Overweight: The Overlooked Risk Factor

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LEARNING OBJECTIVES

At the conclusion of this activity, the family physician should be able to:

- Describe the epidemiology of overweight and obesity in the United States.
- Describe the disease burden associated with being overweight (body mass index 25-30 kg/m^2) and how to broach the topic of weight management with patients.
- Differentiate the safety and efficacy of 2 nonprocedural device treatments for people with overweight.

INTRODUCTION

Trends in body weight

Thirty percent. That's the estimated projected prevalence of adults with overweight in the United States in 2030.[1] Overweight, also called pre-obesity, is defined as having a body mass index (BMI) from 25.0 to <30.0 kg/m^2. Thirty percent is actually a reduction from the 33.1% of US adults who had overweight in 1988-1994 and the 31.6% in 2015-2016. The unfortunate reason for the continued projected decline in the prevalence of adults with overweight is their transition into the obesity classification. Without comprehensive treatment, adults with overweight continue to gain weight, moving steadily into the obesity (BMI 30-39.9 kg/m^2) and severe obesity (BMI ≥40 kg/m^2) categories.[2,3] One of the primary reasons for this transition lies in our dietary habits, eg, overconsumption of highly processed, energy-dense, and palatable foods and beverages in place of naturally fiber-rich foods, and reduced physical activity.[4]

Comparing 1960-1962 with 2015-2016, the mean BMI among US adults increased from 25.1 kg/m^2 to 29.1 kg/m^2 in men and from 24.9 kg/m^2 to 29.6 kg/m^2 in women.[2,5] In fact, despite an increase in mean height of <1 inch in both men and women, the mean body weight among US adults rose sharply, rising from 166.3 pounds in 1960-1962 to 197.9 pounds in 2015-2016 in men and from 140.2 pounds to 170.5 pounds in women.[2,5] By 2030, estimates are that 1 in 2 US adults (48.9%) will have obesity, nearly double the prevalence of 25.7% in 1988-1994.[1,3] Similar trends are observed in youth, particularly those age 5 to 19 years, as the prevalence of obesity increased from 13.9% in 1999-2000 to 18.5% in 2015-2016.[6]

Targeting people with overweight

Among the key trends noted above, one seems to be especially important. That is, people in the overweight category are more likely now than 30 years ago to continue to gain weight and develop obesity. These trends make it clear that early intervention efforts are needed, at lower BMI ranges before patients cross into the obesity classification. Put differently, patients who have overweight represent an important group for targeted treatment to prevent progression to obesity. In fact, patients who are classified as having a healthy weight, ie, BMI from 20 to <25 kg/m^2, are also an important target for preventive measures, because evidence indicates that many of the chronic diseases observed in people with obesity begin to emerge in people who have a healthy weight.

Understanding consequences of excess body weight

Beyond the enormous economic consequences of over-

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DISCLOSURES

Dr. Kushner discloses that he serves on the advisory board for Novo Nordisk and WW (formerly Weight Watchers).

Dr. Primack discloses that he serves as a consultant for Nestle Nutrition, Contrave, on the advisory board for Phenomix and Gelesis, and as a speaker for Novo Nordisk. He also owns stock in Vivus.

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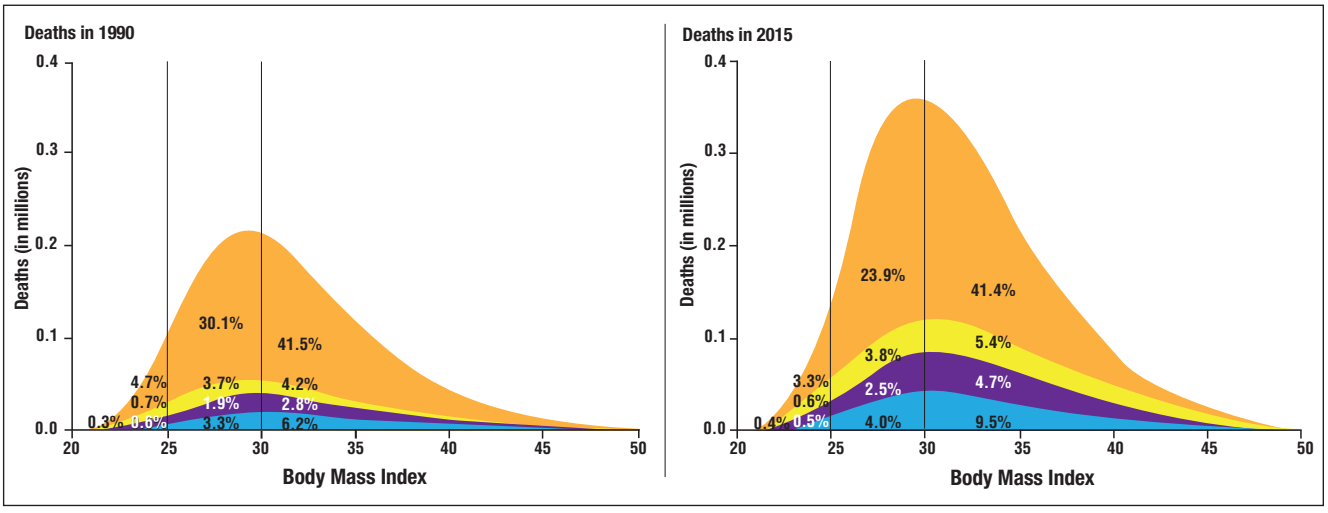
FIGURE 1. **Global deaths by body mass index**



Notes: Number of global deaths (millions) in 1990 (left) and 2015 (right). The 2 vertical lines mark the BMI thresholds for overweight and obesity. The percentages indicate the proportion of the total number of deaths that were contributed by diabetes mellitus (blue), chronic kidney disease (purple), cancers (light orange), and cardiovascular diseases (dark orange).

weight and obesity,[7,8] multiple chronic medical conditions are associated with weight gain and excess adiposity. These include dyslipidemia, type 2 diabetes mellitus, hypertension, coronary heart disease, stroke, gallbladder disease, gastroesophageal reflux disease, respiratory problems, sleep apnea, osteoarthritis, several cancers, urinary incontinence, and depression, as well as higher mortality rates and, most recently observed, an increased risk of complications from COVID-19.[9-19] Many of these chronic comorbidities are observed in children and adolescents with obesity.[20]

DISEASE BURDEN

BMI cutoff of 25 kg/m^2

The upper limit of a healthy BMI, ie, 25 kg/m^2, was established decades ago and reaffirmed in 1995 by the Dietary Guidelines Advisory Committee. This cutoff was based on epidemiological data showing that mortality increased significantly with a BMI >25 kg/m^2.[21,22] In establishing this cutoff, less consideration was given to the evidence showing that the incidence of diabetes, hypertension, and coronary heart disease began to increase well below a BMI of 25 kg/m^2.[23-28]

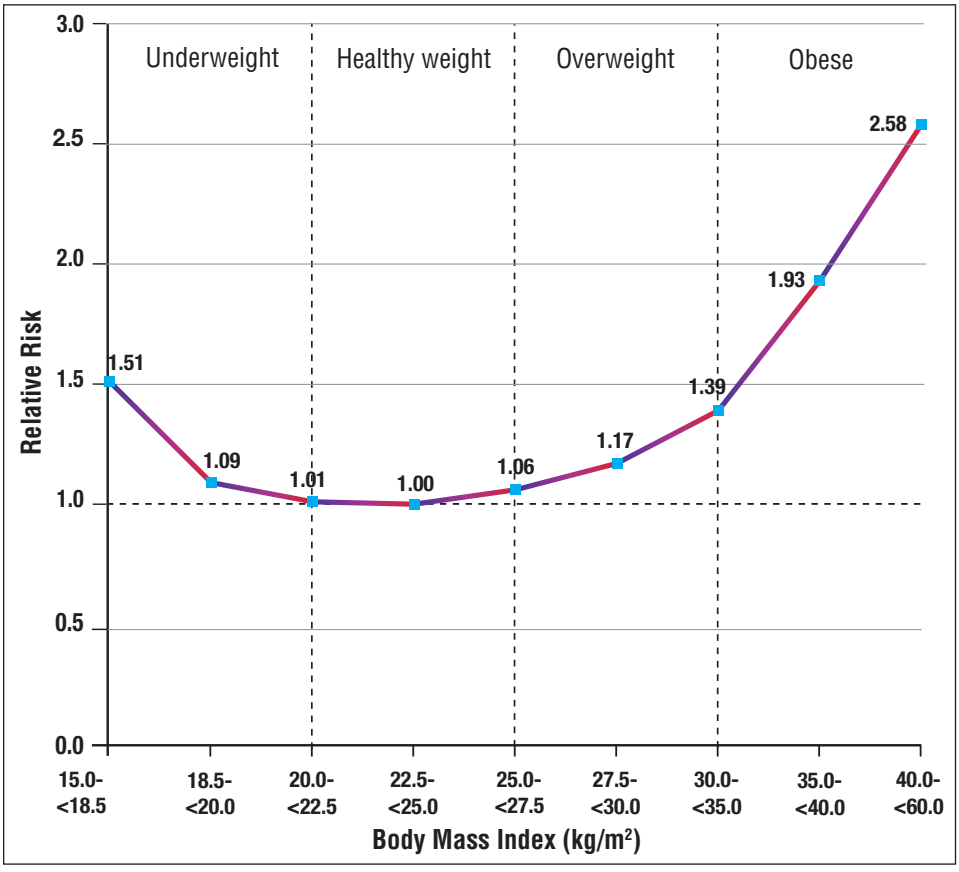
A factor contributing to the committee's decision was that designating a BMI cutoff lower than 25 kg/m^2 for the upper limit of healthy weight (and the lower limit of overweight) would have labeled >50% of US adults as having unhealthy weight. Moreover, the cutoff of 25 kg/m^2 was consistent with then-current recommendations of the American Institute of Nutrition[29] and the World Health Organization.[30]

Mortality burden in overweight

A recent analysis by the Global Burden of Disease (GBD) Obesity Collaborators reinforces that the mortality burden is not restricted to people with obesity.[15] The analysis included data from 68.5 million children and adults in 195 countries between 1980 and 2015. In 2015, 4.0 million weight-related deaths occurred in people with a BMI ≥25 kg/m^2; 39% of these deaths occurred in people with a BMI <30 kg/m^2 (**FIGURE 1**). In people with BMI-related death due to diabetes, for example, 4.5% occurred at a BMI <30 kg/m^2. Similar trends in BMI-related disability were observed.

Details regarding the association of BMI with mortality were provided by a similar analysis by the GBD BMI Mortality Collaborators.[31] The analysis was restricted to never-smokers and excluded preexisting disease and the first 5 years of follow-up. Data involving 1.42 million adults from North America showed that BMI was nonlinearly associated with all-cause mortality, with the overall nadir at BMI from 20.0 kg/m^2 to <25.0 kg/m^2 (**FIGURE 2**). The nadir was age dependent, identified at BMI 22 kg/m^2 for age 35-49 years, BMI 23 kg/m^2 for age 50-69 years, and BMI 24 kg/m^2 for age 70-89 years. These findings confirm the mortality risk in people with overweight and suggest that targeting a BMI well below the cutoff of 25 kg/m^2 may be advisable, particularly in younger adults. These findings also confirm an earlier investigation showing that the relative risk of all-cause and cardiovascular death associated with greater body weight is higher among younger adults than older adults.[32]

FIGURE 2. **Relative risk of all-cause mortality by BMI category in North America[31]***



Abbreviation: BMI, body mass index.

*BMI category from 22.5 to <25.0 kg/m² is set as the reference category. Data are in never-smokers, excluding people with chronic disease at baseline and 5 years of follow-up in geographic regions with >1 million participants.

The GBD BMI Mortality Collaborators analysis also showed that, compared with BMI from 22.5 to <25.0, increasing BMI was strongly positively related to death due to coronary heart disease (hazard ratio [HR] 1.42 per 5 kg/m² increase in BMI), stroke (HR 1.42 per 5 kg/m²), and respiratory disease (HR 1.38 per 5 kg/m²), and moderately positively related to cancer mortality (HR 1.19 per 5 kg/m²).[31] Another analysis showed a reduction in the expected age at death of 0.8 to 1.0 year in a 40-year-old, never-smoker with underweight.[14]

SCREENING

The 2012 guidelines developed by the American Heart Association/American College of Cardiology/The Obesity Society underscore the importance of measuring height and weight and calculating BMI at annual visits or more frequently for all patients.[33] For patients found to have overweight or obesity, measuring the waist circumference at annual visits or more frequently is also recommended. North American waist circumference cutpoints to identify high-risk patients are >40 inches for males and >35 inches for females.[33]

Recently, a task force of The Obesity Society assessed available evidence and concluded that weight history is an essential component of the medical history for patients presenting with overweight or obesity.[34] The weight history should assess the patient's life stage at which unhealthy weight occurred, duration of exposure to obesity, and maximum BMI, as each factor may help predict risk for developing many obesity-related comorbidities. As is often used for ascertaining a patient's chief complaint and history of present illness, the mnemonic "OPQRST" (onset, precipitating events, quality of life, remedy, setting, and temporal pattern) can be used to form an understanding of how and when a patient gained weight, which management efforts have been attempted, and the effect of unhealthy weight on the patient's health and well-being.

Having the conversation about weight

Family physicians are well positioned to address overweight with their patients, in part because patients want and expect weight-loss guidance from their health care providers. Nonetheless, as family physicians prepare for and have these conversations with their patients, it is important to realize that most patients with excess weight, particularly those with obesity, have often been stigmatized as a result of having the disease, including by physicians and other health care providers.[35-37] Consequently, treating the patient with respect and using appropriate language are important. Words such as overweight, unhealthy or excess weight, and increased BMI should be used instead of heaviness, obesity, or excess fat.[38,39]

The conversation about weight should begin by asking for the patient's permission to talk about his or her weight.

If the patient is not interested or ready, acknowledge the importance of discussing weight, but defer the discussion until a future visit. When the patient is ready for the discussion, start with an empathetic statement followed by listening, which can be helpful to avoid the patient feeling embarrassed and to build a trusting relationship. This exchange can be augmented by using a shared decision-making model to find a weight management plan the patient is willing and able to adopt. Inquiring about the patient's experience with weight loss is helpful to establish realistic expectations and inform the treatment plan. These and other suggestions are embodied in the FRAMES model for communicating with patients, which can be found in a discussion guide developed by the STOP Obesity Alliance (http://whyweightguide.org/docs/STOP-Provider-Discussion-Tool.pdf).

TREATMENT OPTIONS FOR OVERWEIGHT

Lifestyle management

Lifestyle management consisting of a calorie-controlled healthy diet and engagement in daily physical activity is a foundational treatment recommendation for weight loss[33] and improved health. After 1 year of treatment, the Look AHEAD trial showed a reduction in mean body weight of 8.6%, which resulted in improved glycemic control, improved lipid profile, and a reduced requirement for medications for diabetes, dyslipidemia, and hypertension.[40] Additional benefits such as improved symptoms of depression and sleep apnea also were observed.[41,42]

A recent analysis of data from the National Health and Nutrition Examination Survey showed that the proportion of overall participants (N=48,026) who had attempted to lose weight increased from 34.3% in 1999-2000 to 42.2% in 2015-2016.[43] The most commonly reported weight-loss strategies were reduced food consumption, exercise, and frequent water intake, used by 31.9%, 31.5%, and 26.3%, respectively, in 2015-2016.

Unfortunately, short- and long-term achievement of 5% to 10% weight loss with lifestyle management alone is difficult.[44-48] The inclusion of behavioral therapy results in modest additional health benefits, with evidence of a dose-response effect with higher intensity interventions resulting in greater improvement.[49,50]

Pharmacologic therapy

With the recent withdrawal of lorcaserin from the US market due to cancer concerns, there are now 4 medications approved for long-term use.[33] Liraglutide, naltrexone/bupropion extended-release, phentermine/topiramate extended-release, and orlistat are approved for weight loss and weight maintenance in patients with obesity or overweight (BMI ≥27 kg/m^2 with ≥1 weight-related comorbidity). In randomized controlled trials, medications currently approved for long-term weight loss have yielded an average weight loss ranging from approximately 3% to 9% relative to placebo at 1 year, and are generally associated with improvements in blood glucose, lipids, and blood pressure.[51]

Although beneficial, use of medications approved for long-term weight loss is low, with 1% to 2% of eligible patients receiving weight-loss medication.[52,53] Several factors may underlie the low prescription rates, including concern about safety and long-term efficacy, failure to recognize obesity as a disease, lack of training, and limited insurance coverage. Furthermore, their approved indications do not include patients with BMI ranging from 25 kg/m^2 to <30 kg/m^2 without comorbidities. Recent investigations show that less than one-quarter of prescribers account for nearly all prescriptions for these medications.[52,53] Suboptimal adherence also appears to contribute. One real-world analysis (N=26,522) showed that 6-month persistence rates ranged from 16% to 42%, while another real-world analysis (N=2.2 million) showed the 4-month and 1-year persistence rates were 52% and 34%, respectively.[53,54] Modest weight reduction may also contribute to the low use and suboptimal persistence, as weight loss over 3 to 6 months is often <5%.[55-58]

Devices

Two nonprocedural devices are approved by the US Food and Drug Administration (FDA) for weight management and may fill a treatment gap, particularly in patients with overweight. One is an ingested, transient, space-occupying device, or oral superabsorbent hydrogel, and the other an oral, removable, palatal space-occupying device. Neither of these devices requires a procedure for use.

Nonsystemic, oral superabsorbent hydrogel

The nonsystemic, oral superabsorbent hydrogel (Plenity™) is indicated for use in conjunction with diet and exercise to aid in weight management in adults with overweight and obesity with a BMI from 25 kg/m^2 to 40 kg/m^2.[59] The availability of Plenity in the US has been delayed until 2021 due to the COVID-19 pandemic.

The oral hydrogel product, which is technically considered a device, is delivered in a capsule taken by mouth that consists of 2 building blocks, cellulose and citric acid.[59] Each capsule (1 dose=3 capsules) contains thousands of salt grain-size particles, which can hydrate up to 100 times their original weight. After oral ingestion with water, each capsule disintegrates in the stomach and releases the particles, which are then hydrated. The hydrated gel particles form a 3-dimensional matrix with viscoelastic properties similar

to solid ingested vegetables and superior to common processed functional fiber supplements such as psyllium.[60] The hydrogel matrix occupies about one-quarter of the average stomach volume, thereby promoting satiety and fullness. The matrix passes through the stomach and small intestine before breaking down in the colon, where the water is released and reabsorbed by the body. The particles are not absorbed and are eliminated in the feces. Consequently, the product has no nutritional or caloric value.

The safety and efficacy of the oral superabsorbent hydrogel product were investigated in a 24-week multicenter, randomized, double-blind, placebo-controlled trial in adults with BMI ≥27 kg/m^2 and ≤40 kg/m^2 and fasting plasma glucose (FPG) ≥90 mg/dL and ≤145 mg/dL (N=436).[61] At baseline, the mean BMIs were 33.5 kg/m^2 and 34.1 kg/m^2 in the oral hydrogel and placebo groups, respectively, with 11.7% and 9.9% classified as overweight. Weight loss ≥5% was achieved by 59% vs 42% of patients, respectively, while weight loss ≥10% was achieved by 27% vs 15%, respectively. Patients treated with the oral superabsorbent hydrogel lost 6.4% body weight compared with 4.4% with placebo (*P*=.0007). In patients with FPG ≥100 mg/dL or drug-naïve type 2 diabetes mellitus at baseline, the mean percentage decrease in body weight was 8.1% with the oral hydrogel and 5.6% for placebo (*P*=NS).

The overall incidence of adverse events (AEs) in the oral superabsorbent hydrogel treatment group was no different from placebo. An AE probably or possibly related to treatment occurred in 39.5% of the oral hydrogel group and 30.3% of the placebo group; most were mild. No serious AEs were reported with the oral superabsorbent hydrogel product. The most common gastrointestinal AEs probably or possibly related to treatment in the oral superabsorbent hydrogel vs placebo groups were diarrhea (10.3% vs 7.6%), abdominal distension (10.8% vs 5.7%), infrequent bowel movements (9.0% vs 4.7%), flatulence (8.5% vs 4.7%), constipation (4.5% vs 4.7%), nausea (3.6% vs 3.8%), and abdominal pain (4.9% vs 2.8%).

Extended treatment was offered to the last 52 patients of the study who lost ≥3% body weight over the 24 weeks. These patients were treated for an additional 24 weeks, with all continuing patients receiving the oral superabsorbent hydrogel. Over weeks 25 to 48, patients in the oral hydrogel–oral hydrogel group lost an additional 0.5% of body weight (7.6% from baseline to week 48), while patients in the placebo–oral hydrogel group lost an additional 2.3% of body weight (9.4% from baseline to week 48). The safety results over weeks 25 to 48 were similar to weeks 0 to 24.

Oral, removable, palatal space-occupying device

The sensor monitored alimentary restriction therapy (SMART) device was approved by the FDA in 2016 as a class II device for weight management or weight loss.[62] It is an oral, removable, upper palatal space-occupying device that is worn during meals to limit bite size and slow the intake of food, thereby reducing the amount of food that is consumed. The device is indicated for people with BMI from 27 kg/m^2 to 35 kg/m^2 in conjunction with behavioral modification instruction.[63] A heat sensor in the device automatically records usage; the data can be uploaded to a secure website for adherence monitoring. The device is made from a mold of the patient's upper oral cavity by a trained health care provider using a mold kit included with the device.

The safety and efficacy of the oral palatal device were assessed in a 16-week, prospective, single-arm, nonrandomized multicenter trial in combination with a video-delivered lifestyle program in adults with BMI 27 kg/m^2 to <35 kg/m^2.[64] Mean weight loss was 2.1% among the 76 intent-to-treat (ITT) subjects and 2.9% among the 40 per-protocol (PP) subjects. PP subjects were required to use the device ≥7 times per week for 14 of 16 weeks, have an overall device usage rate ≥33%, and complete the trial. Weight loss ≥5% at 16 weeks was achieved by 19.7% of the ITT subjects and 30.0% of the PP subjects. Two ITT subjects reported mild/moderate device-related AEs (1 a hard palate abrasion and 2 tongue lacerations).

SUMMARY

While treatment of people with unhealthy weight has typically focused on patients with obesity, evidence indicates that the detrimental effects of excess weight on morbidity and mortality begin at lower BMI categories. Therefore, identifying at-risk patients who have overweight (BMI from 25.0 to <30.0 kg/m^2) and initiating treatment earlier may interrupt the progression toward further weight gain and the development of obesity-related comorbidities. The first step in treatment is broaching the topic of weight with the patient in an empathic and respectful manner. All patients should be provided guidance on following a calorie-controlled healthy diet and engaging in daily physical activity. For some patients, prescription of a medication approved for weight loss may be warranted after reviewing the risks and benefits of the available agents. With the FDA clearance of 2 nonprocedural devices, we now have additional therapeutic options for patients who have a lower BMI, with evidence of modest weight loss and good patient tolerability. ●

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