Why is losing weight so difficult and maintaining weight loss even harder webinar

Frequently asked questions

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COST OF MEDICATIONS

Major down-side to this is cost, $387 per month if on full dose
Rep for one brand said not to use lower than the full 3mg does as it didn't work?
As you know, currently no anti-obesity medications are on the PBS. Some patients might get some money reimbursed if they have private health insurance and their level of cover has provisions for this (variable from my clinical experience ranging from $50-$300/month back OR a capped annual spending budget on non-PBS medication).

In dose-finding studies, the 3mg dose is more effective than lower doses. However, patients may respond to a lower dose of Liraglutide. Just like all general prescribing principles, the aim is to use the lowest effective dose from a side effect, and cost effective point of view Thus it is based on the clinical and the individual patient they are treating.

The product information monograph stipulates that the effective therapeutic dose is 3mg, and the stopping rule mandates "a responder is someone who loses at least 5% of their starting weight after being on the therapeutic 3mg dose for 12 weeks". Obviously if a patient is not responding to any particular medication after a therapeutic trial, then it is not only costly but futile. In such circumstances, the medication should be discontinued and changing to an alternative form of treatment, with a different mechanism of action, should be considered.

Anecdotally, I have some patients who achieve therapeutic satiety response and weight loss with lower than 3mg doses, however they are the minority.

As always, the cost of medication needs to be weighed against the costs, benefits and risks of the alternatives.

WHEN TO CONSIDER MEDICATIONS

Are you giving dietary and lifestyle advice in addition to the medications or VLCD in addition to the medications? I refer you back to Georgia's "3 legged stool analogy"…the intervention in this case being pharmacotherapy, which should be viewed as an "enabler". (see the bariatric surgery webinar in this series). The Australian NHMRC Guidelines talk about successive intensification of treatments i.e. overlaying and reapplying.

The medications themselves do not cause weight loss. They only work by reducing appetite to help adherence to the dietary modifications. They "enable" a patient to lose weight, by

counteracting some of the physiological hormonal changes which occur within the body to defend the weight loss (see Sumithran et al NEJM 2011 paper). Therefore, Lifestyle advice should be the cornerstone of any weight loss strategy including when prescribing anti-obesity medications. VLCD are an effective, evidence based strategy which goes well with pharmacotherapy.

Would you recommend different drugs at different stages? As patients are either "responders" or "non-responders" to medications, pharmacotherapy should be tailored to the person depending on finances, interactions with other medications, side effect profile, other co-morbidities (such as migraines, diabetes, and cardiovascular disease), contraindication (if such exist) and mode of delivery, rather than focussing solely on their stage of obesity.
Anecdotally, I have found that in some patients who were apparently "non-responders" to a particular medication prior to bariatric metabolic surgery, can become "responders" to the same medication (often at a lower dose) after bariatric metabolic surgery. This is consistent with Prof Lee Kaplan's work in USA.

Any role for SSRI or SNRIs as a weight loss therapy independent of mood disorder? There is no real evidence for using SSRI's or SNRI's for weight loss therapy in the absence of a mood disorder. Only bupropion may cause a small amount of weight loss. But at $150 - $170 a month, as a stand-alone therapy, there are better options which are more efficacious like the ones we mentioned in this webinar. It should be noted, that the buproprion/ naltrexone combination is an FDA approved anti-obesity medication which is currently available in America. Furthermore, each individual product has ben safely used in Australia for more than 30 years for other medical indications.

Does metformin have a place in weight management? There is insufficient evidence to recommend metformin as treatment of obesity in adults who do not have diabetes mellitus or polycystic ovary syndrome. Even in the later, it is recognised as off-label use by many regulating bodies. There is limited evidence for the efficacy of metformin in limiting weight-gain induced by atypical antipsychotic agents. In people with T2DM and obesity, metformin is useful in combination with all additional diabetes medications, unless it is contraindicated or not tolerated.

Do you commence these meds once weight loss has already been achieved (to prevent re-gain) or at the start when people are just beginning to implement diet/exercise changes? Medications can be commenced at either time. The appropriate time should be discussed with each individual patient and be tailored to their needs and situation. If they are on medications that cause them to gain weight such as psychotropics, commencing pharmacotherapy straight away may be the right approach. Some studies have shown that if pharmacotherapy is initiated after initial weight loss by other means (intensive lifestyle or VLED), then the addition of pharmacotherapy has resulted in additional weight loss. Using medications either to initiate weight loss or to prevent weight re-gain are both appropriate and effective strategies, and the decision needs to be tailored to the individual.

Is there a BMI or obesity stage/class lower limit you wouldn't prescribe for? eg overweight (not obese) people who have lost 10% weight and worry about regain? Firstly, we should not forget the ethical principle of non-maleficence ie "do no harm"; hence it would be hard to justify prescribing medications for people who have a normal BMI and have no weight- related co-morbidities.

Generally, the best approach is to stick to the recommended guidelines of prescribing in patients with a BMI≥30 or BMI≥ 27 with weight-related co-morbidities. However keep in mind the lower BMI cut offs for people from the Asian and other ethnic groups (refer to NHMRC guidelines).

Using pharmacotherapy for preventing weight re-gain (even 10%) is an effective strategy and just as important as weight loss. We know from the above forementioned Sumithran study and other studies that have shown that the body physiologically defends against weight loss via a cascade of hormonal changes which are under hypothalamic control ie not under voluntary cortical control.

Furthermore, the NHMRC guidelines advise that if a patient regains 3kg after concerted weight management/ health improvement efforts, they should come back for a medical review. It is then up to the discretion of the treating clinician and that patient's particular health profile which will dictate the next course of action. In this scenario, medications or reintroduction of a partial VLED program might be considered amongst other strategies.

With regards to considering initiating medication should we consider when patients are at a certain obesity stage rather than just BMI? If they have no comorbidities from their obesity should medication be considered given the risk of potential serious side effects?

As previously discussed, BMI itself is not a good measure of how "sick" a patient might be. This is where using something like the Edmonton Obesity Staging System, may be of clinical assistance.

In general, all medications come with risk of side effects and therefore patients' needs to be informed and made aware of any "red flag" symptoms they should watch out for; and if these occur to ring their treating clinician. Hence the possibility of the infrequent yet serious side effects are minimised and if they occur, are dealt with earlier.

As above, the use of medications should be discussed with each individual patient and be tailored to their needs and situation. Stage is important regardless of BMI, but I would be reluctant to use medications if BMI is <27. If BMI >27 with weight-related complications, or BMI>30, then I would consider the use of medications, particularly if there are other risk factors (e.g. family history of T2DM or premature cardiovascular disease) and if they have made previous serious attempts at weight loss (and maybe did/did not respond-even if short lived) or have significant hunger or difficulty adhering to their healthier eating plan (due to the body's physiological response eg increased hunger hormone ghrelin etc).

Is Phentermine ok to use in major depression? Phentermine is contraindicated for use in people with major psychiatric conditions and this includes major depression.

ADVERSE EFFECTS/CONTRAINDICATIONS/PRECUATIONS FOR MEDICATIONS

Do you warn patients of the evidence that Liraglutide is linked to increased medullary cell carcinoma in rat studies? Even though there is a link in rodents, it is important to mention this to all patients and to write it in your "notes" (patient electronic medical record) that you have. The key points to highlight to the patient, is that it has been TGA approved, and that the risk indicates that the increased incidence is in rodents only. The mechanism seems to be linked to GLP-1 receptors on thyroid C-cells, which appear to be more numerous and sensitive to stimulation by GLP-1 in rodents compared with humans. The patient can then weigh up the cost benefits of their likelihood of medullary thyroid cancer and their risk of not losing weight. One should also remind patients, that there is an "adverse event" registry which is being maintained globally.

Please comment on TGA decree 2011: The TGA has not approved the use of Topiramate to assist with weight loss and is advising health professionals and consumers that its use for this indication is associated with serious adverse events? Patients need to be informed that Topiramate is not TGA approved for weight management, as part of the discussion of possible risks and benefits. However they need to be made aware that topiramate have been safely used for many years, albeit for other indications such as epilepsy and migraine management. It should be noted, that the topiramate/ phentermine combination is an FDA anti-obesity medication which is currently available in America.

Phentermine is contraindicated in pregnancy, does it mean it is teratogenic? Animal studies have shown that phentermine can cause congenital malformations in newborns (heart defect, cleft lip and cleft palate).
These defects develop at the beginning of pregnancy. Hence why phentermine is not recommended for any women who are trying to fall pregnant or who are pregnant.

Does the drop in mood persist if they stay on the medication? Whether the mood improves over time is very individual. The mood can get better in some but not others. Generally if it has persisted for more than 1 month and it is affecting their day to day function or causing suicidal ideation, I would lower the dose or cease the medication especially in the latter).

Will topiramate impact contraception i.e. OCP. do the dosage of estrogen need to be increased ? Lose dose Topiramate of under 150mg is said not to affect the efficacy of the OCP. However, I always warn patients to use barrier methods around their ovulation time when they are most fertile as an additional precaution. This is also best practice advice for STI prevention.

Can Topiramate be taken with SSRI? Yes. But care must be taken with those on mood stabilisers such as lithium (lithium toxicity) and sodium valproate (serotonin syndrome like effects). Such patients will require closer monitoring, including blood tests to monitor levels etc

Is the fatigue due to hypoglycaemia? The reasons for this can be multifactorial including relative hypoglycaemia, changes in insulin levels & sensitivity, as well as reduction in caloric intake.

The AMH recommends that for doses of Topiramate above 50mg, that we give it in divided doses daily. Do you give it once daily/ BD/ TDS? From a side effect point of view, the doses are split to morning and night if more than 50mg.

DURATION OF MEDICATION USE

Once an effective medication is found for a patient is this possibly lifelong treatment? How long do people have to be prescribed the different options for? With the medications mentioned, do the studies show that the weight stays off long term, or does it also creep back on with time if you don't continue the medication?

Since obesity is a chronic progressive disease, and the compensatory adaptations to weight loss (including increased hunger) are long-standing, the medications are likely to be required in the long-term, as long as they are effective ie patient is responding to it.

The medications are only effective while they are being taken (as is the case for other chronic disease medications e.g. anti-hypertensive or diabetes medications).

Given that obesity is also a progressive condition, some eventual weight regain is to be expected and normal-see the Swedish Obese Study (longitudinal study comparing lifestyle vs bariatric metabolic surgery now for almost 30 years). This does not differ to diabetes and other chronic conditions….progression and relapse is expected and a normal part of the disease process.

However as with any health condition, pharmacotherapy should be discontinued if the patient is non- responsive, unacceptable side effects or other reasons. At a later date, the clinician should discuss with the patient the possibility of initiating a treatment with a different mechanism of action.

However there are 2 caveats: firstly, if a person is regaining weight, adding medications may result in further modest weight loss however, importantly may help them maintain their weight ie prevent further weight regain, which is still a valuable outcome.

Secondly, the literature generally shows that most weight loss with pharmacotherapy occurs in the first 6 months after initiation, and then plateaus. A plateau should not be interpreted as though “the medication has stopped working”, but rather, than it is working by keeping those hormonal counter -regulatory changes at bay…hence reducing the incidence and magnitude of weight regain. However, NHMRC guidelines suggest that if an individual experiences an inadequate response to medical therapy or a relapse, and they meet the NHMRC criteria, the discussion RE possibility a referral for bariatric metabolic surgery should take place.

CAN ANYTHING BE DONE TO COUNTERACT HORMONAL CHANGES?

What is the role of Low carb or LCHF type diets in "hacking" this appetite system? Low carbohydrate ketogenic diets may ameliorate some of the compensatory hormone changes (e.g. preventing the rise in ghrelin and fall in CCK) but are difficult to sustain in the long-term. This option is relatively low in intensity, endorsed by the CSIRO in their cookbooks and clinical papers and is very acceptable to some people. Therefore it could be considered, though as with any intervention, there will be some who respond and some who don't. Currently, there is no other eating pattern which has been shown to modify the hormonal response to weight loss.

As far as I have read this is not happening with repeat/intermediate fasting? To date I am not aware of any studies examining these hormones and intermittent fasting. There is preliminary evidence that the decline in energy expenditure with weight loss may be less with intermittent dieting (2-weeks on/2-weeks off) compared with continuous dieting, but this has not been conclusively shown.

Are the hormonal responses different for different macronutrients? The hormones are each more responsive to some macronutrients than others (e.g. CCK release stimulated by fat, ghrelin suppressed most by carbohydrate) but in practice most meals are mixed.

CHO, Protein, Fat. Will 5-10% wt loss be enough to trigger the hormonal changes that make it harder to keep it off? Is the hormonal changes more significant with much slower rates of weight loss? Weight loss of 5-10% is enough to trigger hormonal changes. The rate of weight loss does not affect the hormonal changes/rate of weight regain (study by Purcell et a Lancet Diabetes Endoc 2014).

Does exogenous leptin administration have a place in weight management? Exogenous leptin administration has been shown to reverse many of the other compensatory adaptations to weight loss but is not available in clinical practice.

In particular this has been helpful to those with genetic true leptin deficiency, rather than the purported leptin resistance which is observed in some individuals with obesity.