with liraglutide compared to placebo (k=2). Food cravings following liraglutide (k=1) or semaglutide (k=6) were improved (k=6) or unchanged (k=1). There was no difference in disinhibition between liraglutide and comparator (k=2) with one study reporting a reduction in both groups. Two non-RCTs reported reduced disinhibition with liraglutide. Overall, limited data are available for the effect of GLP-1RAs on eating behaviours and eating disorders. For most, eating behaviours may improve or remain unchanged. Two trials reported development of eating disorders following GLP-1RAs. Comprehensive assessment of eating behaviours and eating disorder risk are needed to understand potential benefits and risks of treatment.

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Changes in psychosocial outcomes reported in behavioural intervention trials for children and adolescents with overweight and obesity: A scoping review

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Many children and adolescents with obesity have co-occurring psychosocial conditions, which may be impacted by obesity treatment (1). Past systematic reviews have shown positive effects for specific psychosocial outcomes, such as improving eating behaviours and quality of life following behavioural interventions for the treatment of paediatric obesity (2,3). This review aimed to extend these findings by mapping patterns of change for the totality of psychosocial outcomes reported in behavioural intervention trials for children and adolescents with obesity.

We conducted a scoping review following PRISMA-ScR guidelines. Eleven databases were searched to identify behavioural intervention trials for children and adolescents living with overweight or obesity, that measured at least one psychosocial outcome pre- and post-intervention. Outcomes were grouped into categories thematically, and data was synthesised based on the timepoint (post-intervention, latest follow-up), intervention arm (active, no-intervention control), and type of change reported (difference between arms, change over time).

Of 1171 articles screened, 197 articles (169 trials) met inclusion criteria, with a combined sample of 19,256 children and adolescents. A total of 375 psychosocial outcomes were identified and grouped into eight constructs. Across all outcomes and timepoints, most trials reported no difference, or a difference favouring the active intervention arm over the no-intervention control arm. Similarly, most active intervention arms showed improvements or no change over time, though six of 169 trials reported worsening in a psychosocial outcome post-intervention. Most no-intervention control arms showed no change over time.

Behavioural interventions are associated with improvements, or no change in psychosocial health across a broad range of outcomes assessed. Consensus on core psychosocial outcomes is needed to reduce heterogeneity and ensure outcomes are relevant to children and adolescents living with obesity.

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From Weight Loss to Waitlist: Evaluating the Impact of the Tertiary Obesity Multidisciplinary Service

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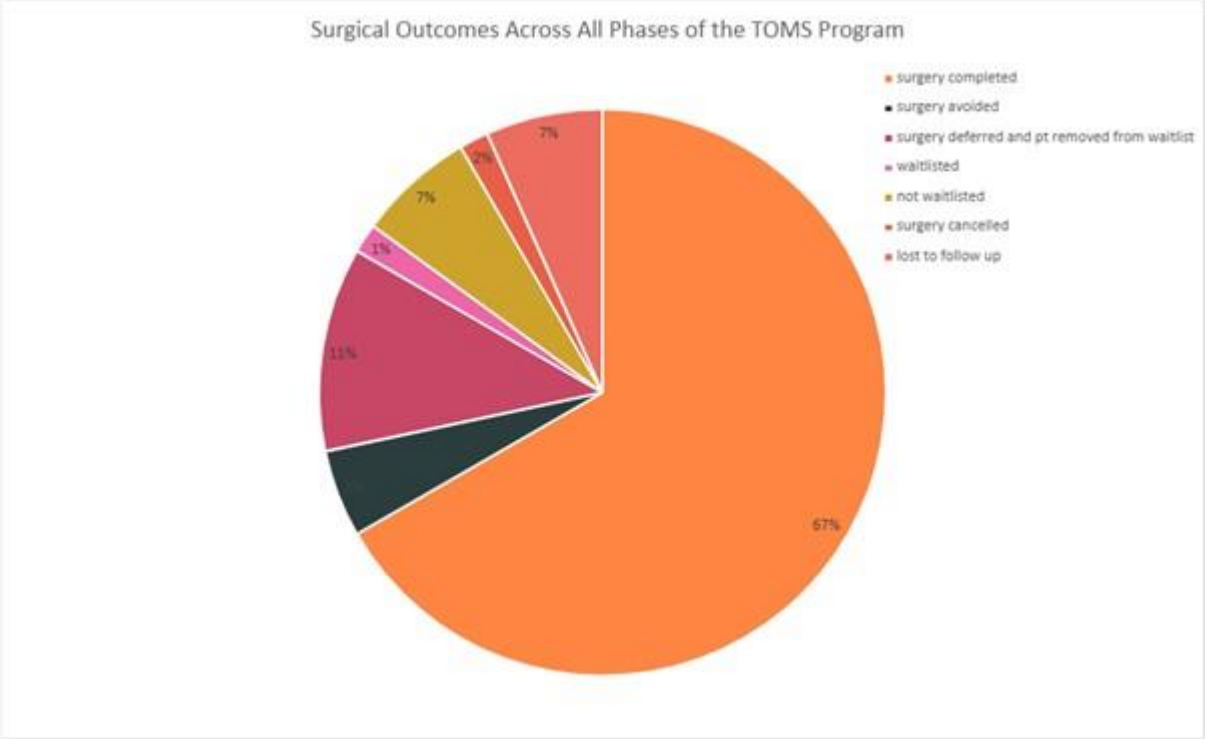
To evaluate the effectiveness of the Tertiary Obesity Multidisciplinary Service (TOMS), a 12-month comprehensive weight-loss program designed to support individuals with complex obesity who face barriers to surgical access due to BMI or weight-related restrictions. Specifically, aiming to achieve weight or BMI goals for non-emergent surgical procedures through coordinated, multidisciplinary care.

Participants who commenced the TOMS program between January 2021 and April 2023 were followed until April 2025. Over the 12-month period, participants were supported by physiotherapists, pharmacists, psychologists, endocrinologists and dietitians to complete a Very Low Energy Diet (VLED), alongside structured education and exercise programs. Surgical waitlisting and operations were tracked for patients referred for pre-surgical weight loss. Key outcomes included surgery completion, avoidance, deferral with removal from the waitlist, and waitlisted status.

A total of 119 patients enrolled in TOMS during the study period. The mean age was 48.8 years (SD 13.7), and the median BMI was 46.4 kg/m² (IQR 40.5–54.8). Of these, 60 patients were referred to TOMS to improve access to non-emergent surgeries, including bariatric, oncological, hernia repair and orthopaedic procedures. Among them, 40 (67%) successfully completed surgery, 3 (5%) avoided surgery, 7 (12%) had surgery deferred and were removed from the waitlist, 1 (2%) had surgery cancelled, 1 (2%) remains waitlisted, 4 (6%) were not waitlisted, and 4 (6%) were lost to follow-up.

The TOMS program demonstrates that coordinated, multidisciplinary care can significantly improve access to non-emergent surgical procedures for individuals with complex obesity through meaningful weight loss. These findings underscore the value of a structured, multidisciplinary based approach in overcoming systemic barriers to surgery, enhancing patient readiness and supporting long-term health outcomes.



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Prevalence of comorbidities in obese New Zealand children and adolescents at enrolment in a community-based obesity programme January 2021-December 2024 vs January 2012 - August 2014

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Aim: The aim of this study was to describe the characteristics at enrolment of children and adolescents referred to an obesity programme and

to determine how the prevalence of comorbidities differed in Indigenous versus non-Indigenous children and how this differed from 2012-2014 to 2021-2024.

Methods: Participants were residents of a semi-rural region of New Zealand (NZ). Eligibility was defined by a body mass index (BMI) of ≥98th percentile

or >91st centile with weight-related comorbidities. Fasting blood, medical and physical assessments were obtained.

Results: During the recruitment period from January 2021 to December 2024 participants (265), aged 3.8–15.8 years, undertook assessment. Average

BMI standard deviation score was 3.04 (compared to 3.09 in 2012-2014). The majority of participants were of either Māori (NZ's indigenous people (41%), 45% in 2012-2014, or NZ European (47%) ethnicity, 45% 2012-2014.

Māori participants were more likely than NZ Europeans to have acanthosis nigricans on examination (32% vs. 12%), elevated fasting Insulin (88% vs 77%), abnormal liver function (66% vs 62%), however low serum high-density lipoprotein cholesterol (HDL) was less likely for Māori vs NZE (7% vs 18%, respectively) and high serum triglyceride (TG) concentration (47% vs. 75%, respectively). This differed from 2012-2014 where low serum HDL for Māori vs NZE was 27% vs 14% , respectively and serum TG was 38% vs 24%.

Conclusion: The unique aspect of this study was the ability to recruit high levels of Māori participants, indicating a high level of acceptability for these target groups. Comorbidities were prevalent in this cohort of overweight/obese school-aged children. While there were some differences in comorbidity prevalence between Māori and NZ Europeans, the overall clinical picture in our cohort, irrespective of ethnicity, was of concern.

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Opportunistic Measurement of Sagittal Abdominal Diameter with Bone Densitometry Predicts Abdominal Aortic Calcification and Major Cardiovascular Events

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Abstract

Background: Visceral adiposity has a crucial Pathophysiological role in the development and progression of cardiovascular disease, the major cause of death globally. Sagittal abdominal diameter (SAD) has been proposed as a simple measure for determining visceral adiposity and has previously shown to predict major cardiovascular events (MACE). However, it remains unclear whether SAD is associated with abdominal aortic calcification (AAC), a marker of subclinical cardiovascular disease, or whether it predicts MACE independent of AAC.

Aims: We sought to investigate the association between SAD adjusted for weight with validated machine learning AAC 24-point score (ML-AAC24), and their joint association with MACE.

Methods: SAD and ML-AAC24 were obtained using Dual-energy X-ray Absorptiometry (DXA) during routine vertebral fracture assessment in the Manitoba BMD Registry. Incident MACE (composite of all-cause mortality, acute myocardial infarction [MI], non-hemorrhagic stroke) was ascertained from linked healthcare databases. Cox proportional hazards models examined the simultaneous relationships of SAD/weight and ML-AAC24 with incident MACE.

Results: The study population comprised 8806 individuals (mean age ± SD 75.1 ± 6.6 years, 93.9% women). ML-AAC24 scores were categorised (low <2, moderate 2<6 and high ≥6). Compared to low, those with moderate and high ML-AAC24 had 1.5% and 3.3% higher mean SAD/weight, respectively. Over follow-up of 3.8 (SD 2.2) years, 993 people (11.3%) experienced a MACE. Each increase in SD of SAD/weight was associated higher relative hazard for incident MACE (HR 1.14, 95%CI 1.07-1.21). The hazard ration (HR) of highest compared with lowest tertile of SAD/weight was 1.37 (95%CI 1.16-1.61). Compared to low ML-AAC24 the hazard ratio for moderate and high ML-AAC24 was 1.45 (95% CI 1.24-1.71) and 1.98 (95CI 1.67-2.35), respectively.

Conclusion: SAD/weight is positively associated with ML-AAC24 in older adults attending routine osteoporosis screening. Both measures were associated with incident MACE independent of each other and multiple cardiovascular risk factors.

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Ketones and Kilograms: Exploring Predictors of Weight Loss Success in a Structured Obesity Program

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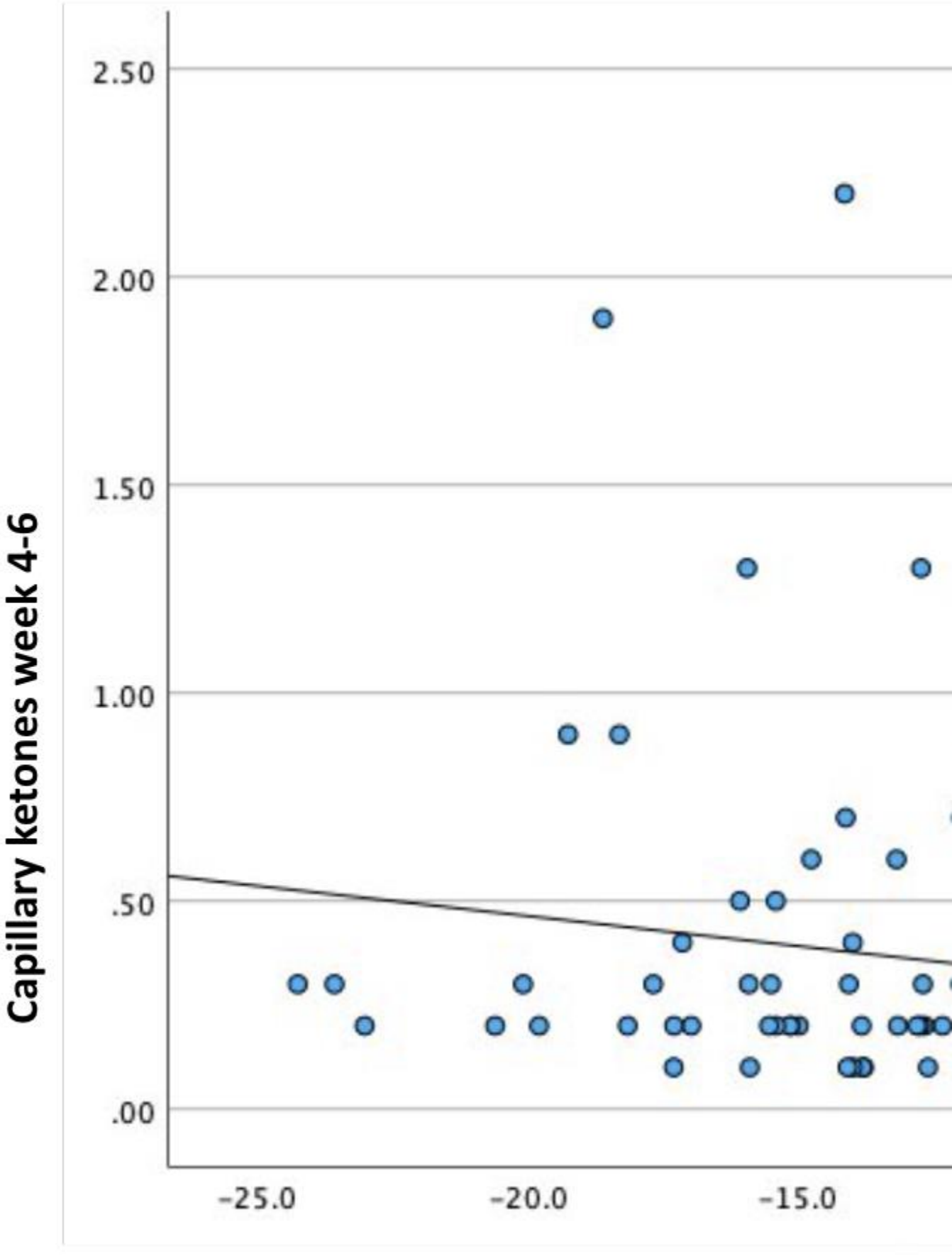
This study investigated whether capillary ketone levels are a predictor of weight loss success during our tertiary obesity multidisciplinary service (TOMS) using a 12-week very low energy diet (VLED) plus exercise with group support.

A total of 108 participants were included for analysis. Capillary ketone levels were measured at week two of the intervention, and weight was monitored throughout the program. Participants were categorised based on their ketone levels into two groups: non ketotic state (0–0.5 mmol/L, n=91) and nutritional ketosis (0.6–2.2 mmol/L, n=17). Weight loss was assessed as a percentage of initial body weight. The association between percentage weight loss and ketone level was assessed with a rank correlation.

Participants in the nutritional ketosis group experienced a greater mean weight loss compared to those in the non ketotic state (12.3% vs 10.7%; SD 5.5, 4.5, p=0.2). The mean ketone level in the non ketotic group was 0.2mmol/L and 1.0 mmol/L for the nutritional ketosis group (SD 0.1, 0.5). Treating percentage change in body weight and ketone levels as continuous variables, there was a moderate, but statistically significant, Spearman rank correlation between the two (rs = 0.258, p 0.007).

This data shows that a positive ketone test is a good predictor of weight loss outcomes, but a negative ketone test has poor predictive value as participants who did not reach nutritional ketosis still achieved clinically significant weight loss. This indicates that nutritional ketosis is not essential for successful outcomes. These findings highlight the potential role of nutritional ketosis as a supportive, but not necessary, factor in weight management strategies. Future research may consider the inclusion of repeated capillary ketone testing throughout the

intervention.


Capillary ketones week 4-6
2.50
2.00
1.50
1.00
.50
.00
-25.0
-20.0
-15.0
Percent weig

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Gestational weight gain and its' association with preeclampsia and blood pressure trends: a retrospective cohort study

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Background: Preeclampsia has a significant negative impact on maternal and foetal health. Excessive gestational weight gain (eGWG) is defined as weight gain in excess of recommendations as per the Institute of Medicine guidelines. eGWG is a risk factor for preeclampsia.

Aims: We aimed to investigate the patterns of gestational weight gain, its relationship to the incidence of preeclampsia, trends in blood pressure and pregnancy outcomes within a hospital network in Sydney, Australia.

Materials and Methods: We conducted a retrospective cohort study within a metropolitan area health network in Sydney, Australia. Participants included all pregnant women who delivered at the facility between 1 January 2018 and 31 August 2024.

Results: 44,852 met the inclusion criteria. 958 (2.14%) women developed preeclampsia.

More women had eGWG (57%) than those with recommended GWG (rGWG) or inadequate GWG (iGWG). eGWG was associated with increased incidence of caesarean section (35.08%) and postpartum haemorrhage (11.48%). eGWG correlated with increased incidence of preeclampsia (2.61% n=668, p<0.001). There appears to be a directly proportional relationship between weight and blood pressure - as BMI increased, blood pressure also increased. Women with preeclampsia had higher blood pressures throughout the pregnancy compared to non-preeclampsia women. eGWG was associated with higher blood pressure throughout the pregnancy.

Conclusions:

Excessive gestational weight gain appears to increase the risk of developing preeclampsia. Pre-pregnancy overweight and obesity increases risk of excessive gestational weight gain as well as blood pressure and incidence of preeclampsia. In pregnancy, weight appears to have a positive linear relationship with blood pressure.

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Active screening for inpatient obesity using a surveillance system

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Obesity is a significant burden in hospitals, yet comprehensive data on its prevalence and impact on healthcare utilisation remain limited. The use of Electronic Medical Records (EMRs) for obesity surveillance is restricted by data completeness and accuracy. This study aimed to determine obesity prevalence across hospital specialties, examine the relationships between body mass index (BMI) and length of stay (LOS), identify patterns of missing anthropometric data, and explore the implications for clinical resource allocation.

A retrospective analysis was conducted on 2,221 patients admitted to Blacktown and Mt Druitt Hospitals in Sydney, NSW, with 1,298 patients meeting the inclusion criteria. Data on patient demographics, BMI, specialty, and LOS were extracted from the EMR. Descriptive statistics and correlation analyses assessed associations between BMI, LOS, and data completeness.

The mean BMI was 29.4 kg/m², with 37.0% of patients classified as obese (Classes I–III). Patients with Class III obesity had the longest average LOS at 15.1 days compared to an overall average of 9.3 days, while underweight patients had an average LOS of 10.5 days. Notably, BMI data were missing in 19.5% of patients, with the highest missing rate (37.0%) in the 17–39 age group.

Although the overall obesity prevalence in the inpatient population reflects community levels, both Class III obesity and underweight statuses are disproportionately represented and linked to prolonged hospital stays. The substantial proportion of missing data underscores significant deficiencies in current documentation practices. Implementation of automated EMR prompts, standardised measurement protocols, and AI-driven risk stratification tools could convert static anthropometric data into dynamic, actionable clinical insights. Such advancements have the potential to improve resource allocation and patient outcomes. These findings emphasise that early, targeted interventions for patients with high-risk BMI categories may optimise hospital resource utilisation and enhance the quality-of-care delivery.

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Machine learning-powered lipidomics identifies serum lipid signature predictive of personalized glycemic changes following 3-year weight loss intervention

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***Aim*:** Over 50% of people with obesity-associated prediabetes fail to sustain long-term glycemic improvements, even after successful weight-loss maintenance through lifestyle interventions. This study aimed to identify baseline lipidomic signatures predictive of personalized glycemic changes following a 3-year structured lifestyle intervention.

***Methods*:** Serum lipidomics was conducted at baseline and annually over 3 years, in 100 participants from the Australian sub-cohort of the PREVIEW randomized controlled lifestyle trial. Longitudinal lipidome dynamics were characterized using multivariate analyses and Fuzzy C-Means clustering. Lipid-glycemic associations across 4 time points were assessed using Response Screening and Bayesian curve fitting. Baseline lipid predictors were identified using the best-performing model, Boosted Neural Networks, among 6 advanced machine learning algorithms.

***Results*:** Lifestyle interventions induced significant serum lipidome remodeling, marked by reductions in ceramides and lysophospholipids, increases in complex sphingolipids and ethanolamine-based lipids, and altered ratios between biologically related lipid subclasses. Several lipid species, particularly from dihydroceramides and lysophospholipids, exhibited longitudinal associations with glycemic changes over time. Notably, a distinct subset of baseline lipids only bearing saturated C14:0 –C24:0 fatty acyl chains accounted for 27% of the leading predictors of 3-year glycemic changes.

***Conclusions*:** Discovered lipidomic dynamics and lipid-glycemic associations illustrate how lifestyle interventions broadly reshape the metabolic landscape, informing potential targets for long-term glycemic monitoring and regulation. In addition, this study demonstrates the utility of advanced machine learning in identifying robust lipid predictors of personalized glycemic outcomes, facilitating early identification of individuals who are less likely to benefit from lifestyle interventions and thus supporting precision prediabetes care.

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Implementing and evaluating an educational intervention for weight stigma reduction among dentistry and oral health therapy students: an implementation study

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Background: There is evidence of weight stigma in the dental setting. However, interventions to reduce weight stigma have been minimally explored and not previously evaluated for their implementation outcomes.

Aims: To assess the implementation outcomes of an educational intervention to reduce weight stigma in students.

Methods: Dentistry and oral health therapy students across all Australian universities were invited to participate. Students were asked to complete and evaluate an educational module intervention to reduce weight stigma. The approaches varied by recruitment strategies, specific groups of students or universities invited, and the presence or absence of a contextual lecture, or follow-up period. Pre- and post-intervention surveys assessed participants' weight stigma levels, attitudes and beliefs regarding obesity. The primary outcome measures were the acceptability, adoption, feasibility and appropriateness, and sustainability of the educational module. An embedded qualitative study explored student perspectives on how the implementation of the weight stigma educational module could be improved for the dental setting.

Results: Across three recruitment approaches, 155 students completed the entire study. Voluntary completion of the weight stigma educational module in the student cohorts was low in settings without curriculum integration (27/94; 28.7%), improved slightly by tangible incentives. The one-session curriculum-embedded intervention was the most effective for student participation. Across all recruitment approaches, the module was evaluated to be useful, relevant and likely to be recommended. Qualitative analysis revealed the most common themes for improving dental relevance were through using examples and by providing education on effective communication, patient management and links between obesity and oral health.

Conclusion: A weight stigma intervention for dental and oral health students was assessed as acceptable, feasible and appropriate and adoption was greater when embedded in the curriculum. Interventions may be enhanced for adoption by providing patient examples and education on non-stigmatising communication approaches with people living with obesity.

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Copy Number Variations (CNV's) and rare genetic mutations associated with childhood obesity at a tertiary obesity management service

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Aims:
Childhood obesity is a worldwide issue. In Australia, 19.3% of children are overweight, and 8.3% are obese. Environmental and polygenic causes remain most common, however, monogenetic causes are significant in the pathogenesis of early onset severe obesity. Identifying monogenetic causes via screening may help tailor therapy. We aimed to identify copy number variants (CNV)'s and monogenetic mutations associated with obesity at an Australian tertiary paediatric obesity service. and key factors predictive of a monogenetic cause in our population.

Methods:
We reviewed databases (January 2008-April 2025), excluding patients with common syndromic causes including Bardet-Beidl and Prader Willi Syndrome. Our site's monogenetic obesity screen encompasses LEP, LEPR, POMC, GHRL, MC4R genes and whole exome sequencing (WES) for CNV's. Data was grouped by age of obesity onset </≥5 years) and presence/absence of neuro-developmental (intellectual, sensory or communication) delays.

Results:
From 2980 records, we identified 52 variants in 44 individuals with abnormal microarray or WES. 100% of patients with monogenetic cause had early onset obesity (mean age 3.2± 3.3years) and neurodevelopmental differences (baseline population prevalence estimate=15.9%). Mean % 95th percentile BMI was 148± 23%. Chromosome 16p CNV's were most common (19.2%). Eight (15.4%) were known pathogenic mutations, two (3.8%) were of unclear clinical significance. Twenty-seven (51.9%) CNV's of unclear clinical significance were identified. Four (9.1%) patients had rare syndromes associated with obesity. Five (11.4%) had pathogenic WES abnormalities. Eight (18.2%) had multiple genetic mutations. Three had commenced GLP1-agonist therapy.

Conclusions:
Consistent with international literature, mutations impacting the leptinmelanocortin pathway were the most common in our cohort. Rates of comorbid neurodevelopmental differences were higher than levels quoted in literature possibly reflecting tertiary centre population and selective testing. With enhanced accessibility to genetic testing, it is likely that rates of monogenic obesity in our cohort are underestimated.

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A study on the effect of Obesity on COVID-19 related outcomes in Sri Lanka

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The aim of this study was to assess the impact of obesity on outcomes in patients with severe COVID-19. This was a prospective observational study of 109 patients with severe COVID-19 treated in either intensive care (ICU) or high dependency care units (HDU) at the National Hospital Kandy, Sri Lanka. The mean BMI of the cohort was 21.5 kg/m^2 (SD 3.53), with the commonest and least common BMI categories being normal BMI (42.2%) and obesity (13.8%) respectively. There was no significant difference in survival rates among the BMI categories (p = 0.301), but 60% people living with obesity survived compared to 32.6% with normal BMI. A lower proportion of people living with obesity compared to those without obesity required ICU care (60% vs. 84%; p=0.028) and intubation and ventilation (13.3% vs. 46.8%; p = 0.015) respectively. People living with obesity required non-invasive-ventilation (NIV) for a longer duration (median 6 days) compared to those with normal BMI (median 3 days), underweight (median 3 days) and overweight (median 2 days) (p = 0.017). People living with obesity had non-significantly higher arterial PaCO2 (median 61 mmHg), followed by people with overweight (median 41 mmHg), normal BMI (median 38), and underweight (median 37 mmHg) (p = 0.076), but had no significant difference in SpO2 (p = 0.273) or PaO2 (p = 0.371) among the BMI categories. The longest duration of insulin infusion was required in people living with obesity (median 181 hours), followed by normal BMI (median 102 hours), underweight (median 35 hours), and overweight (34 hours) (p = 0.01). There was no significant difference in daily insulin dose requirement based on BMI category (p = 0.212). People living with obesity experienced lower rates of ICU admission and intubation, but had more carbon-dioxide retention and required longer durations of NIV and insulin infusion in severe COVID-19.

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The feasibility of overnight time restricted eating in rotating shift workers – a randomised controlled feasibility trial

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Aims: Shift work disrupts circadian rhythms, contributing to increased rates of obesity and related conditions such as insulin resistance and dyslipidaemia. Eating during night shifts may exacerbate weight gain, yet few interventions address this risk. Time-restricted eating (TRE), which aligns food intake with circadian biology, shows promise for metabolic management. This study aims to assess

the feasibility and acceptability of a 7-hour overnight fasting protocol in rotating shift healthcare workers over two weeks, including night shifts.

Methods: This two-week randomised controlled parallel-arm trial assessed the feasibility of time-restricted eating (TRE) in rotating shift workers, including ≥3 consecutive night shifts. Eligible healthcare professionals (n=30) were randomised to either TRE (eating 06:00–23:00, fasting 23:00–06:00) or control (ad libitum eating). Weekly check-ins monitored adherence and adverse events. Post-intervention, participants completed satisfaction ratings and TRE participants were invited to semi structured interviews to evaluate feasibility. The study was coordinated from Macquarie University and the Woolcock Institute of Medical Research, with recruitment from The Sutherland Hospital.

Results: Of 55 pre-screened healthcare workers, 31 (56.4%) met eligibility criteria and were enrolled; 80.6% were female, 83.9% registered nurses, with a mean age of 30.7 years (range 23-55) and BMI of 24.7 kg/m² (range 18.9–37.0). Recruitment spanned 68 days with no refusals post-TRE discussion. Four participants were excluded due to shift schedules or pre-existing fasting and metformin use. Among 16 participants in the TRE group, 81.3% adhered daily to the TRE protocol at the defined compliance threshold (≥13/14 days). No adverse events or dropouts occurred. These findings support the feasibility, acceptability and safety of overnight TRE in rotating shift workers.

Conclusion: We have shown a pragmatic TRE from 23:00-06:00 is feasible and safe intervention for rotating shift healthcare workers. High adherence and absence of adverse events support its acceptability. These data demonstrate feasibility for larger clinical trials.

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Weight loss outcomes with cost-subsidised liraglutide and semaglutide in people with extreme obesity (BMI ≥50kg/m2): a retrospective audit

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Aims: Clinical obesity is a major contributor to adverse health outcomes and treatment remains a significant challenge. Glucagon-like peptide-1 receptor agonists (GLP-1RA) are an effective tool for weight loss, however there is limited evidence for individuals with higher body mass index (BMI) ≥50kg/m2 and costs can be prohibitive. Our aim was to evaluate weight loss outcomes and tolerability of cost-subsidised GLP-1RA in people with extreme obesity (BMI ≥50kg/m2).

Methods: A retrospective audit was performed on individuals treated with cost-subsidised GLP-1RA (semaglutide and/or liraglutide) at a tertiary Complex Obesity Service between March 2021 and June 2025. Eligibility criteria were BMI ≥60kg/m2 or weight ≥180 kg, or BMI ≥50kg/m2 or weight ≥160 kg with ≥1 significant obesity-related comorbidity. The main outcomes were change in weight and BMI at both nadir and last follow-up, treatment duration, and adverse effects.

Results: Thirty-seven individuals were approved for cost-subsidised GLP-1RA therapy, of whom thirty-one had adequate data for analysis. At baseline, the mean (SD) age was 47.3 (13.6) years, median (IQR) weight was 182.4kg (152-246), and BMI was 65.5 kg/m2 (54-75). Median semaglutide dose was 1mg weekly (n=30) and liraglutide dose was 3mg daily (n=10). Median maximal weight loss was 15.5kg (9-26), or 9.3% (5-15), over a median of 10 months (5-15). At last follow-up (median 13 months [8-22]), median weight loss was 14.9kg (7-23), or 7.2% (4-13). Nineteen (61%) individuals achieved ≥5% and 13 (42%) achieved ≥10% weight loss at last follow-up. Twelve (39%) people experienced gastrointestinal adverse effects and six (19%) discontinued due to adverse effects.

Conclusion: Cost-subsidised GLP-1RA enabled clinically significant weight loss in a cohort of people with BMI ≥50kg/m2, and although well-tolerated by most, gastrointestinal adverse effects were common. These results demonstrate a promising role for GLP-1RA in the management of those with extreme obesity.

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Cardiac Autonomic Dysfunction Following Bariatric Surgery: A Case of Presyncope and Postural Intolerance Responsive to Rate-Limiting Therapy

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We describe a case of cardiac autonomic dysfunction following sleeve gastrectomy.

A 54-year-old woman presented with recurrent post operative presyncope described as “blacking out” without loss of consciousness. She underwent sleeve gastrectomy in 2020 with a nadir weight of 93.4 kg, followed by modest weight regain managed with liraglutide. Symptoms occurred up to four times weekly and were associated with palpitations. Orthostatic vitals revealed stable blood pressure (sitting 110/60 mmHg; standing 115/70 mmHg) but a fixed heart rate of 60 bpm with no postural acceleration.

ECG was sinus rhythm. Biochemistry demonstrated no electrolyte abnormalities. Haemoglobin was 141 g/L with low serum ferritin 24 mcg/L (30–165). She received intravenous iron. Preoperative CT coronary angiography and coronary artery calcium score was 0. A loop recorder revealed brief supraventricular tachycardia (186 bpm, 12 beats) correlating with one episode. Multiple device-recorded pauses were confirmed to be artefactual.

The patient was initially treated with metoprolol 25 mg twice daily, which reduced symptom frequency but caused fatigue. She was switched to diltiazem 180 mg extended release, which was well tolerated and led to substantial improvement. Over the next 12 months, she experienced only three to five brief episodes of presyncope, with no further tachycardia or syncope.

Cardiac autonomic dysfunction following bariatric surgery is multifactorial, involving altered baroreflex sensitivity, decreased sympathetic tone, and intravascular volume depletion from weight loss and hormonal changes[1,2]. The efficacy of beta-blockers and calcium channel blockers may relate to modulation of rate variability and supraventricular ectopy[3-5]. Loop recorders provide valuable data to exclude high-risk arrhythmia[6]. Cardiac autonomic dysfunction is a potentially under-recognised complication of rapid weight loss following bariatric surgery. Clinicians should maintain a high index of suspicion for autonomic dysfunction in post-bariatric patients presenting with postural symptoms, especially when standard investigations are unremarkable, and management tailored to symptoms and medication tolerability.

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Severe malnutrition following laparoscopic one anastomosis gastric bypass in a publicly funded bariatric program: A case report

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Background:

Pancreatic exocrine insufficiency (PEI) and chronic pancreatitis (CP) are known complications following bariatric surgery(1) and contribute further to malnutrition, micronutrient deficiency, and deteriorating bone health.(1,2) The risk is higher in bypass operations over sleeve gastrectomy.(1)

Case report:

We report a case of severe malnutrition and chronic diarrhoea with evidence of PEI in a 48-year-old male with insulin-dependent type 2 diabetes following one anastomotic gastric bypass for management of class III obesity through a public multidisciplinary metabolic program. Baseline weight was 193kg (BMI 56kg/m^2) with mixed metabolic and mechanical obesity-related complications. Following 13% (25kg) weight loss pre-op, he lost a further 73kg post-surgery and 98kg overall (43% from surgery, 51% from peak) doing well initially.

Hospital admission with persistent diarrhoea, anasarca, weakness and skin ulceration occurred four years post-surgery. Diarrhoea pre-dated surgery and pre-surgical workup included coeliac testing, stool culture, virology, faecal elastase level, gastroenterology review and colonoscopy but no CT or MR imaging.

Admission bloodshypoalbuminaemia (13g/L), cholestatic liver function derangement, normal amylase/lipase, elevated prothrombin time, thrombocytopenia and fat-soluble vitamin (A, D, K) and trace element (zinc, selenium, ceruloplasmin). Liver screen was normal; elastography negative for fibrosis and abdominal CT and MRI cholangiopancreatogram suggested CP. He had hypogonadism, hypothyroidism, secondary hyperparathyroidism and new severe osteoporosis.

Bypass reversal was considered during his six-week admission. Fortunately, he responded to conservative management via high protein oral diet with nutritional supplementation drinks, high-dose intravenous multivitamins, vitamin K, trace elements, thiamine and vitamin D. Empiric mealtime Creon resulted in rapid diarrhoea resolution. Subsequent faecal elastase was 4ug/L, in keeping with severe PEI.

Conclusion:

PEI symptoms are difficult to differentiate from the usual sequelae of bariatric surgery. Delay in diagnosis and treatment can lead to delayed responses, irreversible damage and death. There is room for developing a structured guideline directed approach and long-term follow-up is crucial.

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Investigating the acute effects of whey protein hydrolysate administration as a preload on postprandial glycaemic metabolism in healthy adults

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Publish consent withheld

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Effectiveness of obesity management education for healthcare professionals: a rapid review with meta-analysis

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Aims: This rapid review and meta-analysis aimed to evaluate the effectiveness of structured education in obesity management for healthcare professionals (HCPs) on practice competencies.

Methods: We systematically searched MEDLINE, EMBASE, CINAHL, Web of Science, ERIC, and Google Scholar. Effect sizes (ESs) were calculated, and a random-effects model was used for meta-analysis. Heterogeneity was quantified using the I^2statistic and tested for statistical significance using the Q-statistic. Subgroup analyses explored sources of heterogeneity. Additionally, several quasi-experimental studies, not included in the meta-analysis, were descriptively synthesised.

Results: Our search yielded 1,683 records, from which 18 eligible studies, published between 2020 and 2025, were selected. These included four RCTs, one non-RCT, ten before-and-after studies, and three studies with both non-RCT and before-and-after designs. Pooled analysis of four RCTs and three non-RCTs revealed a statistically significant moderate positive overall effect (ES=0.413, 95% CI: 0.122 to 0.705, p=0.005), despite substantial heterogeneity (I^2=69%, Q=16.66, p=0.01). Subgroup analysis showed a significant moderate positive effect for RCTs (ES=0.530, 95% CI: 0.104 to 0.956, p=0.015), while the non-RCT subgroup showed a smaller and non-significant effect (ES=0.253, 95% CI: -0.044 to 0.550, p=0.095). Interventions lasting 4 hours or more had a moderate and statistically significant positive effect (ES=0.685 95% CI: 0.304 to 1.066, p<0.001), whereas shorter interventions (under 4 hours) showed a small non-significant effect (ES=0.236, 95% CI: -0.079 to 0.552, p=0.141). Descriptively synthesised quasi-experimental studies supported these findings, revealing improvements in HCPs' knowledge, practice behaviours and skills, confidence, attitudes, in some cases, patient outcomes like weight loss.

Conclusion: Overall, structured education programmes effectively improve HCPs' obesity management competencies. The positive impact is primarily driven by longer, more comprehensive interventions, and more robust studies. These findings highlight the importance of investing in substantial educational initiatives to enhance HCPs' skills in obesity care.

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Should we be worried about normal weight obesity in people with cystic fibrosis

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Aims

People with cystic fibrosis (pwCF) are increasingly at risk of overweight and obesity. The traditional measure of body mass index (BMI) used to commonly define overweight and obesity is crude and there is interest in more sensitive analytics comprising body composition. This study aimed to i) validate bioelectrical impedance assessment (BIA) against clinical standard dual X-ray absorptiometry (DXA) for body composition and ii) compare prevalence of obesity diagnosis based on body composition versus BMI cut-points in pwCF.

Methods

Our adult CF centre at The Prince Charles Hospital used a dual-frequency Tanita BIA machine for body composition in pwCF, with DXA performed contemporaneously for validation (HREC EX/2024/MNHB/110279). BIA validation was defined by a correlation coefficient >0.70. BIA was offered to pwCF attending routine face-to-face outpatient CF clinics across a calendar month where body composition parameters including weight, fat mass and percentage, lean mass, and bone mineral content were collected. General and age- and gender-specific cut-points for BIA-derived body fat percentage were then compared to BMI cut-points.

Results

Eight pwCF (3 females) underwent contemporaneous BIA and DXA analyses. Pearson correlation coefficients for weight (0.99), fat mass (0.94), and muscle mass (0.92) were very high, while bone mass showed moderate correlation (0.68).

Our cross-sectional analyses comprised 15 pwCF (5 females), of whom 80% were on Elexacaftor/Tezacaftor/Ivacaftor and 46% had CF-related diabetes with a mean BMI of 26.4 kg/m². The mean±SD body fat percentage was 33.2%±7.0 in females and 24.5%±6.9 in males. Age and gender-specific body composition cut-points for obesity were met by 73%, in contrast to only 26% using traditional BMI cut-points.

Conclusion
BIA showed strong correlation with DXA for body fat and lean mass in pwCF. Body composition analysis might be more sensitive than BMI for detection of *'normal weight'* obesity, the prevalence of which might be high in pwCF.

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The Role of Fat-Free Mass in Weight-Related Complications in Adults: A Rapid systematic Review

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Aim: To synthesise evidence from observational studies assessing the role of fat-free mass in weight-related complications in adults with overweight or obesity.

Methods: We systematically searched Medline, Embase, Web of Science, and Google Scholar, including observational studies on adults (≥18 years) with overweight or obesity. Effect estimates (risk ratios, odds ratios, hazard ratios) were logarithmically transformed and harmonized to a common reference. Pooled random-effects meta-analyses were conducted for outcomes with three or more studies. Heterogeneity was quantified using the I^2 statistic; when substantial (I^2 > 50%), τ^2) was also considered. Subgroup and sensitivity analyses explored heterogeneity.

Results: Meta-analysis of six studies revealed low FFM to be associated with an increased risk of developing type 2 diabetes mellitus (pooled RR=1.43; 95% CI: 1.15–1.79). Although high heterogeneity was observed (I^2=90.3%; τ^2=0.07), sex-stratified analyses showed similar effects for men and women. Four studies indicated low FFM significantly increased risk of having metabolic syndrome (pooled RR=3.40; 95% CI: 1.63–7.06). High heterogeneity was also observed (I^2=91.6%; τ^2 =0.49), with consistency across sexes. Three studies showed low FFM was associated with over a twofold increased risk of developing cardiovascular disease (pooled RR = 2.03; 95% CI: 1.27–3.26), with low to moderate heterogeneity (I^2=36.1%; τ^2 =0.08). Three studies demonstrated low FFM was associated with more than twice the risk of having non-alcoholic fatty liver disease (pooled RR = 2.24; 95% CI: 1.52–3.32), with substantial heterogeneity (I^2=69.9%; τ^2=0.08). Sensitivity analyses generally affirmed the robustness of these associations.

Conclusion: Low FFM significantly increases the risk of type 2 diabetes, metabolic syndrome, cardiovascular disease, and non-alcoholic fatty liver disease. These associations were largely consistent across sexes, highlighting the critical importance of maintaining adequate FFM to mitigate weight-related health risks in both men and women.

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Understanding weight change perceptions in adults with cystic fibrosis treated with elexacaftor/tezacaftor/ivacaftor

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Aims

Elexacaftor/Tezacaftor/ Ivacaftor (ETI) has transformed the management of cystic fibrosis (CF) leading to marked improvements in lung function and quality of life. However, significant and often rapid weight gain has been observed following ETI initiation with heterogenous responses among individuals.(1) This prospective qualitative study aimed to explore perceptions of weight changes in adults living with CF receiving the CF modulator therapy ETI.

Methods

A consumer survey was co-developed by the CF multidisciplinary team including dietetics and endocrinology, as part of a broader initiative to design the metabolic and diabetes care components of the Cystic Fibrosis Endocrine Service at The Prince Charles Hospital, Queensland. The survey was administered anonymously via Qualtrics^{XTM} and disseminated via social media channels and email to adults with CF attending our centre.

Results

A total of 72 adults with CF completed to the survey (~20% of our entire CF cohort). Most respondents were aged between 19-45 years with equal gender representation. 61% (44/72) were on ETI. Among those on ETI, 69% reported weight gain since therapy initiation with a median gain of 8.72kg. Perspectives varied, with some expressing satisfaction while others feeling very dissatisfied with the weight gain. Thirty-one percent reported that ETI-related weight gain had negatively impacted their health and an equal proportion felt motivated to lose weight. Of note, 60% reported active weight loss efforts through lifestyle modifications primarily through dietary interventions and increased physical activity. In total, three (3) individuals reported using pharmacotherapy for weight loss. Preferred supports included (i) tailored nutrition and exercise plan, (ii) access to smart/wearable technology to promote positive health behaviours and (iii) consistent recommendations. Few (8%) reported interest in anti-obesity clinical trials.

Conclusion

Weight gain associated with ETI is common and variably perceived among adults with CF and many are motivated to manage weight through lifestyle change.

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Evaluating a virtual reality platform for bariatric care education: Enhancing clinical decision-making and safe care practices

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Caring for individuals of larger body size presents multifaceted challenges across healthcare settings. These extend beyond physical demands to include inadequate infrastructure, limited access to specific equipment, inconsistent training, and staff anxiety (1-2). Weight bias further compromises the safety, dignity, and equity of care delivery (3).

Traditional bariatric moving and handling education often focuses on physical techniques and equipment use, overlooking critical aspects such as clinical decision-making, communication, cultural safety, and workplace attitudes. Training environments may lack realism, with limited access to bariatric mannequins and sensitivity concerns when using colleagues as practice subjects.

Aim:
This study aimed to address these gaps by developing a virtual reality (VR) platform to support bariatric care education. The platform was co-designed over 12 months with input from nurses, educators, clinicians, paramedics, patient representatives, equipment manufacturers, and community advocates. It was designed to enhance clinical decision-making and promote safe, respectful care practices for people of larger size.

Methodology:
Using a user-centred, iterative approach, the VR platform was developed with immersive scenarios that integrate clinical reasoning, safety culture, and patient interaction. It enables repeated, risk-free practice and consistent exposure to bariatric care principles. The prototype was evaluated with three end-user groups: nursing students, paramedic and hospital staff, and bariatric equipment providers. Participants experienced the VR educational scenarios and feedback was collected through structured interviews and standardised questionnaires.

Results:
Preliminary findings indicate the platform was engaging and realistic. Participants reported increased confidence and improved understanding of the complexities of bariatric care. The VR experience was valued for addressing both technical and interpersonal aspects of care.

Conclusion:
This VR platform represents a significant advancement in bariatric education, supporting a more equitable, culturally safe healthcare environment for patients of larger size and the professionals who care for them.

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The impact of pre-operative weight loss on 12-month post-bariatric surgery weight outcomes

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Aim:

People attending publicly funded metabolic and bariatric programs often have severe and complex obesity with multiple physical and mental health complications. The aim of this study was to examine whether weight loss achieved before bariatric surgery had an impact on weight loss 12 months after bariatric surgery.

Methods:

All patients (n=40) who underwent bariatric surgery (97% laparoscopic sleeve gastrectomy) at a single publicly funded metabolic and bariatric program in NSW between 2019 and 2022 were included. Clinical and anthropometric parameters were recorded at the commencement of the program (baseline), immediately pre-operatively, and at 12 months post-operatively. All patients received multidisciplinary weight management in the pre-operative and post-operative phases.

Results:

Of the overall cohort (n=40), 75% were female, and at baseline, the mean age participants was 42.7±11.2 years (range 23 to 66 years), weight 149.1±20.6kg, BMI 55.0±7.7kg/m² with 60.7% having type 2 diabetes (T2DM). The mean duration from baseline to surgery was 28 months (range15-55 months) and weight reduced to 138.5±22.7kg pre-operatively, with 8.6±5.1% body weight loss (12.7±8.1 Kg; p<0.001). At 12 months post-operatively, mean weight had decreased to 101.5±19.3 kg (p<0.001) and BMI to 36.8±17.6 kg/m² (p<0.001), with total weight loss from baseline being 31.6±11.0% (47.6±18.9 kg; p<0.001). Pre-operative weight loss was 12.7±8.1kg compared to post-operative weight loss 34.9±19.9 kg (p<0.001). Correlation analysis found no significant association between pre-operative weight loss and total 12-month weight loss (r=0.093, p=0.623).

Conclusion:

Pre-operative weight loss was achieved across the cohort in the weight management program. However, there was a significant wait for people joining the program to access bariatric surgery. While there is often a need for assessment and management of physical and mental health complications, pre-operative weight loss itself did not appear to be a predictor of weight loss following bariatric surgery at 12 months.

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Hepatic steatosis and high-risk coronary plaque: a systematic review

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Publish consent withheld

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Cardiovascular benefits of early childhood obesity prevention: a pragmatic evaluation of a randomised controlled trial in pre-school aged children

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Background: Atherosclerotic cardiovascular disease begins early in life and can be measured non-invasively at a pre-clinical stage using ultrasound-derived intima-media thickness (IMT) [1]. Early childhood efforts to prevent obesity may provide cardiovascular benefits, even without substantial changes in adiposity. The *Communicating Healthy Beginnings Advice by Telephone* (CHAT) trial was a nurse-led, telephone-based intervention conducted in Sydney, Australia, that aimed to support parental behaviours to reduce childhood obesity [2]. This study evaluated the effect of the CHAT intervention on vascular health in preschool-aged children.

Methods: Eligible children from the CHAT trial were invited for an in-person health assessment between the ages of 5 and 6 years. Abdominal aortic IMT (aIMT), the primary outcome, was measured using high-resolution ultrasound. evaluated whether the intervention affected aIMT directly or indirectly via BMI changes from infancy. To explore dose-response effects, participants were grouped by exposure across the trial's two phases (birth–2 years and 2–4 years): no intervention, one phase, or both phases.

Results: The study included 92 mother-child dyads. At follow-up (mean age 5.8 ± 0.2 years), children had mean weight and height z-scores of 0.13 (±1.17) and 0.46 (±1.08), and a BMI z-score of -0.10 (±1.22), indicating a cohort taller and leaner than population

norms. Males and females were evenly distributed. No significant difference in aIMT or BMI was observed between intervention and control groups. A dose-response trend suggested that children who received no intervention across both phases had higher aIMT compared to those with partial or full exposure (p = 0.04). However, the sample size was too small to draw firm conclusions.

Conclusions: Early-life obesity prevention trials may influence vascular health; however, they must be adequately powered. In addition, substantial resources are required to support in-person assessments and imaging. These considerations should be factored into the design and planning of future trials.

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Exploring new strategies to meet the needs of people living with obesity: the role of yoga teachers in multi-disciplinary obesity primary care

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Background: Obesity is a complex, individualized health issue best addressed through multi-disciplinary care teams. However, healthcare system strains—including limited resources, time, and funding—restrict this approach, prompting interest in alternative strategies. Yoga teachers may offer unique value in obesity care, given their physiological knowledge and ability to provide holistic, low-impact, and accessible healthcare.

Objective: This study explores yoga teachers' perspectives on integrating yoga into primary care multi-disciplinary teams to support individuals living with obesity.

Method: A co-designed qualitative study interviewed 15 yoga teachers, analysing perspectives using Braun and Clarke's thematic analysis.

Results: Three key themes emerged: (1) widespread misunderstanding of authentic yoga; (2) alignment between yoga practices and obesity-related health needs; and (3) the need for professional recognition of yoga teachers. Participants voiced frustration with social media's portrayal of yoga as exclusive, advanced postures typically performed by young, thin, white individuals. In contrast, authentic yoga was described as a cross-cultural, holistic, and low-impact health practice with broad accessibility. Teachers emphasized a commitment to "do no harm," likening their ethical standards to the Hippocratic Oath. Notably, weight change was rarely discussed as a yoga benefit; instead, teachers highlighted improvements in psychological and social well-being. All participants stressed the need for certification or accreditation to ensure qualified, safe yoga instruction. While informal clinician referrals were common, teachers preferred formal referral pathways.

Conclusion: Yoga teachers possess strong physiological knowledge, a client-centred approach, and a nuanced understanding of obesity as a complex condition. Participants advocated for integrating yoga into multi-disciplinary care, emphasizing existing precedents such as Pilates referrals. Further research is needed to explore patient perspectives, test pilot referral models, and assess accreditation feasibility within Western healthcare systems.

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Explainable AI for Predicting BMI Trajectories from Childhood to Early Adulthood Using Genetic and Early-Life Factors

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Aims: Childhood obesity is a complex condition influenced by genetic, maternal, and early-life factors. We aimed to develop an interpretable machine learning model to predict body mass index (BMI) from childhood to early adulthood and identify critical risk contributors.

Methods: Data from 2,868 participants in the Raine Study Gen2 cohort were used. BMI was assessed longitudinally at ages 8–27. We integrated over 200 epidemiological features with seven BMI-related polygenic scores (PGS). Models included traditional machine learning methods and Kolmogorov–Arnold Networks (KAN), an explainable deep learning approach capable of producing mathematical formulae for prediction.

Results: The KAN model achieved the highest R^2 (0.81 at age 8, declining to 0.34 at age 27) when using both genetic and epidemiological data. The strongest predictor across all ages was BMI z-score at 5 years, especially for younger age groups. In adolescence and early adulthood, PGS became increasingly influential. Other contributors included maternal/paternal anthropometrics, skinfold measures, and parental education. The model's transparent structure allowed derivation of explicit formulas and visual interpretation of feature influence over time.
Conclusion: This study presents an explainable AI approach for predicting BMI development across the life course. Our findings emphasize the predictive power of early-life BMI and support integrating genetic and epidemiological data for personalized obesity risk assessment. These insights may guide early intervention strategies and clinical decision-making.

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The association between GIS-measured greenspace and adolescents' moderate to vigorous physical activity: A systematic review

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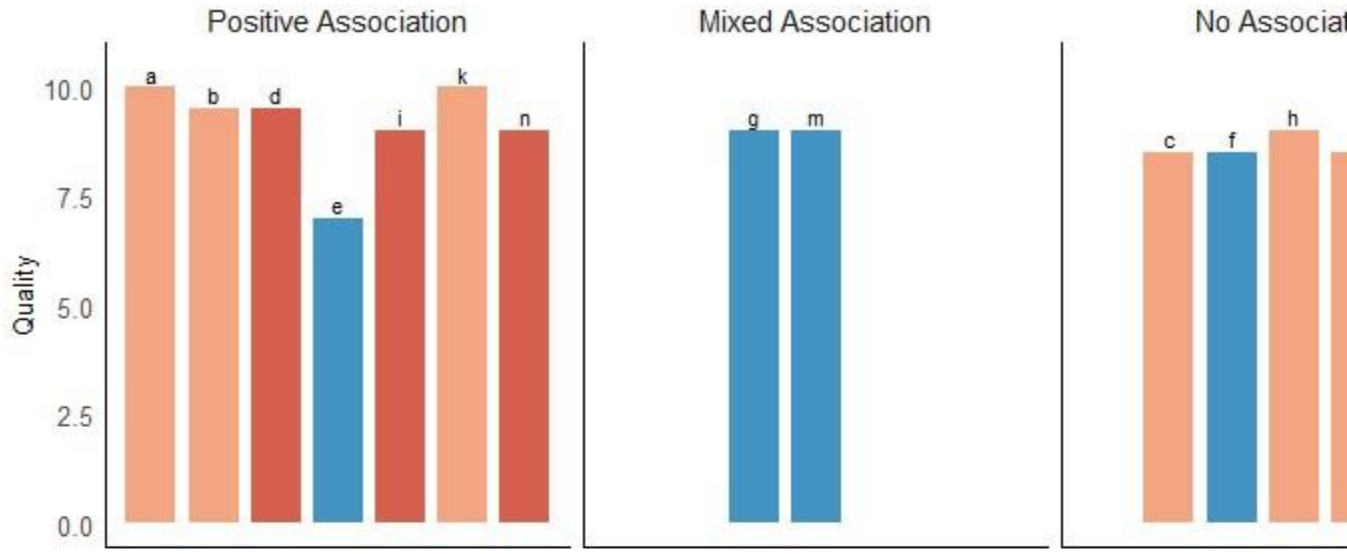
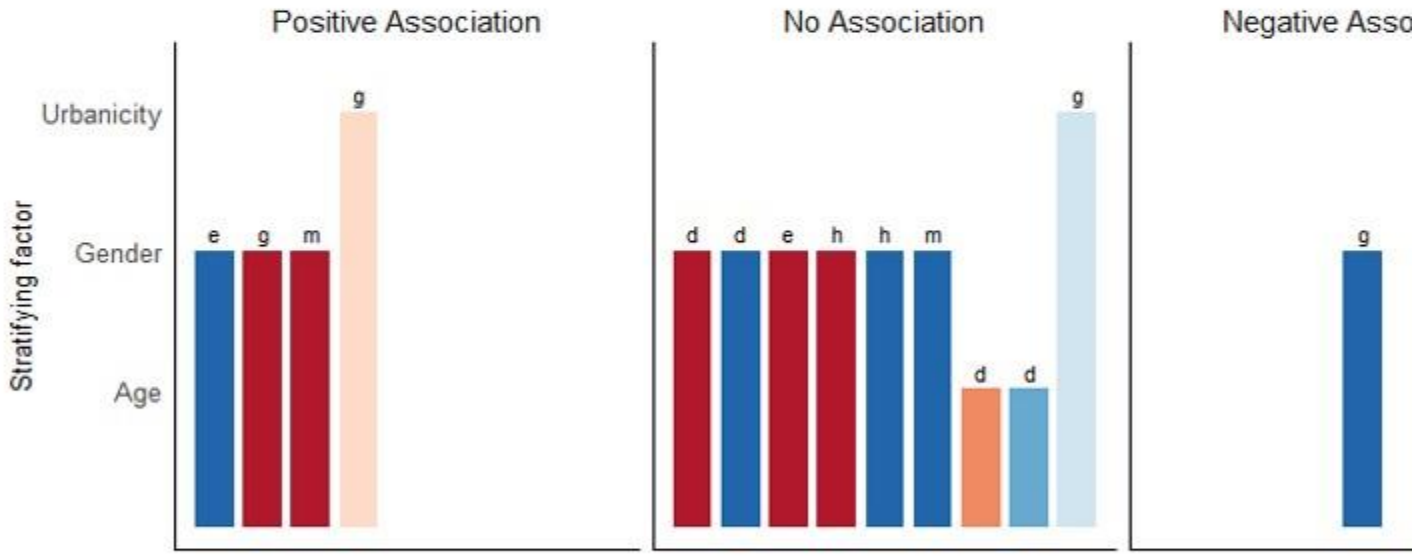
Adolescence is an important life stage characterised by significant social, physical, and psychological development. Physical activity is essential for promoting physical and mental health in adolescents. Activity of a moderate-to-vigorous intensity (MVPA) is associated with numerous benefits, including improved cardio-metabolic health, fitness, bone health, emotional wellbeing, and maintenance of a healthy weight. Greenspace (e.g., trees, parks, etc.) plays an important role in adolescent mental health, but less is known about its links with MVPA. The aim of this research was to undertake a systematic literature review to examine associations between greenspace (measured using geographic information systems; GIS) and MVPA among adolescents (aged 10 to 19 years). We followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines and published our protocol in PROSPERO (https://www.crd.york.ac.uk/PROSPERO/view/CRD42024562009). Search terms were developed from previous research, and included terms for the key categories of adolescence, MVPA, and GIS-measured greenspace. Descriptive and observational studies with either a cross-sectional, experimental or longitudinal design were eligible (qualitative studies, reviews, opinions and conference proceedings were excluded). We searched five databases (SCOPUS, GEOBASE, Medline, EMBASE, and Web of Science) from 1980 onwards. Covidence was used for screening, data extraction and quality assessment. Harvest plots were used to examine patterns in relationships between greenspace and adolescent MVPA. Fifteen articles were included of which ten reported positive relationships between greenspace and adolescent MVPA, while five found non-significant relationships (see Figure). More evidence focusing on adolescents is needed, including longitudinal studies, more detailed examination of greenspace types,

and measurement of greenspace contact.





	Study		
a. Hinckson (2017)	d. Klinker (2014)	g. Markevych (2016)	j. Prins (
b. Hunter (2023)	e. Kowaleski-Jones (2017)	h. Norman (2006)	k. Ries (2
c. Jago (2006)	f. Kuhn (2021)	i. Oreskovic (2015)	l. Scott (

Utilising culturally tailored research methods to understand the acceptability of screening children for type 2 diabetes, from the perspectives of parents of Māori & Pacific Islander descent living in Australia

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The rising prevalence of type 2 diabetes (T2DM) among children remains underdetermined due to inconsistencies in screening methodology and limited availability of research studies (1,2). Māori & Pacific Islander individuals living in Australia are three times more likely to develop diabetes and seven times more likely to develop diabetes-related complications, compared to Australian-born individuals (3). The project aims to utilise culturally appropriate research methods to assess the acceptability of screening children for T2DM, from the perspectives of Māori & Pacific Islander parents.

Māori or Pacific Islander parents living in Australia with at least one child younger than 18 years, will be invited to complete an online survey and/or talanoa/kōrero session *(semi-structured interview).* The project will be guided by Māori & Pacific Islander research methodologies and individuals of Māori or Pacific Islander descent, promoting cultural safety and empowerment. Extensive cultural knowledge will inform participant recruitment and all research questions. Patient-centred outcomes research will be embedded in data collection, to inform acceptable screening strategies and research dissemination.

The project aims to collect ~200 survey responses and ~15 talanoa/kōrero sessions Australia-wide, by the end of 2025. Descriptive statistics and correlation analyses of the survey data will identify trends relating to engagement with the health system, family history of T2DM and screening acceptance. Thematic analyses of the talanoa/kōrero sessions will reveal key themes and a deeper understanding of participant beliefs relating to screening. Results will identify the barriers and enablers to screening children for T2DM, informing future implementation strategies.

By using a combination of design thinking, implementation science and patient-centred outcomes research frameworks, and embedding culturally appropriate research methodologies, this project will be culturally safe and highly acceptable to the Māori & Pacific Islander community. Outcomes will promote community empowerment and the importance of T2DM screening among children, ultimately contributing to T2DM prevention.

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Communicating research findings as recommended by Aboriginal participants

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This study evolved from the Healthy Lifestyle Program for children and young people who are above a healthy weight in Boorloo, Perth, WA.[1] Previous workshop findings, conducted with 29 Aboriginal advisors in April 2024, covered cultural and place-based considerations, including barriers, enablers, and mitigation strategies for adapting the program. From this workshop, it was identified that researchers need to 'close the loop' on findings to participants in a meaningful way. Further, guidelines for communicating with Aboriginal and Torres Strait Islander participants remain limited.[2] The Aboriginal advisors recommended a book to communicate workshop findings to participants.

The study aimed to develop an output reporting cultural and place-based considerations of the Healthy Lifestyle Program for Aboriginal participants that meets their expectations, and to more broadly understand ways of communicating research outcomes with participants.

A workshop was conducted in June 2025 with the Healthy Lifestyle Program Cultural Advisory Group (9 Aboriginal Elders) to understand how best to share these findings with the original participants. An Aboriginal facilitator conducted the workshop, and original study findings were presented. The workshop was audio-recorded, transcribed, and data underwent reflexive thematic analysis.

Themes include ensuring the context and lived realities of participants are recognised when presenting findings, using artwork to further tell participants' stories (including artwork from children involved in the program), and the need for multiple modes of feedback. Tips for researchers working with Aboriginal participants and the book will be presented. The book was noted to have the dual purpose of reporting findings and leaving a legacy for future generations to learn from Elders' views of healthy living.

Ensuring research includes consumer and community involvement is paramount to enabling unique research recommendations to be actioned. Prioritising Aboriginal and community voice in how findings are communicated is critical to genuine partnership in the research process.

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A 'David and Goliath' battle? How do we talk about fast-food outlets to build support for better planning decisions?

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Publish consent withheld

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Nutritional profile and labelling of new packaged lunchbox snacks released in Australia between 2013 and 2024

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Most Australian school-aged children bring lunch from home and the school lunchbox is therefore a key context for influencing their overall diet. The aim of this study was to investigate changes in the nutritional profile and health star labelling of new lunchbox snack products released in Australia coinciding with the introduction of the voluntary Health Star Rating system (HSR). Records of new packaged lunchbox snacks released in Australia between 2013 and 2024 (N=228) were extracted from the Mintel Global New Products Database using a combination of keyword searches and manual coding in August 2024. Nutrient values (/100g/mL), HSRs, and level of processing (NOVA classification) were coded from product images. The most common new lunchbox snack products were muesli bars (27.2%), savoury biscuits/crackers (20.2%), and sweet biscuits/cookies (19.3%). Median nutrition values were 1580 kJ energy/100g/mL, 2.3g saturated fat/100g/mL, 13.2g sugar/100g/mL, 114mg of sodium/100g/mL, 65.5g protein/100g/mL, and 57g fibre/100g/mL. There were significant reductions in sodium and sugar content in new products over time, coinciding with increasing uptake of HSRs, but also significant reduction in fibre content. Overall, less than half of products displayed HSRs (44.7%), and those that did were significantly lower in sugar than those that did not display a HSR. Among products displaying HSRs, approximately two-thirds had a HSR of 3.5 or above (67.7%). Most products were classified as ultra-processed (91.2%), including among products displaying a HSR of 3.5 or above (88.4%). Over the past decade, new packaged lunchbox snack products released in Australia have tended to be high in nutrients of concern and the vast majority are ultra-processed. Mandatory HSRs may encourage reformulation by manufacturers to improve the nutritional profile of lunchbox snack products and assist consumer decision-making, ultimately improving children's diets.

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A snapshot of outdoor food advertising: types, products, and implications for restriction policies

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Most outdoor food advertisements feature discretionary foods, which contribute to excess energy intake. As local governments consider restricting such advertising, the feasibility of applying nutrient profiling models in policy requires evaluation. This study assessed the types of outdoor food advertisements in metropolitan Perth and the availability of nutrition information for the products promoted.

A secondary analysis was conducted using 178 images of outdoor advertising collected in two previous studies: a 500m audit around schools in 16 stratified local government areas (LGAs) in 2019, and full bus shelter audits in four LGAs in 2022. Ads were categorised as 'packaged product', 'food service – chain', 'food service – independent', 'branding only', or 'generic food/beverage'. For ads featuring packaged or food service items, online searches were conducted to obtain product-specific nutrition information from manufacturer and supermarket websites.

Of 168 valid ads, 60 were for packaged products, mainly drinks (e.g. soft drinks, iced teas, energy drinks), confectionery, and snack foods. Chain food service ads (n=34) featured items such as burgers, fried chicken, chips, and sugary drinks. Independent food service ads (n=28) promoted meals like fish and chips, pizza, bacon-and-egg sandwiches, and smoothies, but often lacked specific product depictions. Generic ads (n=28) included both healthy and discretionary items such as fruit, vegetables, pizza, and coffee. Nutrition information was found for 70% of packaged product ads and 68% of chain food service ads, although trans-fat and fibre were rarely reported. Independent outlets provided no nutrition data and rarely depicted identifiable products.

Only 39% of ads featured products for which nutrient profiling could be applied. This limited availability of consistent nutrition data constrains the use of profiling models. A robust and reliable food category-based classification system is likely to offer a more practical and feasible approach for local governments aiming to restrict unhealthy food advertising.

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A Qualitative Study of Community Perspectives on the Development of a Fast-Food Restaurant in the Neighbourhood

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Food environments research is evolving, demonstrating a relationship between fast-food outlets (FFO), poor dietary intake[1] and increasing obesity rates in adults[2] and children[3]. Despite this growing area of investigation, there has been limited study into the experiences of residents living in close proximity to FFOs.

The aim of this study was to categorise the community consultation submissions provided to a local council regarding a McDonald's FFO prior to development, and to qualitatively document the experiences and perceptions of nearby community residents upon completion.

Of the 183 submissions to council between 23 December 2021 and 14 January 2022, 168 were objections to the FFO development and were categorised as close as possible, into overarching themes identified in the resident interviews. In-depth interviews were completed with 11 residents between November 2023 and May 2024, who lived within 300m of the FFO. Thematic analysis identified "perception of the council", "impact on the community" and potential "strategies to foster healthy food environments" as overarching themes. Concern regarding the density of FFO in the surrounding area, impact on health and neighbourhood pollution (light, litter, noise, odour) and antisocial behaviour were predominant in both the community consultation submissions and the interviews.

Results from this study highlight that residents' concerns presented to council prior to the FFO development had become a reality, negatively influencing their perceived quality of life and ongoing community well-being. Despite strong opposition from residents during the consultation period, rejection of planning applications by local councils is impracticable given the current state planning laws that govern planning in Western Australia (WA). Considering the well-being of residents by legislating zoning that limits fast food outlets opening in close proximity to neighbourhoods, schools and playgrounds may positively influence upstream social determinant of urban design and food environments to curb the rise in obesity.

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Early ORIGINS of childhood obesity: Mapping childhood BMI before the age of 5

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Although childhood obesity is extensively researched, a gap remains in longitudinal studies comprehensively examining early predictors using rich, multidimensional data collected from birth through to early childhood. ORIGINS[1] offers a uniquely comprehensive longitudinal dataset, tracking approximately 10,000 families in Western Australia from pregnancy through early childhood. This project

will be using ORIGINS data to explore risk and protective factors of obesity from birth to early childhood. An initial step is to explore the rates of obesity in early childhood in a smaller sub-set of the ORIGINS cohort at the ages of 1, 3 and 5 years. Children's Body Mass Index (BMI) z-score were classified using the World Health Organization BMI-for-age cut-offs[2]. At 1 year of age children (n=1,853) were classified as: thinness (1%), healthy weight (71.7%), and overweight or obese (27.2%). At 3 years of age children (n=1,526) were classified as: thinness (4.3%), healthy weight (78.5%), overweight or obese (17.2%). At 5 years of age children (n=868) were classified as: thinness (3%), healthy weight (78.7%) and overweight or obese (18.3%). Overall, it appears that the majority of children were classified as heathy weight, which remains stable from 1-5 years. The proportion of participants classified as overweight or obese appears to be the highest at 1 year, reduce slightly at 3 years and increase at 5 years. This data provides good insight into the trajectories in early childhood BMI status. However, further exploration is required to ascertain the most appropriate body composition cut-offs to be implemented during early childhood.

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Partnering with local organisations: piloting a new LiveLighter® program systems-level initiative for creating supportive environments

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LiveLighter® is a comprehensive healthy lifestyle promotion and education program, funded by the Western Australian (WA) Department of Health since 2012, and delivered by Cancer Council WA. To strengthen the program's stakeholder engagement activities, a new systems-level initiative was developed and piloted in 2024. This new initiative offered funding to local government agencies (LGAs) for promoting healthy eating and/or movement activities consistent with the needs of their community. This paper describes the initiative's implementation and process outcomes, and critically reflects on how components impacted its success.

LGAs with existing working relationships with Cancer Council WA were offered up to $5000 to support community activities enabling their residents to make small lifestyle changes for health. At conclusion, Cancer Council WA staff were interviewed on the initiative's coordination and the responses thematically analysed to identify facilitators and barriers to its delivery.

Seven LGAs and one community organisation received funding (n=8), with each funding different activities depending on their understanding of what would be most useful in their communities. Funded activities covered healthy eating (n=3), physical activity (n=2) or both (n=3); and new (n=3), extended (n=2) or both new and extended (n=3) activities. Three organisations required greater program staff time to identify how funds could be used for health promotion activities. Two organisations committed to longer-term partnerships after the funding period.

The health promotion experience of Cancer Council WA staff and the flexibility for LGAs to identify health promotion activities that met the unique needs in their area facilitated success of this pilot systems-level initiative. Sharing success stories has added credibility and highlighted the adaptability of the LiveLighter® program to be applied at the grassroots level. This will be important for partnering with local agencies responsible for developing mandated public health plans and creating environments conducive to healthier lifestyles.

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Crunch & Move: adaptation of a primary school nutrition program to get kids moving daily

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Strong evidence demonstrates school-based interventions combining physical activity and nutrition have a beneficial effect on children's obesity. This paper describes adaptations made to a longstanding nutrition program to incorporate daily physical activity practices, and its influence on program reach and impact.

The Crunch&Sip® program, delivered by Cancer Council WA and funded by Healthway is a primary school nutrition program facilitating healthy eating. A new initiative ('Crunch & Move') was trialed to encourage students to eat vegetables only and add an element of physical activity, delivered in classrooms by teachers, for one month. Strategic efforts to recruit more WA primary schools were implemented in 2025. This included organic promotions across multiple channels including, social media platforms, stakeholder networks, and targeted electronic direct mailouts (EDMs). Cancer Council WA developed a suite of resources, including physical activity dice, yoga cards, and classroom prizes, made freely available in print and digital formats upon registration. Teachers were

surveyed on frequency of using resources and their usefulness and provided an estimate of the proportion of children in their class who: crunched on vegetables on most days of the event; and participated in movement breaks on most days of the event.

We found promotional efforts were successful in extending reach and uptake of the initiative in 2025. EDM metrics reported open rates between 27 to 42 per cent. Overall, Crunch & Move saw a 44 per cent increase in registered students (n=10,217), a 112 per cent increase in registered schools (n=117) and a 71 per cent increase in registered classrooms (n=416). Teacher surveys are currently in field and results will be presented.

Program adaptations to encourage more movement alongside healthy eating opportunities improved reach and uptake. Future objectives include refining methodological approach and measurement of daily vegetable consumption and movement participation to assess effectiveness for children's heath.

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Filling the Gap for an Australian Cardiovascular-Kidney-Metabolic Training Program

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Aims

Australia faces a rising burden of obesity and cardiometabolic disease, with disproportionately poor outcomes in First Nations and rural populations [1,2]. Medical obesity management has typically Endocrinology's domain, however Cardiology and Nephrology are developing interest. Despite increasing recognition of cardiometabolic syndrome, no formal Cardio-Kidney-Metabolic (CKM) training program exists. We aim to establish a structured, interdisciplinary program to address critical gaps in knowledge, care, equity, and outcomes.

Methods

To develop this proposal, we drew from local sub-specialty experts and international CKM programs, examining curriculum structures and training models [3,4]. Key elements such as advanced diagnostics, therapeutic strategies, mentorship frameworks, and cultural competency were considered.

Results

Insights from proposed global programs emphasise the importance of a comprehensive curriculum, integrating cardiology, nephrology, and endocrinology over 12 months. This would be offered to trainees from any of these specialties, as well as general physicians (requiring 18 months), with 6 months spent in each rotation outside their primary training program. Essential components include clinical rotations, community-based training, and research opportunities. Specialised obesity clinics during the endocrinology term will facilitate familiarity and expertise in managing type 2 diabetes, metabolic syndrome and its many complications, whilst chronic renal failure and cardiovascular risk management will be explored in-depth during their respective rotations. Cultural immersion experiences would foster relevant Indigenous health expertise, while digital health solutions would improve access in remote areas. A structured mentorship framework would support professional development. We will seek accreditation through the Royal Australasian College of Physicians to formalise this within Australian medicine.

Conclusion

An Australian CKM fellowship represents a transformative step toward bridging healthcare gaps, addressing disparities and equipping specialists with the skills to manage complex multi-system conditions. Establishing this program will improve interdisciplinary patient care and drive equitable health outcomes for patients living with obesity and cardiometabolic syndrome across Australia.


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Unpacking Kids Menus: Perceptions and understandings of parents/caregivers in Perth, Western Australia

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Food environments are a key driver in influencing dietary-related health and in recent years, there has been a substantial shift in the way we dine. Eating out of home was once considered an indulgence, is now commonplace, with venues becoming more family focused. However, such venues continue to encourage the intake of energy dense, nutrient-poor foods and beverages, particularly for children1. In Australia, little is known about what parents/carers think about Kids Menus. Therefore, this study aimed to investigate the perceptions, attitudes and understandings of parents/carers towards Kids Menus and potential innovations for promoting healthier options.

Parents/carers who had at least one child aged 2-12 years old and residing in Perth, Western Australia (n=668) were asked to complete a 65-item online survey. Descriptive statistics were used to summarise participant responses. The most prevalent reason for eating out-of-home with children was “Ease, convenience and accessibility” (59%). Over three quarters (76%) of parent/carers responded that healthy food and drink options should be made available for children when dining out and were supportive of the idea of a *Healthy Kids Menu Venue Accreditation Program.* Data also indicated close to half of participants would likely increase their dining at a venue if it was deemed an accredited *Healthy Kids Menu Venue*.

Findings from this study demonstrate parents/carers not only value the availability of healthier food options for children but also endorse policy and program innovations, such as a Healthy Kids Menu Venue Accreditation Program, as a means of creating positive change. These insights provide a clear opportunity for public health and food policy initiatives to collaborate with the hospitality sector in reshaping the out-of-home food environment to better support children’s health.

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Childcare arrangements and weight status in Australian preschoolers

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Aims: Childhood obesity has detrimental health consequences, persisting into adulthood. Early interventions during the first five years of life are critical. Children aged under five years spend considerable amounts of time in early education and care environments, making them key settings for obesity prevention. This study investigates the association between different childcare types and weight status, using a nationally representative dataset.

Methods: Data from the Longitudinal Study of Australian Children, Waves 2-3, Cohort B (aged 2 to <6 years) were used. The primary outcome was body mass index z-score. The primary exposure was self-reported weekly hours spent in formal, informal and relative care (a subset of informal care, e.g., care by grandparents or other relatives). Logistic regression analyses were performed for nominal panel data, adjusting for key confounders. Results are reported as odds ratios. Sensitivity analyses explored subgroup differences.

Results: Weekly hours spent in formal care are significantly associated with increased odds of overweight/obesity or obesity in both boys and girls. For every additional hour per week in formal care, the odds of having overweight/obesity, and obesity increase by 2.7% (SE: 0.4%, $p<0.05$) and 1.8% (SE: 0.5%, $p<0.05$), respectively, holding other variables constant. Statistically significant associations were observed between weekly hours spent in informal care and odds of overweight/obesity in girls only. The associations between weekly hours spent in relative care and odds of obesity were only statistically significant when boys and girls were analysed as a combined group.

Conclusions: Time spent in formal care was statistically significantly associated with increased odds of overweight and obesity in children aged under six years. Further research is required to understand the role of formal care environments in shaping child weight status, particularly among children with overweight or obesity, and how these settings can be improved to better support child health and wellbeing.

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Burgers for breakfast: Exploring the external school food environment and associated food behaviours of secondary students in Perth, Western Australia

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Obesity among adolescents is a significant public health issue, with increasing prevalence globally. The school food environment plays an important role in shaping adolescent students' food choices, but there is a notable research gap exploring adolescents' perceptions of their school food environment. This study explored how the external school food environment was perceived by secondary students and how it influenced their food behaviours. Four focus groups were conducted in June 2024 with 31 students from a secondary school in Perth, Western Australia. The school was purposively selected as it was located opposite a retail food precinct comprising ten external food outlets. Facilitators used semi-structured questions to guide the focus group discussions. The food outlets' extended opening hours and close proximity to the school increased students' purchase and consumption of unhealthy food. Students' preference for unhealthy food and drinks was influenced by their relative affordability compared to healthier items. The external food outlets provided a meeting place for students to socialise, often resulting in anti-social behaviour (e.g. stealing, loitering and vandalism). Students observed unhealthy food outlet advertising on their school commute and from within the school. Recommendations to improve the external school food environment included initiating planning laws to restrict the presence of fast-food outlets near schools and increasing the cost of unhealthy food. This research provides insights into how the accessibility of the external food environment, availability and affordability of unhealthy food, exposure to advertising and social appeal of food outlets influence adolescents' food preferences and behaviours. strategies to improve their external school food environment, including government interventions that address the accessibility and marketing of unhealthy food near schools.

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Self-Reported Engagement and Utility of a Digital Diabetes Prevention Program in Adults with Obesity and Prediabetes

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Aims

Digital diabetes prevention is a scalable strategy, but its perceived usefulness among Chinese adults with prediabetes remains underexplored. This paper reported the self-report engagement and perceived usefulness of an ongoing digital diabetes prevention program targeting weight loss and lifestyle modification among Chinese adults with prediabetes.

Methodology

Chinese adults (40-60 years) with obesity and prediabetes were recruited to receive a 12-month digital diabetes prevention programme delivered via a smartphone application (app). The app encompasses health data recording, goal setting and self-monitoring, as well as a structured online diabetes prevention curriculum. The online curriculum includes 1) a 6-month core curriculum with weekly nutrition/exercise videos followed by a 6-month post-core curriculum with monthly videos, and 2) exercise videos. An online Qualtrics survey collected participants' feedback at 6 and 12 months.

Results

At 6 months,163 participants completed the online feedback forms (62% females, baseline mean age 53.4±5.9 years, mean BMI 28.0±3.3 kg/m^2, mean HbA1c 6.0±0.3%). Around 20% of participants used the app ≥4 times/ week. Around 47% used the app at least once/month. 86% participants watched the curriculum videos, 68% watched the exercise videos. 25 % and 31% reported exercising with the videos at least weekly and occasionally, respectively.

At 12 months, among respondents who used the app at least monthly, the top activity was watching curriculum videos (82%), followed by watching exercise videos (70%), recording step counts (65%), weight (55%), blood test reports (54%), exercise (42%) and setting goals (42%). Users agreed/strongly agreed that the app enabled better health record management (77%); facilitated active lifestyle (67%), healthy diet (65%) and weight loss (70%). Busy schedules, inconvenience and not used to using the app were the top self-reported barriers to engage user.

Conclusion

The digital diabetes prevention program, including a self-monitoring mobile app and online videos, was perceived as useful by participants.

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Associations between infant feeding practices and maternal sociodemographic characteristics of Indian immigrant mothers in australia - a cross-sectional study

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Suboptimal infant feeding practices can increase the risk of childhood obesity and later life chronic diseases (1). Data collected in 2010 revealed that Indian immigrant mothers in Australia were not meeting infant feeding guidelines (2). The present study examines contemporary infant feeding practices of Indian immigrant mothers in Australia and associations with maternal sociodemographic characteristics.

A cross-sectional online survey in Qualtrics, using convenience sampling, gathered infant feeding practices data (breastfeeding, formula feeding, solids and other liquids) and sociodemographic data from eligible mothers (born in India, with at least one full term child born in Australia at ≥ 37 weeks gestation, aged between 1.5 and 5 years; n=380). Regression analyses assessed the relationship between infant feeding practices and sociodemographic factors.

All mothers were married and had at least a bachelor's degree; approximately half the mothers classified as living with overweight or obesity(47.1%); the majority were Hindus (60%) and migrated from urban India (80%). In multivariable models, every unit increase in maternal BMI (kg/m^2) was associated with a 5% reduction in exclusive breastfeeding at 6 months (OR:1.05,95%CI:1.00,1.1,p=0.04,n=359) and an increased likelihood of introducing other liquids before 12 months (OR:1.06,1.00,1.12,p=0.02,n=276). Christian mothers breastfed for 2.38 months longer than Hindu mothers (β=2.38,p=0.05n=380). Mothers from remote Indian regions had a 3.45 months shorter breastfeeding duration (β=-3.45,p=0.005,n=380) and were 1.9 times more likely to exclusively breastfeed for less than 6 months (OR:1.90,1.07,3.39 p=0.02,n=359) compared to mothers from urban regions. Mothers with one child were 39% less likely to introduce formula compared to those with two or more children (OR:0.61,0.37,0.99,p=0.04,n=365).

Indian immigrant mothers did not meet infant feeding guidelines for exclusive breastfeeding, exposure to other drinks and formula. Maternal religion, Indian region of migration, parity and maternal BMI emerged as crucial determinants highlighting the need for culturally tailored health promotion initiatives targeted at this demographic.

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Maternal Antibiotic use while Breastfeeding and Infant Growth in the First 10 Months.

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The discovery of antibiotics has had a tremendous influence on the treatment of infectious diseases leading to increased life expectancy (1). Antibiotics has been found to disrupt the development of the infant gut microbiome and been associated with weight changes (3). In antibiotic exposed mice, elevated levels of *Firmicutes* have been associated with increased energy harvest (4-5). Maternal antibiotic exposure could reach the infant through diffusion into breast milk leading to enhanced growth (6-8).

To investigate the association between antibiotic exposure through breastfeeding and infant growth in the first 10 months. Also, to examine if effects of antibiotics on growth were sex dependent.

The PANDORA-study used data from the Danish birth and prescription registries. In total 79,179 infants born 2004-20 were included. Exposure: any antibiotic prescribed to the mother while she was breastfeeding. Outcome: change in weight-for-length z-score between a baseline measurement and month 10 using WHO's growth standards. Linear regression analysis was used to examine associations.

Infants exposed to antibiotics through breastfeeding had 0.14 SD units higher change in weight-for-length z-score than unexposed infants after adjustment for covariates (p<0.001), corresponding to a difference of 100 grams between exposed and unexposed infants at month 10. There was no evidence for an interaction between infant sex and antibiotics on growth (p=0.65). When stratified by breastfeeding duration, antibiotic exposure was associated with a significantly higher change in weight-for-length z-score among infants breastfed between 1-2 months (beta=0.20, p=0.04) and 1-4 months (beta=0.15, p=0.007), compared to unexposed infants. No significant differences were observed for exposures among infants breastfed between 3-4 months (beta=0.07, p=0.49) or 5-6 months (beta=0.04, p=0.67).

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Dietary fat and sugar consumption is associated with perceived health of fast-food brand logos

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Background: Discretionary foods high in sugar, salt, and saturated fat are heavily marketed with easily recognisable brand logos. This study investigated whether self-reported consumption of foods high in fat and sugar was associated with attitudes such as liking, familiarity, excitement, and perceived healthiness of fast-food and sugary drink brand logos, and with body mass index (BMI).

Methods: In Study 1, university students in Sydney, Australia completed the study in a lab setting; in Study 2, U.S.-based participants were recruited online and completed the study remotely. Participants rated major commercial fast food and beverage brand logos on liking, familiarity, perceived healthiness, and frequency of interaction, and completed dietary questionnaires (DFS, RED-13) and demographic measures. All hypotheses and analyses for Study 2 were pre-registered. Data analyses included Pearson correlations and hierarchical multiple regressions.

Results: Both studies found a positive association between how much participants liked fast-food brands and how healthy they perceived them to be, a relationship that was not predicted by education level. Liking and healthiness ratings for fast-food brands correlated positively with self-reported fat and sugar consumption, even after controlling for age, gender and education. These associations were not observed for technology and social media brands, suggesting a domain-specific effect. Both reward-based eating and brand attitudes independently predicted dietary patterns. Greater reward-based eating tendencies predicted BMI in the study of U.S.-based participants (Study 2) but not in the study of Australian university students (Study 1).

Conclusions: These findings suggest that positive attitudes toward fast-food and sugary drink brands are linked to poorer diet quality. However, it remains unclear whether positive brand attitudes lead to poorer diets, or if unhealthy eating habits shape more favourable views of these brands. Further research is needed to clarify the directionality and underlying mechanisms of these associations, with important implications for public health.

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Social isolation and loneliness in people with clinically severe obesity: a qualitative study of the perspectives of patients and clinicians

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Background People with clinically severe obesity may experience greater social isolation and loneliness (SIL) leading to poorer health outcomes and reduced treatment engagement. The experience of living with SIL in this population and its clinical consequences remain poorly characterised. As such, understanding and addressing SIL in this population has become increasingly important. Exploring this further is critical to improving treatment engagement and outcomes.

Methods: Qualitative study one-to-one semi-structured interviews with adults living with clinically severe, recruited through targeted and snowball sampling from tertiary metabolic clinics in Sydney and the Weight Issues Network. Concurrently, focus groups with clinicians from the same tertiary clinics were conducted to gain their perspectives on SIL among patients living with obesity in their care. Discussions explored participants' social networks, experiences and drivers of SIL, impacts on mental health and treatment engagement, and potential support strategies. All sessions were audio-recorded, transcribed, and analysed thematically using Quirkos.

Results: n=13 patients and n=14 clinicians across 2 focus groups. Our data shows that SIL is driven by internal (shame, stigma, low self-esteem), external (accessibility, built environment, cost), and social (bullying, judgement) barriers to connection. Additionally, difficulty in addressing SIL stem from a bidirectional relationship with mental health, inconsistent assessment of SIL in clinical practice, and inadequacies of existing support structures. Both patients and clinicians highlighted the need for group-based, in-person activities and peer support but stressed the need for flexible and accessible delivery.

Conclusions: These findings highlight that SIL in clinically severe obesity is driven by complex factors with current supports being neither sufficiently tailored nor sustainable. To overcome these barriers interventions should offer safe, non-judgmental environments; integrate therapeutic, social, and physical activities; and ensure ongoing, meaningful contact - ideally co-designed with patients and clinicians to address barriers and reach those most at risk.

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Make healthy your new habit: developing a new LiveLighter® media campaign

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LiveLighter® is a comprehensive healthy lifestyle promotion and education program, funded by the Western Australian (WA) Department of Health since 2012, and delivered by Cancer Council WA. This paper describes the comprehensive formative evaluation process undertaken to develop the latest TV-led media campaign.

First, previous campaign evaluations and research reports were reviewed and summarized. These identified increased knowledge over time about harms associated with overweight and obesity, unhealthy diet and physical inactivity, as well as findings that those with a higher body weight and regular fast-food consumers were less confident in changing behaviors. Additionally, the need for future campaigns to leave the target audience feeling motivated and confident to adopt and maintain healthy eating behaviors was identified. Second, using this information, a creative agency was briefed and four concepts went into testing with the target audience. Testing was done with 44 participants with BMI 23-32 across eight focus groups. Of the four concepts, 'Habits' tested the best due to its relatability of the depiction of how we have accumulated many unhealthy habits. The tagline – 'make healthy your new habit' – was memorable and motivational. Finally, four iterations of the habits concept were taken into further testing with 21 people with BMI 23-32 across four groups to strengthen the message cohesiveness and relatability.

In conclusion, the need to provide people with achievable solutions to continue eating healthy was a main driver for the new 'Habits' TV-led campaign and also contributed to resource development in the broader program. Through the utilization of previous evaluations and a comprehensive formative evaluation process a relatable, motivational campaign to build self-efficacy in the target audience was created and launched in April 2025.