ilant HEALTH

Value-Based
Obesity Management
& Cardiometabolic Health

Obesity Treatment

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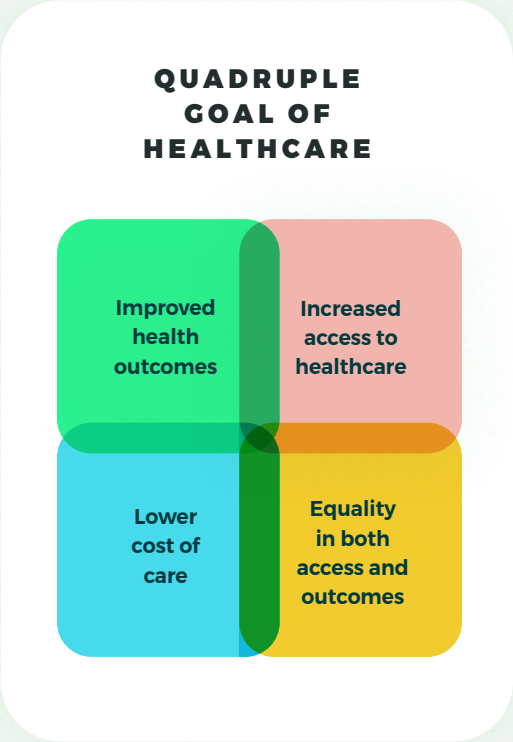
Affecting more than 40% of the US adult population,[1] obesity is a metabolic disorder characterized by excess weight–particularly the gain of adipose (also known as fat) tissue in the stomach area.

Obesity is not a matter of appearance or a negative view of large bodies; it is a chronic health condition and leading public health challenge.

Obesity drives a wide range of over 200+ conditions, and obesity is associated with a general increase in all-cause mortality, with mortality risk increasing with the degree of obesity. In addition to these serious medical impacts, obesity poses a grave health equity challenge. Obesity prevalence is higher for black and brown individuals and in low income communities.[1] Obesity may even 'pass' from one generation to the next based on a combination of genetic, epigenetic, and environmental factors.[2]



These medical and health equity impacts provide strong motivations for addressing obesity. The goal of anti-obesity treatment should align with the quadruple goal of healthcare: improved health outcomes, increased access to healthcare, lower cost of care, and equality in both access and outcomes. Historically, these goals have been difficult to achieve because the ability to treat obesity was limited by a lack of effective treatment options.

However, recent developments have provided significant improvements over existing treatment options, including the use of GLP-1 receptor agonists (21% weight loss on Zepbound; 15% on Wegovy), improvements in bariatric surgery that have resulted in higher safety and lower costs, and 90+ anti-obesity drugs under development. In this white paper, we describe the right approach to matching individuals to treatment to maximize the quadruple goals of healthcare.

Who should receive treatment for obesity?

Who benefits most from obesity treatment? To improve health outcomes, the focus of treatment should be on populations with higher burden of disease and higher healthcare cost. Often, higher disease burden is associated with higher BMI, as obesity both causes and exacerbates many of its comorbidities and can act as a force multiplier that hastens their progression and increases their severity. We have spent significant effort to develop models for identifying from claims data who might benefit most from treatment interventions.

However, even when the right population can be identified, engaging and treating the right individuals can also be hard because of high levels of bias and stigma. For example, 40% physicians report a negative reaction toward a patient who has obesity, and half of primary care providers report regarding patients with obesity as "awkward, unattractive, ugly, and non-compliant".[3] Experiencing this stigma can deter patients with obesity from seeking healthcare services, including preventative care and screenings. 52% of patients with overweight or obesity responded affirmatively to "Has your weight been a barrier to getting appropriate health care?"[3] These two challenges in selecting and engaging the right population create a vicious cycle, where the individuals most likely to get obesity treatment often are those with the lowest acuity and least immediate need.[4] This phenomenon of "adverse selection" in who gets treated impacts obesity just as it does other diseases states with high

levels of stigma and bias. For example, individuals with Class 1 obesity make up the largest segment (40%) of the population who receive treatment by both health systems and direct to consumer offerings.[4-5] In our own analysis of clients' data, we often observe that individuals treated with GLP-1s actually have a lower number of comorbidities on record than those treated for other oral anti-obesity medications intended for individuals at lower levels of acuity. This misalignment of treatment to acuity leads to unnecessary use of treatments that strain healthcare resources without providing meaningful benefits. For example, surging popularity on social media has created shortages of Ozempic which is also used to treat diabetes,[6] leading individuals with diabetes to go without their treatment. The solution is to focus treatment on individuals with high obesity-related acuity in a clinical environment without stigma, and communicate in a non-judgemental and unbiased manner the opportunities for and benefits of treatment.

Selecting the right treatment

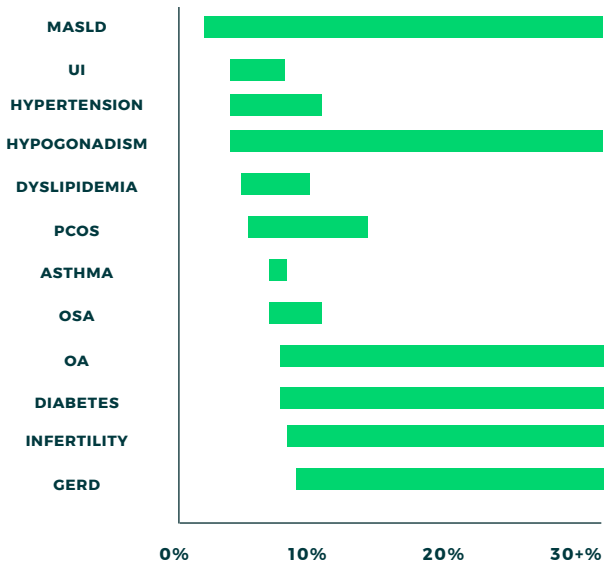
The right strategy for managing treatment for obesity is to select the right treatment for the individual. This requires matching the level of treatment to the level of obesity-related clinical acuity and treatment approach (or mechanism of action) to clinical need.

The first goal of obesity management is better health outcomes, and so effective treatment must set goals for weight reduction that makes the individual's health conditions more manageable and lead to health improvements. Different conditions require different levels of weight loss to slow their progression or reverse their acuity.

For example, the American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice (2016)[7] recommends targeting (at least) approximately 5-10% weight loss for achieving positive improvements in dyslipidemia, fat accumulation in the liver associated with metabolic dysfunction-associated steatotic liver disease (MASLD), male hypogonadism, obstructive sleep apnea, asthma, osteoarthritis (when paired with physical therapy), and urinary incontinence.
For hypertension and polycystic ovarian syndrom (PCOS), they recommended targeting 5-15% reduction. In contrast, more than 10% weight loss is recommended to positively impact diabetes, liver inflammation and fibrosis associated with MASLD, female infertility, osteoarthritis, and gastroesophageal reflux disease (GERD) (see Figure 1).

These goal ranges are useful for illustrating the point that different conditions require different amounts of weight loss to see meaningful benefits. However, these averages mask the real complexity in deciding what level of weight loss an individual person will need to target to drive health improvements. That is because individuals almost never have the 'average' profile, and the averages for each condition collapse across the different stages of severity of disease, and ignore the fact that diseases often co-occur with—and complicate—one another. More severe diseases are harder to impact and so the amount of weight loss needed may be higher.

Figure 1: Estimated Minimum Weight Loss Needed to Drive Health Improvements



Source: 7

Comorbid diseases—especially when an individual has a large number of comorbidities—make it harder to lose weight and may raise the floor for how much weight must be lost to make an impact. For example, an individual with obesity, diabetes and MASLD may need more weight loss to impact their diabetes than a similar individual without MASLD, as MASLD can drive progression of diabetes on its own. In addition, the amount of weight loss needed to achieve health improvements almost certainly varies with starting BMI as well; for an individual with an initial BMI of 60, 5% weight loss may simply not be enough to move the needle.

Lastly, it's always important to remember that almost every condition responds in a dose-dependent manner (meaning more weight loss is better until an optimal body weight is reached), so an individual might need to aim for a target higher than the averages, especially when they have a greater number of comorbid conditions or comorbid conditions that reinforce one another.

What treatment options exist today?

There are now many many obesity treatment options with different treatments suited for different levels of acuity. These treatments range in terms of effectiveness from 2-5% weight loss for intensive behavioral therapy to greater than 35% weight loss for bariatric surgery (See Figure 2).

Figure 2: Types of Treatment for Obesity

Behavioral Therapy

High-touch behavioral coaching intended to improve behaviors and address environmental challenges

2-5% WEIGHT LOSS

- High value for individuals who may not have attempted (structured) weight loss programs previously
- Most likely to drive desired outcomes for individuals close to normal BMI and without significant obesity-related comorbidties

Pharmacotherapy

Medication adjunct to behavioral therapty supporting reductions in hunger and/or increase in metabolism

5-20% WEIGHT LOSS

- High value for individuals with moderate levels of obesity
- Certain medications have been shown to have particularly high-response in different patient populations
- Evidence of cardiometabolic (diabetes, heart disease) impact; emerging other indications

Bariatric Surgery

Surgical procedure to change hormones, reducing hunger, constrict stomach size, and reduce nutrient obsorption

25 - 35% WEIGHT LOSS

- Most impactful for individuals with high levels of obesity (Class 3) and those with more progressed cardiometabolic disease (high A1C/ on insulin diabetes)
- Evidence of remission of diabetes and obstructive sleep apnea
- Evidence of reduction in cancer and non-alcoholic fatty liver disease incidence

Intensive Behavioral Therapy (IBT)

Intensive behavioral therapy (IBT) is high-touch coaching intended to improve behaviors and address environmental challenges. IBT is a clinically validated approach to obesity management, [8] and must be distinguished from simple diet and exercise counseling or other lifestyle advice around weight such as "move more and eat less" which are generally ineffective.

IBT can deliver 2-5% weight loss, although it may not work for every individual. As a result, it is generally best suited for individuals with lower levels of obesity, those without significant comorbidities, or whose weight gain has been recent–especially if these individuals have not tried IBT programs previously. Behavior modification also has the advantage of having no risks or side effects.

Anti-obesity Medications (AOMS)

There are a growing number of medications that can help with obesity. Medications range widely in both their level of impact and how they drive that impact—often known as their mechanism of action - as well as in their related side effects and tolerability (See appendix for full table).

Figure 3: AOM Treatments

Name	Cost	**Weight Loss & Discontinuation rate** due to adverse events ● Discontinuation rate ● Weight Loss
Metformin	$	3% N/A Not approved for obesity for discontinuation rate.
Phentermine (Adipex)	$	5% 6-10%
Orlistat (Xenical, Alli OTC)	$	9% 8%
CONTRAVE (naltrexone ER/bupropion ER)	$	7% 20%
QSYMIA (phentermine /topiramate ER)	$	11% 17%
SAXENDA (liraglutide)	$$$$	7% 9%
WEGOVY (semaglutide)	$$$$	15% 8 - 12%
ZEPBOUND (tirzepatide)	$$$$	21% <5%

The most exciting of these is a new class of drug known as GLP-1 receptor agonists (often called GLP-ras or GLP-1s) which have captured popular attention due to their high efficacy in both weight loss and in treating other cardiometabolic diseases, including diabetes and heart disease.[9-10] In March 2024, Wegovy (a drug of this class) became FDA approved for reducing the risk of major cardiovascular events,[11] capturing the excitement that GLP-1 receptor agonists can simultaneously address weight loss and some of the most serious comorbidities associated with obesity. In fact, GLP-1s are now under investigation for their ability to treat chronic kidney disease[12-13] and obstructive sleep apnea,[14] in addition to their existing indications for diabetes, cardiovascular disease, and obesity.

Although GLP-1s have taken the space over by storm, the speed of innovation has not slowed and 86 new drugs are on the horizon[16] (see Table 2). Seven of these drugs are currently in Phase 3 trials which means that if safety and efficacy benchmarks are met, there may soon be many more treatment options available. Perhaps the most exciting aspect of these new treatments is that many are innovating on novel methods of action.

For example, Zepbound—the most recently of the GLP-1 receptor agonists—also has a second mechanism of action by acting as a glucose-dependent insulinotropic polypeptide (GIP) agonist, mimicking a chemical that increases sensitivity to insulin so that the same amount of insulin has a greater effect. and reduces the amount of acid produced by the stomach further slowing digestion.[17]

Eight of the upcoming drugs will use this same combination of dual GLP-1/GIP agonism, and other exciting mechanisms of action are being explored such as myostatin inhibitors which may preserve a greater amount muscle during weight loss, microRNA-22 inhibitors, and leptin sensitization.

WHAT IS

A GLP-1 RECEPTOR AGONIST?

A GLP-1 receptor agonist is an artificial drug that has been engineered to trick the body into thinking it is glucagon-like peptide (commonly abbreviated as GLP-1), a naturally occurring hormone produced in the small intestine that helps regulate blood sugar by triggering insulin release and also slows the movement of food from the stomach to the intestine. [15]

That is, these drugs imitate the natural signals of the body and allow physicians to turn those signals up.

The practical effects of these drugs is that (1) blood sugar will be better controlled due to improved insulin regulation—which is why GLP-1s are prescribed for managing diabetes and individuals taking GLPs often see reductions in the hbA1c—and (2) the stomach is full for longer and so fewer nutrients (i.e. calories, fat) will be absorbed by the small intestine at a slower rate.

Figure 4: R&D Pipeline for New AOMS

Phase	GLP-1 Receptor Agonist	GLP-1 Combination	Other
Phase 3	3	4	0
Phase 2	4	7	12
Phase 1	6	7	19
Preclinical	1	4	14
Total	14	22	45

Note: See full Table in Appendix

Who will benefit from an AOM?

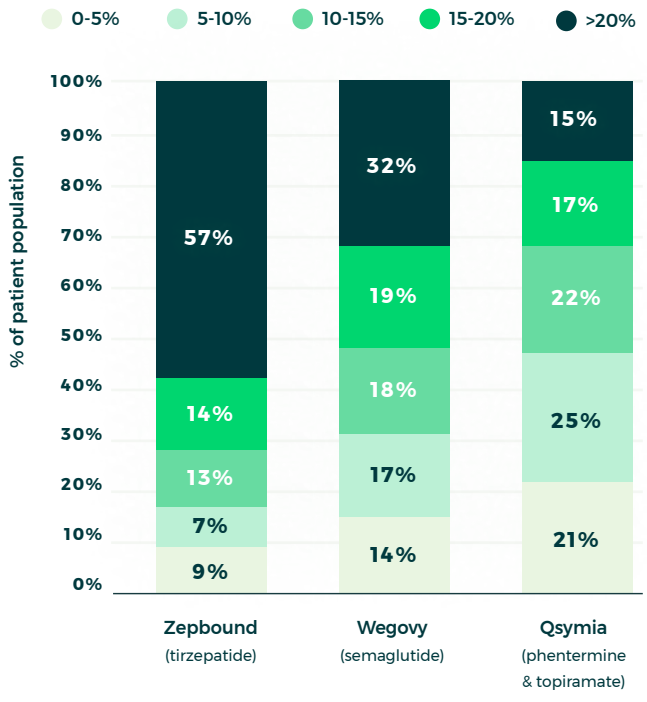
When thinking about an approach for medication treatment of obesity, it is extremely important to de-average care. That is, we cannot decide how to treat an individual based on averages alone; because the averages overlook that individuals have different comorbid conditions, and so the amount of average weight loss is not the most important deciding factor. Instead, the ideal approach is to determine which mechanism of action is most likely to improve the individual's health—will it directly treat the individual's comorbid conditions? Will it produce the right level of weight loss to reduce their severity or put them into remission? And, crucially, will the medication be safe in the context of those conditions? For example, an individual with diabetes might benefit more from treatment with a GLP-1 because they increase insulin release; similarly, an individual with OSA might benefit from treatment with Qysimia because its mechanism of action involves inhibiting carbonic anhydrase–one result of which is improved breathing. On the other side of the equation, phentramine is contraindicated in patients with uncontrolled hypertension,[18] similarly, Qysimia is contraindicated in patients with a history of glaucoma, and almost all anti-obesity medications are contraindicated in pregnancy and cannot be taken by those planning to become pregnant.

Effective treatment must also take into consideration an individual's metabolic history, as well as their prior experience with obesity treatments, as individuals may react differently to different medications. For example, a subset of people who try a GLP-1 have no significant weight reduction—these individuals are known as "non-responders" (See Figure 3)—and it is unlikely that prescribing that medication again to someone with a history of non-response will be successful. Even among responders, the amount of weight loss varies widely)—on Wegovy, the same number of people experience 5-10% weight loss is virtually identical to the number who achieve 10-15% and 15-20% weight loss. 29% of people treated with Zepbound have less than 15% weight loss whereas, 32% of people treated with Qysimia–a less effective medication on average–had more than 15% weight loss.

Consequently, the average responses cannot tell the whole story, and that a host of biological and environmental factors determine how successful a medication's method of action will be for an individual. This is why the availability of medications with different methods of action are so exciting, as they allow a non-responder on one medication to find successful treatment on another. Until the science advances and we can use labs and biomarkers to predict how much an individual will respond to a given AOM, the best data for determining treatment is understanding the potential mechanism of impact for that treatment, as well as what has and hasn't worked for the individual. Thus, effective management will require a personalized approach followed by continuous monitoring and ongoing evaluation of its efficacy.

We focus on delivering that personalized approach at scale using a clinical decision support algorithm to assess the host of factors that need to be considered to optimize treatment for each individual.

Figure 5: Weight Reduction by Anti-obesity Medication



De-averaging care means that we must also take into account that side effects will prevent some individuals from pursuing particular courses of treatment over an extended period of time (see below for further discussion on the consequences of non-adherence). For GLP-1s, the most common side effects are nausea (25%), vomiting (12%), diarrhea and constipation (11%), dyspepsia (6.4%) as well as a small risk of developing thyroid cancer,[19] for Contrave, the most common side effects are nausea (33%), constipation (19%), headache (18%) and vomiting (11%).[19] In addition, patients treated with GLP-1s must be monitored for hypoglycemia while those on Contrave need to be monitored for blood pressure. Side effects should be appropriately managed with education in adapting to a treatment regime and regular clinical contact including ongoing screening for adverse events; however, the existence of adverse side effects mean that different people will end up requiring different treatment journeys.

Bariatric surgery

Bariatric surgery is a minimally invasive surgery (typically between 20 and 60 minutes) that involves reducing stomach size, and in some cases, re-arranging the intestines. These procedures cause the stomach to feel full upon consuming smaller amounts of food and also reduce the production of certain hormones in the stomach. Bariatric procedures deliver 25-35% weight loss, and have been observed to reverse diabetes and 27-58% see full remission,[20-21] bariatric surgery also often (60%) achieves remission of hypertension[22] and reduces major adverse cardiovascular events (MACE) by 50-80%.[23-25] These surgical procedures are generally targeted at individuals with higher levels of obesity or diabetes. Bariatric procedures are safer than most other common surgeries, such as knee replacement, and their mortality rate is <0.1%—equivalent to the risk of drowning in the US, and has a complication rate of 7.6% of cases, many of which are minor complications,[26-27] with 4.3% having one or more major adverse event.[28] Many people experience side effects such as nausea and constipation.

More recently, innovations are transforming gastric and bariatric procedures; robotic assisted surgery promises to reduce complication rates and speed up recovery time. Innovative endoscopic techniques have been developed, which offer even less invasive procedures for weight loss.[29] In an endoscopic sleeve gastroplasty, physicians lower a camera-guided suturing device down the esophagus and sutures the stomach into a smaller shape, which will fill up and feel full sooner. Another endoscopic option for weight loss is the insertion of an intragastric balloon–a silicon device filled with saline that partially fills the stomach leaving less room for food.[30] After a year, endoscopic sleeve gastroplasty typically achieves 18% weight loss, and intragastric balloons 10%,[31] although these procedures achieve lower levels of weight loss than bariatric surgery–and the durability of weight loss has not yet been studied longitudinally–they are exciting additions to the armamentarium for patients for whom bariatric surgery may not be the right fit.

What drives the best treatment outcomes?

In addition to selecting the right treatment for the individual, effective management of obesity treatment depends upon the right care model for delivering that treatment. The key elements of the care model are (1) the care team, (2) meeting the behavioral needs of the patient, (3) aligning nutrition for weight loss, and (4) establishing habits of physical activity. When paired with the right treatment, these factors will drive outcomes in both the short and long-term.

Integrated care teams (ICTs) that can treat the whole person and touch upon all aspects of how obesity impacts someone's life deliver better results for managing obesity treatment. Integrated care teams improve continuity of care, create higher patient satisfaction, and achieve higher rates of preventative screenings, such as kidney screenings for individuals with diabetes.[32]

Importantly, an integrated care team for managing obesity treatment should always be led by a licensed obesity medicine physician as medical schools traditionally spend very little time on education about obesity and how to counsel and treat patients.[33] Obesity medicine training and certification has emerged so that providers are prepared to address the common cause–obesity and metabolic syndrome–as well as treat and manage the substantial number of comorbidities. These obesity medicine physicians can be best supported by experienced RNs to manage side effects; as reviewed above, many treatments for obesity can have common and severe side effects which if left untreated can cause both lower quality of life as well as unnecessary visits to the urgent care or emergency room for treatment. Setting expectations and catching side effects early can help; and a call line staffed by experienced RNs can give patients a method to get timely help and head off unpleasant adverse events.

Behavioral health support is another key component of integrated care both in ensuring that individuals are able to make changes and effectively cope with significant changes that a change in weight may drive. Behavioral health support can help individuals develop healthier coping mechanisms and improve mood, while addressing weight-related concerns such as emotional consequences of weight loss or regain, and encourage supportive environments with opportunity for social connection and shared experience, which can help foster motivation and adherence to a new lifestyle. In addition, integrating behavioral health support recognizes that obesity and mental health have a bi-directional relationship–for example, individuals with obesity are at increased risk for mood disorders[34] and these mental health concerns can in turn lead to maladaptive eating behaviors–supporting the care team in addressing mental health and obesity in a comprehensive manner (see also Ilant Health Mental Health White Paper).

The care team must also address an individual's nutrition as a core component of managing their treatment. Developing a better diet for weight management often involves increasing fiber intake, which can promote satiety and gut health,[35] along with higher protein intake, which increases satiety and thermogenesis.[36] Making these changes goes beyond just weight reduction. For example, diets high in processed foods and unhealthy fats can lead to nutritional deficits like Vitamin D deficiency which impacts metabolism and energy regulation;[37] displacing these foods with higher-nutrient options can restore these vitamin levels and improve metabolism. Adapting diet is especially important when initiating treatment on a GLP-1—which lowers appetite—or after bariatric surgery—which limits the amount of nutrients absorbed and can create risk of more severe deficiencies as well as hypoglycemia. To successfully modify diet behavior, nutritional guidance must be tailored to an individual's background—it's deeply unreasonable to expect someone to stop eating the foods their parents and grandparents made for them and switch to a cookbook written for a different audience. Socioeconomic status must also be considered when developing a treatment plan. Low socioeconomic status is associated with a higher risk of obesity and additional cardiovascular risk;[38] in part, because of the low cost of non-nutritious and highly-processed foods relative to the higher cost of healthy food. Dietary advice that emphasizes swapping out foods without recognizing potential economic costs is less likely to be followed and will sound out of touch with a person's actual life. This is why it is critical to have a nutritional program that is individualized and delivered by experts who are able to jointly solve across medical needs, socio-economic dynamics, and personal preferences.

Finally, physical activity and exercise are critical factors for maintaining effective treatment. Physical activity expends energy and can boost resting metabolic rate even after the activity is over, leading to increased calorie burning throughout the day.[39] Exercise promotes muscle growth—especially strength training—and can reduce visceral fat and improve sensitivity to insulin[40-41]. Muscle growth is particularly important, given that weight loss due to restricted appetite will include muscle loss and muscle growth will be necessary to even maintain the starting amount of muscle. Last, physical activity has many psychological benefits as well; exercise can reduce stress, boost confidence and feelings of self-efficacy, and potentially reduce or prevent unhealthy eating behaviors like emotional eating.[42-43]

All of the best support in the world will not work if patients do not trust the care team, and trust can be very hard to establish for populations that have historically experienced bias and poor care. This is one of the reasons why, in addition to the clinical team, we employ peer navigators with lived experience with obesity and obesity medicine treatments. Peer support leads to better self-monitoring and self-management (e.g. see [44] for success in blood glucose monitoring), and we have found that lived-experience peer navigators make treatment programs far more engaging, and create personal connections that people undergoing treatment deeply value. Peer navigators from different backgrounds help to narrow the gap between clinical advice and the daily experience of the real person undergoing treatment; for example, genetic background and differences in cultural body image standards can affect body composition and fat distribution,[38] and a care team that cannot communicate effectively within that context will not achieve success.

Challenges In Managing Obesity Treatment

Obesity management is a continuous lifelong journey and driving positive outcomes requires a focus on achieving long-term adherence to the treatment program and behavior modifications. Maintaining a long-term treatment program is harder than it seems; even GLP-1s—which are very effective and have captured the public imagination in this space—have low long-term adherence rates, with 68% of individuals taking GLP-1s stopping treatment within a year.[45] Even more worryingly, a recent study found that only 42% individuals using GLP-1s for weight loss adhered to treatment for at least 12 weeks–the benchmark for successful treatment.[46]

This challenge of adherence is hard to address because we rarely know the root cause of why someone stopped taking a medication–side effect and adverse events, changing beliefs about the value of treatment (such as deciding that the course of treatment is complete), or cost of the medication; and this challenge of adherence applies to virtually every medication–it is not an obesity-only issue.

The importance of maintaining treatment long-term is that many people will regain some or all of the weight once treatment stops—and put the health benefits of treatment in jeopardy. In one study, people on tirzepitize were switched to a placebo and regained 67% of the weight they had lost;[47] in another, 44% of individuals who stopped GLP-1 treatment regained weight, and 18% regained all of the weight they had lost–or even gained weight over their pre-treatment weight ([48], see [49] for discussion of the health consequences). Weight regain also occurs in behavioral and nutritional counseling with many people regaining a third of the weight in the first year, and the almost all regaining all the weight after 5 years[50] and bariatric surgery (approximately 40% of patients will regain at least a quarter of what they had lost after 6 years).[51] Weight regain can have a substantial psychological impact including feelings of frustration, disappointment or a sense of failure. These feelings may impede future efforts at weight loss; indeed the number of weight loss attempts is a negative predictor of successful weight loss,[52] and so it is crucial to get someone treated with obesity onto a program they can sustain, and provide the care and resources to help them maintain it over the long haul.

Our experience with well-managed obesity medicine treatment has led us to a few best practices to support long-term adherence. First, people will lose motivation if they do not see results, and we strongly recommend following FDA guidelines to discontinue a treatment approach that fails to drive at least 5% weight reduction within 12 weeks.[53] Second, the care team must be prepared to manage expectations and address inevitable weight gains or setbacks that occur; helping the individual going through treatment to not judge themselves harshly or lose feelings of self-efficacy. Reframing goals away from a weight loss number and into wellness goals such as managing levels of psychological distress can help; as can perceiving the difficulties in one's life that might have contributed to fluctuations in weight or adherence, and making adjustments to their life related to their new weight.[54] Habit building regarding eating, drinking, sleeping, exercise is also crucial for meeting these new wellness goals.[55] Habits related to the treatment program itself are also important; for example, support groups for weight loss often find that a higher session attendance results in greater weight loss.[56]

DEPRESCRIBING

How and when can a care team remove a medication that a patient previously depended on? This is a critical, thorny issue for care management–but an issue that raises itself in many aspects of managing obesity treatment.

One of the primary goals of obesity treatment is to reduce the impact of disease, which may enable individuals to come off existing medication. For example, medications for hypertension can be removed when put into remission by weight loss after bariatric surgery.[22]

At the same time, the cost of GLP-1 medications, their use among individuals who are young (and could therefore conceptually be on medications for 50+ years), as well as expectations around weight loss "curing" obesity have led to wide-spread discussion on the potential to "de-prescribe" GLP-1s or stop treatment once a certain level of weight loss has been reached. To-date, there have been two key studies on deprescribing GLP-1s. One, a randomized control trial, showed that majority [80%] of people regained most the weight.[47] Another based on observational data from prescribers on Epic showed that as many as 50% may maintain weight loss.[48] A recent talk at the European Congress on Obesity observed that titrating doses of GLP-1s down prior to stopping resulted in less weight loss than an abrupt stop [57]

Ultimately—as with determining when and what time of obesity treatment should be provided—the path on de-prescribing needs to be individualized. As we learn more—both from studies and from personal preferences and needs (e.g., a woman who comes off medication to become pregnant)—we will be able to more accurately predict who may need to stay on medication for life, who may be able to change dose or type of medication, and who may be able to come off the medication entirely. Identifying the individualized path for weight maintenance will be important not just in supporting cost management but also in managing adherence and long-term results.[58]

The final challenge is in ensuring equitable access to treatments for those who need it.

Inappropriate use of GLP-1s for weight loss in the absence of metabolic disorders creates shortages which deny access to treatment to people with diabetes who rely on GLP-1s for blood sugar control, and people with metabolic disorders who would see direct health benefits from weight loss.

This trend must be combatted because it is unfair, unsafe, and perpetuates a fundamentally misguided approach to obesity treatment. Treatment equity also extends to addressing disparity in access due to geography, age, socioeconomic status, and other social determinants of health as these may exacerbate existing health inequities.

For example, there is wide concern that white individuals may be more likely than black individuals to receive a prescription for semaglutide,[59] even though white individuals have lower prevalence of diabetes and obesity.[1] Individuals covered by Medicare and Medicaid also face limited access to medications for treating obesity, as these medications are covered predominantly only for diabetes management and not weight loss.

WANT TO LEARN MORE?

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Appendix

Table 1: R&D Pipeline for New AOMS

Name	Mechanism of Action	Method	Most common adverse events
Phentermine (Adipex)	Sympathomimetic amine, anorectic (suppresses appetite, decreases food intake)	Once daily oral	Dry mouth, constipation, insomnia
Orlistat (Xenical, Alli OTC)	Intestinal lipase inhibitor (blocks fat absorption)	Oral up to three times daily	Increased defecation and fecal incontinence
CONTRAVE (naltrexone ER/ bupropion ER)	Opioid antagonist & aminoketone antidepressant	Oral ranging from one tablet weekly to a 4 daily	Nausea, constipation, headache, vomiting, dizziness, insomnia, dry mouth and diarrhea
QSYMIA (phentermine /topiramate ER)	Sympathomimetic amine anorectic, inhibits carbonic anhydrase, appetite suppression and satiety enhancement via GABA and glutamate receptors	Once daily oral.	Paraesthesia, dizziness, dysgeusia, insomnia, constipation, and dry mouth
SAXENDA (liraglutide)	Glucagon-like peptide (GLP-1) receptor agonist Decrease hunger and delay gastric emptying, which increases satiety, reducing overall energy intake.	Injectable once daily	Nausea, diarrhea, constipation, vomiting, injection site reactions, headache, hypoglycemia, dyspepsia, fatigue, dizziness, abdominal pain, increased lipase, upper abdominal pain, pyrexia, and gastroenteritis
WEGOVY (semaglutide)	GLP-1 receptor agonist Decrease hunger and delay gastric emptying, which increases satiety, reducing overall energy intake.	Injection once weekly	Nausea, diarrhea, vomiting, constipation, abdominal pain, headache, fatigue, dyspepsia, dizziness, abdominal distension, belching, hypoglycemia, flatulence, gastroenteritis, and gastroesophageal reflux disease
ZEPBOUND (tirzepatide)	GLP-1/ glucose-dependent insulinotropic polypeptide (GIP) dual receptor agonist The GLP-1/GIP agonists decrease hunger and delay gastric emptying which increases satiety reducing overall energy intake. Reduce appetite, energy intake and fat mass	Injection once weekly	Nausea, diarrhea, vomiting, constipation, abdominal pain, dyspepsia, injection site reactions, fatigue, hypersensitivity reactions, belching, hair loss, gastroesophageal reflux disease.
Metformin	Biguanide Thought to modulate hypothalamic appetite-regulatory centers, hepatic glucose regulation, decreased insulin production	Oral multiple times daily	Diarrhea, nausea, vomiting, flatulence, asthenia, indigestion, abdominal discomfort, and headache

Table 2: R&D Pipeline for New AOMS

Phase	GLP-1 Receptor Agonist	GLP-1/ GIPR	GLP-1/ GCGR	GLP-1/ Amylin	GLP-1/ GIPR/ GCGR	Other GLP-1 dual/triple agonist	Amylin Analogue	Leptin Sensitizer	Myostatin Inhibitor	MicroRNA22	Other
Phase 3	3	0	2	1	1	0	0	0	0	0	0
Phase 2	4	3	1	0	0	3	0	0	0	0	12
Phase 1	6	3	1	2	0	1	3	1	2	1	12
Preclinical	1	2	1	0	1	2	1	1	1	2	9