Making the Connection

CV risk in people with obesity

Prevalence rates of obesity among adults in the United States are on the rise[1,2,a]:

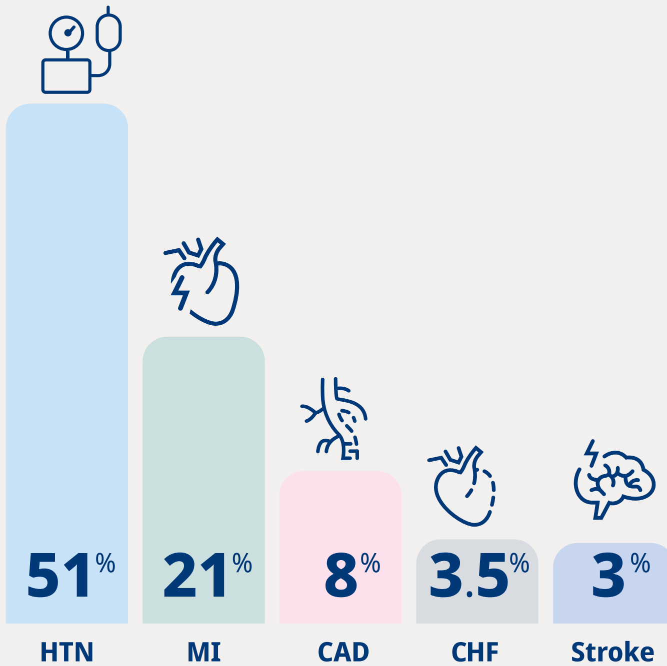
BMI	Classification	US prevalence
25 to 29.9 kg/m^2	Overweight	30.7%
30+ kg/m^2	Obesity	42.4%
40+ kg/m^2	Severe obesity	9.2%

The increasing prevalence of obesity is considered a major contributor to the rising burden of CVD in the United States[3]:

CVD is a leading cause of death and disability in people living with overweight or obesity[5]

- In 2015, more than ⅔ of obesity-related deaths were caused by CVD[6,b]
- 34% of obesity-related disability adjusted life years were caused by CVD among individuals with obesity[6,b]

Prevalence of CVD complications in adults with obesity (BMI ≥30 kg/m^2)[4,c]:



Developed by Novo Nordisk in partnership with PCNA and ADCES. These associations have received financial support from Novo Nordisk for their collaboration in the creation of this educational program and related co-promotional and advertising opportunities.

BMI=body mass index; CAD=coronary artery disease; CHF=congestive heart failure; CV=cardiovascular; CVD=cardiovascular disease; HTN=hypertension; MI=myocardial infarction. [a]Age-adjusted percentage of US adults with overweight, obesity, and severe obesity, 2017–2018 data from the National Health and Nutrition Examination Survey (NHANES). [b]As estimated by the Global Burden of Disease investigators. [c]The 2005–2012 NHANES compared 100,000 people with obesity (BMI <30 kg/m^2 to >40 kg/m^2) with 100,000 people of normal weight (BMI<25 kg/m^2).

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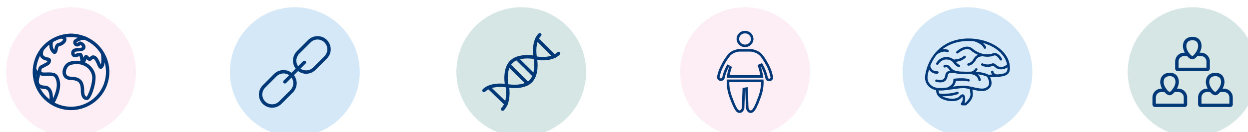
Pathophysiology of obesity

The Obesity Medicine Association (OMA) defines obesity as

"a chronic, progressive, relapsing, and treatable multifactorial, neurobehavioral disease, wherein an increase in body fat promotes adipose tissue dysfunction and abnormal fat mass physical forces, resulting in adverse metabolic, biomechanical, and psychosocial health consequences." [7]

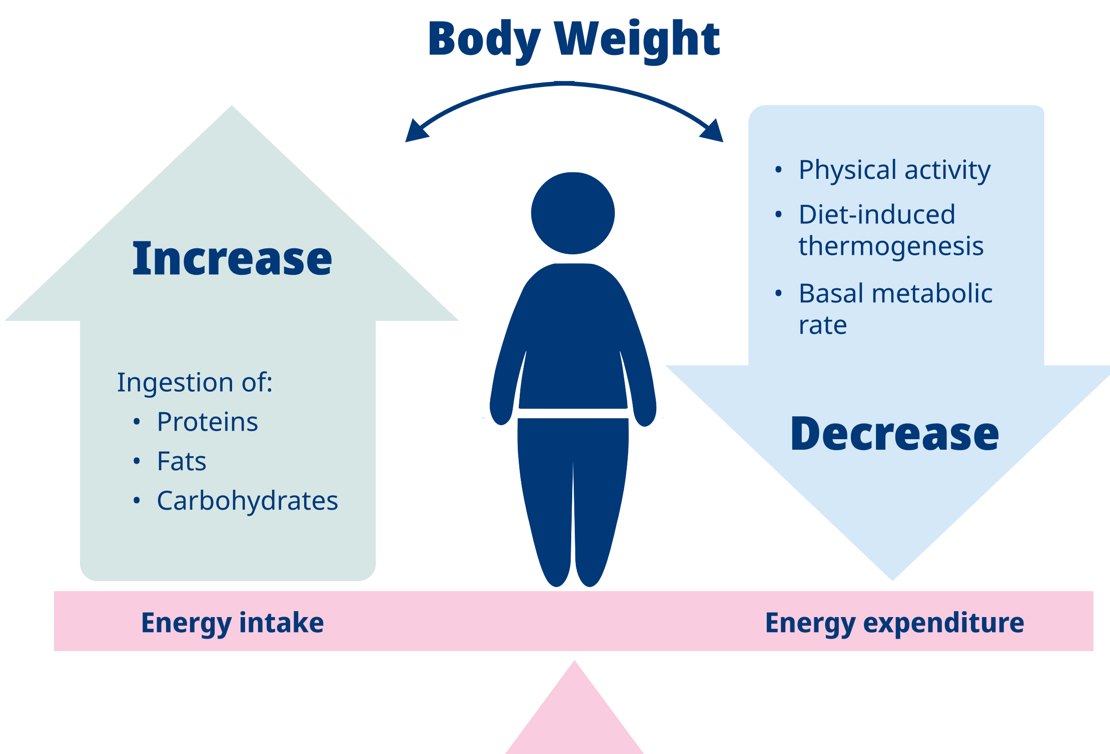
Obesity has multiple pathophysiologic origins that lead to an imbalance between energy intake and expenditure during an extended period[8]:

Environmental **Epigenetic** **Genetic** **Physiological** **Behavioral** **Sociocultural**



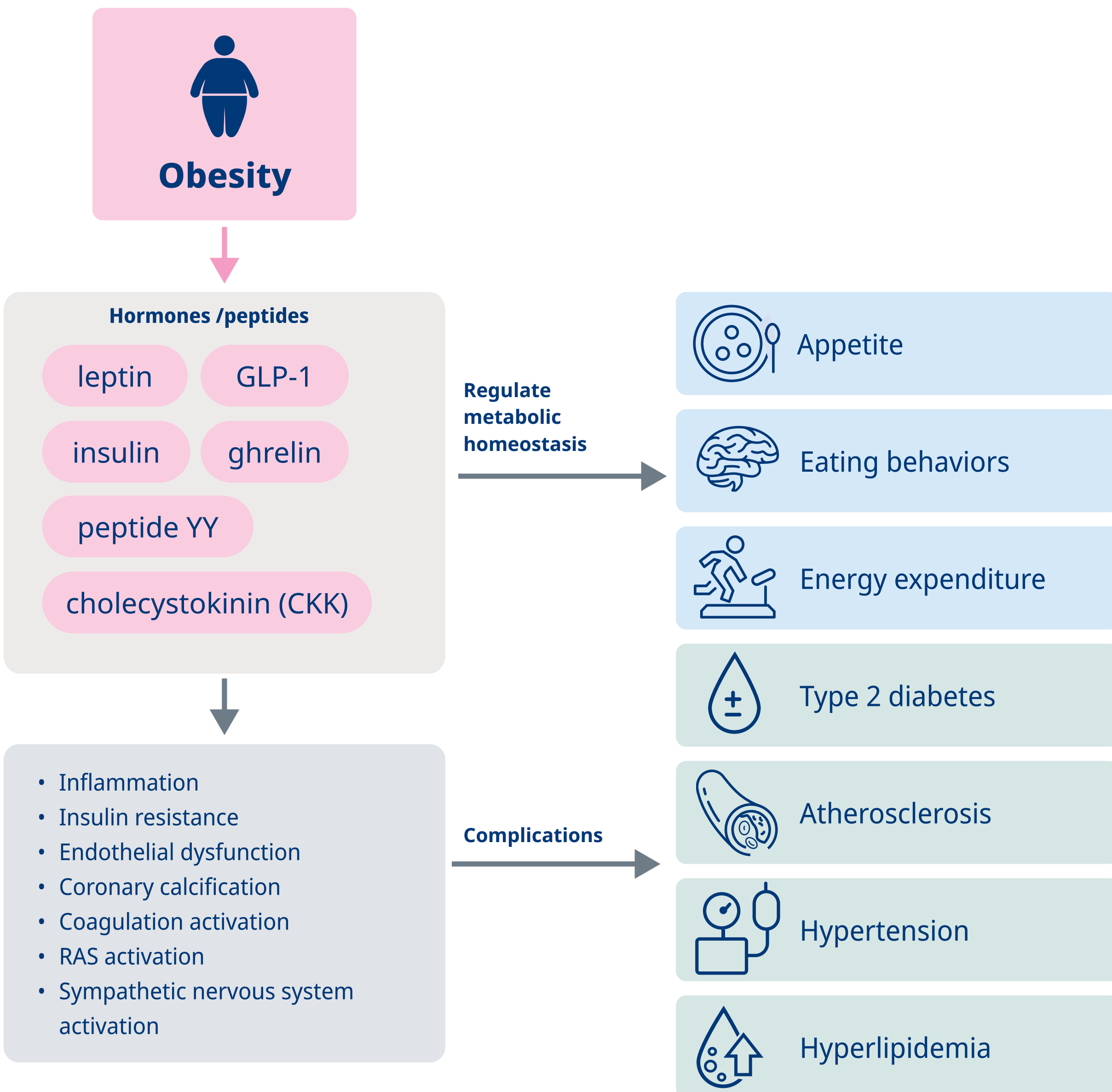
Growing evidence suggests that obesity is a complex disease of abnormal physiology that involves more than the passive accumulation of calories[9]

- Obesity results from pathophysiological processes that lead to the failure of normal weight and energy regulatory mechanisms; this in turn can lead to an elevated, biologically defended body fat mass
- Although the homeostatic mechanisms appear to drive maintenance and defense of excess body-fat mass, evidence suggests it is a failure of this energy balance homeostasis that results in the pathogenesis of obesity



Relationship between obesity and CVD

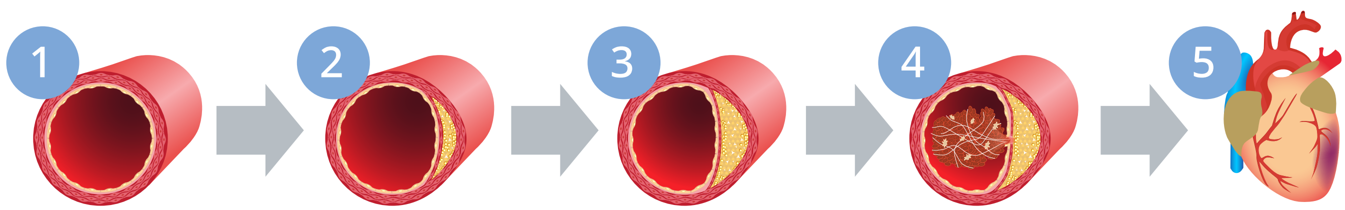
- Adipose tissue is associated with metabolic and inflammatory systems, with protective effects on energy homeostasis[10]
- Peptides and proteins secreted by adipose tissue regulate biological and physiological conditions and play an important role in obesity, insulin resistance, inflammatory and immune functions, atherosclerosis, and CVD[10]



CVD=cardiovascular disease; GLP-1 glucagon-like peptide-1; RAS=renin angiotensin system.

Obesity and atherosclerosis

- Obesity and increased adipose tissue can influence the pathogenesis of atherosclerosis[10]
- Obesity accelerates early atherosclerotic changes through several mechanisms, including insulin resistance and inflammation[6]
- Obesity may increase pericardial fat, intracardial fat, visceral fat, and liver and skeletal muscle fat[7]
- Visceral and epicardial fat share the same mesodermal embryonic origin, both increase the risk for atherosclerosis, and both are highly correlated with coronary artery calcification[7]



1 Healthy artery

2 Fatty streak and atheroma formation

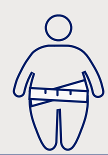
3 Vulnerable plaque formation

4 Plaque rupture and thrombosis

5 ASCVD event such as:
- Angina
- Stroke
- MI
- Sudden cardiac death

Abdominal obesity and increased risk of CV events

- Central adiposity, has been associated with increased cardiometabolic and ASCVD risk[6,11,a]
- High WC, even in individuals with normal weight, may unmask higher CVD risk[11]
- Several organizations recommend combining WC and BMI to assess obesity-related risk in clinical evaluations[6,11]



Disease risk (relative to normal weight and waist circumference)

	Men <40 in (102 cm) **Women <35 in** (88 cm)	**Men >40 in** (102 cm) **Women >35 in** (88 cm)
Healthy Weight 18 kg/m² – 24.9 kg/m²	—	**High**
Overweight 25 kg/m² – 29.9 kg/m²	**Increased**	**High**
Obesity Class I 30.0 kg/m² – 34.9 kg/m²	**High**	**Very High**
Obesity Class II 35.0 kg/m² – 39.9 kg/m²	**Very High**	**Very High**
Obesity Class III ≥40.0 kg/m²	**Extremely High**	**Extremely High**

ASCVD=athersclerotic cardiovascular disease; BMI=body mass index; CVD=cardiovascular disease; MI=myocardial infarction; WC=waist circumference. [a]According to data from the National Health and Nutrition Examination Survey, those in the US population with a waist-to-hip ratio indicative of central obesity had a higher risk of CV mortality compared to those with the same BMI but without central adiposity.

Management of obesity and CVD risk factors[12-15]

Clinical component	Weight-loss goal	Clinical goals	Guidelines recommend
Metabolic syndrome	10%	• Prevention of type 2 diabetes • Reduce CV risk	Per AACE/ACE and AHA/ACC/TOS guidelines: • Assess risk of CVD and presence of weight-related comorbidities in people with overweight and obesity • The Expert Panel recommends by expert opinion to manage CV risk factors or other obesity-related conditions if found, regardless of weight loss efforts
Hypertension	5-15% or more	• Lower systolic and diastolic BP • Reductions in number and/or doses of antihypertensive medications	Per AACE/ACE and OMA guidelines: • Evaluate BP in all people with overweight/obesity • Target BP of less than 130/80 mm Hg • Lifestyle therapy to achieve BP reduction goals
Dyslipidemia	5-15% or more	• Lower triglycerides, LDL-C, non-HDL-C • Raise HDL-C	Per AACE/ACE, ACC/AHA, and OMA guidelines: • Obtain lipid panel in all people with overweight/obesity • Lifestyle therapy to achieve therapeutic targets • Consider medication-assisted weight loss combined with lifestyle therapy when necessary to achieve sufficient improvements in lipids
Type 2 Diabetes	5-15% or more	• Reduction in A1C • Reduction in number and/or doses of glucose-lowering medications • Improvement in intermediate CV risk factors	Per AACE/ACE and ADA guidelines: • Obtain A1C or other glycemic measure in all people with type 2 diabetes and overweight/obesity • Lifestyle therapy to achieve A1C target with consideration of weight • Consider glucose-lowering agents that are proven to reduce CV risk (label indication) • Consider bariatric surgery in people with obesity (BMI >30 kg/m^2)
MASLD	5% or more	Reduction in intrahepatocellular lipid	Per AACE/ACE guidelines: • Evaluate for MASLD (formerly known as NAFLD) in all people with overweight/obesity

AACE= American Association of Clinical Endocrinologists; ACC= American College of Cardiology; ACE=American College of Endocrinology; ADA=American Diabetes Association; AHA=American Heart Association; BMI=body mass index; BP=blood pressure; CV=cardiovascular; CVD=cardiovascular disease; HDL-C=high density lipoprotein cholesterol; LDL-C= low density lipoprotein cholesterol; MASLD=metabolic dysfunction-associated steatotic liver disease; NAFLD=nonalcoholic fatty liver disease; OMA=Obesity Medicine Association.

Talking to patients about weight and CV risk

The 5As provide a framework to start a conversation. Consider that weight is a sensitive and personal topic. Discussions about weight can be difficult for the individual, leaving them open to feelings of embarrassment, fear, and blame.[16]

Ask
- Ask for permission to discuss weight
- Explore readiness for change

Assess
- Assess obesity class and stage
- Assess for drivers, complications, and barriers

Advise
- Explain benefits of modest weight loss
- Explain need for long-term strategy
- Discuss treatment options

Agree
- Agree on realistic weigh-loss expectations and focus on behavioral goals and health outcomes
- Agree on treatment plan

Assist
- Provide education and resources
- Refer to appropriate providers
- Arrange follow-up

When CV risk is communicated well, it can serve as a key motivator to initiate and carry out treatment plans and lifestyle changes

Effective CV risk communication can[17]:

- Help individuals make informed decisions
- Foster patient engagement
- Increase alignment with treatment recommendations
- Help individuals be aware of adverse events
- Strengthen the patient-clinician relationship
- Improve quality of care

For CV risk discussions to be effective[17,18]:

- Make risk communication meaningful
- Use plain language and active listening
- Put risk into context
- Use shared decision making

Making the Connection Education Program at ObesityMakingTheConnection.com

CV=cardiovascular.

References

1. Hales CM et al. Hyattsville, MD: National Center for Health Statistics. 2020. **2.** National Institute of Diabetes and Digestive and Kidney Diseases. Accessed October 7, 2023. https://www.niddk.nih.gov/health-information/health-statistics/overweight-obesity. **3.** Lavie CJ et al. *Prog Cardiovasc Dis.* 2016;58(5):537-47. **4.** Su W et al. *J Med Econ.* 2015;18(11):886-897. **5.** Lopez-Jimenez F et al. *Eur J Prev Cardiol.* 2022:29(17);2218-2237. **6.** Powell-Wiley TM et al. *Circulation*. 2021;143:e984-e1010. **7.** Tondt J et al. Obesity Algorithm, presented by the Obesity Medicine Association 2023. **8.** Bray GA et al. *Lancet*. 2016;387(10031):1947-1956. **9.** Schwartz MW et al. *Endocr Rev.* 2017;38(4):267-296. **10.** Cercato C, Fonseca FA. *Diabetol Metab Syndr*. 2019;11:74. **11.** Arnett DK et al. *JACC*. 2019:74:e177-e232. **12.** Garvey WT et al. *Endocr Pract.* 2016;22(suppl 3):1-203. **13.** Jensen MD et al. *Circulation*. 2014;129(25 Suppl 2):S102-138. **14.** American Diabetes Association. *Diabetes Care.* 2023;46(suppl 1):S1-S291. **15.** Nguyen A et al. *Diabetes*. 2023;72(4):496-510. **16.** Vallis M et al. *Can Fam Physician.* 2013:59(1):27-31. **17.** American College of Cardiology. Accessed October 5, 2023. https://www.acc.org/-/media/Non-Clinical/Files-PDFs-Excel-MS-Word-etc/Tools-and-Practice-Support/Risk-Communications/2-Full-Toolkit.pdf?la=en&hash=81C9701F0FFFE490F854FD6AC224D5611D7A4360. **18.** Imbus J, Funk LM. (2019). Quality in Obesity Treatment. Springer, Cham. https://doi.org/10.1007/978-3-030-25173-4_17.

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