Care of the Obese Patient

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General Principles

Epidemiology

In 2014 more than one-third of adults (78.6 million) in the United States of America (USA) were obese with annual costs for obesity estimated at $147 billion in 2008 US dollars [1]. The overall prevalence of obesity in the USA doubled between 1994 and 2014, and the prevalence of extreme obesity rose from 3.9 % to 6.6 % between 2000 and 2010 [2]. Childhood obesity has more than tripled in the last 40 years from 5 % between 1963 and 1970 to 17 % in 2003–2004, although the rate has stabilized in children in the last decade [1, 3]. Obesity rose from a prevalence no greater than 14 % in any state in 1990 to no state having a prevalence less than 20 % in 2010, with the national average at 34.9 % [4] (Fig. 1). This rapid increase has led to an alarm of an "obesity epidemic." In 2013 the American Medical Association initiated designation of obesity as a disease "requiring a range of medical interventions to advance obesity treatment and prevention" and "help change the way the medical community tackles this complex issue" [5].

Racial and socioeconomic disparity in obesity rates is clearly evident in children, adolescents, and adults. Among US adults, non-Hispanic blacks have the highest age-adjusted rate of obesity (47.8 %), followed by Hispanics (42.5 %), non-Hispanic whites (32.6 %), and non-Hispanic Asians (10.8 %) with a similar racial trends in children and adolescents except that Hispanic youth have a

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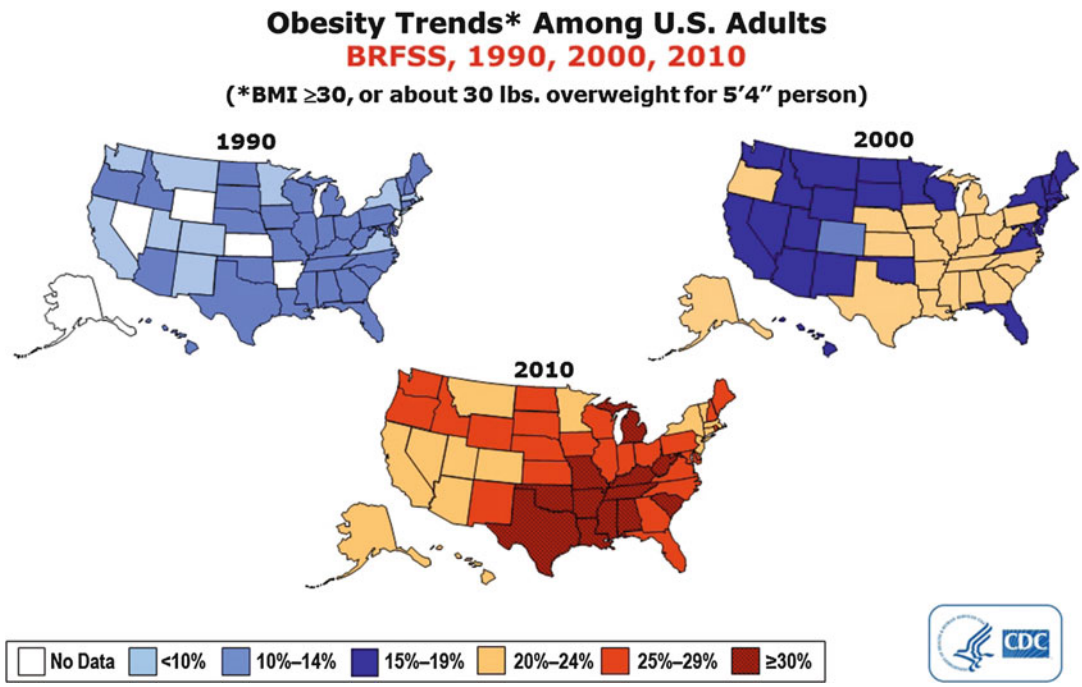

Fig. 1 Prevalence of obesity (BMI $\geq$ 30 kg/m^2) among US adults ages from 1990 to 2010 [4]. CDC's Obesity Prevalence maps, available at: http://www.cdc.gov/obesity/data/prevalence-maps.html. Abbreviations: *BMI* body mass index

greater incidence of obesity than non-Hispanic black youth (22.4 % vs. 20.2 %) [1]. Income and educational status have both been associated with trends in obesity, but the specific effects vary between races and gender. These medical disparities highlight the need for individualized treatment plans that factor in cultural and social realities.

Effects

Obesity has long been known to be associated with or increase the risk of developing many of the most common chronic diseases (see Table 1) and has been shown to increase risks of both cardiovascular disease (CVD) mortality and all-cause mortality [6].

The converse is also true in that even a modest weight loss of 3–5 % has been found to improve outcomes for some cardiovascular risk factors including progression of diabetes and hypertension, with larger weight loss resulting in greater benefits [6].

Definition

Obesity is a disease condition of excess body fat that may put a person at health risk [1, 7], but in reality percentage body fat is a difficult thing to measure. Thus, worldwide the definition of obesity is based on body mass index (BMI). Population studies have consistently shown that when BMI is viewed as a continuous variable, all-cause mortality steadily increases above a BMI of 22 kg/m^2, and recent guidelines support the current cut points for defining overweight and obesity [3, 8]. BMI is calculated by dividing a patient's weight in kilograms by their height in meters squared (kg/m^2). Simple web-based calculators and apps are widely available, and most EMRs are now configured to automatically calculate BMI from the height and weight values.

In adults, obesity is diagnosed in those with a BMI over 30. Overweight and obesity are subdivided as follows: BMI 25–29.9 (overweight), BMI 30–34.9 (class I obese), BMI 35–39.9 (class II obese), and BMI > 40 (class

Table 1 Obesity-associated comorbidities and complications by organ system

Obesity-Associated Comorbidities and Complications by Organ System [7,8]	
Cardiovascular	***Psychological***
Heart disease	Depression
Hypertension	Discrimination
Dyslipidemia	Emotional distress
Congestive heart failure	Impaired psychological functioning[a]
Cardiovascular disease death	Social stigmatization
Stroke	***Reproductive***
Endocrine	Amenorrhea
Type 2 diabetes mellitus	Infertility
Reduced fertility	Menorrhagia
Gastrointestinal	Negative fetal outcomes
Barrett's esophagus	Increased maternal complications
Cholesterol gallstones	***Respiratory***
Hiatal hernia	Asthma[a]
Reflux disease	Obesity hypoventilation syndrome
Musculoskeletal	Sleep Apnea
Injuries/Fractures[a]	***Urological***
Osteoarthritis	Stress Incontinence
Pain[a]	
Neoplasms	
Breast Endometrium Ovaries	
Cervix Kidney Prostate	
Colon Liver Rectum	

[a]Pediatric complications

III obese or "extreme obesity") [6]. In children, obesity is based on BMI percentile in reference to CDC growth charts. High BMI in children has been found to predict future adiposity, morbidity, and death leading to recommended diagnostic terminology of children being "overweight" when their BMI is between 85th and 94th percentiles and "obese" when their BMI is at or above the 95th percentile [3].

Etiology

Obesity is the result of a chronic imbalance between energy intake and energy expenditure leading to the storage of excess energy as fat, primarily in white adipose tissue [8]. However, the underlying reasons for this imbalance are multifactorial and complex and include genetic makeup, cultural beliefs, environment, habits, physical activity, dietary intake, and occupation [7, 8]. Contrary to social stigmatization, evidence supports that obesity is not simply a problem of the lack of willpower or self-control, but stems from a disordered regulation of appetite and energy metabolism associated with a variety of comorbid illnesses [7].

Weight homeostasis involves a complex and redundant neurobiological system with signaling primarily between the central nervous system, adipose tissue, and the gastrointestinal (GI) system to regulate metabolic rate and drive eating behavior [8]. Recent research has focused on peripheral signaling hormones that seem to promote satiety or decreased food intake in hopes of designing therapies to combat obesity or assist with weight maintenance. Anorexigenic hormones secreted from the GI system

(cholecystokinin (CCK), pancreatic polypeptide, peptide tyrosine-tyrosine (PYY), glucagon-like peptide-1 (GLP-1), and oxyntomodulin) and adipokines (leptin, adiponectin) produced by white adipose tissue are potential candidates. Research has uncovered that most markers of satiety are reduced and most measures of appetite enhanced in patients who have lost weight, which partly explains the difficulty patients experience in sustaining weight loss [8].

Yet, while "nature" plays a clear role, "nurture" is also at work. The demographics in western societies have shifted over the last half century from that of a largely rural population frequently involved in manual labor to a heavily urban demographic with more sedentary lifestyles. Compounding this are vast changes in food – both in quantity and in kind. Highly processed foods have become widely available and some of the lowest costing foods are calorie dense and contain high levels of fat, sugar, and salts.

Diagnosis

History

Obesity is overwhelmingly a primary process: imbalance of caloric intake to caloric expenditure. As noted, there are myriad reasons for this imbalance, but elucidation of individual factors can be an intensely sensitive topic. Review of a patient's weight trajectory plotted over time, typical caloric intake, and typical physical activity can be used to guide initial work-up of obesity and subsequent office-based recommendations. Further insights can be gleaned when the patient annotates significant life occurrences (i.e., employment changes, tobacco cessation, end in a relationship, etc.) on the weight trajectory timeline. Ideally, patients complete oral intake diaries recording all beverages, meals, snacks – anything a patient puts in their mouth – as well as daily physical activity including the time.

As obesity usually derives from a primary etiology, work-up for secondary causes of obesity in adults should be based on specific symptoms or risk factors coupled with a physician's index of suspicion. Medications should be reviewed for potential obesogenic medications as some common drug classes are clearly associated with weight gain including atypical antipsychotics, anti-depression medications, and diabetic medications. History should ensure there is no comorbid psychiatric illness leading to weight gain such as eating disorders, depression, or body dysmorphia, and in women a detailed menstrual history should be obtained to evaluate for polycystic ovarian syndrome.

Physical Exam

Appropriate height and weight are paramount in children and adults alike. Additional screening of waist circumference in adults with a BMI between 25 and 35 may be undertaken as such individuals have an elevated CVD-related and overall mortality if their waist circumference is >102 cm (~40 in.) for males and 88 cm (~35 in.) for females [6]. Measuring waist circumference when BMI is greater than 35 is generally not indicated as such patients can be expected to have increased waist sizes. Physicians should also have a keen eye for physical markers associated with the uncommon causes of secondary obesity including acanthosis nigricans, goiter, moon faces, buffalo hump, central obesity, striae, and hirsutism.

Additional Testing

Most lab testing is geared toward evaluating for comorbidities of obesity rather than ruling out causes. Screening for impaired fasting glucose or frank diabetes (fasting glucose), nonalcoholic fatty liver changes (AST/ALT), and dyslipidemia to complete cardiovascular risk assessment (lipid panel) is appropriate at least biannually starting at age 10 [3]. While thyroid disease is associated with obesity, TSH is of limited benefit even in adults and is not recommended as a screening test in the pediatric population. In the pediatric population, lab tests ought be performed only in those with short stature (<5th percentile),

developmental delays, dysmorphic features, or who have clear signs or symptoms of underlying endocrine abnormalities especially as cortisol, and TSH levels are often elevated in children with obesity [9].

Treatment Plan

In 2013, a seminal Guideline for Management of Overweight and Obesity in Adults was authored collaboratively between the American College of Cardiology (ACC), the American Heart Association (AHA), and The Obesity Society (TOS) and includes an evidence-based treatment algorithm with recommendations on the management of patients with overweight and obesity. After diagnosis of obesity, or overweight with comorbidities, physicians are encouraged to assess for patient willingness to change. Once patients are committed to weight loss, a "high-intensity comprehensive lifestyle intervention" becomes the cornerstone of therapy – with or without adjunct use of pharmacotherapy or surgery [6]. Such an intervention is defined as being greater than or equal to 14 face-to-face sessions in a 6 month time frame and includes three principle components: a moderately reduced calorie diet, an increased physical activity program, and the use of behavioral strategies to better comply with the diet and exercise programs [6].

Dietary Management of Overweight and Obese Patients

In today's targeted consumer-based market, new diets appear almost every season claiming to be more effective than their predecessors. Certain diet plans focus on altering macronutrients, while others emphasize creating a negative energy balance through cutting overall calories. Combination plans combine diet type (i.e., low carbs) with behavior interventions, such as group meetings, calorie counting, or food journals. Patients often want quick results which are often impractical, lead to treatment failures, and cause patient dissatisfaction.

Recent meta-analysis of 48 original RCTs showed overweight and obese adults randomized to any popular diet or meal replacement plan lost significant weight at 6-month and 12-month intervals (approx. 8 and 7 kg, respectively), on any low-carbohydrate or low-fat diet [10]. Thus, the landmark 2013 guidelines by the ACC/AHA/TOS encourage physicians to recommend a weight-loss diet based on patient adherence rather than the diet type [6]. A daily energy deficit of greater than 500 kcal can usually be accomplished with 1,200–1,500 kcal/day for women and 1,500–1,800 kcal/day for men, but very low-calorie diets (800 kcal/day) should be confined to patients within a medical care setting where close medical monitoring and high-intensity lifestyle interventions are available [6].

There may be benefits to a diet beyond weight loss, and dietary composition may affect cardiovascular biomarkers (triglycerides, HDL cholesterol, glucose, and insulin) [11], whether through loss of adipose tissue or an independent mechanism. Data published over the last decade touted that Mediterranean-type diets – those rich in nuts, whole grains, vegetables, poultry, and fish instead of red meats – may help patients achieve better glucose or insulin control. However, a 2014 systematic review showed no difference between diet types (low carbohydrate vs. isoenergetic balanced) in overweight and obese adults when it came to preventing or reducing cardiovascular risk factors (blood pressure, lipids, and fasting blood glucose) [12].

Exercise

Patients often resort to increased physical activity and binge exercise as a weight-loss tool, but data shows that these measures only result in modest weight loss, even over the long term. Moderate intensity aerobic exercise programs have been shown to net participants 1.7 kg (3.7 lbs) weight loss versus controls over 12 months, and exercise also increases weight loss in those dieting by an additional 1.1 kg (2.4 lbs) [13]. Exercise of any intensity can improve cardiovascular outcomes and metabolic profiles, but results vary for each

patient and activity. Similar to recommending a diet, family physicians should encourage patients to partake in activities of moderate intensity that are enjoyable and those to which the patients will adhere.

Pharmacological Management of Obesity

There are several pharmacological agents approved by the Food and Drug Administration (FDA) for use in the short- (<12 weeks) and long-term (>52 weeks) management of obesity. Such agents have various targets and mechanisms of action and include two new medications approved by the FDA in 2012. Physicians should view medications as adjunctive therapy to other interventions, started when initial management strategies including diet, exercise, and intensive behavior therapy fail to yield clinical results. Weight-loss drugs have a long and tarnished history, with many drug recalls and associated adverse events, especially increased cardiovascular risks. Pharmacotherapy should be discussed with patients as early as at the first encounter, including various options, side effects, and any associated adverse events. As with any other therapeutic interventions, physicians need to monitor compliance, respond to treatment, and manage expectations carefully. Significant weight loss can take over a year, and most patients will regain some weight after an initial period of response.

Pharmacotherapy alone is not more effective than diet and exercise; however, when used as adjuvant therapy, physicians and patients can expect to see significant results over the long term. Table 2 summarizes agents currently approved by the FDA for weight loss, along with dosing info, weight-loss results, and most commonly reported adverse events.

Surgical Management of Obesity

Surgical treatment for obesity has been around since the 1950s when it was incidentally discovered that procedures resulting in restriction, size limitation, or malabsorption syndromes of the gut (i.e., gastric and bowel resections) led to postoperative weight loss over both the short and long term. These surgeries were initially considered too risky for obesity management due to high rates of complications and significant morbidity and mortality. The field was transformed in 1991 after the NIH Consensus Conference concluded that vertical banded gastroplasty and Roux-en-Y gastric bypass procedures were safe and effective treatment options for morbidly obese patients (BMI > 40 or BMI > 35 with comorbidities present) [23]. The consensus statement, along with the rise of laparoscopy in the early 1990s, led to standardization and advent of safer techniques.

Clinical evidence demonstrates that surgical treatment of obesity results in greater weight loss than any other conventional pharmacological treatment or lifestyle modifications, including diet, exercise, and intensive behavior therapy [24]. The Swedish Obese Subjects (SOS) study showed long-term mortality was lower in the surgical group (>10 year) [25], and several large randomized trials have shown superior efficacy of bariatric procedures for treating T2DM and inducing remission at 2 years [3]. Observational data has shown improvement in quality of life and a decrease in the incidence of diabetes and certain types of cancer [26].

A 2013 meta-analysis directly comparing bariatric surgery with nonsurgical treatments (lifestyle modifications including diet, exercise, and various pharmacotherapy) for obesity concluded that surgical treatment leads to greater body weight loss and higher remission rates of T2DM and metabolic syndrome [27]. This review included 11 trials and looked at the most commonly used open and laparoscopic techniques: Roux-en-Y gastric bypass (RYGB), adjustable gastric banding (AGB), sleeve gastrectomy (SG), biliopancreatic diversion, or biliopancreatic diversion with duodenal switch. Most common adverse events were anemia (iron deficiency) and reoperations [27]. For the best outcomes, it is recommended that patients be sent to specialty hospitals that perform high volumes of bariatric cases annually.

RYGB has a greater cardiovascular mortality risk reduction and leads to much greater weight

Table 2 FDA-approved pharmacotherapy for obesity management

	DRUG(FDA Approval) *TRADE NAME*	PHARMACOLOGY / DOSING	TOTAL (PLACEBO SUBTRACTED) WEIGHT LOSS & EFFECTS	SIDE EFFECTS[A]
Long-Term (>52 wks)	**Lorcaserin** (2012) *Belviq ©*	Selective 5-HT2C receptor agonist 10mg PO BID	4.5% (3%) after 1 year[14,15] Decrease in BP[16] Decrease in LDL & HgbA1C Appetite suppression	Headache[17] Nausea Fatigue Dizziness URI/Nasopharyngitis Cardiovascular Risk? [B]
	Naltrexone-bupropion SR (2014) *Contrave ©*	Opioid receptor antagonist; DA/NE reuptake inhibitor 8/90 mg ER titrated up to 2 tabs PO BID	6.5% (4.6%) after 1 year[18,19] Reduced food intake Decreased visceral fat and waist size	Nausea Headache Constipation Sleep disturbance Anxiety
	Orlistat (1999) *Xenical ©* *Alli © (OTC - 2007)*	Lipase inhibitor 120mg PO TID (RX) 60mg PO TID (OTC)	11% (5%) after 1 year 6.9% (2.8%) after 4 years[14] Decrease in LDL cholesterol & HgbA1C Prevention of Type II DM (37% RR reduction)	Flatus with discharge[17] Oily spotting Fecal urgency/incontinence Steatorrhea Fat-soluble vitamins deficiency **Approved for use in adolescents**
	Phentermine/Topiramate ER (2012) *Qsymia ©*	Sympathomimetic / anti-epileptic; exact MOA unknown High Dose: 15mg/92mg ER PO QAM Low Dose: 7.5/46mg ER PO QAM	10.9% (9.3%) at 56 weeks for High Dose[20] 5.1% (3.5%) at 56 weeks (Low Dose) Decrease Systolic & Diastolic BP Decrease in LDL and triglycerides	Paresthesia[19,20] Dry mouth Constipation Dysgeusia Insomnia Mood & cognition related events were reported more frequently in High-Dose treatment group
Short-Term	**Phentermine** (1959) *Adipex-P ©; Fastin ©; others*	Appetite suppression via sympathomimetic action 15mg - 37.5mg PO ONCE DAILY	Paucity of long term trial data to establish weight-loss compared to baseline	*CNS:* insomnia, elevation in heart rate, dry mouth, taste alterations, dizziness, tremors, headache, anxiety, and restlessness *GI:* diarrhea, constipation, and vomiting
Novel Agents	**GLP1-Receptor Agonist** *Liraglutide © - approved for T2DM*	Appetite suppression via GLP1-R agonism *Dose ranges in Phase II / III trials* 1.8mg to 3mg PO ONCE DAILY	8% (5.4%) after 1 year[16] Improvement in plasma glucose[16] Decrease in systolic BP Decrease in triglyceride concentration	Nausea[16] Vomiting Constipation Diarrhea Headache Unclear association with pancreatitis
	Peripheral MetAP2 Inhibitors *Beloranib © (Phase III)*	Peripheral inhibition of angiogenesis in adipose tissue; stimulates energy expenditure, fat utilization, and lipid excretion[21] 0.9 mg/m2 IV TWICE WEEKLY for 4 weeks	3.5% (2.9%) after 4 weeks[21] Appetite suppression[21] Decrease in Triglyceride concentration Decrease in CRP levels	Headache; infusion site injury; nausea; diarrhea

A) In order of frequency reported in randomized trials.
B) Valvulopathy-rates, as seen on echocardiography, were similar in treatment and placebo group at 1 year but FDA has requested a post-approval trial to see long term cardiovascular effects.[16,22]

[a]In order of frequency reported in randomized trials
[b]Valvulopathy rates, as seen on echocardiography, were similar in treatment and placebo group at 1 year, but FDA has requested a post-approval trial to see long-term cardiovascular effects [16, 22]

loss compared to AGB at 2 years but has a higher risk of short-term (30 days) complications [28]. Some high-volume bariatric surgery centers are able to achieve similar weight loss at 2 years following either ABG or RYGB [P24]. AGB may appear to have a lower rate of short-term risk, but the procedure has a rate of band removal as high as 50 % due to "failure to achieve or maintain clinically significant weight loss; band malfunction, slippage, or erosion; or patient intolerance of the gastric restriction" [29].

Although SG is fast becoming one of the most common bariatric procedures [30], there is limited long-term outcomes data; ongoing trials are expected to yield results in the near future on long-term outcomes data [24]. A Cochrane Review© published in 2014 showed similar weight-loss results (based on BMI at 2-year follow-up) after either SG or RYGB [28]. Endoscopic techniques are a novel treatment option in the past few years, but again there is a paucity of outcomes data at this time. Endoscopic sleeve gastroplasty

(ESG), which aims to reduce gastric volume via placement of full-thickness sutures, showed weight loss of 30 % in 10 patients at 6 months, with no significant adverse events [31].

A big challenge for the primary care physician is deciding when to refer a patient to a surgeon for this invasive and life-altering treatment. As with any other surgical treatment, patients need to be made aware of all the risks and benefits and both short- and long-term complications. There is limited long-term data on aspects of bariatric surgery not related to weight loss, including mental health and reproductive outcomes, or for long-term management of complications due to weight loss [15]. Patients having undergone bariatric surgery are advised long-term follow-up and ongoing nutrition and lifestyle management to monitor for any nutritional deficiencies [29].

Prevention

In obesity, an ounce of prevention may well be worth more than a pound of cure given the clinical realities experienced by those trying to lose and maintain weight loss, not to mention the potential risks of medication or bariatric surgery. A focus on promoting healthy weight in those who are normal weight or overweight may be a more profitable strategy, especially when focusing on children. Family physicians can leverage their understanding of the familial realities in helping individual patients and their families arrive at healthful lifestyle measures that will prevent obesity. Consistent evidence supports family physicians recommending limiting consumption of sugary beverages, limiting screen time (2 h max in children over age 2), limiting eating out, limiting portion size, promoting regular consumption of breakfast, and promoting eating family meals together [3].

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