difference in relative expression of stem cell markers (SOX2, CD133, Nestin) between tumours with and without distinct cell lineage.

Conclusions: Our study is the first to biologically characterise plurihormonal tumours without distinct lineage differentiation. PitNETs without distinct lineage differentiation exhibit a higher expression of the stem cell marker SOX2 compared with other lineage-differentiated tumours, suggesting possible involvement of stem cells in their development. By expanding our knowledge of pituitary tumourigenesis, we aim to develop scope for targeted therapies that may be used to treat tumours in early stages.

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Pregnancy outcomes following bariatric surgery in Queensland, Australia: A data-linkage report

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In Australia, bariatric procedures doubled between 2005 and 2015 with 80% of surgeries performed on women of child bearing age [1]. Pregnancy following bariatric surgery is associated with mixed maternal and fetal outcomes. Limited data are available regarding pregnancy outcomes after laparoscopic sleeve gastrectomy.

A statewide hospital and perinatal data register linked cohort matched study was performed. In total, 2,018 births in 1,677 women with prior maternal bariatric surgery were registered in the Queensland Hospital Admitted Patient Data Collection and matched with deliveries during 2013-2018 in the Perinatal Data Collection. The first singleton pregnancy following bariatric surgery for each woman was used for analysis. Women were excluded if BMI was missing or if bariatric surgery procedures had been reversed, revised or ambiguously coded. A total of n=1282 cases and n=12820 controls were analyzed matched on BMI, smoking, age and parity. Continuous variables were analyzed using paired t-tests and categorical variables were analyzed using Pearson's Chi-square or Fisher's exact test.

Of 1282 women with a singleton delivery after bariatric surgery, 93% had undergone laparoscopic sleeve gastrectomy. In women with previous bariatric surgery, there was more assisted reproductive technology use (10.7% vs 8.0%, p<0.001) and preterm birth (<37 weeks) (10.5% vs 7.8%; p=0.007). Offspring had lower absolute birthweight (3223g ± 605g vs 3418g ± 595g; p<0.001), lower percent of large for gestational age (LGA) (8.6% vs 14.1%; p<0.001) and higher percent of SGA infants (10.7% vs 7.3%; p<0.001) than offspring born to matched women. Percent of GDM was lower in women with previous bariatric surgery (15% vs 20%; p<0.001).

Glycaemic and metabolic shifts caused by pre-pregnancy bariatric surgery modify obesity associated pregnancy and neonatal outcomes. Our results suggest that pregnancy outcomes following maternal bariatric surgery differ from matched controls in a cohort of women with primarily gastric sleeve surgery.

1. 1. AIHW, Weight loss surgery in Australia 2014–15: Australian hospital statistics. 2017.

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The effect of cyproterone and spironolactone on breast development in transgender women: a randomised controlled trial

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Objective: Transgender women commonly use cyproterone or spironolactone as anti-androgens with estradiol to assist with feminisation. However, the optimal anti-androgen is unclear. We aimed to assess the effect of these anti-androgens on breast development and hypothesised that cyproterone would result in greater breast development than spironolactone due to greater androgen receptor antagonism and suppression of serum total testosterone.

Design: Double-blind, randomised controlled trial

Methods: Transgender women newly commencing estradiol were randomised to spironolactone 100mg daily or cyproterone 12.5mg daily for six months. The primary outcome was measurement of breast development via breast chest distance with secondary outcomes of estimated breast volume using the BreastIdea Volume Estimator application and serum total testosterone.

Results: Fifty-five participants were included in per protocol analysis (cyproterone group n=28, spironolactone group n=27). Baseline age, body mass index, breast indices, serum estradiol and serum total testosterone were comparable. At six months, the mean (standard deviation) breast chest distance was 9.2cm (3.0) in the cyproterone group versus 8.3cm (2.7) in the spironolactone group (p=0.27). The mean (SD) estimated breast volume was 190.25 mL (158.60) in the cyproterone group and

157.84mL (112.03) in the spironolactone group (p=0.39) with significant inter-individual variation (range 20.27 – 787.77 mL). The mean (SD) serum total testosterone was 1.48 nmol/L (3.45) in the cyproterone group and 4.29 nmol/L (5.44) in the spironolactone group (p=0.04). Serum estradiol levels were comparable. Use of cyproterone was associated with mild hyperprolactinaemia and spironolactone with an increase in serum urea and creatinine.

Conclusions: Choice of anti-androgen should be individualised based on clinician and patient preference, with consideration of associated side effects. Further research is needed to optimise breast development in transgender women.

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RANKL inhibition creates a pro-osteoclastic environment, leading to an overshoot in serum TRAP and accelerated bone resorption following treatment withdrawal.

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Denosumab withdrawal triggers rapid bone mineral density (BMD) loss via accelerated bone resorption. Development of optimal sequential therapy is hindered by poor understanding of the cellular mechanisms and sub-optimal serum turnover marker assessment. We compared temporal changes in RANKL, serum TRAP5b and osteoclast precursors to CTX, P1NP and BMD, to define alternative tools to guide sequential treatment.

Seven week female C57BL/6 mice received 2-weeks of saline or thrice-weekly OPG:Fc (10mg/kg) to inhibit RANKL, then withdrawn from therapy (OPG-W). Following longitudinal BMD and serum measurement, mice were harvested at weeks 2, 8, 11 and 13 for RANKL, TRAP5b, P1NP and CTX. Week 8, marrow-flushed, long-bone samples were assessed for RANKL mRNA. Week 6 bone marrow samples were analysed for osteoclast precursors ($NK1.1^-$ $Ter119^-$ $CD3^-$ $Ly6G^-$, $B220^-$, $CD11b^{lo}$, $CD117^{int}$, $CD115^+$).

Following OPG:Fc withdrawal, BMD increased 24% at week 8 in OPG-W ($p<0.01$), declining at week 10 and normalised to vehicle at week 13. At week 8, serum TRAP, CTX and P1NP were all suppressed in OPG-W ($p<0.001$). At week 11, serum TRAP was elevated in OPG-W ($p=0.01$), P1NP and CTX remained equivalent to vehicle. At week 13, serum TRAP, P1NP and CTX were all greater in OPG-W ($p<0.01$).

Serum RANKL levels at week 2 were elevated with OPG:Fc ($p<0.001$), peaking 13-fold higher at week 8 ($p<0.0001$), returning to vehicle at week 11. Prior to the overshoot in serum TRAP levels in OPG-W (at week 11), bone RANKL mRNA was elevated at week 8 ($p<0.01$) and osteoclast precursors at week 6 ($p<0.05$).

Rebound BMD decline preceded the increase in clinical turnover markers (P1NP, CTX). Elevated serum TRAP occurs earlier, prior to bone loss, and may better guide sequential therapy. Increased serum and bone RANKL levels and an accumulation of osteoclast precursors were detected prior to the overshoot in TRAP.

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Anti-Müllerian hormone regulates organ-size in the ovary.

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Anti-Müllerian hormone is a TGFβ-superfamily member that inhibits primordial follicle activation, induces early preantral follicle atresia, promotes late preantral/early antral growth and inhibits FSH-responses and aromatase expression in antral follicle granulosa cells. Of these diverse actions, the induction of preantral follicle atresia has the greatest effect on the number of developing follicles in the ovary but the reason for this role has not yet been determined. Our research suggests that without substantial amounts of preantral follicle atresia, the ovary would not be able to contain the large number of antral follicles growing rapidly in the follicular phase. AMH released from large follicles appears to be a key regulator, preventing excessive numbers of antral follicles from developing to the antral stage. We also show that most proteolytic cleavage of the inactive precursor form of the protein (proAMH) occurs in the theca and stroma. The AMH in follicular fluid is predominantly the inactive form, with small quantities of cleaved, active form ($AMH_{N,C}$) that performs the growth-promoting functions of AMH. When the AMH leaves follicular fluid, the majority is converted to the $AMH_{N,C}$ where in high concentrations it performs the inhibitory functions, including suppression of primordial follicle activation and induction of preantral follicle atresia. In this way, AMH can have two divergent functions in the same organ.

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Reproductive function of men conceived with intra-cytoplasmic sperm injection

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Since its introduction for male factor infertility, the use of intra-cytoplasmic sperm injection (ICSI) has increased. Given the strong genetic basis of male infertility, the risk of transmitting infertility to future generations is concerning. Furthermore, offspring health is affected by paternal health and sperm quality, irrespective of genetic causes of infertility. Concerns regarding the use of ICSI include the heritability of infertility, the effects of poor-quality spermatozoa on offspring health, and the potential for the technique itself to induce epigenetic changes with long-term health effects. Given the prevalence of male infertility and