

# Obesity 2021: Current Clinical Management of a Chronic, Serious Disease

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## CONTINUING MEDICAL EDUCATION

### LEARNING OBJECTIVES

At the end of the activity, participants will be able to:

- Recognize obesity as a chronic, relapsing, serious disease warranting long-term management and early intervention to minimize disease burden and decrease associated morbidity and mortality.
- Destigmatize obesity to initiate and enhance patient engagement.
- Apply guideline-recommended care for screening, diagnosis, and individualized treatment of adults and others with obesity.
- Incorporate practical practice management strategies.

### KEY TAKEAWAYS

- Obesity is deeply rooted in genetic, psychosocial, behavioral, and environmental factors that are intertwined with a complex pathophysiology involving persistent adaptations in numerous gut hormones and neuropeptides.
- Destigmatizing obesity in the health care environment is needed and can be accomplished through recognition that obesity is a chronic disease, improved communication facilitated by motivational interviewing, and properly equipping the office environment.
- Nonpharmacologic therapy is the foundation of comprehensive treatment for patients with obesity.
- There are 5 antiobesity medications currently approved for long-term use, and these should be considered for patients who are unable to achieve weight management goals with lifestyle treatment alone.
- Injectable semaglutide is a glucagon-like peptide-1 receptor agonist recently approved based on the results of clinical trials showing it to be safe and well tolerated in patients with obesity, enabling one-half of patients without diabetes to achieve significant weight loss.

### TARGET AUDIENCE

Family physicians and clinicians who wish to gain increased knowledge and greater competency regarding primary care management of obesity.

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In the 1950s, the prevalence of obesity (body mass index [BMI]  $\geq 30$  kg/m<sup>2</sup>) in the United States was 10.2% for men and 13.9% for women.<sup>1</sup> In 2018, 43.0% of men and 41.9% of women had obesity.<sup>2</sup> From 1999 to 2016, mean body weight, waist circumference, and BMI increased for all adult age groups in the United States.<sup>3</sup> These trends over the past 7 decades are concerning since obesity serves as an independent risk factor for several of the most debilitating conditions in adults age <65 years,<sup>4</sup> being linked to 10% to 20% of all cancer cases,<sup>5-7</sup> 50% to 85% of all type 2 diabetes mellitus (T2D) cases,<sup>8,9</sup> and 15% to 30% of all osteoarthritis cases.<sup>10</sup>

Advancements in disease understanding and treatment approaches provide opportunities to implement 5 strategies aimed at curbing obesity trends and improving health outcomes. A toolbox of resources for each of the 5 strategies is available at <https://www.pcmg-us.org/obesitytoolkit>. Not discussed in this review is another important part of the continuum of obesity care, metabolic and bariatric surgery (MBS). Referral to qualified MBS centers should be considered for patients with BMI >40 kg/m<sup>2</sup> or those with BMI >35 kg/m<sup>2</sup> with obesity-related comorbidities.<sup>11</sup>

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## STRATEGY #1

### Recognize that obesity is a chronic, relapsing, serious disease with diverse causes.

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An important barrier to the management of individuals with obesity was the common belief that obesity was simply a consequence of an individual's personal decisions regarding his/her own lifestyle and behaviors. This belief began to change in 2012 when the American Association of Clinical Endocrinology designated obesity as a chronic disease.<sup>12</sup> The American Medical Association (AMA) followed suit in 2013,<sup>13</sup> with the World Health Organization, World Obesity Federation, The Obesity Society, and other organizations subsequently making similar designations.

Designation of obesity as a disease was based on an improved understanding of the complex system that integrates external and internal information throughout the initiation, procurement, consummatory, and metabolic phases of eating (FIGURE).<sup>14</sup> The critical role of several gut hormones and neuropeptides, ie, the "gut-brain axis," was made clear by Sumithran et al, who demonstrated long-term persistence of hormonal adaptations to weight loss.<sup>15</sup> Their investigation in 50 patients with overweight/obesity showed that 1 year after diet-induced weight loss (mean 30 lbs), levels of circulating mediators of appetite that promote weight regain did not revert to levels prior to weight loss. Subjects reported increased hunger and less fullness driven by changes in key

mediators including leptin, peptide YY, cholecystokinin, insulin, ghrelin, gastric inhibitory polypeptide, and pancreatic polypeptide. The investigators concluded that the body actively adapts numerous gut and neurohormonal mediators to protect fat mass in people with overweight/obesity.

In addition to metabolic adaptations, obesity is deeply rooted in genetic, psychosocial, behavioral, and environmental factors. Environmental factors include the ready availability of food—particularly calorie-dense, nutrient-deficient, ultra-processed food—fast-paced lifestyle making food preparation and physical activity a greater challenge, and the cultural norm of engaging in social activities that involve food.

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## STRATEGY #2

### Destigmatize obesity by creating an office environment that is sensitive to the needs and experiences of patients with obesity.

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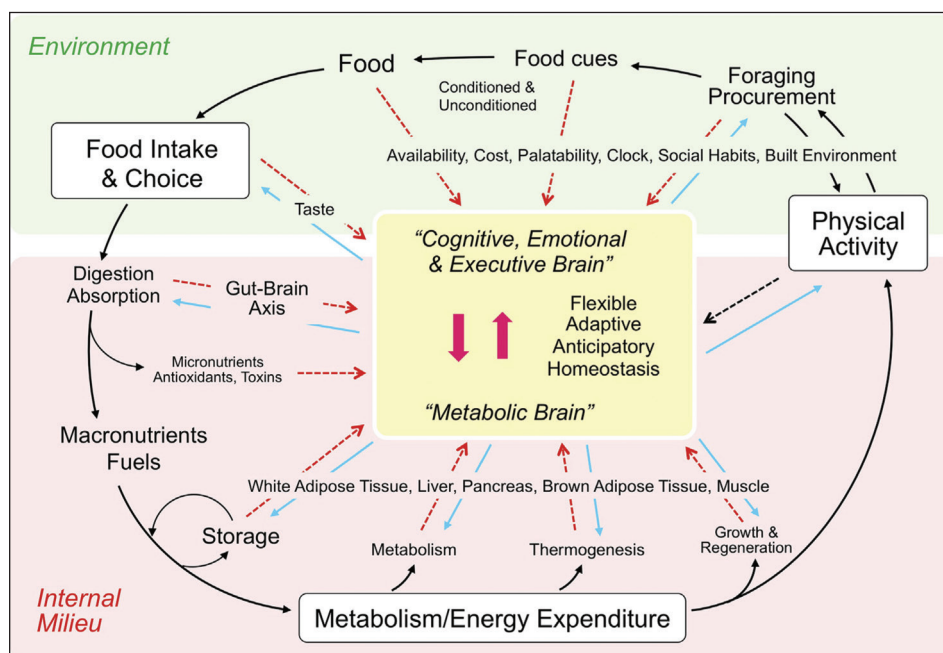
Evidence over the past 2 decades indicates that weight bias is common within the healthcare environment with clinicians often viewing patients with obesity as lacking self-control, lazy, unintelligent, and annoying.<sup>16-20</sup> Moreover, as patient BMI increases, physicians report having less patience, less respect, and less desire to help the patient.<sup>21</sup> In turn, patients with obesity feel berated and disrespected and believe their health concerns are not taken seriously. Delaying or canceling healthcare appointments, including preventive care, is common.<sup>22</sup> Overall, evidence indicates that weight bias within healthcare contributes to a cycle that perpetuates obesity.

## ATTITUDES AND BELIEFS

Destigmatizing obesity is of critical importance within healthcare and requires creating an office environment that is sensitive to the needs and experiences of this patient population. An important first step is to change how clinicians and staff view obesity and patients who are afflicted. This necessitates accepting that obesity is a disease just like T2D, hypertension, cancer, and coronary heart disease, and that obesity is a product of genetic and environmental factors that kindle a complex pathophysiology.

## COMMUNICATION

A second step is to improve patient-clinician communication since the simple act of discussing a patient's weight is more likely to promote patient self-efficacy.<sup>23,24</sup> In fact, a successful conversation with patients with obesity can be 10% to 20% more effective than didactic delivery of recommendations in increasing patient motivation and encouraging action that

FIGURE. The system that regulates eating is complex<sup>14</sup>

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results in sustained changes.<sup>25</sup>

Good communication includes using supportive language that avoids placing blame and emphasizes health improvement. Using people-first language is helpful to avoid placing blame. Instead of referring to “the obese patient,” it is more welcoming to use people-first language and refer to “the patient with obesity.” The AMA adopted a resolution in 2017 that encourages the use of people-first language as an important communication strategy for patients with obesity.<sup>26</sup> The AMA resolution also encourages the use of preferred terms such as weight and unhealthy weight, rather than stigmatizing terms such as obese, morbidly obese, and fat.

## MOTIVATIONAL INTERVIEWING

Because psychosocial, behavioral, and other environmental factors generally serve as modifiable causes of obesity, identifying targets related to the patient’s lifestyle is fundamental to treatment. To do this, motivational interviewing (MI) can be very helpful. MI is a patient-centered guiding method for enhancing intrinsic motivation to change behavior by exploring and resolving ambivalence.<sup>27</sup> MI has much in common with shared decision-making, but relates more to behaviors in which there clearly is a healthier option.

MI is based on 4 key principles: 1) expressing empathy; 2) supporting self-efficacy; 3) rolling with resistance; and 4) developing and resolving discrepancies. The need for the

clinician to roll with resistance occurs when a patient displays resistance to changing one or more behaviors despite recognizing the need to do so to achieve a goal. Instead of trying to fix or solve the problem, the clinician should sidestep the resistance, helping the patient resolve the ambivalence or discrepancy between behavior and goals or values. Helping the patient resolve the discrepancy can be facilitated by constructing a 2 by 2 matrix of the benefits/pros vs costs/cons of making the change or not making the change (this is one example of an MI technique; there are many others).

One model of MI is known by the acronym OARS: 1) open-ended questions; 2) affirmative statements; 3) reflections; and 4) summary statements.<sup>27</sup> By

encouraging patients to talk about their goals rather than focus on their obstacles, OARS can enable patients to make behavioral changes about which they have been ambivalent or previously found difficult.

As a method of communication, MI is inherently collaborative, beginning by inviting the patient to set the agenda, often by identifying the behavior they feel most contributes to their obesity and/or the behavior they are most ready to address. For MI to be most effective, clinicians should resist finding solutions for the patient, instead helping the patient find solutions they are willing to implement. A key role for the clinician is to then educate and support the patient so that they are able to successfully change behavior. Using MI in the office setting can take time. However, with experience and skill building, it is rewarding and helps to create an improved patient-provider relationship.

Examples of MI for patients with obesity are provided in the toolbox of resources for this article.

## PHYSICAL OFFICE ENVIRONMENT

Finally, the physical office environment in which care is provided is also of importance and should be welcoming to the patient with obesity. In its 2017 resolution, the AMA emphasized the importance of equipping healthcare facilities with properly sized furniture, medical equipment, and gowns for patients with obesity. The AMA also noted the importance

of weighing patients respectfully, which involves asking the patient for permission to weigh them, measuring weight in a private setting, and recording the weight silently and without judgment, reserving the discussion about weight for the privacy of the examination room.<sup>28,29</sup>

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### STRATEGY #3

#### Set individualized and realistic short- and long-term treatment goals in collaboration with the patient.

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Most patients with obesity are not aware that modest weight loss of 5% has significant health and quality of life (QoL) benefits.<sup>30</sup> In fact, patients with obesity often strive to lose 15% or more of their body weight.<sup>31</sup> A frank discussion of realistic expectations and the importance of long-term weight management (WM) is essential. MI is helpful to establish treatment goals and can be facilitated by using the SMART strategy: 1) specific; 2) measurable; 3) attainable; 4) realistic; and 5) timely. Establishing attainable goals, particularly at the beginning, is especially important to sustain and enhance patient motivation by building on success.

In the discussion of health benefits with weight loss, it is important to consider not only the general health benefits with weight loss, but also the benefits for an individual patient. For example, all patients should be educated about the cardiovascular benefits. But talking about QoL benefits with the patient who has difficulty climbing stairs or who cannot play with their grandchildren due to shortness of breath can be very motivating.

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### STRATEGY #4

#### Identify the role of nonpharmacologic therapy.

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Nonpharmacologic therapy is the foundation of comprehensive treatment for patients with obesity. There are 3 components: dietary intervention, increased physical activity, and behavioral modification, with each component affecting the others, as well as being influenced by biological, cultural, and environmental factors along with attitudes and beliefs.

Creating a negative energy balance is the key to weight loss.<sup>30,32</sup> A systematic review showed that among 17 dietary patterns, none was superior in terms of ability to produce and sustain weight loss.<sup>11</sup> Consequently, the best dietary intervention is the one that provides needed nutrients and that the patient is willing and able to follow.<sup>33</sup>

For weight loss, aerobic physical activity (eg, a brisk walk) >150 minutes per week is recommended.<sup>11,34</sup> Engaging in weekly physical activity of greater intensity and for longer

duration results in greater short- and long-term weight loss.<sup>35</sup> Recent evidence shows that compared with a person who takes 2,000 steps per day, a person who regularly takes 10,000 steps per day has one-third the cardiovascular mortality rate and one-half the cancer mortality rate.<sup>36</sup> Resistance training is recommended at least 2 days per week to promote loss of fat mass and reduce health risk; it does not, however, enhance weight loss.<sup>35</sup> Some patients, particularly those who have led a sedentary lifestyle, may find it difficult to achieve the recommended level of physical activity initially, but should be encouraged through education that even 5 minutes of physical activity daily has real health benefits.<sup>34</sup>

To achieve and sustain the dietary and physical activity habits needed for WM, changing behavior is required. Successful behavioral interventions often use MI and combine education with behaviorally oriented counseling to help patients acquire the skills, motivation, and support needed to alter the targeted behavior. The Centers for Medicare & Medicaid Services has developed a program guide and reimbursement structure for behavioral therapy for obesity (<https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=353>).

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### STRATEGY #5

#### Individualize therapy with approved medications (liraglutide, naltrexone/bupropion, phentermine/topiramate, orlistat, semaglutide) for long-term use.

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Two groups of medications are available for weight loss, those that are approved by the US Food and Drug Administration (FDA) for short-term use (8-12 weeks) and those that are FDA approved for long-term use. Medications currently approved for long-term use are liraglutide, naltrexone/bupropion extended-release (ER), orlistat, phentermine/topiramate ER, semaglutide, and setmelanotide. Setmelanotide is indicated for weight loss in a small group of children and adults with specific genetic deficiencies and will not be discussed further.<sup>37</sup> The glucagon-like peptide-1 receptor agonist (GLP-1 RA) semaglutide, which is approved for T2D, was approved in June 2021 by the FDA for once-weekly administration for weight loss.

#### APPROVED MEDICATIONS FOR LONG-TERM WEIGHT LOSS

The 5 antiobesity medications currently approved for long-term weight loss are indicated as adjunctive therapy to help patients who do not achieve health and weight targets with lifestyle management alone. Weight loss at 1 year among the 4 medications ranges from 6% to 11%.<sup>38</sup> Medication selec-

TABLE 1. **Key patient characteristics in selecting a medication approved for long-term weight loss**<sup>39-42</sup>

Patient characteristic	Recommendations <sup>a</sup>
Pregnancy	LIR, NB, OR, PT: C/I
Age ≥65 years	NB, PT: use with caution OR: limited experience
Moderate renal impairment	LIR: use with caution NB: do not exceed 16/180 mg daily PT: do not exceed 7.5/46 mg daily
Moderate hepatic impairment	LIR: use with caution NB: do not exceed 16/180 mg daily PT: do not exceed 7.5/46 mg daily
History of depression	NB, PT: caution
History of hypertension	NB: C/I if uncontrolled PT: monitor BP if being treated for HTN; if hypotensive symptoms develop, adjust antihypertensive drug regimen
History of seizure	NB: C/I
History of kidney stones	PT: avoid due to increased risk of calcium oxalate stones; increase fluid intake
History of pancreatitis	LIR: use with caution
Personal or family history of medullary thyroid cancer or MEN type 2	LIR: C/I
History of cognitive impairment	PT: caution about operating automobiles, hazardous machinery

BP, blood pressure; C/I, contraindicated; HTN, hypertension; LIR, liraglutide; MEN, multiple endocrine neoplasia; NB, naltrexone/bupropion extended-release; ORL, orlistat; PT, phentermine/topiramate extended-release.

<sup>a</sup>Information for semaglutide is not included in this table due to its approval as the article was about to go to press.

tion is based on individual patient factors, eg, comorbidities and differences among the medications, and patient preference. Individual differences include mechanism of action, route of administration, contraindications, warnings, adverse events, drug interactions, and cost (TABLE 1).<sup>39-42</sup>

Weight loss of 5% to 10% over 6 months is the recommended weight loss target.<sup>11</sup> Treatment response should be evaluated after approximately 3 to 4 months. If a patient has not lost at least 4% to 5% of baseline body weight, the medication should be discontinued and alternative treatment initiated.<sup>11</sup> The exception is for phentermine/topiramate.

TABLE 2. **Topline results from the semaglutide STEP 1 through 4 clinical trial program**

	STEP			
	1 <sup>43</sup> (N=1961) Overweight or obesity, without diabetes	2 <sup>44</sup> (N=1210) Overweight or obesity, with diabetes	3 <sup>45</sup> (N=611) 8-week LCD and 30-week IBT	4 <sup>46</sup> (N=803 <sup>a</sup> ) Overweight or obesity, without diabetes
Treatment duration	68 wks	68 wks	68 wks	20-wk run-in <sup>b</sup> followed by 48-wk randomized period
Mean change in BW (placebo-corrected)	-12.7 kg	-6.2 kg	-10.6 kg	Run-in <sup>b</sup> : -11.1 kg Randomized: SEM: -7.1 kg PBO: 6.1 kg
Mean % change in BW (placebo-corrected)	-12.4%	-6.2%	-10.3%	Run-in <sup>b</sup> : -10.6% Randomized: SEM: -7.9% PBO: 6.9%
% Achieving WL ≥15% (placebo-corrected) <sup>c</sup>	45.6%	22.6%	42.6%	Wk 0 to 68: 54.5%

BW, body weight; IBT, intensive behavioral therapy; LCD, low-calorie diet; PBO, placebo; SEM, semaglutide; WL, weight loss.

<sup>a</sup>Patients who completed the 20-week run-in period and were randomized.

<sup>b</sup>All patients received semaglutide during the 20-week run-in period.

<sup>c</sup>Based on the number of participants for whom data were available at the week 68 visit (n=1212 semaglutide; n=577 placebo).

mate ER, where the dose can be increased to the maximum daily dose of 15 mg/92 mg, if tolerated.<sup>11</sup> As when initiating treatment, MI is helpful to inform treatment modification, including lifestyle management.

## Semaglutide

The safety and efficacy of semaglutide 2.4 mg injected subcutaneously once weekly for the treatment of patients with obesity has been investigated in the STEP 1–4 clinical trial program: 1) WM<sup>43</sup>; 2) WM in T2D<sup>44</sup>; 3) WM with intensive behavioral therapy<sup>45</sup>; and 4) sustained WM.<sup>46</sup> Results of the STEP 1 through 4 trials have been published. The primary endpoint in all STEP trials is change in body weight from baseline to end of treatment at 68 weeks.

In the STEP 1 through STEP 3 trials, the mean change in placebo-corrected body weight from baseline to week 68 ranged from -6.2% to -12.4%. Weight loss  $\geq 5\%$  was achieved by 68.8% to 86.6% of semaglutide patients and 28.5% to 47.6% of placebo patients. Weight loss  $\geq 15\%$  was achieved by 25.8% to 55.8% of semaglutide patients and 3.2% to 13.2% of placebo patients (TABLE 2). The STEP 4 trial showed that semaglutide resulted in substantial weight loss during the 20-week run-in dose titration phase, with further weight loss over an additional 48 weeks compared with weight gain in patients switched to placebo following the run-in phase.

In STEP 1–4, gastrointestinal events, such as mostly transient mild to moderate nausea, were observed in 49% to 83% of semaglutide patients and 26% to 63% of placebo patients. Rates of acute pancreatitis and malignant neoplasms were low and similar in the semaglutide and placebo groups. ●

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