

Impact of Obesity and Weight-Related Comorbidities



What is obesity?

Obesity, commonly misperceived as a lifestyle choice, is a multifaceted, chronic condition influenced by social, environmental, genetic, and behavioral elements¹

Major medical associations refer to obesity:



The **American Medical Association (AMA)** asserts that "obesity is a disease state with multiple pathophysiological aspects requiring a range of interventions to advance obesity treatment and prevention."²



The **American Association of Clinical Endocrinology (AACE)** also recognizes "obesity as a complex, multifactorial condition characterized by excess body fat. It must be viewed as a chronic disorder that essentially requires perpetual care, support, and follow-up. Obesity can cause many other diseases, and it warrants recognition by healthcare providers and payers."³

The link between obesity and comorbidities

Obesity-related comorbidities may have far-reaching consequences, affecting not only physical health but also daily life.⁴

Select examples of weight-related comorbidities^{5-7,a}



The comorbidities of obesity may pose a serious threat to individuals within your organization.^{5,6} There are also ways that obesity can impact how the body responds to certain infections.⁷ **The subsequent pages/sections will explore the above-mentioned comorbidities in more detail**.

^aThe above list is not exhaustive and is intended to illustrate only a range of key complications. ^bMASLD was formerly known as nonalcoholic fatty liver disease (NAFLD).

Prevalence of obesity and cases of comorbidities attributable to obesity

Obesity continues to be a significant concern in the United States, with its prevalence on a steady rise.¹

- The adult obesity prevalence rate in the United States increased from 30.5% during the period of 1999-2000 to 41.9% for 2017-March 2020^{8,a}
- The link between obesity and numerous severe diseases and health conditions is extensively documented¹

Disease	Total Attributable Cases
Asthma	4,766,263
Congestive heart failure	1,481,286
Coronary heart disease	4,119,416
Type 2 diabetes	13,183,232
Dyslipidemia	17,881,860
Hypertension	35,048,396
Osteoarthritis	25,493,351
Stroke	1,841,188

Attributable cases of select obesity-related comorbidities, 2018^{1,b}



^bPopulation attributable risk (PAR) was used to calculate the approximate number of cases of a particular disease that are attributed to obesity.¹

The economic burden of obesity and associated health conditions

- Calculating the full economic impact of obesity is complex. Medical (direct) costs and missed workdays (indirect cost) are just part of the broader expenses linked to obesity¹
- The combined (direct and indirect) estimated costs for people who have obesity with comorbidities are high; the costs are shown in the table below

Annual estimated costs attributable to obesity in select obesity-related comorbidities in the United States (2018 costs adjusted to 2023 costs)^{1,a}

Disease	Direct Costs in Millions⁵	Indirect Costs in Millions ^ь	Total Costs in Millions
Asthma	\$10,041	\$16,111	\$26,152
Congestive heart failure	\$7,326	\$2,837	\$10,164
Coronary heart disease	\$20,373	\$31,605	\$51,979
Type 2 diabetes	\$107,074	\$198,668	\$305,742
Dyslipidemia	\$16,156	\$0	\$16,156
Hypertension	\$33,746	\$519,383	\$553,129
Osteoarthritis	\$60,421	\$157,060	\$217,480
Stroke	\$12,518	\$13,421	\$25,939

^aInflation adjusted using the United States Consumer Price Index inflation calculator at https://data.bls.gov/cgi-bin/cpicalc.pl, with December 2018 and July 2023 as the index dates.

^bDirect cost includes medical treatment and indirect costs were determined by lost workdays (absenteeism, etc), calculated as lost employee output.¹

Obesity and certain weight-related comorbidities can increase risk of cardiovascular diseases¹⁰

- Obesity contributes to certain cardiovascular risk factors such as dyslipidemia, type 2 diabetes, and hypertension (HTN)¹⁰
- Every 5 kg/m² increase in body mass index (BMI) is associated with an increased risk of adverse cardiovascular outcomes for the following^{11,a}:



Overweight and obesity are linked to increased cardiovascular disease risk¹²

No.

A meta-analysis established a significant association between overweight and obesity with the incidence of cardiovascular diseases.¹²

		Obesity increases risk
CAD	≥1.7x ^{12,b}	
Stroke	~1.5x ^{12,b}	Obesity is estimated to impact 18% to 44% of stroke patients ¹³

CAD=coronary artery disease; CHD=coronary heart disease; HF=heart failure.

^aAnalysis was performed using 12 systematic reviews and 53 meta-analyses (including >501 cohort studies) and 12 Mendelian randomization (informing causality) studies that were published until January 2021 to evaluate the association between obesity-related indices and CVD risks (eg, coronary heart disease, heart failure, hypertension, 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 Mendelian randomization studies.¹¹

^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. 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.¹²

Obesity and dyslipidemia: contributors to cardiovascular disease¹⁴

BMI (between 25 and 34.9 kg/m²) and/or a high waist circumference may be associated with increased risk of type 2 diabetes, dyslipidemia, hypertension, and cardiovascular disease^{10,15}

In clinical practice, waist circumference predicts health-risk more accurately than BMI alone.¹⁴

In one study, compared with individuals of normal weight, the prevalence of dyslipidemia was higher in those with overweight and obesity.^{16,17,a} $\uparrow 55\%$ adults with overweight obesity adults with obesity

Clinical data showed¹⁸:

- Weight reduction ranging from **2.5% to over 15%** is associated with **triglyceride reductions** (applicable across all BMI classes)
- Similarly, weight reduction ranging from **5% to over 15%** is associated with **increased HDL levels**, excluding BMI >40 kg/m²

Obesity increases diabetes risk^{14,19}



A meta-analysis suggests that obesity can increase the risk of T2D 6.7x in men and 12.4x in women.^{12,b}



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Overweight or obesity affects **90% of patients with diabetes**.²⁰

According to the American Diabetes Prevention Program, an average body-weight reduction of ~6% (5.6 kg), achieved through lifestyle modification, reduced the incidence of diabetes by 58%.^{21,c}

The study analyzed NHANES survey data from 1999-2010, involving 10,568 adults aged 18 and older. Cardiovascular risk factors (eg, diabetes,

hypertension, dyslipidemia, and smoking) were assessed. Prevalence and temporal trends of these risk factors within each BMI group were estimated.¹⁶ ^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 (9 studies met the inclusion criteria and were included). 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.¹²

^cIn this lifestyle intervention study, patients without diabetes (N=3243, average BMI=34 kg/m²) with elevated fasting and post-load plasma glucose levels were randomly assigned to 1 of 3 groups: placebo, 850 mg metformin twice daily, or a lifestyle modification program. The program aimed for at least a 7% body weight loss and at least 150 minutes of weekly physical activity.²¹

The risk of developing MASLD is increased for patients with obesity^{22,23,a,b,c}

Obesity is independently (ie, irrespective of other metabolic factors) linked with MASLD.^{22,23}

• People with obesity have a **3.5-fold higher risk** of MASLD compared to lean individuals

Polycystic ovary syndrome (PCOS) and overweight or obesity

PCOS is one of the most prevalent (range 5% to 13%) endocrine disorders in reproductive-aged women.²⁴ Epidemiological data suggest that between 38% and 88% of women with PCOS have either overweight or obesity.25

Obesity can exacerbate PCOS, which can lead to issues such as hyperandrogenism, hirsutism, and pregnancy complications.²⁶

· Benefits in reproductive and metabolic outcomes can be achieved with a modest weight reduction of **5% to 10%**. Lifestyle changes demonstrate benefits even if women stay within the overweight or obesity range²⁶

A systematic review and meta analysis showed that women with PCOS are almost twice as likely to have overweight (1.95 relative risk) and nearly three times as likely to have obesity (2.77 relative risk) compared to women without PCOS.^{27,d}

Obesity may be associated with reproductive health issues, especially in women²⁸



There is a 3% increased risk of infertility associated with each 1-unit increase in BMI in women whose BMI is ≥19.5 kg/m².^{29,e}

^aMASLD (metabolic dysfunction-associated steatotic liver disease) was formerly known as non-alcoholic fatty liver disease (NAFLD).

^bA meta-analysis of 21 cohort studies (13 prospective and 8 retrospective, with a total of 381,655 participants) was performed to assess the NAFLD risk associated with obesity or increased BMI. The data was analyzed for pooled relative risks (RRs) with 95% confidence intervals (CIs) using a randomeffects model.23

^cThe data in these studies were utilizing the NAFLD definition.

^dA systematic review and meta analysis was performed using a literature search using different search engines for studies reporting the prevalence of overweight, obesity, or central obesity in women with and without PCOS. The data were presented as prevalence (%) and RR (95% CI). Random-effect models were used to calculate the pooled RR.²⁷

eThe study's design was a cross-sectional analysis including 3623 adult females ages 18 to 45 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 was assumed to be "fertile" status.²⁹

Obesity and overweight may be associated with cancers throughout the body³⁰

Obesity and overweight have been linked with an increased risk of at least **13 types of cancer**, such as adenocarcinoma of the esophagus; cancers of the breast (in postmenopausal women), colon and rectum, endometrium (corpus uterus), gallbladder, gastric cardia, kidney (renal cell), liver, ovary, pancreas, and thyroid; meningioma, and multiple myeloma.³⁰

Notably, **40%** of all cancers diagnosed in 2014 were linked to overweight or obesity.³⁰



Obesity's impact on the chest wall and lung mechanics: links to asthma and reactive airway disease³¹

Obesity affects ~38% of adults (aged 18 years and older) with asthma³¹

The risk of developing asthma is increased for people with overweight and obesity compared with individuals with a BMI in the normal range.^{32,a}

Patients with severe or difficult to treat asthma and overweight or obesity who gained at least 5 pounds reported worse asthma control and a greater number of steroid bursts than those who had stable weight or lost at least 5 pounds.^{33,b}

Classification ³²	BMI ³²	Increased risk ³²
Overweight	25 to <30 kg/m ²	12%
Class I Obesity	30 to <35 kg/m ²	37%
Class II Obesity	35 to <40 kg/m ²	64%
Class III Obesity	40 to <50 kg/m ²	97%
	≥50 kg/m²	149%

The link between obesity and obstructive sleep apnea (OSA)

~45% of adults with obesity have OSA^{34,c}



Individuals with mild OSA are 6x more likely to experience OSA progression if they gain 10% or more of their initial weight.³⁴



The risk of OSA may decrease with increased physical activity.^{35,36,d}

^aThis retrospective cohort study analyzed electronic health record 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.³²

^bIn this study, baseline and 12-month follow-up data of TENOR patients aged 18 years and older with severe or difficult-to-treat asthma were analyzed using 2396 patients (1730 women, 666 men). Patients were categorized into 3 groups (\geq 5 lb loss, stable, or \geq 5 lb gain) based on a \pm 5 lb difference between baseline and 12-month follow-up weight. Five pounds were chosen for assessing weight gain or loss, because changes of that magnitude were sufficiently common in the cohort to allow for comparisons. Main objective of the study was to evaluate the effect of weight change on asthma control, asthma-related quality of life, asthma symptoms, and number of steroid bursts.³³

^cObesity is only one of the risk factors for OSA.³⁴

^dIn this prospective study, 50,332 women (Nurses' Health Study 2002-2012), 68,265 women (Nurses' Health Study II 1995-2013), and 19,320 men (Health Professionals Follow-up Study 1996-2012) were followed. Recreational physical activity and sedentary time were assessed every 2 to 4 years, and physician-diagnosed OSA incidence was identified via self report. Hazard ratios for OSA incidence associated with physical activity and sedentary behavior was determined using Cox models.³⁵

Obesity contributes to soft tissue damage and osteoarthritis (OA) of the hip and knee³⁷

Obesity may increase the risk of OA and is associated with an increased need for joint replacement surgery.^{37,38}

Patients undergoing total joint arthroplasty in the United States³⁷



A reduction of 5% to 10% in weight may improve knee functionality, walking speed and distance, and pain.¹⁸

Gastroesophageal reflux disease (GERD)

GERD affects up to 70% of people with severe obesity³⁹

In one analysis, compared to people of normal weight, the likelihood of experiencing GERD	1.5x greater	2.0x greater
symptoms was ^{40,a} :	People with overweight	People with obesity

A reduction of 5% to 10% of body weight in women and \geq 10% in men may reduce GERD symptoms.^{41,b}

^aA 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.⁴⁰

^bIn this prospective cohort study, 332 adult subjects (mean age 46 years, 66% women) were enrolled. Participants with overweight or obesity (BMI 25-39.9 kg/m²) joined a structured weight reduction program involving dietary changes (including reduced calories), increased physical activity, and behavioral modifications. Baseline and 6-month assessments included measurements of BMI, waist circumference, and completion of a validated reflux disease questionnaire.⁴¹

The interrelationship between obesity and depression is complex



43% of adults aged ≥20 years in the United States with depression have obesity.⁴²

There is a bidirectional connection between depression and obesity, with obesity increasing the risk of depression and vice versa.^{43,44}

Association between obesity/overweight exposure and depression onset, and vice versa: findings from a systematic review and meta analysis

Overweight or obesity $ ightarrow$ depression44	Depression $ ightarrow$ overweight or obesity44
27% greater risk for people with overweight	20% greater risk of developing overweight
55% greater risk for people with obesity	58% greater risk of developing obesity

Obesity increases the risk of complications and adverse outcomes from acute illnesses and infections⁴⁵

Obesity also affects respiratory infections⁴⁵

Obesity can contribute to⁴⁵:

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

In contrast to adults with a normal weight, the likelihood of hospitalization related to respiratory issues during the influenza season are^{46,a}: BMI 30.0 kg/r

1.45x ↑	2.12x ↑
BMI 30.0 kg/m² to <35 kg/m²	BMI ≥35.0 kg/m ²

^aA cohort study conducted over 12 influenza seasons (1996-2008) in Ontario, Canada, included 82,545 respondents aged 18 to 64 years who had completed population health surveys. Individuals who had responded to a survey within 5 years prior to the beginning of an influenza season were enrolled for the study. Logistic regression was employed to investigate the association between self-reported BMI and hospitalization for specific respiratory diseases (pneumonia and influenza, acute respiratory diseases, and chronic lung diseases) in both the entire cohort and when stratified by chronic condition status for the analysis. The study's main focus was to assess hospitalization rates for pneumonia and influenza as its primary outcome measure.⁴⁶

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