

different sub-groups of persons with obesity. This study aimed to investigate the potential impact if such levels of weight loss could be achieved nationally and the cost implications.

The study used NCDMod [2], a microsimulation model that simulates inter-relationships of risk factors (including obesity), chronic disease and health system costs. NCDMod operates in 5 year cycles projecting to 2030. The main scenario simulated 20% of potential patients with obesity achieving their target weight loss and maintaining weight loss for the 15 year simulation. Sensitivity analysis was done including addition of drop-out/failure to lose weight despite starting treatment as set out by the obesity management algorithm. Key health outcomes were: Decrease in body mass index, cardiovascular disease events averted, quality adjusted life years gained and health system cost offsets.

In comparison to weight trajectories remaining at historical levels, implementation of the Obesity Management Algorithm estimates almost 500,000 less persons with obesity in 2030, resulting in a cost offset in the health system over the 15 years to 2030 of Au\$12.7 billion to potentially fund the required weight management programs. Even assuming that 40% of those that start the program either drop-out or fail to lose weight, there still would be 280 000 less persons with obesity in 2030 providing health system cost-offsets of Au\$7.7 billion.

The need to facilitate multifaceted, intensive weight management programs described in The Australian Obesity Management Algorithm is illustrated in this simulation, showing the potential decrease in persons with obesity over time and the freeing of health system funding to pay for such services.

## References

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### The role of the pro-apoptotic protein BIM in glucose homeostasis and preservation of islet mass in type 2 diabetes



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### IL-22-based tissue-targeted therapeutics for type 2 diabetes



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### The interplay between insulin and the NPY system



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Insulin has been shown to have effects not only in the peripheral tissues, but also in the brain particularly in the arcuate nucleus of the hypothalamus to regulate glucose and energy homeostasis. The importance of the central neuropeptide Y (NPY) system in the regulation of appetite and energy metabolism is well established. Although insulin is known to influence NPY expression, the precise physiological role of insulin action in these neuronal cells remains unknown. A closely related peptide, PYY released from L-type cells of the gut, is also expressed in  $\alpha$ -cells in the pancreatic islets. It has been shown that application of PYY decreases glucose stimulated insulin secretion from rat and mouse islets. PYY can activate Y1, Y2 and Y5 receptor to regulate feeding and energy balance, however, little is known as to which Y receptor(s) mediate PYY's effect in the pancreatic islets. We have recently identified that the Y1 receptors are expressed in the  $\beta$ -cells both in mice and humans. In this presentation, I will discuss the role of insulin action in NPY-expressing neurons and provide evidence addressing the role of Y1 receptor in the regulation of  $\beta$ -cell function and how inhibition of this receptor could improve islet transplantation outcome.

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### Cafeteria diet-induced cognitive impairment is prevented by oral minocycline in association with changes in the microbiome



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Obesogenic diets and obesity are associated with cognitive impairment in both humans and animals. While the underlying mechanisms remain controversial, a key potential driver is increased inflammatory signalling associated with obesity. The anti-inflammatory antibiotic minocycline hydrochloride has been routinely used to depress microglial activity as it easily crosses the blood brain barrier. We used a rodent model to test the hypothesis that minocycline would alleviate the cognitive impairment produced by a high-fat high-sugar "cafeteria" diet. The study was a 2 × 2 design, where rats were exposed to either vehicle (syrup) or minocycline (40 mg/kg/day) while consuming either regular chow or cafeteria diet. Memory was tested using novel object and place recognition tasks (NOR and NPR, respectively) and EchoMRI determined body composition across 6 weeks of intervention. Rats fed the cafeteria diet and vehicle were impaired on the hippocampal-dependent NPR at 2, 4 and 6 weeks but minocycline administration spared NPR performance in cafeteria-fed rats (similar exploration ratios as chow and vehicle). Of interest, chow rats treated with minocycline performed worse than those treated with vehicle. Cafeteria-fed rats irrespective of drug treatment consumed 150% more energy over the experiment and gained 100% more fat mass relative to rats fed chow. Faecal microbiota alpha diversity was reduced by both cafeteria diet and minocycline,

but these reductions were not associated with performance on the NPR. However, abundances of specific OTUs within *Bacteroides* and *Lactobacillus* were associated with place task performance. Minocycline did not affect gene expression of IL-1B, TNF or IL6 in retroperitoneal white adipose tissue, although rats fed cafeteria diet and minocycline exhibited significantly increased expression of TLR-4. In summary, cafeteria diet produced persistent deficits in NPR that were prevented by minocycline cotreatment. The differences in behaviour observed correlated with differences in microbiome composition, but not with inflammatory gene expression in retroperitoneal fat.

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### Genetic architecture of a healthy diet in *Drosophila*



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Obesity is the strongest risk factor for type 2 diabetes, however, excess body fat does not fully explain the etiology of diabetes as several human populations develop diabetes at a lower level of obesity than others, and about 20% of obese people display normal metabolism. A major recommendation is to reduce calorie intake, yet the contribution of individual macronutrients to individuals risk of developing metabolic diseases is poorly understood. There is no clear consensus on what comprises the optimal healthy diet, and emerging evidence shows tremendous variation on health effects of different diets between individuals and populations. The aim of this study was to understand how the genetic background defines a framework for a healthy diet. To this end, we have used the *Drosophila* Genetic Reference Panel (DGRP), a collection of 200 inbred fly strains derived from a single outbred natural population, to dissect the gene-diet interaction across various macronutrients. Our study shows that genetic background determines the survival of flies on different diets. Functional validation of candidate SNPs identified a large number of genes previously unknown to control the metabolism and utilization of macronutrients. Isolating genes that predispose to better health outcomes in response to different nutrients will have considerable impact on public health and provides a first step towards the development of personalized nutrition as a practice to manage metabolic diseases.

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### Metformin and dietary advice for pregnant women who are overweight or obese: the GROW randomised trial



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**Introduction:** Maternal overweight and obesity is associated with well-recognised pregnancy complications. Our aim was to evaluate the role of metformin in addition to dietary and lifestyle advice for pregnant women who were overweight or obese.

**Methods:** We conducted a double blind, placebo controlled, randomised trial. Eligible women with a live singleton pregnancy

between 10<sup>+0</sup> and 20<sup>+0</sup> weeks gestation, and were overweight or obese (BMI  $\geq$ 25.0 kg/m<sup>2</sup>) at their first prenatal visit were recruited from public maternity hospitals in Adelaide, South Australia.

All women received an antenatal dietary intervention and were randomly allocated to receive either metformin to a maximum dose of 2000 mg per day, or an identical appearing placebo.

The primary outcome was the proportion of infants with birth weight >4000grams. Secondary outcomes included gestational weight gain (GWG), maternal pregnancy, labour and birth, and infant outcomes. Statistical analyses adopted intention to treat principles.

**Results:** 524 women were randomized (261 Metformin; 263 Placebo). There was no significant difference in the proportion of infants with birth weight >4000 g (15.63% Metformin versus 14.34% Placebo; aRR 0.97; 95% CI 0.65–1.47;  $p=0.899$ ). Women receiving metformin had lower weekly GWG (0.38+0.34 kg Metformin vs 0.47+0.35 kg Placebo; aMD -0.08; 95% CI -0.14–0.02;  $p=0.007$ ), and were more likely to gain below the Institute of Medicine recommendations (39.2% Metformin vs 27.0% Placebo; aRR 1.46; 95% CI 1.10–1.94;  $p=0.008$ ). Total GWG was not statistically significantly different (7.48+6.95 kg Metformin versus 8.72+6.91 kg Placebo; aMD -1.18; 95% CI -2.37 to 0.01;  $p=0.053$ ). There was no evidence of impact on pregnancy and birth outcomes.

**Conclusion:** There was some evidence that metformin as an adjunct therapy to a dietary and lifestyle intervention in overweight and obese pregnant women reduced GWG measures, but there was no evidence of an impact on pregnancy and birth outcomes.

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### The importance of good dialogue between healthcare professionals and people with obesity



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**Background:** The ACTION (Awareness, Care, and Treatment In Obesity maNagement) study examined perceptions, attitudes and behaviours related to obesity management among people with obesity (PwO) and healthcare professionals (HCPs).

**Methods:** A cross-sectional, US-based, stratified sampling of 3008 adults with obesity and 606 HCPs completed an online survey assessing perceptions, attitudes and behaviours associated with obesity management. Both groups self-reported on their height and weight and perceptions of obesity-related discussions between PwO and HCPs.

**Results:** Most PwO (82%) agreed weight loss (WL) is completely their responsibility and most HCPs (72%) agreed they are responsible to contribute to PwO WL efforts. PwO believe reaching a target weight is central to success. Half of PwO reported receiving a formal obesity diagnosis; however, PwO were more likely to have an obesity diagnosis if they were actively seeking treatment (57% vs. 51%)