Actor portrayal.



the weigh forward >>

MODULE 1 Why obesity management matters to your organization

A new understanding of obesity guidelines, obesity management, and anti-obesity medications (AOMs)

Obesity is a chronic disease. Previously, obesity was viewed as just a lifestyle issue

"Our AMA recognizes obesity as a disease state with multiple pathophysiological aspects requiring a range of interventions to advance obesity treatment and prevention."

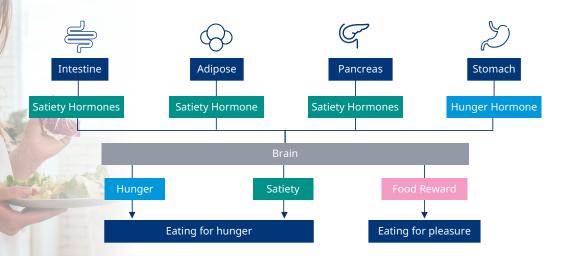
American Medical Association (AMA)

"Obesity is a complex, multifactorial condition characterized by excess body fat. It must be viewed as a chronic condition that essentially requires perpetual care, support, and follow-up. Obesity causes many other diseases, and it warrants recognition by healthcare providers and payers."²

American Association of Clinical Endocrinology/ American College of Endocrinology Obesity Task Force

National organizations recognize obesity as a multifaceted, chronic disease and a significant threat to public health.¹⁻³ Obesity is an excess accumulation of adipose (fat) tissue that may impair health. Its presence can be estimated by a body mass index ≥30 kg/m² in many populations.⁴

Appetite regulation is affected by hormones signaling from the body to the brain⁵⁻⁹



Appetite regulation results from complex communication between the gastrointestinal (GI) tract, adipose tissue, and the nervous system.¹⁰

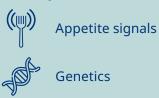
Actor portrayal.

Actor portrayal.

Metabolic adaptations can complicate obesity management^{11,12}

Multiple factors affect weight management. For many people with obesity, lifestyle modifications alone are not enough to maintain long-term weight reduction and there may be a gradual weight regain over time.^{3,13}

Multiple factors affect weight management^{12,14-16}:



Behavior

Environment

In people with obesity, the body will try to put the weight back on for at least 12 months after weight reduction.¹²

Appetite signals

- Multiple hormonal signals influence appetite¹⁷
- When weight is lost through caloric restriction, the body increases the hunger hormone and decreases fullness hormones¹²
- Hormonal adaptations in response to weight reduction favor weight regain¹⁷

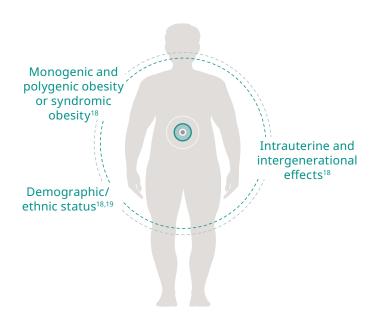
Hormones ¹⁷	Food intake ^{17,a}	Site of secretion ¹⁷	
Ghrelin	\uparrow	Stomach	
GLP-1	\checkmark	Intestines	
ΡΥΥ	\checkmark	Intestines	
ССК	↓ Small intestir		
OXM	\checkmark	Intestines	
Amylin	\checkmark	Pancreas	
РР	\checkmark	Pancreas	

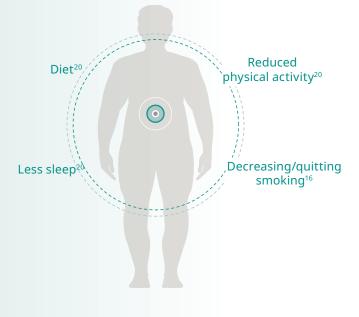
Actor portrayal.

^aArrows indicate whether the particular hormone encourages increased or decreased food intake. CCK=cholecystokinin; GLP-1=glucagon-like peptide 1; OXM=oxyntomodulin; PP=pancreatic polypeptide; PYY=peptide tyrosine-tyrosine.

Genetics

- Genes may play an important role in who is impacted by obesity^{14,15}
- A person's genetics may determine the extent to which external factors impact their weight¹⁴



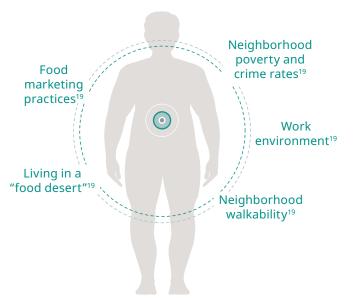


Behavior

• Diet, not enough sleep, lack of physical activity, and smoking status may be contributing factors¹⁶

Environment

 Having healthy food may be challenging (eg, location, price, time to prepare), which may result in buying more convenient, fatty, and calorie-dense foods. Some individuals have no place to exercise^{15,16}



Obesity is classified as BMI ≥30 kg/m² and is often associated with weight-related comorbidities³

BMI is the primary method for identifying people with obesity or overweight. It provides a more accurate measure of total body fat compared with body weight alone.²¹



Assessing obesity in a clinical setting is often done with the following practical tools²¹:

• BMI

Waist Circumference



Although other methods of evaluating body fat exist, BMI, along with clinical assessment, is still used to evaluate patients for obesity treatment options.^{3,22}

BMI	ciu	sincation of over	weight and obesity	
	25-29.9 kg/m ² Overweight	30-34.9 kg/m ² Obesity Class I	35-39.9 kg/m ² Obesity Class II	≥ 40 kg/m ² Obesity Class II

In most EHRs, a patient's BMI is autogenerated from height and weight measurements obtained during the visit²³

- Diagnoses of obesity are always clinically significant and should always be reported through coding
- Physicians generally do not report a diagnosis of overweight without the presence of weight-related comorbidities

Actor portrayal.

EHR=electronic health record.

BMI is the primary method for identifying people with obesity or overweight²¹

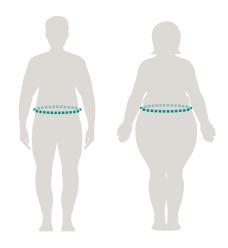
BMI provides a more accurate assessment of total body fat compared with body weight alone

Calculating BMI²⁴: Weight (kg) ———— = BMI (kg/m²) Height squared (m²) Interpretation of BMI should take into consideration patient-specific factors such as age, gender, ethnicity, hydration, and other factors. BMI cannot accurately estimate body fat in some people, including persons who are very muscular or who have lost muscle mass.²¹

The role of waist circumference²¹

Waist circumference can be measured to assess risk for obesity-related comorbidities in patients with BMI <35 kg/m²

Measuring waist circumference is a useful method to evaluate a patient's abdominal fat before and during obesity treatment



Examples of BMI Ranges^{3,25}

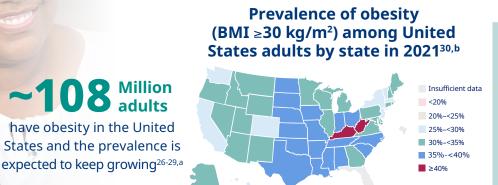
Based on average national heights for men and women in the United States, the table below shows examples of weight correlated with BMI ranges^a

Class BMI		Men Average Height: 69.0 inches (5'9")	Women Average Height: 63.5 inches (5'3.5")	
Normal weight	≥18.5 kg/m ² to 24.9 kg/m ²	≥125 lbs to 169 lbs	≥106 lbs to 142 lbs	
Overweight	≥25 kg/m² to 29.9 kg/m²	≥169 lbs to 202 lbs	≥143 lbs to 171 lbs	
Obesity Class I	≥30 kg/m ² to 34.9 kg/m ²	≥203 lbs to 236 lbs	≥172 lbs to 200 lbs	
Obesity Class II	≥35 kg/m² to 39.9 kg/m²	≥237 lbs to 270 lbs	≥201 lbs to 229 lbs	
Obesity Class III	≥40 kg/m²	≥271 lbs	≥229 lbs	

^aAdults aged 20 and older.

Obesity's prevalence and associated comorbidities

Obesity is highly prevalent within your ecosystem and the statistics are rising





Explore obesity prevalence by region

Actor portrayal.

By 2030, nearly **1 in 2 adults** in the United States are projected to have obesity (BMI \ge 30 kg/m²) and nearly **1 in 4** are projected to have Class II or III obesity (BMI ≥35 kg/m² or ≥40 kg/m²).²⁸

Actor portrayal.

Approximately 73% of the adult population have overweight or obesity^{31,c,d}

Breakdown by BMI category^{31,d,e}

26.0%

Normal Weight

(BMI ≥18.5 kg/m² to 24.9 kg/m²)

31.4% Overweight

(BMI ≥25 kg/m² to 29.9 kg/m²)

22.0% Obesity Class I

 $(BMI > 30 \text{ kg/m}^2 \text{ to } 34.9 \text{ kg/m}^2)$

10.5% 8.6% Obesity **Class II** (BMI ≥35 kg/m²) to 39.9 kg/m²)

Obesity **Class III**

From 1999-2020 through 2017-2018, the age-adjusted United States obesity prevalence increased from 30.5% to 41.9%. During the same time, the prevalence of severe obesity nearly doubled, from 4.7% to 9.2%.³²

^aAdults aged ≥18 years.²⁷

^bPrevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.

^cAdults aged ≥20 years.

^dBased on data from 2015-2018.³¹

ePercentages do not sum to 100 because the percentage of people with BMI <18.5 kg/m² is not shown and the percentage of people with obesity is a subset of the percentage with overweight and obesity.³

Regardless of your industry or occupation, obesity and overweight can have an impact on your workforce

Among full-time employees:



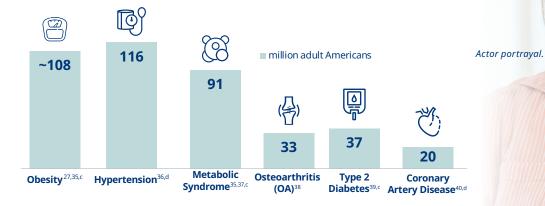
full-time employees have^{33,a} Obesity (BMI ≥30 kg/m²)



or ~45,350,000 full-time employees have^{33,a} Overweight (BMI ≥25 kg/m² to 29.9 kg/m²)

Obesity may be associated with many health complications that can drive up healthcare costs. Obesity can also increase indirect costs such as absenteeism and disability costs.³⁴

How does the prevalence of obesity compare with that of other chronic diseases?^b



Note that these conditions are **not mutually exclusive**; an individual may have more than one of these conditions at the same time

^aUnited States adults aged ≥18 years, as of 2018.

^bThese are approximations based on currently available statistics.

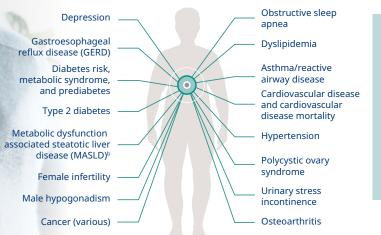
^cAdults aged ≥18 years.

Actor portrayal.

^dAdults aged ≥20 years.

The comorbidities of obesity may pose a serious threat to individuals within your organization^{41,42,a}

Examples of obesity-related comorbidities^{41,42}



According to the Obesity Medicine Association, there may be



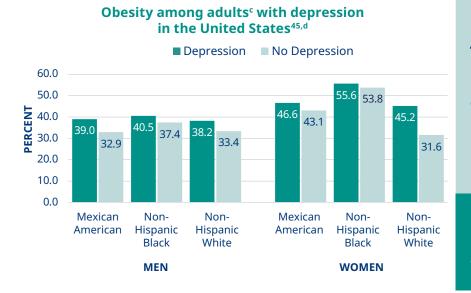
Obesity is a debilitating disease that is likely already impacting the health of people in your organization.

There are also some ways that obesity can impact **mortality** and the way the body responds to acute illnesses and infection44

Actor portrayal.

DEPRESSION

43% of adults aged ≥20 years in the United States with depression have obesity⁴⁵



Which comes first?

Does the impact of overweight lead to depression?

The answer may be yes to both.46

Both depression and obesity have been associated with many health risks, including cardiovascular disease, diabetes, and functional limitations.45

^aThe above list is not exhaustive and is intended to illustrate only a range of key complications.

^dData from National Health and Nutrition Examination Survey, 2005-2010.⁴⁵

Or does depression itself cause excess weight gain?

^bMASLD was formerly known as non-alcoholic fatty liver disease (NAFLD).

^cAged ≥20 years.⁴⁵

OBSTRUCTIVE SLEEP APNEA

Obesity is associated with obstructive sleep apnea (OSA)^a

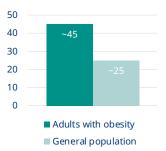
What is OSA?47

Obesity and sleep⁴⁸

Sleep apnea is a disorder in which people experience disrupted breathing while they are sleeping.

In OSA, disruptive breathing occurs because of a narrow or blocked upper airway. People who have obesity (BMI ≥30 kg/m²) have a shorter duration of sleep and twice as many subjective sleep problems compared with people without obesity.





What can be done?

Weight reduction of 10% or more may improve apnea-hypopnea index in OSA.⁵⁰

Increased physical activity and decreased sedentary behavior were associated with lower OSA incidence.⁵¹

OSA adversely affects multiple organs and systems, and may be associated with cardiovascular disease, hypertension, insulin resistance, systemic inflammation, visceral fat deposition, and dyslipidemia.⁴⁹

DIABETES RISK, METABOLIC SYNDROME, AND PREDIABETES

BMI and/or waist circumference may be associated with risk of metabolic disorders^{52,53}



^aObesity is only 1 of the risk factors for OSA.⁴⁹

^bA meta-analysis was performed using 89 prospective cohort studies with a sample size of at least 200 subjects with risk estimates based on the incidence of disease (7 studies were available for T2D). Incidence rate ratios and risk ratio proportions were used to obtain pooled risk ratios with 95% CIs to provide a review of the incidence of comorbidities related to obesity and overweight.⁵⁶ T2D=type 2 diabetes.

CARDIOVASCULAR DISEASE AND CARDIOVASCULAR DISEASE MORTALITY

Obesity and certain weight-related comorbidities can increase risk of cardiovascular diseases



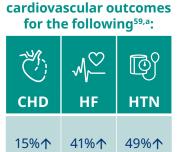
Obesity contributes to certain cardiovascular risk factors such as dyslipidemia, T2D, and HTN.⁵⁸



People with a BMI of 30 kg/m² or greater have an increased risk for developing HTN and CHD.⁵⁶



A meta-analysis established a significant association between overweight and obesity with the incidence of cardiovascular diseases.⁵⁶



Every 5 kg/m² increase in

BMI is associated with an

increased risk of adverse

Overweight and obesity are linked to increased cardiovascular disease risk:

	Obesity increases risk		
CAD	≥1.7x ^{56,b}		
Stroke	~1.5x ^{56,b} Obesity is estimated to impact 18% to 44% of stroke patients ⁶⁰		

FEMALE INFERTILITY

Obesity is associated with reproductive health issues in women⁶¹

Potential Complications—Infertility^{62,c}

3% increased risk of infertility per 1-unit increase in BMI ≥19.5 kg/m²

POLYCYSTIC OVARY SYNDROME

Polycystic ovary syndrome (PCOS) is one of the most prevalent endocrine disorders in reproductive-aged women⁶³



Data suggest that between **38%** and **88%** of women with PCOS have obesity or overweight.⁶⁴



As of 2020, PCOS is associated with **\$8 billion in healthcare costs**.⁶⁵

Although clinical efficacy can vary among individuals, even modest reduction of 5% of total body weight may result in clinically meaningful improvements of PCOS symptoms (including restoration of ovulation, normal menstruation, and androgen levels).^{41,66}

^aAnalysis was performed using 12 systematic reviews and 53 meta-analyses (including >501 cohort studies) and 12 Mendelian randomization (MR) (informing causality) studies that were published until January 2021 to evaluate the association between obesity-related indices and CVD risks (eg, CHD, HF, HTN, etc). In this review, the all-cause and CVD-specific mortality risks increased with adiposity in cohorts, while there was no causal effect of adiposity on all-cause mortality demonstrated in the MR studies.⁵⁹

^bA meta-analysis was performed using 89 prospective cohort studies with a sample size of at least 200 subjects. Pooled risk ratios with 95% CIs were used to determine the incidence of comorbidities related to obesity and overweight.⁵⁶

^cThe study's design was a cross-sectional analysis including 3623 adult females using the NHANES database's 2013-2018 cycle. With BMI serving as the independent variable and reproductive status as the dependent variable, the survey's main goal was to investigate the association between infertility and BMI in women of childbearing age. The reproductive health questionnaire (eg, have you ever attempted to become pregnant over a period of at least a year without becoming pregnant?) was used to self-report infertility; a "yes" response indicated "infertile" status, while a "no" response suggested "fertile" status.⁶²

CAD=coronary artery disease; CHD=coronary heart disease; CVD=cardiovascular disease; HF=heart failure; HTN=hypertension.

ASTHMA/REACTIVE AIRWAY DISEASE

Obesity affects the mechanics and function of the chest wall and lungs and is associated with various respiratory disorders⁶⁷

Obesity affects ~38% of adults ^a with asthma ^{68,69,b}					
Increased risk of developing asthma12%37%64%97%149%					
BMI	25 to <30 kg/m ²	30 to <35 kg/m ²	35 to <40 kg/m ²	40 to <50 kg/m ²	≥50 kg/m²

Respiratory disorders are costly

Asthma		
Direct costs	\$61.9 billion ^{70,71,c}	
Indirect costs	\$2.1 billion ^{71,72,c}	

GASTROESOPHAGEAL REFLUX DISEASE (GERD)

GERD affects up to 70% of people with severe obesity⁷³



In one analysis comparing people of normal weight, the likelihood of experiencing GERD symptoms was^{74,d}:

1.5x greater People with overweight People with obesity



Costs in 2009 ^e			
Prevalence among all adults ^f	18.1% to 27.8% ⁷⁵		
Direct costs	\$17.5 billion ^{71,76}		
Facility charges	\$2.2 billion		
Physician charges	\$1.1 billion		
Ambulatory care	\$2.0 billion		
Prescriptions	\$11.1 billion		
Indirect costs	\$744 million ^{71,76}		

Weight reduction of $\geq 10\%$ can help reduce GERD symptoms⁴¹

^aAged 18 years and older.⁶⁹

^bThis retrospective cohort study analyzed EHR data from 2012-2013, covering 2.8 million adults with a BMI of ≥23.0 kg/m² who were enrolled in 9 different health plans across the United States. The study investigated the association between obesity (body weight), asthma control, and the incidence of adult-onset asthma.69

^cCosts were adjusted for inflation in 2023.

^dA meta-analysis of published literature spanning from 1966-2004, this study explored the link between obesity (BMI) and GERD symptoms. The analysis was performed using the data from 9 pooled studies identified through a Medline search based on risk estimates and defined criteria for exposure and reporting outcomes.74

Costs in 2009 United States dollars (USD) were adjusted for inflation in 2023.

fAged 20-95 years.75

METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE

The risk of developing metabolic dysfunction-associated steatotic liver disease (MASLD) may be increased for patients with obesity⁷⁷



Obesity is independently (ie, irrespective of other metabolic factors) linked with MASLD. People with obesity have a^{77,78,a,b,c}

3.5 fold

independently higher relative risk of MASLD compared to lean individuals



Prevalence among United States adults		
MASLD ⁷⁹	~25%	



Modeling estimates the burden of MASLD per patient per year in the United States to be⁸⁰

\$1613

CANCER (VARIOUS)

Obesity and overweight are associated with select cancers throughout the body⁸¹

Obesity and overweight have been linked with an increased risk of at least 13 types of cancer:

Liver

Ovarv

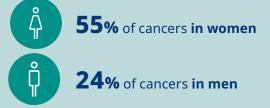
Gallbladder

Kidney (renal cell)

- Esophagus
- Breast
- Colon and rectum
- Endometrium (corpus uterus)

- Pancreas
- Gastric cardia
 Thyroid
 - Meninges
 - Multiple myeloma

40% of all cancers diagnosed in 2014 were linked to overweight or obesity



OSTEOARTHRITIS

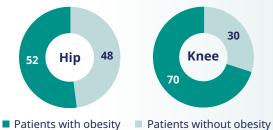
Obesity contributes to soft-tissue damage and osteoarthritis (OA) of the hip and knees⁸²



Obesity may increase the risk of knee OA and may be associated with an increased need for joint replacement surgery.^{82,83}



In one study using the Canadian Joint Replacement Registry data, people with Class I obesity^d were **~8.5x more likely** to require knee replacement surgery compared with the general population.⁸⁴ Patients undergoing total joint arthroplasty in the United States⁸²



 $^{\rm a}\mathsf{MASLD}$ was formerly known as non-alcoholic fatty liver disease (NAFLD). 77

^bA meta-analysis of 21 cohort studies (13 prospective and 8 retrospective, with a total of 381,655 participants) was performed to assess the MASLD risk associated with obesity or increased BMI. The data was analyzed for pooled relative risks with 95% CIs using a random-effects model.⁷⁸ ^cThe data in these studies were utilizing the NAFLD definition.

^dClass I obesity: BMI 30-34.9 kg/m^{2.84}

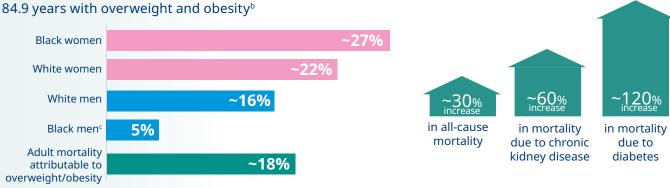
CI=confidence interval.

MORTALITY

Increased BMI may be associated with adult obesity-related mortality⁴⁴

Overweight and obesity may be associated with ~18%^a increased mortality for Black and White adults in the United States⁴⁴

Estimated percentage of deaths among adults aged 40 to 84.9 years with overweight and obesity^b One analysis of 57 prospective studies found that for every 5 kg/m² BMI increment above 25 kg/m², there was a^{15,85}:



Obesity is a chronic disease that may have an incremental impact on lifespan, with younger people with obesity **losing the most years** of their lives (up to 8 years for men with severe obesity aged 20 to 39 years).^{86,d} Healthy life years were also lost due to chronic illnesses such as T2D or CVD.⁸⁶

ACUTE ILLNESSES AND INFECTION

Obesity increases the risk of complications and adverse outcomes from acute illnesses and infections

Obesity can contribute to⁸⁷:

- Greater risk of getting certain infectious diseases
- Greater infectious disease severity

The systemic changes that occur in patients with obesity have an impact "across the spectrum of critical illness"⁸⁸

- Pulmonary system
- Nosocomial infections (eg, pneumonia)
- Renal system
- Musculoskeletal system
- Cardiovascular system

When associated with an infection like COVID-19, the odds of needing invasive mechanical ventilation increase with increasing BMI.⁸⁹

Patients hospitalized with COVID-19 who have class II or III obesity are also at an increased risk of death.⁸⁹

Odds ratio (95% CI)			
Overweight	1.27		
Obesity class I	1.48		
Obesity class II	1.89		

Obesity class III 2.31

Obesity could also jeopardize the effectiveness of vaccines

- **COVID-19:** Obesity is significantly associated with decreased antibody response^{90,e,f}
- **Influenza:** Obesity blunts immune responses, enabling virus transmission and extending the duration of infection⁹¹

^dBased on modeling of data from the 2003-2010 NHANES, including 3992 non-Hispanic, White participants.⁴⁴

eStudies analyzed antibody response after at least one dose of COVID-19 vaccine, and did not include boosters.⁹⁰

^fBased on a meta-analysis of 11 studies (n=7956, of which 1869 had obesity).⁹⁰

^aAggregated and standardized by race/ethnicity and sex distribution of deaths in the United States among Black and White men and women between 1986 and 2006.⁴⁴

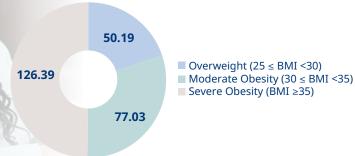
^bBased on a study of all-cause mortality from 19 consecutive waves of the National Health Interview Survey (NHIS) between 1986 and 2004.⁴⁴ 'This finding was not significant (CI -6.8, 18.3).⁴⁴

The costs of obesity to your organization

Obesity is a costly disease

As of 2019, **obesity was associated with \$1861 in excess annual medical costs per person** for adults^a in the United States⁹²

Population level excess cost (billions) compared to normal weight by BMI category^{92,b}





Medical expenditures associated with obesity increase depending on a number of factors, including BMI.⁹²



In major United States industries, direct and indirect costs of obesity increase with rising BMI.³⁴

Actor portrayal.

WARD STUDY

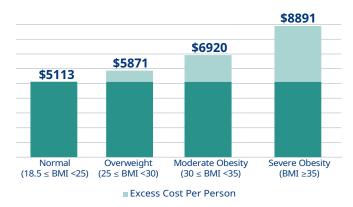
Medical expenditures associated with obesity increase depending on degree of obesity^{c-e}

Obesity may be costing your organization more than you know, since obesity itself may **cause or exacerbate** costly conditions.⁹³

Obesity-related costs per person increase depending on a number of factors, including BMI⁹²

Age	Around age 30, obesity-related excess costs begin to increase and continue to increase until about age 65 ⁹²
Gender	Medical expenditures are higher in general for adult women ⁹²
BMI	A one-unit increase in BMI is associated with an additional average cost of \$309 annually per person ^{71,92}

Total and excess annual medical costs associated with overweight and obesity^{71,92,f}



^aAged 20 years and older.

^bPopulation-level costs were estimated by scaling the per-person excess costs using BMI category prevalence estimates from NHANES 2011-2016 and 2019 population estimates of the civilian, non-institutionalized population.⁹²

^eExcess costs were estimated by assuming that all respondents would instead follow the BMI distribution observed in the reference category, then calculating the difference between the current predicted costs and the predicted costs for the reference weight population.

^fCosts in 2021 USD were adjusted for inflation in 2023.

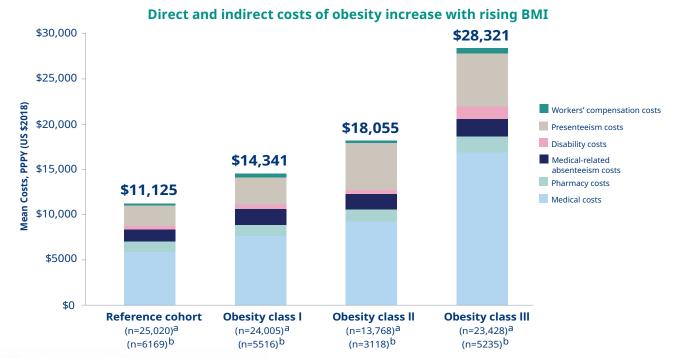
^{&#}x27;Total cost based on Medical Expenditure Panel Survey data 2011-2016 (n=175,726, adults aged 20 years and older n=139,143).92

^dTotal cost per person is a mean of predicted costs for respondents in each BMI category, controlling for age, sex, and other covariates in the two-part model.⁹²

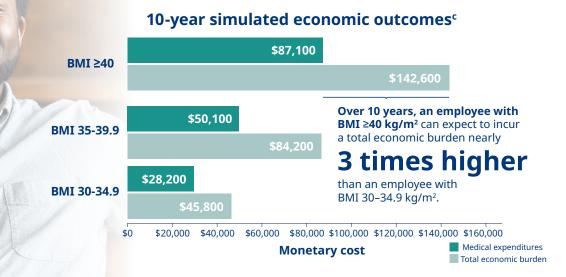
RAMASAMY STUDY

Actor portrayal.

Obesity was a strong predictor of high direct and indirect costs in a study of major United States industries³⁴



The economic burden of comorbidities increases exponentially over time⁹⁴



^aTotal sample size for direct costs (eg, medical and pharmacy costs).³⁴

^bSample size for indirect costs (eg, medical-related absenteeism, disability, presenteeism, and worker's compensation), representing the number of employees with work-loss coverage.³⁴

^cPopulation included 100,000 adults with obesity and 100,000 demographically matched normal-weight adults. Data taken from 2005-2012 NHANES and shown in the graph as cumulative over 10 years and as medical expenditure and total economic burden.⁹⁴

PPPY=per-patient per-year.

The complications of obesity result in significant direct medical costs

Total direct medical costs of obesity-related complications in a hypothetical health plan of 100,000 members^{71,95,96,a}







T2D ~\$33,356,661

~\$18,820,186

4030 affected members **7792** affected members **1259** affected members ~\$6,345,575

> The impact of obesity-related comorbidities can be seen in your medical and pharmacy costs.

Actor portrayal.

Obesity is associated with high indirect costs for employers

Absenteeism

 Nationally, presence of obesity increases job absenteeism by 3.00 workdays per worker per year (a 128% increase). Compared with workers with normal weight, national-level per-worker job absenteeism increases97,b:

Class I Obesity	Class II Obesity	Class III Obesity
2.07 days (88.5% 个)	3.67 days (156.8% 个)	7.13 days (304.7% ↑)

 The average loss of productivity due to job absenteeism related to obesity ranges from ~\$344 to ~\$688 per worker annually, an aggregate national loss of ~\$17.0 billion to ~\$34.1 billion per year^{71,97,c}

Short-term disability⁹⁸

- Employees with obesity-related complications are nearly 2x as likely to file claims
- The number of claims can increase by 37% as BMI increases

Workers' compensation⁹⁹

Claims were 160% higher for employees with obesity^d

^dStudy specific to the Louisiana Workers' Compensation Corporation Claims Payment Database for open claims. Study included ~2300 injured employees filing workers' compensation claims.99

CAD=coronary artery disease; OA=osteoarthritis.

^aCosts were calculated in 2018 USD and adjusted for inflation in 2023.

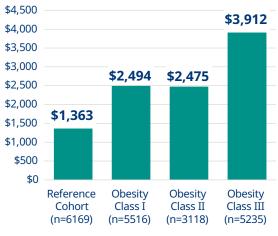
^bStudy sample included 50,789 employed adults aged 20 to 65 years with data from the 2001-2016 Medical Expenditure Panel Survey (MEPS), a nationally representative survey of civilian, non-institutionalized adults in the United States. For the purposes of estimating the number of workdays lost, "affected workdays" were those in which respondents lost half or more of the day due to illness and injury." ^c2017 USD were adjusted for inflation in 2023.

The direct and indirect costs associated with obesity vary across industries^{100,a}

In a study of medical, pharmacy, absenteeism, and disability costs, costs increased with higher obesity classes for all industries. Industries studied included:

- Government, education, and religious services
- Manufacturing and energy
- Finance and insurance
- Technology
- Transportation
- Healthcare
- Retail stores and consumer goods
- Other (food, entertainment, and other services)





Mean Total Cost

Compared with employees in the healthcare industry, the following industries had significantly higher direct healthcare costs among employees with obesity:

- Government, education, and religious services
- Other (food, entertainment, and other services)
- Technology

Actor portrayal.

Impact on cost of treatment

Obesity may increase the cost of drugs with weight-based dosing. Here are examples of various weight-based dosage drugs for select chronic conditions and their annual cost.^{101,b}

Potential annual costs for weight-based dosage drugs for select chronic conditions				
	Routine prophylaxis to prevent or reduce bleeding episodes	Chronic inflammatory demyelinating polyneuropathy	Metastatic breast cancer	Colorectal cancer
Patient A Body weight: 70 kg Height: 170 cm	\$643,860	\$228,899	\$163,900	\$182,138
Patient B Body weight: 150 kg Height: 170 cm	\$1,379,700	\$490,497	\$351,213	\$251,809
Difference in treating patients A and B	\$735,840	\$261,599	\$187,313	\$69,671

The methodology for selecting drugs in this category involved considering weight-based dosed branded treatments across various clinical categories.

^aA retrospective longitudinal cohort study of 39,196 employees was conducted between 2010 and 2017 using data from the Optum Health Reporting and Insights employer claims database. Costs are reported in 2018 USD.¹⁰⁰

^bFor estimation purposes only. A single product in each category was selected. The annual costs were calculated based on the September 2023 wholesale acquisition costs (WAC) of the selected medications from Redbook and the dosing information from the package inserts as of February 2024 of the selected medications. The inputs for the calculation included actual body weight and cost per mg or mL. The annual cost per patient was determined, and the difference in cost of 1 year of treatment is noted between Patient A and Patient B.

GERS=government, education, and religious services.

Obesity treatment guidelines

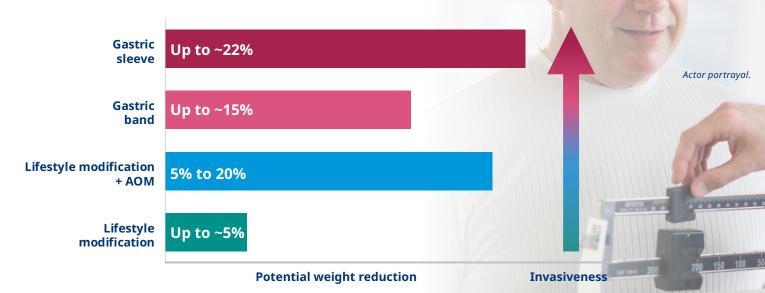
Obesity management may require several treatment approaches^{3,22,a}

Treatment	BMI category (kg/m²)									
ireatment	25-26.9	27-29.9	30-34.9	35-39.9	≥40					
Diet, physical activity, and behavior therapy	Yes, with comorbidities	Yes	Yes	Yes	Yes					
benavior eneropy										
Pharmacotherapy		Yes, with comorbidities	Yes	Yes	Yes					
Surgery			Yes, with comorbidities	Yes	Yes					

Actor portrayal.

Providing a comprehensive range of weightmanagement options may help meet the needs of individuals with obesity

Available treatments for obesity vary in indication, effectiveness, and invasiveness^{3,41,102-104}



^a"Yes" alone means that the treatment is indicated regardless of presence or absence of comorbidities. The solid arrow signifies the point at which treatment is initiated.

Multiple major medical associations support using AOMs in a treatment approach for obesity

AOMs, along with lifestyle modifications for appropriate individuals as a part of a comprehensive obesity management approach, are indicated by the following societies:

- American Heart Association (AHA)/American College of Cardiology (ACC)/The Obesity Society (TOS)³
- American Association of Clinical Endocrinology (AACE)/American College of Endocrinology (ACE)⁴¹
- American Medical Association (AMA)¹⁰⁵
- American Gastroenterological Association (AGA)¹⁰⁶

Actor portrayal.

Guidelines from AACE/ACE agree on AOM recommendations⁴¹

AOMs are supported by AACE/ACE as an adjunct to lifestyle therapy in 3 situations⁴¹:



When individuals experience failure on lifestyle therapy alone



When individuals with overweight and at least 1 weightrelated comorbidity or obesity experience weight regain after initial success on lifestyle therapy alone



When individuals with overweight and at least 1 weight-related comorbidity or obesity experience weight-related complications (particularly if severe)

Actor portrayal.

AGA GUIDELINES

The AGA recommends adding AOMs to lifestyle interventions over continuing lifestyle interventions alone¹⁰⁶

The current AGA recommendations on pharmacological interventions for management of obesity suggest:



• Adding an AOM to lifestyle interventions over continuing lifestyle interventions alone in adults with obesity or overweight with weight-related complications who have had an inadequate response to lifestyle interventions alone



portraya

- AOMs generally need to be used chronically
- The selection of the medication or intervention should be based on the clinical profile and needs of the patient, including (but not limited to):
 - Comorbidities
 - Patient preferences
 - Costs
 - Access to the therapy

The AMA supports health insurance coverage parity for evidence-based treatments for obesity¹⁰⁵

The AMA recognizes that:

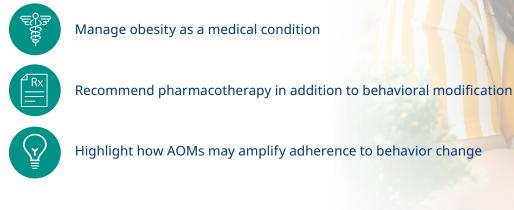
- The cost of weight-reduction medication can be a significant access barrier for people with obesity unless their health plan provides coverage
- Insurance coverage barriers limit broad access to medications
- Providing evidence-based treatment options, including AOMs, aligns with a comprehensive approach to manage obesity

The AMA's policy includes coverage of FDA-approved medications without exclusions or additional carve-outs. "The AMA will urge health insurers to provide coverage of available FDAapproved weight-loss medications...to demonstrate a commitment to the health and well-being of our patients."

AMA Trustee Bobby Mukkamala, M.D.

Currently, AOMs are more accessible than in the past and are intended for use with lifestyle modification^{107,108}

The current Endocrine Society Clinical Practice Guidelines from the Pharmacological Management of Obesity emphasize the need to¹⁰⁸:



Actor portrayal.

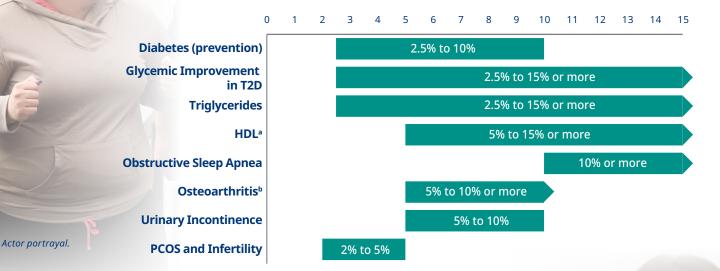
FOR THE FIRST TIME IN 15 YEARS, Adolescent treatment guidelines from the AAP have been updated¹⁰⁹

	Pharmacotherapy	Bariatric Surgery
Population	Adolescents 12 years and older with obesity (BMI ≥95 th percentile)	Adolescents 13 years and older with severe obesity (BMI ≥120% of the 95 th percentile for age and sex)
Recommendation	Pharmacotherapy, according to medication indications, risks, and benefits, as an adjunct to healthy behavior and lifestyle treatment	Evaluation for metabolic and bariatric surgery to local or regional comprehensive, multidisciplinary, pediatric, metabolic, and bariatric surgery centers

AAP=American Academy of Pediatrics.

Weight reduction of 2% to >15% can lead to clinical improvements in many comorbidities associated with obesity⁵⁰

Clinical benefits provided by percent weight reduction



Studies indicate that a 5% to 10% weight reduction can help curb the economic impact of costly comorbidities⁴¹

Estimated impact per each case avoided in the United States over 10 years^{101,110}:

Coronary heart disease and stroke • 3.3 million cases avoided • ~\$2.97 PMPM associated savings	 Hypertension 3.6 million cases avoided ~\$0.41 PMPM associated savings
Diabetes	Arthritis
• 4.1 million cases avoided	• 1.9 million cases avoided
• ~ \$2.08 PMPM associated savings	• ~ \$0.55 PMPM associated savings

Actor portrayal.

Another study found that, with a given percent reduction in BMI, savings were greater for^{111,c}:

- Individuals with higher BMI
- Those with diabetes than for those without diabetes
- The economic benefits of sustained weight reduction are contingent upon the appropriate weightmanagement approach being available for all obesity classes.

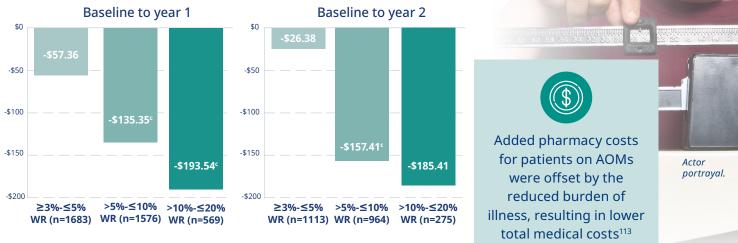
^bWhile weight reduction of 5% or more may provide a clinical benefit to the signs and symptoms of osteoarthritis, no change is evident in knee MRIs or X-rays.⁵

^cUsing data from the Medical Expenditure Panel Survey for 2000-2010, 2-part models of instrumental variables were estimated. Models were estimated for all adults, as well as separately for those with and without diabetes. Study investigators calculated the causal impact of changes in BMI on medical care expenditures, cost savings for specific changes in BMI, and total excess medical care expenditures caused by obesity. HDL=high-density lipoprotein; PCOS=polycystic ovarian syndrome; PMPM=per-member-per-month.

^aNot true for BMI >40 kg/m².⁵⁰

Healthcare cost savings were greater for individuals with obesity who had a larger magnitude of weight reduction

In a retrospective cohort study, adjusted mean per-patient-per-month (PPPM) total healthcare savings were greater in all weight reduction groups compared with no weight change^{112,a,b}

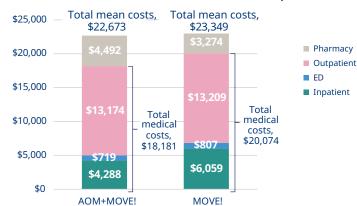


AOM usage was low (<0.5%) among the study population.¹¹²

Added pharmacy costs for patients on AOMs were offset by reduced burden of illness, resulting in lower total medical costs¹¹³

- The Motivating Overweight/Obese Veterans Everywhere! (MOVE!) program, introduced by the VA in 2006, uses lifestyle modifications to aid in obesity management
- Compared with those who only participated in lifestyle modifications (the MOVE! cohort), participants who also received AOMs (the AOM+MOVE! cohort)^d:
- Were more likely to have a weight decrease of >5% to 10% at 6 months, a trend that persisted at 12 and 24 months
- Had improved measures of cardiometabolic parameters at 6 months^e
- Had lower rates of inpatient visits and emergency department visits

Total costs for AOM+MOVE! vs MOVE! cohorts, 2010-2020



The AOM+MOVE! cohort experienced \$1893 less total medical costs compared with the MOVE! cohort.

^bHealthcare costs were measured as PPPM all-cause costs and included inpatient visits, physician office visits, emergency room visits, and pharmacy costs.¹¹²

°P<0.05.112

^dIn a retrospective cohort study from January 2010 to April 2020, the AOM+MOVE! and MOVE! cohorts were matched in a 1:2 ratio. The AOMs used for the study were orlistat, liraglutide, phentermine/topiramate ER, and naltrexone ER/bupropion ER.¹¹³

^eMeasures included systolic and diastolic blood pressure, total cholesterol, LDL cholesterol, and HbA1c.¹¹³

ED=emergency department; ER=extended release; HbA1c=hemoglobin A1c; LDL=low density lipoprotein; VA=U.S. Department of Veterans Affairs; WR=weight reduction.

^aThis retrospective, longitudinal cohort study utilized claims data from IBM MarketScan® and Explorys® EHR databases, focusing on patients covered by United States employer-sponsored private health insurance from January 1, 2012, to June 30, 2014. The objective of the study was to assess the short-term (1 year) and sustained (approximately 2 years) effects of nonsurgical weight loss on PPPM total all-cause healthcare costs among commercially insured adults (aged 18–64 years) with obesity (BMI ≥30 kg/m²). Participants' BMI measurements at 12, 24, and 36 months were utilized to categorize them into no-weight-change cohorts, and weight-loss cohorts from the index date for data analysis. Additionally, it's important to note that the study specifically targeted adults with obesity receiving care at Tier 1 medical facilities offering comprehensive medical, surgical, psychological, nutritional, and other care. Therefore, the findings may not be generalizable to patients in ambulatory or primary care settings.¹¹²

Impact of 10% weight reduction on drug costs¹⁰¹

Examples of annual costs for four branded weight-based dosed drugs before and after 10% weight reduction for select chronic conditions.^a

Plaque Psoriasis						
Patient Characteristics	Annual Drug Cost					
Body weight: 110 kg, Height: 170 cm	\$116,395					
Loss of 10% body weight: 99 kg	\$58,197					
Difference in annual drug cost after reduced body weight: \$58,197 (50% cost reduction)						

Actor portrayal.

Colorectal cancer						
Patient Characteristics	Annual Drug Cost					
Body weight: 110 kg, Height: 170 cm	\$38,574					
Loss of 10% body weight: 99 kg	\$28,909					
Difference in annual drug cost after reduced body weight: \$9,665 (25% cost reduction)						

Metastatic breast cancer					
Patient Characteristics	Annual Drug Cost				
Body weight: 110 kg, Height: 170 cm	\$93,657				
Loss of 10% body weight: 99 kg \$67,901					
Difference in annual drug cost after reduced body weight:					

\$25,756 (27% cost reduction)

		•					•	•	1
Routine	nronh		n rovo ni	OF FOR		000			

Patient Characteristics	Annual Drug Cost				
Body weight: 110 kg, Height: 170 cm	\$367,920				
Loss of 10% body weight: 99 kg	\$266,742				
Difference in annual drug cost after reduced body weight:					

\$101,178 (27% cost reduction)

^aFor estimation purposes only. A single product in each category was selected. The annual costs were calculated based on the September 2023 wholesale acquisition costs (WAC) of the selected medications from Redbook and the dosing information from the package inserts as of September 2023 of the selected medications. The inputs for the calculation included actual body weight and cost per mg or mL. The annual cost per patient was determined, and the difference in cost of 1 year of treatment is noted between Patient A and Patient B.

Summary



Obesity is...

- A chronic disease^{1,2}
- Highly prevalent, and the prevalence has been increasing³²
- Associated with more than 200 comorbidities⁴³



Obesity is costly due to...

- Excess medical expenditures⁹²
- Obesity-related complications^{41,95}
- Indirect costs for employers, such as absenteeism, disability, and workers' compensation⁹⁷⁻⁹⁹



AOMs are...

- Part of a comprehensive treatment approach to weight reduction, in addition to ongoing lifestyle modifcations³
- Supported by recognized third-party guidelines⁴¹
- More accessible today than in the past^{107,108}



Obesity treatment can result in...

- Improve certain obesity-related comorbidities⁴¹
- Healthcare cost savings¹¹²

Actor portrayal.

References:

- 1. Recognition of obesity as a disease H-440.842. American Medical Association. Accessed January 17, 2023. https://policysearch.ama-assn. org/policyfinder/detail/obesity?uri=%2FAMADoc%2FHOD.xml-0-3858.xml
- 2. Mechanick JI, Garber AJ, Handelsman Y, Garvey WT. American Association of Clinical Endocrinologists' position statement on obesity and obesity medicine. *Endocr Pract*. 2012;18(5):642-648. doi:10.4158/EP12160.PS
- Jensen MD, Ryan DH, Apovian CM, et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. *Circulation*. 2014;129(25 Suppl 2):S102-S138. doi:10.1161/01.cir.0000437739.71477.ee
- 4. Obesity. World Health Organization. Accessed March 8, 2023. https://www.who.int/health-topics/obesity#tab=tab_1
- 5. Farr OM, Li CR, Mantzoros CS. Central nervous system regulation of eating: insights from human brain imaging. *Metab Clin Exp.* 2016;65:699-713. doi:10.1016/j.metabol.2016.02.002
- 6. Guyenet SJ, Schwartz MW. Clinical review: regulation of food intake, energy balance, and body fat mass: implications for the pathogenesis and treatment of obesity. *J Clin Endocr Metab*. 2012;97(3):745-755. doi:10.1210/jc.2011-2525
- 7. Cassidy RM, Ton Q. Hunger and satiety gauge reward sensitivity. Front Endocrinol (Lausanne). 2017;8:104. doi:10.3389/fendo.2017.00104
- 8. Druce MR, Small CJ, Bloom SR. Minireview: gut peptides regulating satiety. Endocrinology. 2004;145:2660-2665. doi:10.1210/en.2004-0089
- **9.** Berthoud HR, Münzberg H, Morrison CD. Blaming the brain for obesity: integration of hedonic and homeostatic mechanisms. *Gastroenterology*. 2017;152(7):1728-1738. doi:10.1053/j.gastro.2016.12.050
- 10. Badman MK, Flier JS. The gut and energy balance: visceral allies in the obesity wars. *Science*. 2005;307(5717):1909-1914. doi:10.1126/ science.1109951
- **11.** Lam YY, Ravussin E. Analysis of energy metabolism in humans: a review of methodologies. *Mol Metab.* 2016;5(11):1057-1071. doi:10.1016/j.molmet.2016.09.005
- Sumithran P, Prendergast LA, Delbridge E, et al. Long-term persistence of hormonal adaptations to weight loss. N Engl J Med. 2011;365(17):1597-1604. doi:10.1056/NEJMoa1105816
- 13. Wadden TA, Tronieri JS, Butryn ML. Lifestyle modification approaches for the treatment of obesity in adults. *Am Psychol.* 2020;75(2):235-251. doi:10.1037/amp0000517
- 14. Hebebrand J, Hinney A, Knoll N, Volckmar AL, Scherag A. Molecular genetic aspects of weight regulation. *Dtsch Arztebl Int.* 2013;110(19):338-344. doi:10.3238/arztebl.2013.0338
- **15.** Bray GA, Kim KK, Wilding JPH. Obesity: a chronic relapsing progressive disease process. A position statement of the World Obesity Federation. *Obes Rev.* 2017;18(7):715-723. doi:10.1111/obr.12551
- 16. Schwartz MW, Seeley RJ, Zeltser LM, et al. Obesity pathogenesis: an Endocrine Society scientific statement. *Endocr Rev.* 2017;38(4):267-296. doi:10.1210/er.2017-00111
- 17. Suzuki K, Jayasena CN, Bloom SR. Obesity and appetite control. Exp Diabetes Res. 2012;2012:824305. doi:10.1155/2012/824305
- **18.** Tirthani E, Said MS, Rehman A. *Genetics and Obesity*. StatPearls [Internet]. Updated July 31, 2023. Accessed January 26, 2024. https://www.ncbi.nlm.nih.gov/books/NBK573068/
- Lee A, Cardel M, Donahoo WT. Social and Environmental Factors Influencing Obesity. In: Feingold KR, Anawalt B, Blackman MR, et al, eds. Endotext. South Dartmouth (MA): MDText.com, Inc.; October 12, 2019. Accessed January 26, 2024. https://www.ncbi.nlm.nih.gov/books/ NBK278977/
- 20. Obesity. Mayo Clinic. Updated July 22, 2023. Accessed January 26, 2024. https://www.mayoclinic.org/diseases-conditions/obesity/ symptoms-causes/syc-20375742
- **21.** The practical guide: identification, evaluation, and treatment of overweight and obesity in adults. NIH Publication No. 00-4084. National Institutes of Health. National Heart, Lung, and Blood Institute. Published October 2000. Accessed January 26, 2024. https://www.nhlbi.nih. gov/files/docs/guidelines/prctgd_c.pdf
- **22.** Eisenberg D, Shikora SA, Aarts E, et al. 2022 American Society for Metabolic and Bariatric Surgery (ASMBS) and International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO): indications for metabolic and bariatric surgery. *Surg Obes Relat Dis.* 2022;1-12. doi:10.1016/j.soard.2022.08.013
- 23. Bernard SP. Let's get on the same page when coding BMI and obesity. AAPC. Published February 27, 2019. Accessed January 26, 2024. https://www.aapc.com/blog/45879-lets-get-on-the-same-page-when-coding-bmi-and-obesity/
- 24. About adult BMI. Centers for Disease Control and Prevention. Accessed January 17, 2023. https://www.cdc.gov/healthyweight/assessing/ bmi/adult_bmi/index.html
- **25.** Body measurements. Centers for Disease Control and Prevention. National Center for Health Statistics. Accessed August 14, 2023. https://www.cdc.gov/nchs/fastats/body-measurements.htm
- 26. QuickFacts: United States. United States Census Bureau. Accessed January 17, 2023. https://www.census.gov/quickfacts/fact/table/US/ PST045222
- 27. Stierman B, Afful J, Carroll MD, et al. National Health and Nutrition Examination Survey 2017–March 2020 prepandemic data files development of files and prevalence estimates for selected health outcomes. Centers for Disease Control and Prevention. Accessed January 17, 2023. https://www.cdc.gov/nchs/data/nhsr/nhsr158-508.pdf
- 28. Ward ZJ, Bleich SN, Cradock AL, et al. Projected U.S. state-level prevalence of adult obesity and severe obesity. N Engl J Med. 2019;381(25):2440-2450. doi:10.1056/NEJMsa1909301
- 29. Prevalence of obesity and severe obesity among adults: United States, 2017–2018. Centers for Disease Control and Prevention. Accessed March 6, 2023. https://www.cdc.gov/nchs/products/databriefs/db360.htm
- 30. Explore by topic. Centers for Disease Control and Prevention. Accessed January 17, 2023. https://nccd.cdc.gov/BRFSSPrevalence/rdPage. aspx?rdReport=DPH_BRFSS.ExploreByTopic&irbLocationType=StatesAndMMSA&islClass=CLASS14&islTopic=TOPIC09&islYear=2021 &rdRnd=56160
- **31.** Trend tables. Health, United States, 2019 [supplement]. Centers for Disease Control and Prevention. National Center for Health Statistics. Accessed August 4, 2023. https://www.cdc.gov/nchs/data/hus/2019/026-508.pdf
- 32. Adult obesity facts. Centers for Disease Control and Prevention. Updated May 17, 2022. Accessed January 17, 2023. https://www.cdc.gov/ obesity/data/adult.html

- **33.** Summary health statistics: National Health Interview Survey, 2018: table A-15a. Centers for Disease Control and Prevention. Accessed January 17, 2023. https://ftp.cdc.gov/pub/Health_Statistics/NCHS/NHIS/SHS/2018_SHS_Table_A-15.pdf
- **34.** Ramasamy A, Laliberté F, Aktavoukian SA, et al. Direct and indirect cost of obesity among the privately insured in the United States: a focus on the impact by type of industry. *J Occup Environ Med*. 2019;61(11):877-886. doi:10.1097/JOM.00000000001693
- **35.** QuickFacts: United States. United States Census Bureau. Accessed July 26, 2023. https://www.census.gov/quickfacts/fact/table/US/ PST045221
- **36.** Facts about hypertension. Centers for Disease Control and Prevention. Accessed May 30, 2024. https://www.cdc.gov/high-blood-pressure/data-research/facts-stats/?CDC_AAref_Val=https://www.cdc.gov/bloodpressure/facts.htm
- **37.** Hirode G, Wong RJ. Trends in the prevalence of metabolic syndrome in the United States, 2011-2016. *JAMA*. 2020;323(24):2526-2528. doi:10.1001/jama.2020.4501
- **38.** Osteoarthritis (OA). Centers for Disease Control and Prevention. Accessed May 30, 2024. https://www.cdc.gov/arthritis/types/ osteoarthritis.htm
- **39.** Type 2 diabetes. Centers for Disease Control and Prevention. Accessed May 30, 2024. https://www.cdc.gov/diabetes/about/about-type-2-diabetes.html?CDC_AAref_Val=https://www.cdc.gov/diabetes/basics/type2.html
- **40.** Heart disease facts. Centers for Disease Control and Prevention. Accessed May 30, 2024. https://www.cdc.gov/heart-disease/data-research/facts-stats/?CDC_AAref_Val=https://www.cdc.gov/heartdisease/facts.htm
- **41.** Garvey WT, Mechanick JI, Brett EM, et al; Reviewers of the AACE/ACE Obesity Clinical Practice Guidelines. American Association of Clinical Endocrinologists and American College of Endocrinology comprehensive clinical practice guidelines for medical care of patients with obesity. *Endocr Pract.* 2016;22(suppl 3):1-203. doi:10.4158/EP161365.GL
- **42.** Obesity and cancer. Centers for Disease Control and Prevention. Accessed May 30, 2024. https://www.cdc.gov/cancer/risk-factors/obesity. html?CDC_AAref_Val=https://www.cdc.gov/cancer/obesity/index.htm
- **43.** What is obesity? Obesity Medicine Association. Published July 31, 2023. Accessed December 21, 2023. https://obesitymedicine.org/what-is-obesity/
- **44.** Masters RK, Reither EN, Powers DA, Yang YC, Burger AE, Link BG. The impact of obesity on US mortality levels: the importance of age and cohort factors in population estimates. *Am J Public Health*. 2013;103(10):1895-1901. doi:10.2105/AJPH.2013.301379
- **45.** Pratt LA, Brody DJ. Depression and obesity in the U.S. adult household population, 2005-2010. NCHS Data Brief No. 167. Published October 2014. Accessed January 23, 2023. https://www.cdc.gov/nchs/data/databriefs/db167.pdf
- **46.** Engstrom D. Obesity and depression. Obesity Action Coalition. Accessed January 23, 2023. https://www.obesityaction.org/wp-content/uploads/Depression-and-Obesity.pdf
- 47. Dempsey JA, Veasey SC, Morgan BJ, O'Donnell CP. Pathophysiology of sleep apnea. *Physiol Rev.* 2010;90(1):47-112. doi:10.1152/ physrev.00043.2008
- **48.** Jehan S, Zizi F, Pandi-Perumal SR, et al. Obstructive sleep apnea and obesity: implications for public health. *Sleep Med Dis Int J.* 2017;1(4):93-99. doi:10.15406/smdij.2017.01.00019
- **49.** Romero-Corral A, Caples SM, Lopez-Jimenez F, Somers VK. Interactions between obesity and obstructive sleep apnea: implications for treatment. *Chest*. 2010;137(3):711-719. doi:10.1378/chest.09-0360
- **50.** Ryan DH, Yockey SR. Weight loss and improvement in comorbidity: differences at 5%, 10%, 15%, and over. *Curr Obes Rep.* 2017;6(2):187-194. doi:10.1007/s13679-017-0262-y
- 51. Liu Y, Yang L, Stampfer MJ, Redline S, Tworoger SS, Huang T. Physical activity, sedentary behavior and incidence of obstructive sleep apnoea in three prospective US cohorts. *Eur Respir J.* 2022;59(2):2100606. doi:10.1183/13993003.00606-2021
- **52.** National Institutes of Health. The practical guide: identification, evaluation, and treatment of overweight and obesity in adults. Published October 2020. Accessed April 6, 2023. https://www.nhlbi.nih.gov/files/docs/guidelines/prctgd_c.pdf
- 53. Ryan DH, Ravussin E, Heymsfield S. COVID 19 and the patient with obesity the editors speak out. *Obesity (Silver Spring)*. 2020;28(5):847. doi:10.1002/oby.22808
- **54.** Waters H, Graf M. America's obesity crisis: the health and economic costs of excess weight. Milken Institute. Published October 2018. Accessed April 6, 2023. https://milkeninstitute.org/sites/default/files/reports-pdf/Mi-Americas-Obesity-Crisis-WEB_2.pdf
- 55. Klop B, Elte JW, Cabezas MC. Dyslipidemia in obesity: mechanisms and potential targets. *Nutrients*. 2013;5(4):1218-1240. doi:10.3390/ nu5041218
- 56. Guh DP, Zhang W, Bansback N, Amarsi Z, Birmingham CL, Anis AH. The incidence of co-morbidities related to obesity and overweight: a systematic review and meta-analysis. *BMC Pub Health*. 2009;9:88. doi:10.1186/1471-2458-9-88
- **57.** Grant B, Sandelson M, Agyemang-Prempeh B, Zalin A. Managing obesity in people with type 2 diabetes. *Clin Med (Lond)*. 2021;21(4):e327-e231. doi:10.7861/clinmed.2021-0370
- **58.** Powell-Wiley TM, Poirier P, Burke L, et al. Obesity and cardiovascular disease: a scientific statement from the American Heart Association. *Circulation*. 2021;143:e984–e1010. doi:10.1161/CIR.00000000000973
- **59.** Kim MS, Kim WJ, Khera AV, et al. Association between adiposity and cardiovascular outcomes: an umbrella review and meta-analysis of observational and Mendelian randomization studies. *Eur Heart J.* 2021;42(34):3388-3403. doi:10.1093/eurheartj/ehab454
- **60.** Kernan WN, Inzucchi SE, Sawan C, Macko RF, Furie KL. Obesity: a stubbornly obvious target for stroke prevention. *Stroke*. 2013;44:278-286. doi:10.1161/STROKEAHA.111.639922
- **61.** Weight and fertility. American Society for Reproductive Medicine. Updated 2015. Accessed December 21, 2023. https://www.reproductive facts.org/globalassets/_rf/news-and-publications/bookletsfact-sheets/english-pdf/weight_and_fertility_factsheet.pdf
- **62.** Zhu L, Zhou B, Zhu X, et al. Association between body mass index and female infertility in the United States: data from National Health and Nutrition Examination Survey 2013-2018. *Int J Gen Med*. 2022;15:1821-1831. doi:10.2147/IJGM.S349874
- **63.** Kurt RK, Okyay AG, Hakverdi AU, et al. The effect of obesity on inflammatory markers in patients with PCOS: a BMI-matched case-control study. *Arch Gynecol Obstet.* 2014;290(2):315-319. doi:10.1007/s00404-014-3199-3
- 64. Barber TM, Franks S. Obesity and polycystic ovary syndrome. *Clin Endocrinol (Oxf)*. 2021;95:531-541. doi:10.1111/cen.14421
- **65.** Riestenberg C, Jagasia A, Markovic D, Buyalos RP, Azziz R. Health care-related economic burden of polycystic ovary syndrome in the United States: pregnancy-related and long-term health consequences. *J Clin Endocrinol Metab.* 2022;107(2):575-585. doi:10.1210/clinem/dgab613

- **66.** Teede H, Deeks A, Moran L. Polycystic ovary syndrome: a complex condition with psychological, reproductive and metabolic manifestations that impacts on health across the lifespan. *BMC Med.* 2010;8:41. doi:10.1186/1741-7015-8-41.
- **67.** Dixon AE, Peters U. The effect of obesity on lung function. *Expert Rev Respir Med.* 2018;12(9):755-767. doi:10.1080/17476348.2018.1506331
- **68.** Baffi CW, Winnica DE, Holguin F. Asthma and obesity: mechanisms and clinical implications. *Asthma Res Pract*. 2015;1:1. doi:10.1186/ s40733-015-0001-7
- **69.** Koebnick C, Fischer H, Daley MF, et al. Interacting effects of obesity, race, ethnicity and sex on the incidence and control of adult-onset asthma. *Allergy Asthma Clin Immunol*. 2016;12:50. doi:10.1186/s13223-016-0155-8
- **70.** Nurmagambetov T, Kuwahara R, Garbe P. The economic burden of asthma in the United States, 2008-2013. *Ann Am Thorac Soc.* 2018;15(3):348-356. doi:10.1513/AnnalsATS.201703-259OC
- 71. CPI inflation calculator. U.S. Bureau of Labor Statistics. CPI inflation calculator. Accessed May 24, 2024. https://www.bls.gov/data/ inflation_calculator.htm
- 72. Song HJ, Blake KV, Wilson DL, Winterstein AG, Park H. Medical costs and productivity loss due to mild, moderate, and severe asthma in the United States. J Asthma Allergy. 2020;13:545-555. doi:10.2147/JAA.S272681
- 73. Thalheimer A, Bueter M. Excess body weight and gastroesophageal reflux disease. Visc Med. 2021;37:267-272. doi:10.1159/000516050
- 74. Hampel H, Abraham NS, El-Serag HB. Meta-analysis: obesity and the risk for gastroesophageal reflux disease and its complications. *Ann Intern Med.* 2005;143:199-211. doi:10.7326/0003-4819-143-3-200508020-00006
- **75.** El-Serag HB, Sweet S, Winchester CC, Dent J. Update on the epidemiology of gastro-oesophageal reflux disease: a systematic review. *Gut.* 2014;63(6):871-880. doi:10.1136/gujnl-2012-304269
- **76.** Everhart JE, Ruhl CE. Burden of digestive diseases in the United States part I: overall and upper gastrointestinal diseases. *Gastroenterology*. 2009;136(2):376-386. doi:10.1053/j.gastro.2008.12.015
- 77. Polyzos SA, Kountouras J, Mantzoros CS. Obesity and nonalcoholic fatty liver disease: from pathophysiology to therapeutics. *Metabolism*. 2019;92:82-97. doi:10.1016/j.metabol.2018.11.014
- **78.** Li L, Liu DW, Yan HY, Wang ZY, Zhao SH, Wang B. Obesity is an independent risk factor for non-alcoholic fatty liver disease: evidence from a meta-analysis of 21 cohort studies. *Obes Rev.* 2016;17(6):510-519. doi:10.1111/obr.12407
- **79.** Nonalcoholic fatty liver disease (NAFLD). American Liver Foundation. Updated December 21, 2023. Accessed December 21, 2023. https://liverfoundation.org/liver-diseases/fatty-liver-disease/nonalcoholic-fatty-liver-disease-nafld/
- **80.** Wong RJ, Kachru N, Martinez DJ, Moynihan M, Ozbay AB, Gordon SC. Real-world comorbidity burden, health care utilization, and costs of nonalcoholic steatohepatitis patients with advanced liver diseases. *J Clin Gastroenterol*. 2021;55:891-902. doi:10.1097/MCG.000000000001409
- **81.** Steele CB, Thomas CC, Henley SJ, et al. Vital signs: trends in incidence of cancers associated with overweight and obesity-United States, 2005-2014. *MMWR Morb Mortal Wkly Rep.* 2017;66(39):1052-1058. doi:10.15585/mmwr.mm6639e1
- **82.** Obesity and musculoskeletal care. American Academy of Orthopaedic Surgeons. Updated February 2022. Accessed March 9, 2023. https://www.aaos.org/globalassets/about/bylaws-library/information-statements/1040-obesity-and-musculoskeletal-care.pdf
- **83.** Narouze S, Souzdalnitski D. Obesity and chronic pain: systematic review of prevalence and implications for pain practice. *Reg Anesth Pain Med.* 2015;40(2):91-111. doi:10.1097/AAP.0000000000218
- **84.** Bourne R, Mukhi S, Zhu N, Keresteci M, Marin M. Role of obesity on the risk for total hip or knee arthroplasty. *Clin Orthop Relat Res.* 2007;465:185-188. doi:10.1097/BLO.0b013e3181576035
- **85.** Whitlock G, Lewington S, Sherliker P, et al; Prospective Studies Collaboration. Body-mass index and cause-specific mortality in 900,000 adults: collaborative analyses of 57 prospective studies. *Lancet.* 2009;373(9669):1083-1096. doi:10.1016/S0140-6736(09)60318-4
- **86.** Grover SA, Kaouache M, Rempel P, et al. Years of life lost and healthy life-years lost from diabetes and cardiovascular disease in overweight and obese people: a modelling study. *Lancet Diabetes Endocrinol*. 2015;3(2):114-122. doi:10.1016/S2213-8587(14)70229-3
- **87.** Pugliese G, Liccardi A, Graziadio C, Barrea L, Muscogiuri G, Colao A. Obesity and infectious diseases: pathophysiology and epidemiology of a double pandemic condition. *Int J Obes (Lond)*. 2022;46(3):449-465. doi:10.1038/s41366-021-01035-6
- **88.** Shashaty MG, Stapleton RD. Physiological and management implications of obesity in critical illness. *Ann Am Thorac Soc*. 2014;11(8):1286-1297. doi:10.1513/AnnalsATS.201404-159FR
- **89.** Kim TS, Roslin M, Wang JJ, et al. BMI as a risk factor for clinical outcomes in patients hospitalized with COVID-19 in New York. *Obesity (Silver Spring)*. 2021;29(2):279-284. doi:10.1002/oby.23076
- 90. Ou X, Jiang J, Lin B, et al. Antibody responses to COVID-19 vaccination in people with obesity: a systematic review and meta-analysis. Influenza Other Respir Viruses. 2023;17(1):e13078. doi:10.1111/irv.13078
- **91.** Honce R, Schultz-Cherry S. Impact of obesity on influenza A virus pathogenesis, immune response, and evolution. *Front Immunol.* 2019;10:1071. doi:10.3389/fimmu.2019.01071
- **92.** Ward ZJ, Bleich SN, Long MW, Gortmaker SL. Association of body mass index with health care expenditures in the United States by age and sex. *PLoS ONE*. 2021;16(3):e0247307. doi:10.1371/journal.pone.0247307
- **93.** Mocarski M, Tian Y, Smolarz BG, McAna J, Crawford A. Use of International Classification of Diseases, Ninth Revision codes for obesity: trends in the United States from an electronic health record-derived database. *Popul Health Manag.* 2018;21(3):222-230. doi:10.1089/ pop.2017.0092
- **94.** Su W, Huang J, Chen F, et al. Modeling the clinical and economic implications of obesity using microsimulation. *J Med Econ.* 2015;18(11):886-897. doi:10.3111/13696998.2015.1058805
- 95. Lopez C, Bendix J, Sagynbekov K. Weighing down America: 2020 update. A community approach against obesity. Published December 2020. Accessed April 17, 2023. https://milkeninstitute.org/sites/default/files/reports-pdf/Weighing%20Down%20America%20v12.3.20_0.pdf
- **96.** ACS demographic and housing estimates. US Census Bureau. Accessed April 17, 2023. https://data.census.gov/ table?q=population+2018&tid=ACSDP1Y2018.DP05
- 97. Cawley J, Biener A, Meyerhoefer C, et al. Job absenteeism costs of obesity in the United States: national and state-level estimates. J Occup Environ Med. 2021;63(7):565-573. doi:10.1097/JOM.0000000002198
- **98.** Van Nuys K, Globe D, Ng-Mak D, Cheung H, Sullivan J, Goldman D. The association between employee obesity and employer costs: evidence from a panel of U.S. employers. *Am J Health Promot*. 2014;28(5):277-285. doi:10.4278/ajhp.120905-QUAN-428

- 99. Tao XG, Su PY, Yuspeh L, Lavin RA, Kalia-Satwah N, Bernacki EJ. Is obesity associated with adverse workers' compensation claims outcomes? *J Occup Environ Med*. 2016;58(9):880-884. doi:10.1097/JOM.0000000000834
- **100**. Ramasamy A, Laliberté F, Aktavoukian SA, et al. Direct, absenteeism, and disability cost burden of obesity among privately insured employees: a comparison of healthcare industry versus other major industries in the United States. *J Occup Environ Med.* 2020;62(2):98-107. doi:10.1097/JOM.00000000001761
- 101. Data on file. Novo Nordisk Inc.; Plainsboro, NJ.
- 102. FEHB program carrier letter No. 2023-01. U.S. Office of Personnel Management. January 18, 2023.
- **103**. Courcoulas AP, Christian NJ, Belle SH, et al. Weight change and health outcomes at three years after bariatric surgery among patients with severe obesity. *JAMA*. 2013;310 (22):2416-2425. doi:10.1001/jama.2013.280928
- **104**. Berry MA, Urrutia L, Lamoza P, et al. Sleeve gastrectomy outcomes in patients with BMI between 30 and 35-3 years of follow-up. *Obes Surg.* 2018;28:649-655. doi:10.1007/s11695-017-2897-x
- **105.** AMA urges insurance coverage parity for emerging obesity treatment options [press release]. American Medical Association. Published November 14, 2023. Accessed December 13, 2023. https://www.ama-assn.org/press-center/press-releases/ama-urges-insurance-coverage-parity-emerging-obesity-treatment-options
- **106**. Grunvald E, Shah R, Hernaez R, et al. AGA clinical practice guideline on pharmacological interventions for adults with obesity. *Gastroenterology*. 2022;163(5):1198-1225. doi:10.1053/j.gastro.2022.08.045
- **107**. Dieguez G, Pyeneson B, Tomicki S, et al. Obesity in a claims-based analysis of the commercially insured population: prevalence, cost, and the influence of obesity services and anti-obesity medication coverage on health expenditures. Milliman Report. March 2021. Accessed May 31, 2024. https://www.novonordiskworks.com/content/dam/nnw/resource-library/pdf/milliman-white-paper.pdf
- 108. Apovian CM, Aronne LJ, Bessesen DH, et al. Pharmacological management of obesity: an Endocrine Society clinical practice guideline [published correction appears in J Clin Endocrinol Metab. 2015;100(5):2135-2136]. J Clin Endocrinol Metab. 2015;100(2):342-362. doi:10.1210/jc.2014-3415
- **109.** Hampl SE, Hassink SG, Skinner AC, et al. Clinical practice guideline for the evaluation and treatment of children and adolescents with obesity. *Pediatrics*. 2023;151(2):e2022060640.
- **110**. Levi J, Segal LM, St Laurent R, Lang A, Rayburn J. F as in fat: how obesity threatens America's future. Robert Wood Johnson Foundation. Published September 2012. Accessed January 23, 2023. https://www.tfah.org/report-details/f-as-in-fat-how-obesity-threatens-americasfuture-2012/
- 111. Cawley J, Meyerhoefer C, Biener A, Hammer M, Wintfeld N. Savings in medical expenditures associated with reductions in body mass index among US adults with obesity, by diabetes status. *Pharmacoeconomics*. 2015;33(7):707-722. doi:10.1007/s40273-014-0230-2
- **112**. Ding Y, Fan X, Blanchette CM, Smolarz BG, Weng W, Ramasamy A. Economic value of weight loss in adults with obesity. *J Manag Care Spec Pharm*. 2021;27(1):37-50. doi:10.18553/jmcp.2020.20036
- **113**. Garvey TW, Cheng M, Ramasamy A, et al. Clinical and cost benefits of anti-obesity medication for US veterans participating in the MOVE! weight management program. *Popul Health Manag.* 2023;26(1):72-82. doi:10.1089/pop.2022.0227

