



Actor
portrayals
throughout.

FOR PATIENTS WITH WEIGHT-RELATED COMORBIDITIES
**BRING OBESITY TO THE
FOREFRONT**



Explore the role obesity can
play in your patients' health



Obesity is the first thing you see. Don't make it the last thing you talk about



Depression
Obstructive sleep apnea (OSA)
Gastroesophageal reflux disease (GERD)
Cardiovascular disease (CVD)
Asthma/reactive airway disease
Nonalcoholic fatty liver disease (NAFLD)
Polycystic ovary syndrome (PCOS)
Female infertility
Urinary stress incontinence
Male hypogonadism
Osteoarthritis (OA)
Prediabetes
Type 2 diabetes (T2D)
Hypertension
Dyslipidemia
Cancers (various)

Obesity is associated with at least 60 comorbidities, some of which can be improved through weight loss.¹⁻⁴

While the majority of patients and HCPs agree that weight loss of 10% may be beneficial to their health, patients may be waiting for HCPs to take that important first step and discuss weight management.^{5*}



It's time to bring obesity to the forefront

Weight-related comorbidities are just that: medical conditions that may often be associated with obesity.

Weight loss of **5% to 15%** or greater may result in improvements in many of these comorbidities.²

*Data from a survey that examined obesity-related perceptions, attitude and behaviors among ~3000 adults with obesity and ~600 HCPs.



Don't ignore the connection between obesity and cardiovascular disease

It's time to make weight loss a priority

In one study, patients 16 years of age and older with an elevated BMI were

~2x
as likely

to have hypertension⁶

Obesity can be associated with some common CVD risk factors, including⁷:

- Hypertension
- Dyslipidemia
- Type 2 diabetes

Obesity and its related risk factors can lead to development of cardiovascular diseases, including⁷⁻⁹:

- Coronary artery disease
- Myocardial infarction
- Heart failure



How does obesity affect cardiovascular disease?

Nearly

3 MILLION

obesity-related cardiovascular deaths occurred worldwide in 2015¹⁰

Obesity can lead to enlarged adipose tissue cells, or adipocytes, which promote low-grade systemic inflammation.¹¹ This can^{8,12}:

- Lead to vascular breakdown
- Cause structural and functional myocardial damage

Increased adipose tissue can further lead to endothelial dysfunction and cardiovascular conditions.¹²

BRING OBESITY TO THE FOREFRONT WITH YOUR PATIENTS WITH CVD RISK FACTORS

A **5% to 15% weight loss** can improve²:
triglycerides | HDL cholesterol | diastolic blood pressure



Don't overlook obesity in your patients with NAFLD

A systematic review and meta-analysis reveal that NAFLD was present in nearly 60% of patients with obesity¹³

1 in 4

adults worldwide have NAFLD¹⁴

Nonalcoholic fatty liver disease is a buildup of excess fat in the liver.¹⁵

Obesity, as well as dietary and environmental factors, can lead to raised levels of¹⁵:

- **Free fatty acids (FFAs)**
- **Free cholesterol**
- **Other lipid metabolites**

This increase in hepatic FFAs can lead to fat accumulation in the liver in the form of triglycerides and ultimately NAFLD.¹⁵

An increase in hepatic FFAs can lead to fat accumulation in the liver in the form of triglycerides; in certain patients, inflammation and liver damage can follow.^{15,16}



Waist circumference—more than elevated BMI—can increase risk for NAFLD¹⁷



BRING OBESITY TO THE FOREFRONT WITH YOUR PATIENTS WITH NAFLD

AACE/ACE guidelines recommend that patients with obesity and NAFLD should be managed with lifestyle intervention, targeting **5% to 10% weight loss**.³



What role does obesity play in your patients' PCOS?

PCOS is one of the most common endocrine disorders in women^{18,19}

Nearly
5 MILLION

US women of reproductive age have PCOS^{18,19}

Symptoms include^{20,21}:

- **Menstrual irregularities**
- **Excess androgen levels**
- **Enlarged and dysfunctional ovaries**
- **Metabolic disturbances such as insulin resistance**

Obesity and excess adipose tissue are underlying factors that may worsen PCOS²²

From
38%-88%

of women with PCOS are overweight or living with obesity²²⁻²⁴

Increased fat distribution is associated with **higher circulating levels of insulin**, which leads to increased insulin resistance and causes further androgen excess.^{22,25}

Obesity can influence gonadotropin production, and imbalances lead to further **ovulatory dysfunction and menstrual abnormalities**.^{25,26}



BRING OBESITY TO THE FOREFRONT WITH YOUR PATIENTS WITH PCOS

With a **5% to 15% or greater weight loss**, your patients can improve certain PCOS symptoms, including^{3*}:
hyperandrogenism | oligomenorrhea | anovulation

*Clinical efficacy can vary among individual patients.



How often do your patients with obesity present with joint pain?

Patients with obesity are associated with an increased risk of knee OA³

The damaging impact of obesity on OA may be due to mechanical stress and other factors²⁷⁻³¹

Mechanical stress

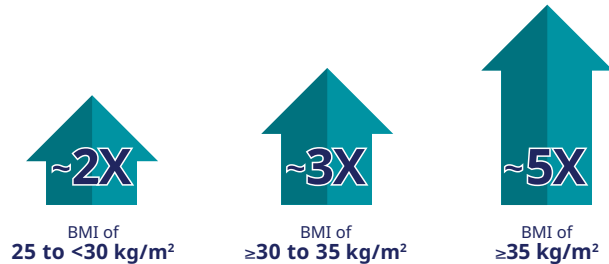
- Structural damage
- Abnormal cell activities
- Inflammation of synovial membrane

Metabolic impact through the functions of adipokines

- Additional inflammation
- Cartilage degeneration
- Bone remodeling

A meta-analysis of patients with OA showed that obesity is associated with greater pain, long-term disability, and complications following hip or knee arthroplasty.³²

Increased BMI can mean an increased risk of knee osteoarthritis³³



A population-based cohort study involving data from approximately 1.7 million Spanish adults, at least 40 years of age, over a median of about 4.5 years. The study aimed to analyze the effect of overweight and obesity on the incidence of diagnosed knee, hip, and hand osteoarthritis.



BRING OBESITY TO THE FOREFRONT WITH YOUR PATIENTS WITH OSTEOARTHRITIS

With a **5% to 10% weight loss**, knee functionality, speed, walking distance, and pain can improve—and the more weight lost, the greater the improvement.^{2,34*}

*Knee MRI and x-ray findings do not change after weight loss.



What is the relationship between obesity and your patients' type 2 diabetes?

Obesity can increase the risk of prediabetes, which can lead to type 2 diabetes³⁵

In patients with obesity and prediabetes

10%
WEIGHT LOSS

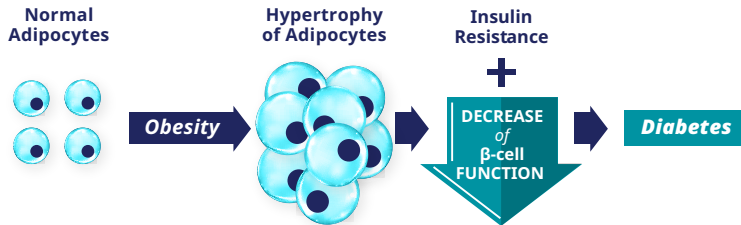
reduces the risk of developing diabetes^{2,3}

70% of patients with prediabetes—
an A1C from 5.7% to 6.4%—often
go on to develop type 2 diabetes.^{36,37}
In patients with type 2 diabetes,
a higher BMI is associated with higher
A1C (glycated hemoglobin) levels.³⁸



What is a potential mechanism linking obesity to diabetes?

Obesity is associated with insulin resistance and decreased β -cell function, which can lead to the development of diabetes.^{39,40}



Evidence suggests that genetic risk factors may be necessary for the occurrence of β -cell dysfunction.⁴⁰

BRING OBESITY TO THE FOREFRONT WITH YOUR PATIENTS WITH PREDIABETES

Weight loss may prevent or delay progression to type 2 diabetes, with an **average weight loss of 6.7% being shown to reduce the onset of diabetes by 58%**.^{2,11}

The American Diabetes Prevention Program (ADPP) was a trial of adults at high risk for development of type 2 diabetes (N=3,234) who were randomized to receive intensive lifestyle intervention, pharmacotherapy, or placebo.



Can addressing obesity improve sleep apnea?

It is estimated that nearly half of all people with obesity also have obstructive sleep apnea⁴¹

Obesity is associated with fat deposition in the upper respiratory tract, which can lead to mechanical, hormonal, and inflammatory effects, impacting the severity of OSA.^{42,43}

- Mechanical load increase** → **respiratory stress**
- Proinflammatory cytokines** → **reduced CNS activity and upper airway control**
- Oxidative stress increase** → **lowered upper airway function**

A 10% weight gain in people with an average BMI of 29 kg/m² increases the likelihood of developing moderate to severe OSA by **6 times**, and incidence increases with BMI.^{44*}

BMI	OSA Incidence^{41,45†}
25 kg/m ² to 34.9 kg/m ²	33%
35 kg/m ² to <40 kg/m ²	71%
40 kg/m ² to <50 kg/m ²	74%
50 kg/m ² to <60 kg/m ²	77%
≥60 kg/m ²	95%

*This study was population-based, prospective cohort study of 690 patients that measured the independent longitudinal association between weight change and change in sleep-disordered breathing severity.

†The intent of this study was to determine the prevalence of OSA in 290 patients with obesity presenting for weight-loss surgery.



BRING OBESITY TO THE FOREFRONT WITH YOUR PATIENTS WITH OSA

AACE guidelines recommend a weight-loss goal of **7% to 11% or more** for patients with obesity and obstructive sleep apnea.³





Bring obesity to the forefront when looking at your patients' health

Consider the following:

1. When evaluating your patients, make obesity a priority right from the start
2. Educate patients on how obesity can play a role in certain comorbid conditions
3. Design a comprehensive treatment plan together

Learn more about the impact weight loss may have on some comorbidities at

[FocusOnObesity.com](https://www.FocusOnObesity.com)



References: 1. Bays HE, McCarthy W, Christensen S, et al. Obesity algorithm 2020. Presented by the Obesity Medicine Association. Accessed November 21, 2022. <https://obesitymedicine.org/obesity-algorithm>

2. Ryan DH, Yockey SR. Weight loss and improvement in comorbidities: differences at 5%, 10%, 15% and over. *Curr Obes Rep.* 2017;6:187-194.

3. Garvey WT, Mechanick JL, Brett EM, and 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.

4. Cancers associated with overweight and obesity make up 40 percent of cancers diagnosed in the United States. Centers for Disease Control and Prevention. Accessed November 22, 2022. <https://www.cdc.gov/media/releases/2017/p1003-vs-cancer-obesity.html>

5. Kaplan LM, Golden A, Jinnett K, et al. Perceptions of barriers to effective obesity care: results from the national ACTION study. *Obesity (Silver Spring).* 2018;26(1):61-69.

6. Bramlage P, Pittrow D, Wittchen H-U, et al. Hypertension in overweight and obese primary care patients is highly prevalent and poorly controlled. *Am J Hypertens.* 2004;17:904-910.

7. Powell-Wiley TM, Poirier P, Burke LE, et al. Obesity and cardiovascular disease. *Circulation.* 2021;143:e984-e1010.

8. Cohen JB. Hypertension in obesity and the impact of weight loss. *Curr Cardiol Rep.* 2017;19:98.

9. Thomsen M, Nordestgaard BG. Myocardial infarction and ischemic heart disease in overweight and obesity with and without metabolic syndrome. *JAMA Intern Med.* 2014;174:15-22.

10. Afshin A, Forouzanfar MH, Reitsma MB; GBD 2015 Obesity Collaborators. Health effects of overweight and obesity in 195 countries over 25 years. *N Engl J Med.* 2017;377:13-27.

11. Heymsfield SB, Wadden TA. Mechanisms, pathophysiology, and management of obesity. *N Engl J Med.* 2017;376:254-266.

12. Cercato C, Fonseca FA. Cardiovascular risk and obesity. *Diabetol Metab Syndr.* 2019;11:74.

13. Le MH, Yeo YH, Li X, et al. 2019 global NAFLD prevalence: a systematic review and meta-analysis. *Clin Gastroenterol Hepatol.* 2021;S1542-3565(21)01280-5.

14. Yanoussi ZM, Koenig AB, Abdelatif D, et al. Global epidemiology of nonalcoholic fatty liver disease—meta-analytic assessment of prevalence, incidence, and outcomes. *Hepatology.* 2016;64:73-84.

15. Buzzetti E, Pinzani M, Tsochatzis EA. The multiple-hit pathogenesis of non-alcoholic fatty liver disease (NAFLD). *Metabolism.* 2016;65:1038-1048.

16. Godoy-Matos A, Silva WS, Valerio CM. NAFLD as a continuum: from obesity to metabolic syndrome and diabetes. *Diabetol Metab Syndr.* 2020;12:60.

17. Cotter TG, Rinella M. NAFLD 2020: the state of the disease. *Gastroenterology.* 2020;158:1851-1864.

18. Centers for Disease Control and Prevention. PCOS (polycystic ovary syndrome) and diabetes. Updated March 24, 2020. Accessed June 15, 2022. <https://www.cdc.gov/diabetes/basics/pcos.html>

19. De Leo V, Musacchio MC, Cappelli V, et al. Genetic, hormonal and metabolic aspects of PCOS: an update. *Reprod Biol Endocrinol.* 2016;14:38.

20. The American College of Obstetricians and Gynecologists. Polycystic ovary syndrome (PCOS). Updated January 2022. Accessed July 27, 2022. https://www.acog.org/womens-health/faqs/polycystic-ovary-syndrome-pcos?utm_source=redirect&utm_medium=web&utm_campaign=otr

21. Endocrine Society. Patient resources: polycystic ovary syndrome. Updated January 23, 2022. Accessed June 15, 2022. <https://www.endocrine.org/patient-engagement/endocrine-library/pcos>

22. Barber TM, Franks S. Obesity and polycystic ovary syndrome. *Clin Endocrinol (Oxf).* 2021;95:531-541.

23. Balen AH, Conway GS, Kaltsas G, et al. Polycystic ovary syndrome: the spectrum of the disorder in 1741 patients. *Hum Reprod.* 1995;10:2107-2111.

24. Legro RS. The genetics of obesity: lessons for polycystic ovary syndrome. *Ann N Y Acad Sci.* 2000;900:193-202.

25. Cena H, Chiovato L, Nappi RE. Obesity, polycystic ovary syndrome, and infertility: a new avenue for GLP-1 receptor agonists. *J Clin Endocrinol Metab.* 2020;105:e2695-e2709.

26. Snider AP, Wood JR. Obesity induces ovarian inflammation and reduces oocyte quality. *Reproduction.* 2019;158:R79-R90.

27. Chen L, Zheng JY, Li G, et al. Pathogenesis and clinical management of obesity-related knee osteoarthritis: impact of mechanical loading. *J Orthop Transl.* 2020;24:66-75.

28. Xie C, Chen Q. Adipokines: new therapeutic target for osteoarthritis? *Curr Rheumatol Rep.* 2019;21:71.

29. Presle N, Pottie P, Dumond H, et al. Differential distribution of adipokines between serum and synovial fluid in patients with osteoarthritis. Contribution of joint tissues to their articular production. *Osteoarthritis Cartilage.* 2006;14:690-695.

30. Tsuchida AI, Beekhuizen M, Hart MC, et al. Cytokine profiles in the joint depend on pathology, but are different between synovial fluid, cartilage tissue and cultured chondrocytes. *Arthritis Res Ther.* 2014;16:441.

31. Ushiyama T, Chano T, Inoue K, Matsusue Y. Cytokine production in the infrapatellar fat pad: another source of cytokines in knee synovial fluids. *Ann Rheum Dis.* 2003;62:108-112.

32. Pozzobon D, Ferreira PH, Blyth FM, Machado GC, Ferreira ML. Can obesity and physical activity predict outcomes of elective knee or hip surgery due to osteoarthritis? A meta-analysis of cohort studies. *BMJ Open.* 2018;8:e017689.

33. Reyes C, Leyland KM, Peat G, Cooper C, Arden NK, Prieto-Alhambra D. Association between overweight and obesity and risk of clinically diagnosed knee, hip, and hand osteoarthritis: a population-based cohort study. *Arthritis Rheumatol.* 2016;68:1869-1875.

34. Gersing AS, Solka M, Joseph GB, et al. Progression of cartilage degeneration and clinical symptoms in obese and overweight individuals is dependent on the amount of weight loss: 48-month data from the Osteoarthritis Initiative. *Osteoarthritis Cartilage.* 2016;24:1126-1134.

35. Miao Z, Alvarez M, Ko A, et al. The causal effect of obesity on prediabetes and insulin resistance reveals the important role of adipose tissue in insulin resistance. *PLoS Genet.* 2020;16:e1009018.

36. Riddle MC, et al. Classification and diagnosis of diabetes: standards of medical care in diabetes—2022. *Diabetes Care.* 2022;45:S17-S38.

37. Rett K, Gottwald-Hostalek U. Understanding prediabetes: definition, prevalence, burden and treatment options for an emerging disease. *Curr Med Res Opin.* 2019;35:1529-1534.

38. Boye KS, Lage MJ, Shinde S, Thieu V, Bae JR. Trends in HbA1c and body mass index among individuals with type 2 diabetes: evidence from a US database 2012–2019. *Diabetes Ther.* 2021;12:2077-2087.

39. Wondmunk YT. Obesity, insulin resistance, and type 2 diabetes: associations and therapeutic implications. *Diabetes Metab Syndr Obes.* 2020;13:3611-3616.

40. Al-Goblan AS, Al-Alfi MA, Khan MZ. Mechanism linking diabetes mellitus and obesity. *Diabetes Metab Syndr Obes.* 2014;7:587-591.

41. Romero-Corral A, Caples SM, Lopez-Jimenez F, Somers VK. Interactions between obesity and obstructive sleep apnea: implications for treatment. *Chest.* 2010;137:711-719.

42. Dobrosielski DA, Papanicolaou C, Patil SP, Salas-Salvado J. Diet and exercise in the management of obstructive sleep apnoea and cardiovascular disease risk. *Eur Respir Rev.* 2017;26:160110.

43. Jehan S, Zizi F, Pandi-Perumal SR, et al. Obstructive sleep apnea and obesity: implications for public health. *Sleep Med Disord.* 2017;1:00019.

44. Peppard PE, Young T, Palta M, Dempsey J, Skatrud J. Longitudinal study of moderate weight change and sleep-disordered breathing. *JAMA.* 2000;284:3015-3021.

45. Lopez PP, Stefan B, Schulman CI, Byers PM. Prevalence of sleep apnea in morbidly obese patients who presented for weight loss surgery evaluation: more evidence for routine screening for obstructive sleep apnea before weight loss surgery. *Am Surg.* 2008;74:834-838.



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