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Obesity Surgery WA

Identifying Cause / Contribution of Obesity is important for Management

Choosing the wrong management will **LIMIT** effectiveness of treatment

Identifying Obesity without Metabolic or Obesity with Metabolic does not help in the management but rather points towards the **URGENCY** needed for treatment of the Obesity

	Diet	Exercise and physical activity	Behaviour therapy
Hungry brain	Volumetric, high-fibre, low-calorie diet* 1-2 meals per day		
Hungry gut	Low-calorie diet* with pre-meal protein supplementation 3-5 meals per day		
Emotional hunger			Behavioural counselling plus weekly CBT sessions
Slow burn	Low-calorie diet* with post-workout protein supplementation	HIIT plus resistance training (supervised once per week)	

HUNGRY BRAIN – Knows when full but keeps eating and eats more calories at each meal

High Fibre (Volume) diet 1-2 meals a day

HUNGRY GUT – Feels hungry all the time – rapid stomach emptying

Premeal Protein, Split meals over 3-5 meals a day (Use GLP1)

EMOTIONAL EATING – Eating in response to emotional stimulation negative (and positive)

Needs Counselling and Therapy (Use Contrave)

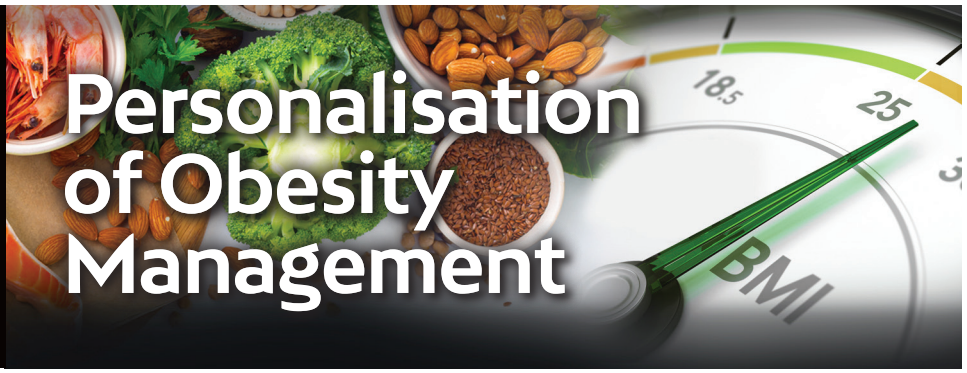
SLOW BURN – Body just doesn't burn calories

Needs Low Calorie Diet and hi Intensity training (Phentermine)

Summary by A/Prof HS Chandraratna

A RESEARCH REVIEW™
SPEAKER SERIES

Personalisation of Obesity Management



Making Education Easy 2023

About the expert

Dr Andres J. Acosta,
MD, PhD, ABOM dip

Dr Andres Acosta is Assistant Professor of Gastroenterology at the Mayo Clinic, where he co-directs the Nutrition Obesity Research Program and directs the Precision Medicine for Obesity Program. He is board-certified in Internal Medicine, Gastroenterology and Hepatology, as well as Obesity Medicine and Nutrition.

Dr Acosta's research focuses on precision medicine for obesity with the aim of identifying the right therapy for the right patient. He is a recognised international speaker, with over 100 peer-reviewed publications, including the Lancet, Gut and Gastroenterology, and book chapters. He is principal investigator and co-investigator on research funded by the National Institute of Diabetes and Digestive and Kidney Diseases.

Abbreviations used in this review
BMI = body mass index
BP = blood pressure
CBT = cognitive behavioural therapy
CV = cardiovascular
CVD = cardiovascular disease
ER = extended-release
GORD = gastro-oesophageal reflux disease
GLP1 RA = glucagon-like peptide-1 receptor agonist
HADS-A = hospital anxiety and depression scale (anxiety)
HDL = high-density lipoprotein
HIIT = high-intensity interval training
LDL = low-density lipoprotein
NEAT = non-exercise activity thermogenesis
OSA = obstructive sleep apnoea
RCT = randomised controlled trial
RYGB = Roux-en-Y gastric bypass
SEM = standard error of the mean
SSRI = selective serotonin reuptake inhibitor
SR = sustained release
TBWL = total body weight loss
T2D = type 2 diabetes

This publication summarises an online presentation given by Mayo Clinic obesity expert Dr Andres Acosta in April 2023. Over three consecutive evenings, Dr Acosta presented a case study led discussion on the selection of anti-obesity interventions based on patient phenotypes. The webinar and review article were sponsored by iNova Pharmaceuticals Pty Limited.

Dr Acosta began his talk by presenting real-world case studies from his practice that he would use to illustrate the implementation of precision medicine in the treatment of obesity (**Table 1**). The goal of Dr Acosta's presentation was to demonstrate that these three patients are not the same, despite their similar clinical histories, and that they require different approaches for obesity management to be successful.

Table 1: Three real-word cases who presented to Dr Acosta requesting obesity management

Case 1	Case 2	Case 3
41-year-old female Obesity, uncontrolled T2D, hypertension, dyslipidaemia, GORD, osteoarthritis, depression, obstructive sleep apnoea	41-year-old female Obesity, uncontrolled T2D, hypertension, dyslipidaemia, GORD, osteoarthritis, depression, obstructive sleep apnoea, anxiety	41-year-old male Obesity, uncontrolled T2D, hypertension, dyslipidaemia, GORD, osteoarthritis, depression, obstructive sleep apnoea, severe back pain

Obesity: the number one chronic disease

More than 1 billion adults are affected by obesity worldwide. Obesity is an important chronic disease because it leads to heart disease, stroke, T2D, cancer, and premature death. Dr Acosta emphasised the importance of treating obesity to prevent premature mortality. Multiple, large epidemiological studies clearly demonstrate that obesity is an independent risk factor for mortality.[1,2] Obesity should not be viewed only as a disease that is a risk factor for other conditions, but as a serious chronic condition associated with an increased risk of mortality in its own right.

Obesity is also associated with significant healthcare expenditure.

The efficacy of the current approaches to obesity management is related to the degree of risk associated with the interventions. Education is associated with almost no risk but as lifestyle, medications, endoscopic and surgical procedures are introduced the patient is exposed to an increasing risk of adverse effects, as the efficacy of the weight-loss interventions increase. Currently, clinicians stratify obesity management based on this model by assessing patient risk and benefit. But this approach is not consistently effective. Obesity prevalence in the United States is projected to be approximately 50% by 2030, demonstrating that it is not currently well managed.[3]

The challenges of treating obesity

Dr Acosta emphasised that the "one-size-fits-all" approach to obesity management is not working. This point is illustrated by the heterogeneity in efficacy of weight loss interventions. After 3 months of treatment, there is a wide variety in responses to interventions including diet (**Figure 1**), anti-obesity medicines, and also surgery. Some patients may lose significant amounts of weight, while others may even gain weight.

Dr Acosta's approach is to identify the patients who derive a significant benefit from each approach so that they can be provided with individualised care.

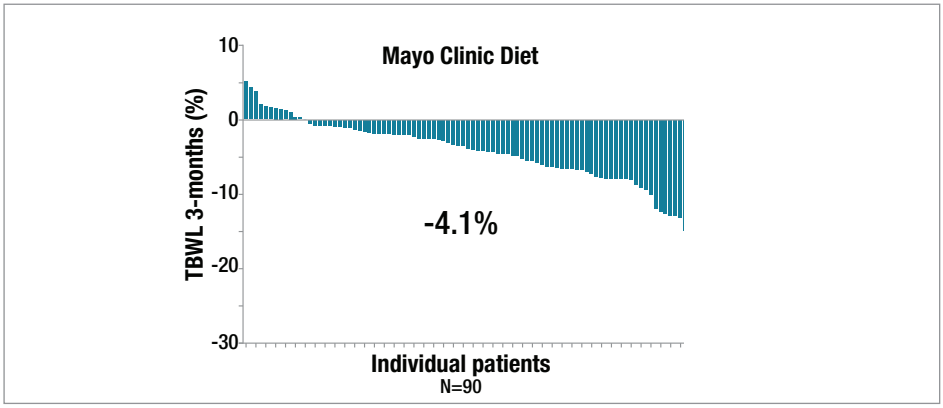


Figure 1: Heterogeneity of response to the Mayo Clinic diet. Data presented by Dr Acosta (2023).

Why is there heterogeneity in effectiveness?

The current obesity classifications focus on obesity cardiovascular or co-morbidity risk (severity) and not on obesity stratification (segmentation). For example, BMI with or without waist circumference is a classification system based on risk of mortality or of developing CVD.[4] This does not inform clinicians as to how patients should be managed. Similarly, dividing patients into metabolically healthy or metabolically unhealthy obesity is not necessarily helpful in guiding the management of a patient who wishes to lose weight.[5]

Precision medicine for obesity

The traditional approach to treatment groups phenotypes into one disease to allow for drug discovery and clinical trials. Precision medicine investigates a disease to determine if there is a unique factor present, e.g. a genotype, before attempting drug discovery and targeted trials.

Examples of precision medicine in obesity management include a family with leptin deficiency where treatment with leptin resulted in immediate weight loss, and rare genetic disorders of the leptin-melanocortin pathway being treated with a melanocortin-4 receptor agonist.[6,7]

Genetics do not provide a complete explanation for obesity. A disease stratification approach is therefore required whereby obesity is divided into phenotypes that can be identified by biomarkers to facilitate drug discovery with companion diagnosis and targeted trials. This requires an appreciation of how lifestyle and environment interact with a person's genetics to produce their phenotype, which is a snapshot of current health.

Obesity phenotypes based on pathophysiology

When Dr Acosta explains obesity to patients, he describes a disease of energy balance with excess intake and insufficient expenditure. Most obesity classifications focus on the storage of excess energy to identify both adiposity toxicity and who is at risk of developing CVD (**Figure 2**). Dr Acosta's approach is to focus on the energy balance of obesity and to classify this into phenotypes.

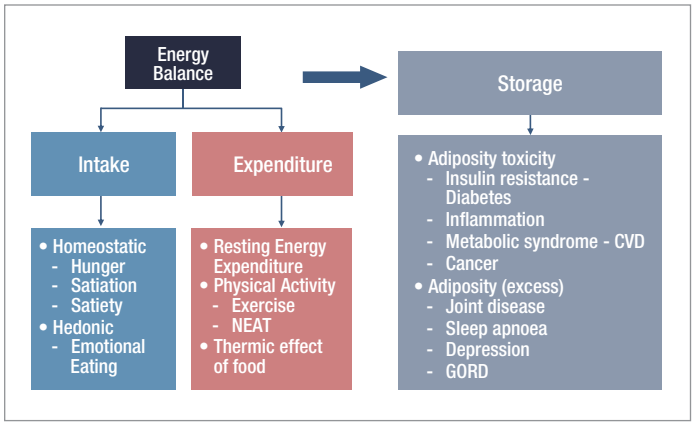


Figure 2: Obesity phenotype based on pathophysiology

How do we phenotype patients?

Dr Acosta's team phenotypes patients with obesity over 1 day, beginning with an energy expenditure assessment by indirect calorimetry and a body composition assessment with collection of blood, saliva and stool samples. Patients are given a breakfast (320 kcal) containing radioactive eggs to assess gastric emptying. Over the next 4 hours the movement of food is examined via scintigraphy and the patient's appetite is assessed. When the patient feels hungry, they are provided with an *ad libitum* buffet meal and the calories consumed quantified.

In Dr Acosta's experience, there is a substantial heterogeneity in energy balance traits between patients and this is consistent with the literature. For example, when satiation is measured in 660 patients, i.e. the number of calories eaten until experiencing maximal fullness, the results range from 444-2860 kcal.[8] Similarly, after following patients for 2 hours after maximal fullness, there is substantial variation in postprandial fullness. Between-patient variation is also seen in the extent to which anxiety influences eating and in resting energy expenditure versus predicted resting energy expenditure (**Figure 3**).

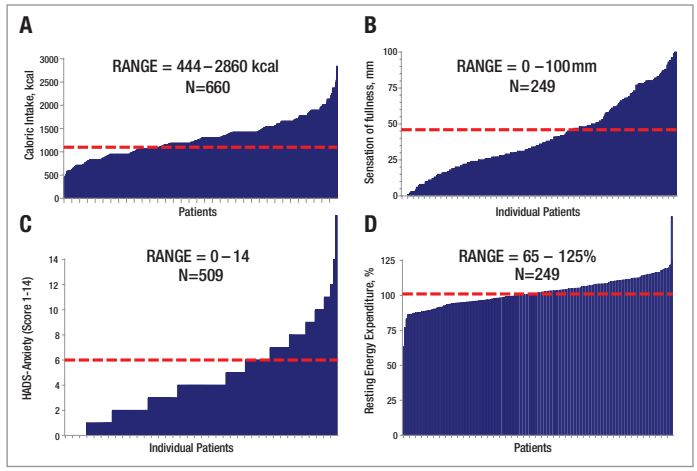


Figure 3: Results of (A) satiation test assessing maximum fullness, (B) satiety test measuring 2-hour postprandial fullness, (C) emotional eating (anxiety) and (D) resting energy expenditure. Adapted from Acosta *et al* (2015).[8]

Dr Acosta noted that the variation in energy balance traits mirrors the variation in the efficacy of obesity interventions. This led Dr Acosta and colleagues to perform a pragmatic trial in which they classified obesity phenotypes.[9] They found that sex was the most significant biological factor in determining energy balance. Therefore, females and males need to be separated in terms of obesity phenotypes. For example, the mean number of kilocalories needed to achieve satiation in a cohort of 100 patients was 803 kcal (range 660-1054), however, in females the mean value was 762 kcal (631-894) and in males it was 1104 kcal (802-1376).[9] This shows that if the mean for the cohort (803 kcal) is used as a cut-off, this will almost exclusively select females.

After dividing patients into male and female, Dr Acosta's group used inter-quartile percentiles to define what is normal and what is abnormal for the analysed traits.[9] They arbitrarily identified four obesity phenotypes using the 75th percentile from the median value of 450 obese patients in a study at the Mayo clinic:[9]

1. Hungry brain (satiation) – knowing when the meal is over. This phenotype eats more calories at each meal.
2. Hungry gut (postprandial satiety) – ability to not eat between meals. This phenotype feels hungry in a relatively short period after eating a meal.
3. Emotional hunger (hedonic eating)– eating in response to negative and/or positive emotions. This is the phenotype most typically associated with obesity.
4. Slow burn (energy expenditure) – an abnormally low basal metabolic rate and low overall activity level. This phenotype does not burn sufficient calories.

In reality, patients may have more than one phenotype (**Figure 4**). Dr Acosta's team found that 15% of patients with obesity did not meet the criteria for any of the four phenotypes.[9]

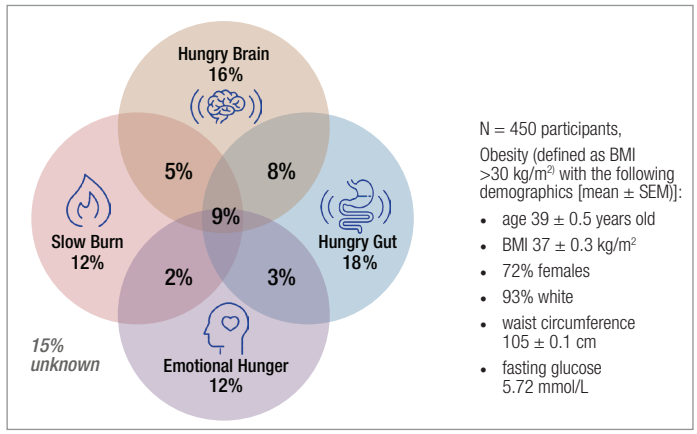


Figure 4: Distribution of obesity phenotypes in 450 patients. Adapted from Acosta *et al* (2021).

Dr Acosta and colleagues are currently compiling data from patients to develop unique pathological signatures to identify each obesity phenotype.

Can phenotypes enhance weight loss interventions?

Dr Acosta's clinical approach is to identify patients who are most likely to respond positively to existing weight loss interventions and to tailor treatment according to their obesity phenotype. This strategy has resulted in different lifestyle interventions for each phenotype (**Table 2**). This contrasts with recommending that all patients undergo the same treatment.

Table 2: Phenotype-tailored lifestyle and counselling interventions. Adapted from Cifuentes *et al* (2023).[10]

	Diet	Exercise and physical activity	Behaviour therapy
Hungry brain	Volumetric, high-fibre, low-calorie diet* 1-2 meals per day		
Hungry gut	Low-calorie diet* with pre-meal protein supplementation 3-5 meals per day		
Emotional hunger			Behavioural counselling plus weekly CBT sessions
Slow burn	Low-calorie diet* with post-workout protein supplementation	HIIT plus resistance training (supervised once per week)	

*Resting energy expenditure measured by indirect calorimetry minus 500 kcal

Dr Acosta's team reported that the mean TBWL in patients with obesity following a phenotype-tailored diet was -7.2% at 12 weeks, while those following the Mayo Clinic diet lost -3.5% TBWL.[10] There were also significant differences between the two diets in the percentage of responding patients able to achieve -5% and -10% TBWL (p<0.001).

When the data from this trial was analysed according to the phenotype-defining variable, the effectiveness of the phenotype-tailored approach became more apparent.

Hungry brain phenotype

Patients with the hungry brain phenotype achieved approximately -8% TBWL on the phenotype diet versus approximately -2% on the Mayo Clinic diet (**Figure 5A**).[10] There was no difference in the total calories consumed per day before and 12 weeks after the introduction of the Mayo Clinic diet. However, patients following the hungry brain diet consumed approximately 1000 fewer kcal per day, compared to baseline (**Figure 5B**).

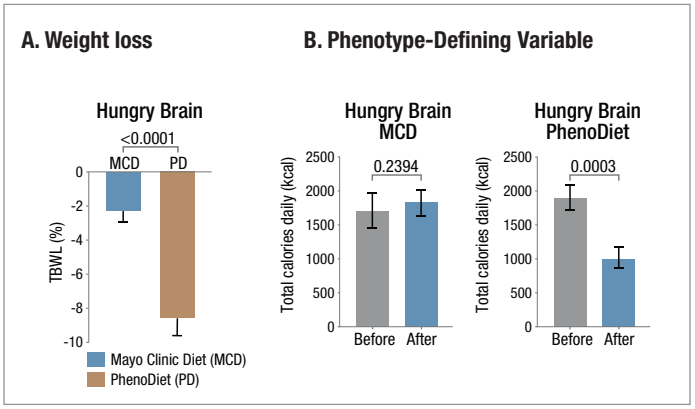


Figure 5: Outcomes at 12 weeks for patients with obesity with the hungry brain phenotype following the Mayo Clinic diet and the hungry brain diet for (A) total body weight loss, and (B) total daily calories consumed before and after the intervention. Adapted from Cifuentes *et al* (2023).[10]

Hungry gut phenotype

Patients with the hungry gut phenotype achieved approximately -6% TBWL, compared to approximately -1% on the Mayo Clinic diet (**Figure 6A**).[10] The objective phenotype-defining variable in this group, i.e. rate of gastric emptying, was no different before and after patients began the Mayo Clinic diet, however, in those following the hungry gut diet the rate of gastric emptying was reduced (p=0.032; **Figure 6B**). The finding that pre-meal protein supplementation is associated with decreased rates of gastric emptying was consistent with earlier studies in the literature.

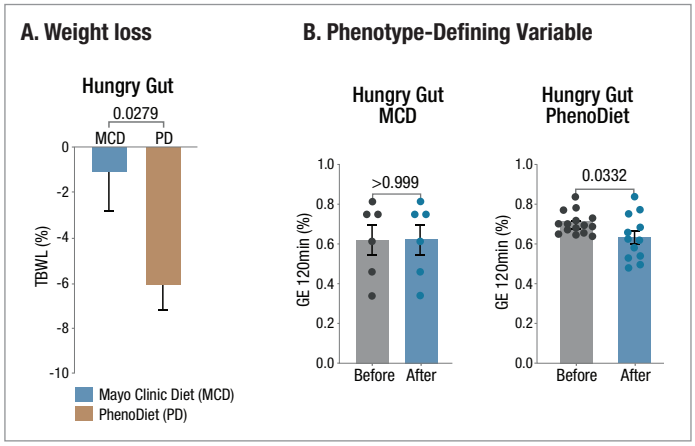


Figure 6: Outcomes at 12 weeks for patients with obesity with the hungry gut phenotype following the Mayo Clinic diet and the hungry gut diet for (A) total body weight loss, and (B) rate of gastric emptying before and after the intervention. Adapted from Cifuentes *et al* (2023).[10]

Emotional hunger phenotype

Patients with obesity with the emotional hunger phenotype achieved approximately -7% TBWL on the phenotype-tailored diet, compared to approximately -6% TBWL on the Mayo Clinic diet (p=0.563; **Figure 7A**).[10]

There was no difference in anxiety levels in patients with the emotional hunger phenotype who were following the Mayo Clinic diet (p=0.8857), however, there was a significant reduction in anxiety associated with the emotional eating diet (p=0.001; **Figure 7B**). This suggests that the Mayo Clinic diet does not address the underlying issue that is potentially causing weight gain, despite it being equally effective as the phenotype diet combined with counselling in terms of TBWL at 12 weeks.

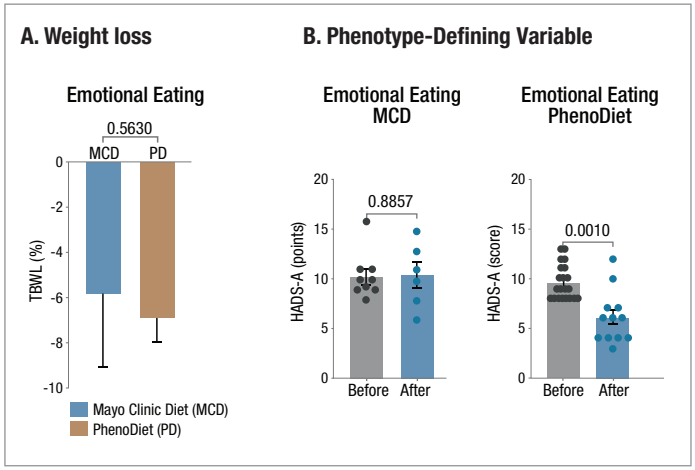


Figure 7: Outcomes at 12 weeks for patients with obesity with the emotional eating phenotype following the Mayo Clinic diet and the emotional eating diet for (A) total body weight loss, and (B) anxiety before and after the intervention. Adapted from Cifuentes *et al* (2023).[10]

Slow burn phenotype

Patients with obesity with the slow burn phenotype achieved approximately -8% TBWL on the phenotype-tailored intervention, compared to approximately -3% TBWL on the Mayo Clinic diet (p=0.0001; **Figure 8A**).[10] This suggests that increasing exercise is an effective weight loss strategy, if the recommendation is made to patients who are most likely to benefit. There was no change in lean muscle mass for patients with the slow burn phenotype following the Mayo Clinic diet (p=0.3663; **Figure 8B**). However, there was a significant increase in lean muscle mass for patients following the phenotype-tailored intervention (p=0.0062), despite these patients achieving -8% TBWL. This suggests that the low resting energy expenditure of patients with the slow burn phenotype may be improved by increasing their muscle mass.

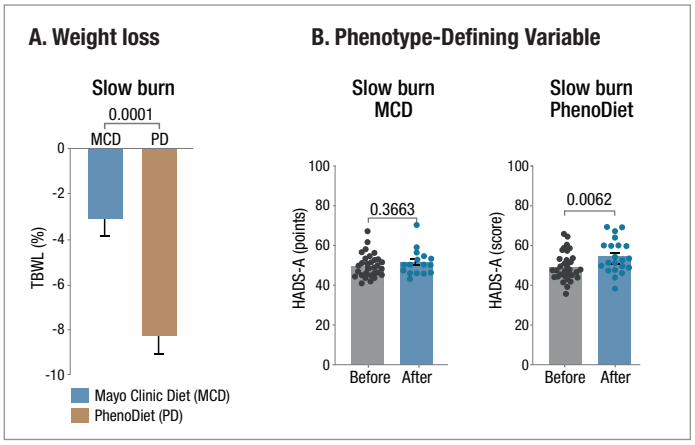


Figure 8: Outcomes at 12 weeks for patients with obesity with the slow burn phenotype following the Mayo Clinic diet and the slow burn intervention for (A) total body weight loss, and (B) lean muscle mass before and after the intervention. Adapted from Cifuentes *et al* (2023).[10]

Dr Acosta cautioned that the results of these interventions were at 12 weeks and are therefore a proof-of-concept. His group aims to replicate the results in a 1-year RCT to show the long-term feasibility of a phenotype-tailored approach to weight loss management.

A pragmatic trial

A pragmatic trial was conducted in which patients were prescribed different anti-obesity medications according to phenotype-guided or non-phenotype-guided treatment regimens. **Table 3** shows the anti-obesity medications that were prescribed to the two groups of patients in this real-world trial.[9]

Table 3: Anti-obesity medications used in the real-world trial. Adapted from Acosta *et al* (2021).[9]

Medication	Phenotype-guided therapy	Non-phenotype-guided therapy
Naltrexone-bupropion SR	19 (29%)	14 (6%)
Liraglutide	12 (18%)	41 (21%)
Lorcaserin*	10 (14%)	5 (3%)
Phentermine	7 (10%)	34 (17%)
Phentermine-topiramate ER*	20 (30%)	106 (53%)

*Not available in Australia

At 12 months, 98% of patients using a phenotype-guided intervention had achieved >5% TBWL, compared to 74% of those receiving a non-phenotype-guided intervention (p<0.001; **Figure 9**).[9]

The phenotype-guided intervention was also associated with a significantly higher proportion of patients achieving >10%, >15% and 20% TBWL, compared to non-phenotype guided interventions. Overall, the phenotype-guided interventions resulted in a -16% TBWL compared to -9% TBWL in the non-phenotype-guided cohort.

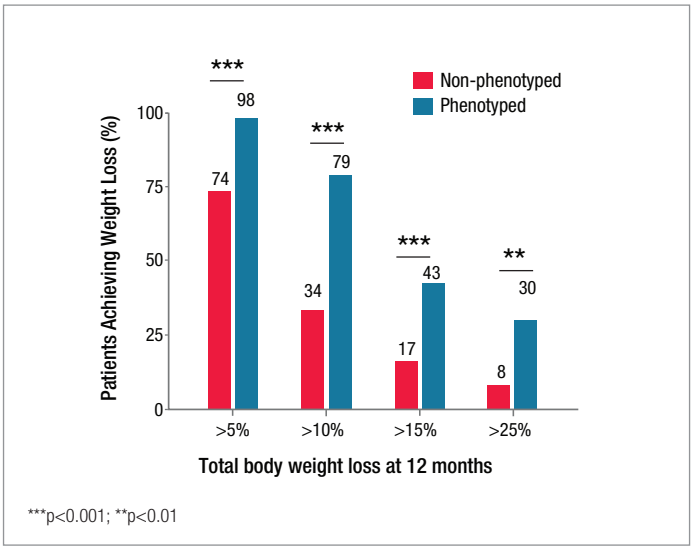


Figure 9: Weight loss at 12 months for phenotype-guided and non-phenotype-guided interventions. Adapted from Acosta *et al* (2021).[9]

These results show that phenotyping patients with obesity to determine the most appropriate interventions can approximately double the amount of weight loss that patients can achieve.

Dr Acosta acknowledged that informing patients that they would receive phenotype-guided treatment may act as a placebo. This is a positive bias, however, that is clinically helpful to include in conversations when treatment decisions are being made.

For patients with obesity with the hungry brain phenotype, Dr Acosta believes a vagal nerve block and endoscopy sleeve gastroplasty would be the most appropriate endoscopy procedures, and laparoscopic sleeve gastrectomy would be the most appropriate surgical procedure.

For patients with hungry gut, intragastric balloons and gels are likely to be the most appropriate endoscopic procedures, and RYGB would be the most appropriate surgical procedure.

There are no initial procedures or devices that are likely to be appropriate for emotional hunger or slow burn phenotypes.

As the investigations used to phenotype patients with obesity are not available in the community, biomarker tests are being developed using genetic, metabolic and hormonal testing. The first test to identify hungry gut has already been deployed in the United States.

Dr Acosta returned to the three real-world case studies he presented earlier.

Case Study One

A 41-year-old female: BMI 43 kg/m^2, height 165 cm, weight 118 kg, BP 142/91 mmHg. Her food intake is >2000 kcal/day and she drinks >700 mL/day of soft drinks. Her daily physical activity is unknown and she does not like to exercise. Medications she is taking are cyclobenzaprine (muscle relaxant)*, ibuprofen, levothyroxine and sertraline. The physical examination indicated central adiposity. Blood testing indicated an elevated fasting glucose with normal LDL, HDL, cholesterol and triglycerides. Her obesity phenotype results are shown below.

*Not available in Australia

Investigation	Patient	Reference
Gastric emptying ($t_{1/2}$ mins)	113	>101
Calories to fullness (kcal)	789	<894
HADS-A (anxiety)	**9**	**<7**
Resting energy expenditure (kcal)	1865	1897

Dr Acosta classified Case Study One as having obesity class III with an emotional hunger phenotype. The patient set a weight goal of 68 kg (TBWL = -50 kg).

The recommended treatment plan was:

- Diet – low calorie, 1000 kcal per day
- Physical activity – goal 10,000 steps per day (recommending 500 more per week) and 150 minutes of walking per week
- Behavioural plan – group therapy
- Medication – stop sertraline (depression well controlled) and start anti-obesity medication, naltrexone-bupropion SR to help manage the cravings.

After 1 month, Dr Acosta could tell the treatment was effective because the patient reported decreased food cravings and her emotional eating had improved. There were no adverse effects from the medication, and she continued to stay connected with the group therapy that she had started via text. The patient steadily lost weight and after three years her TBWL was -21.4% (-24 kg).

She now has controlled obesity (BMI <30 kg/m^2) with treated emotional hunger phenotype, and controlled hypertension and controlled T2D. Her weight has not rebounded during the COVID pandemic and despite other challenges she has faced. Critically, the patient no longer has cravings that are driving her to eat, therefore her weight loss may be sustainable.

Case Study Two

A 41-year-old female: BMI 41.3 kg/m^2, height 170.6 cm, weight 119.5 kg, BP 124/70 mmHg. She consumes 1700-1800 kcal per day, drinks water or black coffee and completes >10,000 steps per day and >150 minutes of exercise per week. Medications she is taking are montelukast, metformin and a multivitamin. The physical examination revealed central adiposity.

Dr Acosta accepted the patient's reported food intake and performed an obesity phenotype (see below).

Investigation	Patient	Reference
Gastric emptying ($t_{1/2}$ mins)	**95**	**>101**
Calories to fullness (kcal)	835	<894
HADS-A (anxiety)	5	<7
Resting energy expenditure (kcal)	1865	1916
Predicted resting energy expenditure (%)	97.4	100
Body fat (%)	51.8	20-32%

The results indicated that the patient's gastric emptying was fast and that her percentage body fat was 51.8%, despite exercising regularly and eating a healthy diet. This was consistent with the patient's reported craving for food between meals. Dr Acosta pointed out that the rate of gastric emptying cannot be controlled by the patient.

Dr Acosta classified Case Study Two with medically complicated obesity class III with hungry gut phenotype. The patient's target bodyweight was 75 kg (-45 kg TBWL).

The recommended treatment plan was:

- Diet – 1000 kcal/day, high protein
- Medication – liraglutide injection

After 1 month, the patient had not experienced medication adverse effects. She reported not "*feeling hungry all the time as I used to...*" and she was able to adhere to a low-calorie diet. From August 2017 to March 2019, the patient reduced her bodyweight from 120 kg to 74 kg and her body fat percentage dropped from 52% to 32.8%.

The patient has subsequently maintained her goal bodyweight. She has controlled obesity with treated hungry gut phenotype. She was able to lose weight easily once the issue underlying her weight gain was addressed.

Case Study Three

A 41-year-old male: BMI 56.86 kg/m^2 with back pain and the same co-morbidities as the previous case studies and with the following vital signs: height 188 cm, weight 201 kg, BP 142/88 mmHg. His physical examination was normal. Blood testing revealed impaired fasting glucose (14.04 mmol/L), elevated LDL (4.09 mmol/L), triglycerides (4.84 mmol/L) and very high C-reactive protein (15.7 mg/L).

Typically, the patient would not feel hungry on waking and would drink a powdered drink during the morning. At lunch, he often did not feel full and would try to control his portions and had cravings in the afternoon. At dinner, he would often have two servings and would eat snacks later at night. The patient was preparing for bariatric surgery, but his claim was denied by his insurance company. Medications he was taking were gabapentin, glipizide, NPH insulin, sertraline, atorvastatin, lisinopril, and hydrochlorothiazide.

Dr Acosta phenotyped Case Study Three (see below) and classified him as medically complicated obesity class III with emotional hunger and hungry gut phenotypes.

Investigation	Patient	Reference
Gastric emptying ($t_{1/2}$ mins)	**81**	**>88**
Calories to fullness (kcal)	900	<894
HADS-A (anxiety)	**11**	**<7**
Resting energy expenditure (kcal/day)	2762	2700
Predicted resting energy expenditure (%)	93	>94
Body fat (%)	59.1	20-32

The recommended treatment plan was:

- Diet: 1400 kcal/day
- Behavioural therapy
- Medication:
  - Naltrexone-bupropion SR
  - GLP1 RA: Semaglutide injection

After one month, the patient did not experience any adverse effects from the medications and his cravings improved. He no longer drank the powdered drink during the morning and was no longer hungry between meals. Over the next 6 months, Dr Acosta withdrew glipizide and decreased insulin treatment by 15 units. From October 2022 to February 2023, the patient experienced -11.4% TBWL (-20 kg).

Case Study Three has improving obesity with treated emotional hunger and hungry gut phenotype. Dr Acosta noted that the withdrawal of medicines associated with weight gain probably contributed to the success of the treatment.

Questions and answers

1. **Do you have plans to perform a randomised trial with your approach?**
   No grant applications have been approved as yet for funding a study of this type.
2. **How were the case studies categorised into their phenotypes?**
   Each patient completed a phenotype panel to identify their abnormal traits.
3. **In Case Study 1, why was the sertraline stopped?**
   Dr Acosta's preference is not to have dual agents treating the same condition, unless required. In this case, the patient's depression was well controlled, therefore the sertraline appeared to be unnecessary. Based on pharmacogenetic data, we know that some patients taking SSRIs may gain weight. In general, and where appropriate, Dr Acosta withdraws medicines that are associated with weight gain.
4. **What questions can be used to help identify potential phenotypes in obese patients, in the absence of phenotype testing?**
   The HADS anxiety questionnaire is widely available to identify patients with emotional eating phenotypes as is the Three-Factor Eating questionnaire. By introducing these questionnaires into clinical practice after approximately 20 patients an idea of what is normal will begin to emerge that can be paired with clinical decision making. For example, whether to prescribe Contrave® or recommend group therapy or to use the two approaches together. Specific tests are currently required to identify the hungry gut, hungry brain and slow burn phenotypes.

TAKE-HOME MESSAGES

- Obesity is the number one chronic disease in the world.
- A "one-treatment-fits-all" approach to obesity management is not working.
- Obesity is a complex and heterogenous disease with multiple phenotypes.
- Phenotyping patients with obesity doubles weight loss and facilitates personalised interventions involving diet, lifestyle and pharmacotherapy.
- Four obesity phenotypes have been identified as seen in the pragmatic trial, each with different approaches.

	Hungry Brain	Hungry Gut	Emotional Hunger	Slow Burn
LIFESTYLE INTERVENTIONS	• Hungry Brain diet: Volumetric, high-fibre, low-calorie diet 1-2 meals per day	• Hungry Gut diet: Low-calorie diet with pre-meal protein supplementation 3-5 meals per day	• Behavioural therapy • Hungry Feelings diet: 3 meals per day and either no snacks or only fruit/vegetables as snacks	• Slow burn diet: Low-calorie diet with post-workout protein supplementation or healthy protein snacks Intensive exercise plan
MEDICATION	• Phentermine-topiramate ER*	• Liraglutide • Semaglutide	• Naltrexone-bupropion SR	
ENDOSCOPY	• Vagal nerve block • Endoscopy sleeve gastroplasty	• Intragastric balloons • Intragastric gels		
SURGERY	• Laparoscopic sleeve gastrectomy	• Roux-en-Y gastric bypass		

*Not available in Australia

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