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POSITION PAPER
Prevention in practice

Obesity and cardiovascular disease: mechanistic insights and management strategies. A joint position paper by the World Heart Federation and World Obesity Federation

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The ongoing obesity epidemic represents a global public health crisis that contributes to poor health outcomes, reduced quality of life, and >2.8 million deaths each year. Obesity is relapsing, progressive, and heterogeneous. It is considered a chronic disease by the World Obesity Federation (WOF) and a chronic condition by the World Heart Federation (WHF). People living with overweight/obesity are at greater risk for cardiovascular (CV) morbidity and mortality. Increased adiposity (body fat), particularly visceral/abdominal fat, is linked to CV risk and CV disease (CVD) via multiple direct and indirect pathophysiological mechanisms. The development of CVD is driven, in part, by obesity-related metabolic, endocrinologic, immunologic, structural, humoral, haemodynamic, and functional alterations. The complex multifaceted nature of these mechanisms can be challenging to understand and address in clinical practice. People living with obesity and CVD often have concurrent chronic physical or psychological disorders (multimorbidity) requiring multidisciplinary care pathways and polypharmacy. Evidence indicates that intentional weight loss (particularly when substantial) lowers CVD risk among people with overweight/obesity. Long-term weight loss and maintenance require ongoing commitment from both the individual and those responsible for their care. This position paper, developed by the WOF and the WHF, aims to improve understanding of the direct and indirect links between overweight/obesity and CVD, the key controversies in this area and evidence relating to cardiometabolic outcomes with available weight management options. Finally, an action plan for clinicians provides recommendations to help in identifying and addressing the risks of obesity-related CVD (recognizing resource and support variances between countries).

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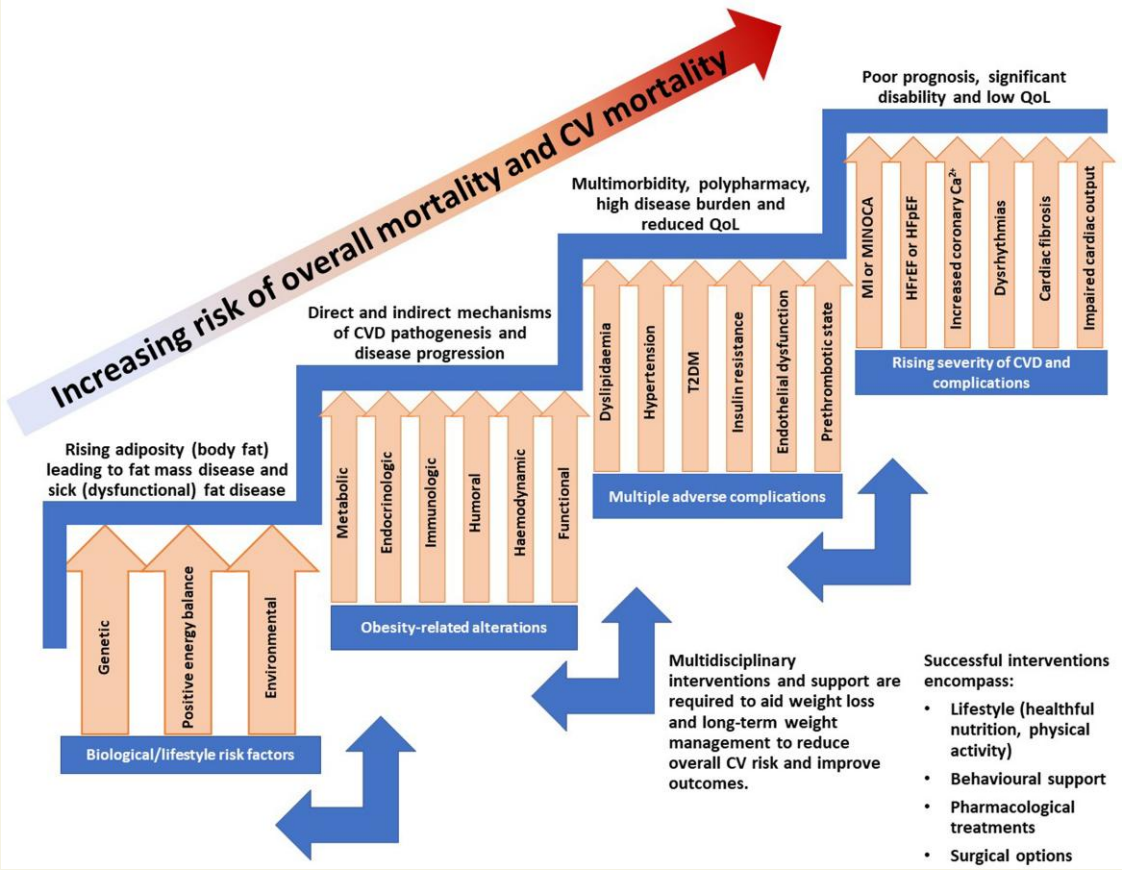
Graphical Abstract



Biological/lifestyle factors drive rising adiposity leading to fat mass and 'sick fat' disease. Obesity-related alterations increase the onset of multiple adverse cardiometabolic complications via direct and indirect mechanisms causing further complications and rising severity of CVD. Bidirectional relationships exist between each of these steps, with the potential to reverse complications and lower CV risk through effective reduction of body fat.

Keywords Adiposity • Cardiometabolic complications • Cardiovascular disease • Cardiovascular risk • obesity • Overweight

Introduction

Worldwide obesity has almost trebled since 1975 with at least 2.8 million deaths occurring each year due to associated adverse health outcomes.[1,2] Cardiovascular disease (CVD), including myocardial infarction (MI), stroke, and heart failure (HF), is a leading cause of death and disability in people living with overweight or obesity and early detection of cardiovascular (CV) risk is critical in reducing mortality and preserving quality of life (QoL).[1,3] The World Heart Federation (WHF) and the World Obesity Federation (WOF) have joined forces to provide educational materials for healthcare professionals (HCPs) with the aim of addressing this public health crisis.[4] The WOF describes obesity as a chronic disease, while the WHF defines obesity as a chronic condition.[5] Both organizations consider overweight/obesity to be relapsing and progressive in nature and requiring continuous effort to control.[5] This position paper aims to provide greater clarity on the direct and indirect links between overweight/obesity and CVD, to discuss the ongoing controversies associated with weight gain and CV risk, and to highlight clinical approaches for the management of obesity.

Search strategy and selection criteria

This paper summarizes the key topics of concern that were discussed during a joint WHF and WOF panel meeting, convened in January 2021, to address the growing issue of obesity and CVD comorbidity. Relevant original articles and review papers focusing on aspects of obesity-related CVD considered by the panel to be a priority were identified using PubMed and MEDLINE searches. The following search terms (or combination of terms) were used: 'obesity', 'adiposity', 'adiposopathy', 'ectopic fat', 'visceral adipose tissue or visceral fat', 'epicardial adipose tissue', 'cardiovascular disease', 'cardiovascular risk', 'coronary artery disease', 'coronary heart disease',

Table 1 World Health Organization recommendations for body mass index and waist circumference cut-off points for overweight or obesity, and association with disease risk[1,13,18]

Classification	Body mass index (kg/m^2)	Disease risk (relative to normal weight and waist circumference)	
Caucasian populations		Men <102 cm	Men >102 cm
		Women <88 cm	Women >88 cm
Underweight	<18.5	Very high	—
Healthy weight	18.5–24.9	—	High
Overweight	25.0–29.9	Increased	High
Obesity class I	30.0–34.9	High	Very high
Obesity class II (morbid obesity)	35.0–39.9	Very high	Very high
Obesity class III (severe obesity)	≥40.0	Extremely high	Extremely high
South Asian, Chinese and Japanese populations		Men <90 cm	Men >90 cm
		Women <80 cm	Women >80 cm
Underweight	<18.5	Low (increased risk of other clinical problems)	Average
Healthy weight	18.5–22.9	Average	Increased
Overweight (at risk)	23.0–24.9	Increased	Moderate
Obesity class I	25.0–29.9	Moderate	Severe
Obesity class II	≥30.0	Severe	Very Severe

Global consensus and specific recommendations regarding the diagnosis of obesity according to the measurement of body fat percentage are currently lacking.
Adapted from: World Health Organization. Waist circumference and waist–hip ratio: report of a WHO expert consultation, Geneva, 8–11 December 2008 and World Health Organization. Regional Office for the Western Pacific. The Asia-Pacific perspective: redefining obesity and its treatment. 2000.

'atrial fibrillation', 'heart failure', 'cardiometabolic', 'comorbidity or comorbidities', 'type 2 diabetes', 'obstructive sleep apnoea, or obstructive sleep apnoea or OSA', 'metabolic-associated fatty liver disease or MAFLD', 'polycystic ovary syndrome or PCOS', 'insulin resistance', 'migraine', 'depression', 'arthritis', 'body mass index or BMI', 'waist circumference', 'waist-hip ratio', 'body composition', 'normal weight obesity', 'obesity paradox', 'metabolically healthy obesity', 'weight loss', 'pharmacotherapy or medication', 'anti-obesity', 'bariatric surgery', 'quality of life', 'psychological impact', 'guidelines' and 'recommendations'.

Epidemiology of obesity and cardiovascular disease

CVD is responsible for an estimated 17.9 million deaths per year, the majority being preventable through population interventions, appropriate management, and clinical interventions that target risk factors associated with overweight and obesity.[3] The World Health Organization (WHO) estimates that approximately 1.9 billion adults worldwide (around 39% of the world's population) are considered within the overweight category.[1] Of those, more than 650 million are living with obesity (approximately 13% of the global population).[1] Although traditionally viewed as a problem associated with urbanization in high income countries, people living with obesity are well distributed across the globe with prevalence increasing in developing and rural areas at a comparable rate to affluent cities.[6–8] By 2025, global obesity prevalence in adults is projected to reach 18% in men and above 21% in women, although relative sex distribution will vary in different countries.[6]

Accumulation of excess body fat (adiposity), particularly central/abdominal fat, is a well-established health risk. While body mass index (BMI), defined by weight (kg) divided by height squared (m^2), is used most widely as a pragmatic indicator of excess weight, waist circumference (WC) and waist-hip ratio (WHR) are better predictors of fat distribution and central obesity and have a closer association with morbidity.[6,9–15] Waist to height ratio has also shown utility in the stratification of individuals according to CV risk.[16,17] The WHO has published recommended BMI and WC thresholds as indicators of CVD risk (*Table 1*).[13,18] Caucasian individuals with a BMI between 25 and 29.9 kg/m^2 and ≥30 kg/m^2 are generally defined as having overweight and obesity, respectively.[1,13] A WC measuring >102 cm in men and >88 cm in women is associated with elevated CV and mortality risk, but complexities exist and factors such as age and body weight trajectory over life-course influence risk levels.[1,9,10,13–15,18–24] Different WC and BMI recommendations reflect variations in risk relating to ethnicity.[13,18] For example, lower BMI thresholds have been suggested for Asian populations, with overweight (increased risk) defined as ≥23 kg/m^2 and obesity (high risk) as ≥27.5 kg/m^2, and a WC measuring >90 cm (men) or >80 cm (women) representing an increased CV risk in these populations.[1,9,10,13–15,18–24]

The limitations of BMI as an indicator of obesity/adiposity are well recognized and numerous anthropometric measures have been explored in an effort to improve assessment and prediction of CV risk, including WC, WHR, waist to height ratio, bioimpedance, 3D scanning and dual energy x-ray absorptiometry (DEXA).[25–28] A lack of clarity

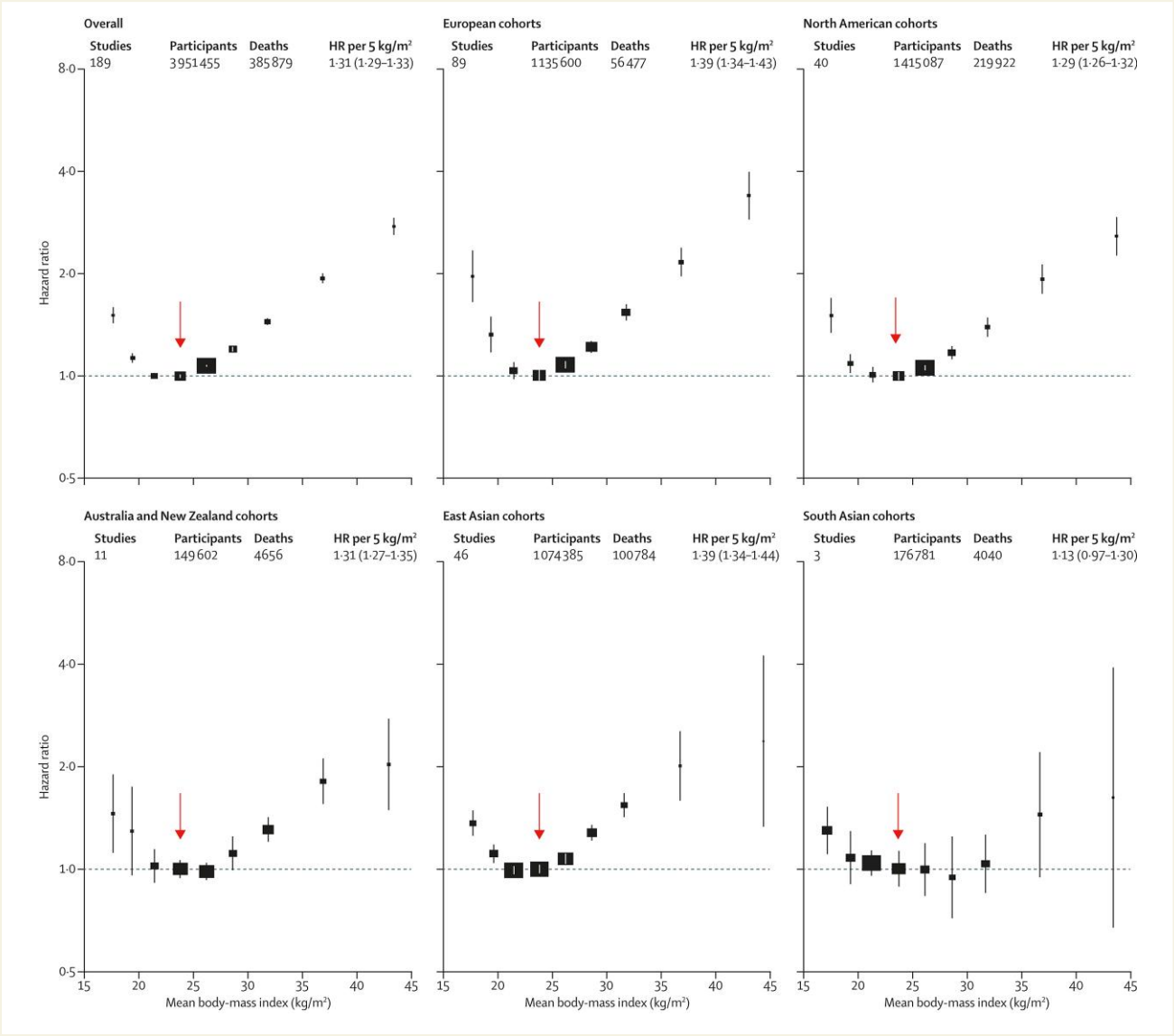


Figure 1 Association of body-mass index with all-cause mortality, by geographical region.[30] Boxes are plotted against the mean body mass index in each group. The hazard ratio per 5 kg/m^2 higher body mass index and its 95% confidence interval (CI) are calculated only for body mass index more than 25.0 kg/m^2. Analyses restricted to never smokers without pre-existing chronic disease, excluding the first 5 years of follow-up. The reference category is shown with the arrow and is 22.5 to <25.0 kg/m^2. CIs are from floating variance estimates (reflecting independent variability within each category, including reference). Areas of squares are proportional to the information content (i.e. inverse of the floating variance). From Global Body Mass Index Mortality Collaboration. Body mass index and all-cause mortality: individual-participant-data meta-analysis of 239 prospective studies in four continents. *Lancet*. 2016; 388:776–786. doi: 10.1016/S0140-6736(16)30175-1. This article is available under the terms of the Creative Commons Attribution License (CC BY).

exists regarding the most appropriate parameters for use in clinical practice and each measure will have different implications regarding CV risk and mortality.[25–28] Furthermore, inequity concerning resources precludes the global use of some newer high cost methodologies in many locations.[28] Cost and better measurement accuracy are probably the reasons that BMI continues to be widely used.[28]

Although data are limited on the association of fat distribution and CV mortality, a largely non-linear association exists between BMI and all-cause mortality risk.[8,29–31] The relationship is similar across different continents and countries, regardless of age or sex, with the possible exception of Africa and South Asia where there are limited data on BMI and mortality (*Figure 1*).[29–31] On average, in the populations studied (largely Caucasians from higher income countries), obesity class III (BMI ≥40 kg/m^2) shortens life-expectancy by approximately 10 years and obesity class I (BMI 30–34.9 kg/m^2) reduces life duration by around 3 years, relative to normal weight, with the number of years lost varying according to age, sex, and severity of obesity.[32,33]

A BMI above 25 kg/m^2 is strongly and positively associated with higher risk of CVD death, particularly coronary heart disease (CHD) and

ischaemic stroke (*Figure 2*).[30] Historically, the relationship between increased adiposity and CVD mortality was believed to be indirectly driven through the upstream acceleration of risk factors and chronic diseases associated with poor CVD outcomes, but growing evidence suggests that direct mechanisms also link overweight/obesity with increased CVD mortality.[34–37] Indirect associations are evidenced by studies showing that different indicators of increased adiposity (e.g. BMI, WC) raise the chances of developing or exacerbating conditions

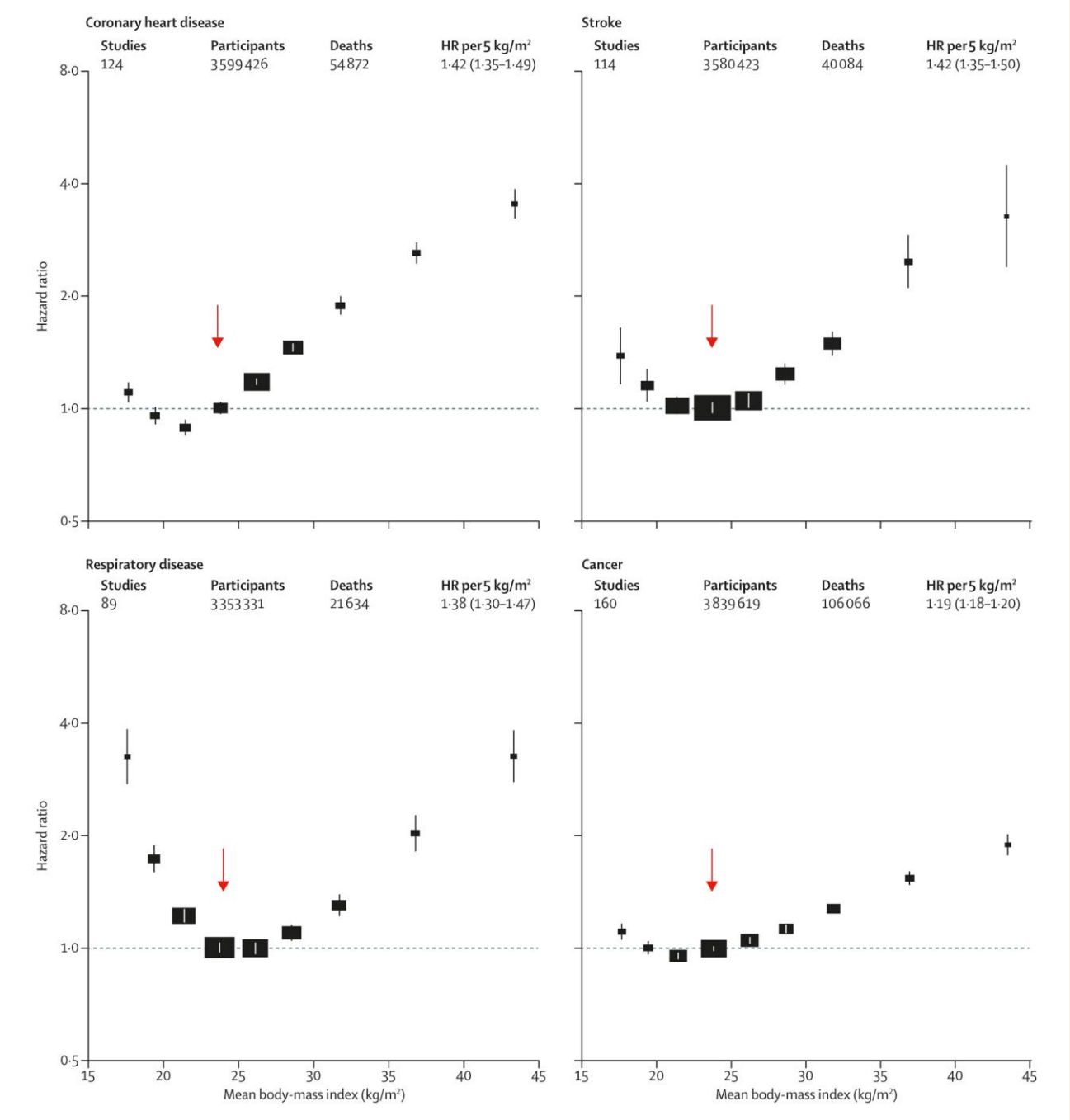


Figure 2 Association of body mass index with mortality, by major underlying cause.[30] The hazard ratio per 5 kg/m^2 higher body mass index and its 95% CI are calculated only for body mass index more than 25.0 kg/m^2. Analyses restricted to never-smokers without pre-existing chronic disease, excluding the first 5 years of follow-up, and include data from all geographical regions. The reference category is shown with the arrow and is 22.5 to <25.0 kg/m^2. CIs are from floating variance estimates (reflecting independent variability within each category, including reference). Areas of squares are proportional to the information content. From Global Body Mass Index Mortality Collaboration. Body mass index and all-cause mortality: individual-participant-data meta-analysis of 239 prospective studies in four continents. *Lancet*. 2016; 388:776–786. doi: 10.1016/S0140-6736(16) 30175-1. This article is available under the terms of the Creative Commons Attribution License (CC BY).

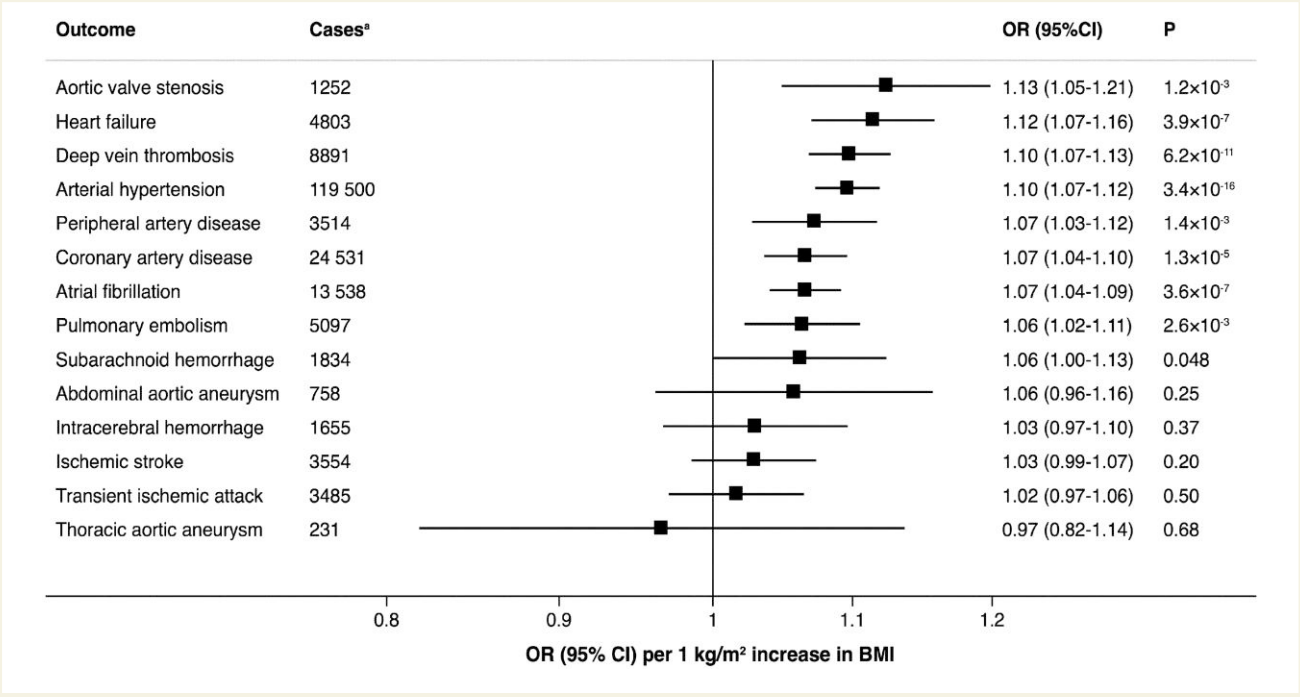


Figure 3 Associations of genetically predicted 1 kg/m^2 increase in body mass index with 14 cardiovascular conditions in UK Biobank.[39] [a]Total number. From Larsson SC, Bäck M, Rees JMB, Mason AM, Burgess S. Body mass index and body composition in relation to 14 cardiovascular conditions in UK Biobank: a Mendelian randomization study. *Eur Heart J.* 2020; 41:221–226. doi: 10.1093/eurheartj/ehz388. This is an Open Access article distributed under the terms of the Creative Commons Attribution License http://creativecommons.org/licenses/by/4.0/. CI, confidence interval; OR, odds ratio.

that carry high CV mortality risk (e.g. sleep apnoea, thromboembolic disease) and/or cardiometabolic diseases, including hypertension, dyslipidaemia, and type 2 diabetes mellitus (T2DM).[29,34,37] These associations have been shown to be independent of age, sex, socioeconomic status, alcohol intake and smoking history in the white US population.[37] Evidence for direct links between obesity and CVD followed the discovery of more than 140 chromosomal regions that predispose to increased adiposity, many involving genes highly expressed in the central nervous system, indicating neuronal mechanisms in the development of obesity (e.g. dysregulation of appetite/satiety pathways).[38–40] Mendelian randomization studies using data from UK Biobank and HUNT studies (Trøndelag Health Study) have also shown that higher lifelong BMI (particularly when associated with high percentage body fat) is causally linked with increased risk of CVD mortality, aortic valve stenosis and many other CVDs (*Figure 3*).[38,39] Genetic and population-based cohort analysis have revealed a direct relationship between adiposity and a range of other high risk CV traits including aortic diseases, HF, deep vein thrombosis, hypertensive heart disease, peripheral artery diseases, and atrial fibrillation (AF).[39,41,42]

It is important to recognize that obesity is often associated with both poor diet quality (e.g. high saturated fat and sugar, ultra-processed foods, lower than optimal intakes of fresh fruit and vegetables) and reduced physical activity and/or increased sedentary behaviour, all of which may be linked with poor socioeconomic status, and each factor independently increases CVD risk.[5,42–45] Nevertheless, the data summarized above clearly show that, once present, obesity is causally related to several CV conditions, albeit to differing extents.[30,34–41]

How does obesity affect the heart?

Table 2 summarizes the key CV changes or abnormalities that are commonly associated with obesity.[5,37,42,46–58] Multiple obesity-related mechanisms drive structural, functional, humoral and haemodynamic alterations believed to underpin the development of CVD, most notably coronary artery disease (CAD), HF, and arrythmias.[42,46–48,52,54]

Among the adverse consequences of obesity are 'fat mass disease' and 'sick fat disease' (termed 'adiposopathy' by the Obesity Medicine Association; *Figure 4*).[42,46–52,54,59] Fat mass disease includes the biomechanical complications of obesity, such as obstructive sleep apnoea (OSA) and joint stress and damage.[42,46]

Sick fat disease: obesity increases cardiovascular risk factors

Positive energy balance results in adipocyte hypertrophy and ectopic fat accumulation that leads to organelle dysfunction (e.g. mitochondrial and endoplasmic reticulum stress) as well as metabolic abnormalities (sometimes called metabolic syndrome) and endocrine disturbance, which include dyslipidaemia, insulin resistance and beta-cell dysfunction, polycystic ovary syndrome (PCOS) in women, and low testosterone in men.[46–48,52] Under these conditions, the most common CVD risk factors (atherogenic dyslipidaemia, T2DM and

Table 2 An overview of key electrocardiographic, haemodynamic, structural and functional changes associated with adiposopathy and fat mass disorders[5,37,42,46–54,57–59]

	Cardiovascular abnormalities/changes associated with adiposopathy and fat mass disorders
Electrocardiographic	Increased heart rate
	Increased PR interval
	Increased QRS interval
	Decreased QRS voltage[a] (although sometimes increased)
	Increased QTc interval
	Abnormal signal-averaged electrocardiogram late potentials
	ST–T-wave abnormalities
	Left-axis deviation[a]
	Flattening of the T waves (inferolateral leads)[a]
	Left atrial abnormalities
	False positive criteria for inferior myocardial infarction[a]
Haemodynamic	Increased heart rate (in physically inactive individuals)
	Increased blood volume
	Changes in stroke volume (will increase in early stages, and decrease in later stages)
	Increased cardiac output
	Increased systemic vascular resistance (in those with hypertension and insulin resistance)
	Increased arterial pressure, including systolic and diastolic Increased left ventricular wall stress
	Increased left ventricular stiffness
	Increased end diastolic left ventricular filling pressure
	Increased pulmonary artery pressure
	Altered atrial and ventricular pressure (in those with sleep apnoea)
Structural	Myocardial steatosis, apoptosis, fibrosis
	Left ventricular remodelling and hypertrophy
	Left atrial enlargement
	Right ventricular hypertrophy
	Increased pericardial and perivascular adipose tissue
Functional	Hypoxia due to sleep apnoea, atherosclerosis, thrombosis
	Left ventricular diastolic and systolic dysfunction
	Coronary obstruction
	Myocardial ischemia
	Tachyarrhythmias, including atrial fibrillation, atrial flutter, ventricular tachycardia, inappropriate sinus tachycardia
	Right ventricular failure
	Deep vein thrombosis
	Pulmonary embolism

[a]Changes that are likely related to the recording of the ECG rather than pathologic changes.

hypertension) become highly prevalent, exacerbating CVD risk.[46–48] Abdominal visceral and subcutaneous fat accumulation is typically accompanied by pro-inflammatory adipocytokine expression that promotes recruitment and proliferation of pro-inflammatory macrophages and may lead to tissue damage and oxidative stress.[52,60,61] Incident CVD and mortality are associated with insulin resistance, but whether this has a primary aetiological role remains uncertain. This is probably because insulin resistance is itself associated with other risk factors including obesity, hypertension, OSA, abnormal glucose metabolism and dyslipidaemia.[52,60–65] In CHD, the ischaemic myocardium switches from using predominantly fatty acids to glucose.[66] People who have HF with preserved ejection fraction (HFpEF) and T2DM requiring insulin therapy have a 50% greater risk of death compared with those not treated with insulin or individuals without T2DM.[67] However, this may simply reflect more advanced diabetes. Randomization to insulin was shown to be neutral regarding CV outcomes in the Outcome Reduction with an Initial Glargine Intervention (ORIGIN) trial, which examined the effect of insulin glargine treatment in 12 537 people (aged 50 years and above) with CV risk factors and impaired fasting glucose, impaired glucose tolerance, or T2DM.[68]

Fat mass disease: direct and indirect effects on cardiovascular risk

The association between adipose tissue and CVD appears to be causal, involving direct mechanisms and indirect pathways mediated through obesity-related comorbidities.[42,46] For example, obesity is in the causal

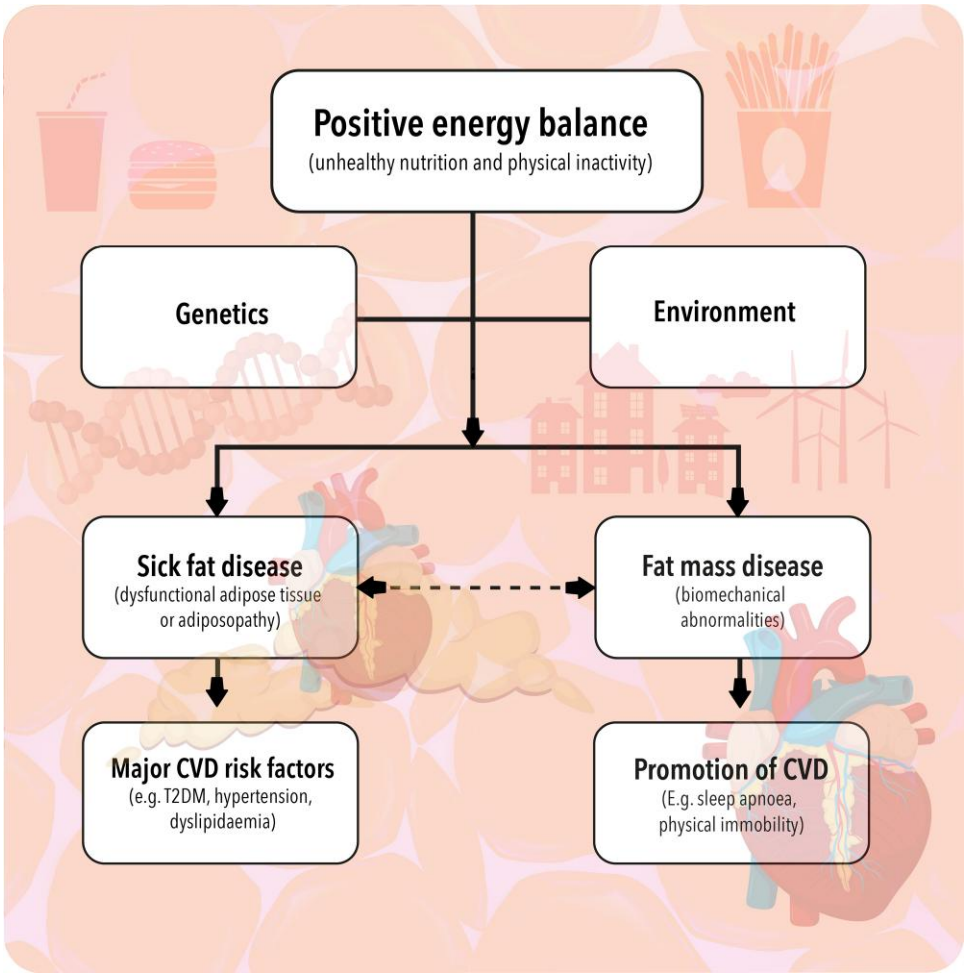


Figure 4 The adverse consequences of obesity: fat mass disease and sick fat disease.[42,46–55] Fat mass disease and sick fat disease (adiposopathy) are among the adverse consequences of obesity. Fat mass disease includes the biomechanical complications, such as obstructive sleep apnoea and joint stress/damage. CVD, cardiovascular disease, T2DM, type 2 diabetes mellitus.

pathway of several traditional CV risk factors such as atherogenic dyslipidaemia, hypertension and diabetes.[42,46] Obesity-related OSA contributes to CVD risk through promotion of hypoxia, cardiac dysrhythmias, insulin resistance, and hypertension.[49,50] In the next section (clinical interactions with other obesity complications) we provide several examples to illustrate how obesity may indirectly cause CVD, mediated through different obesity-associated comorbidities.

For years, it was assumed that the association between obesity and CVD was indirect, yet recent decades have revealed a significant body of evidence demonstrating a more direct causal relationship between obesity and CVD.[5,47,52] For example, an excessive increase in body weight impairs mobility and physical activity and/or worsens musculoskeletal comorbidities (e.g. osteoarthritis), and subsequently reduces energy expenditure resulting in a vicious cycle of weight gain and escalating CV risk.[42,47,48,51] Total blood volume and cardiac output are higher in people with overweight/obesity, contributing to structural and functional changes to the heart and vascular system.[42,46–48,55] Increased intravascular volume and neuro-humoral mechanisms lead to left ventricular hypertrophy (LVH), a major risk factor for elevated left ventricular filling pressure, commonly associated with left ventricular diastolic dysfunction and predisposition to HF.[42,46–48,55] Causative associations are supported by recent Mendelian randomization studies.[69,70] Obesity-related HF with reduced ejection fraction (HFrEF) or HFpEF can occur and may be worsened or accompanied by obesity-induced kidney compression as well as upregulation of the renin-angiotensin-aldosterone system (RAAS) and the sympathetic nervous system, which also contribute to hypertension and stroke risk.[55,71,72]

Studies indicate that different types of adipose tissue may be associated with varying metabolic and atherogenic risks and response to weight loss might also vary according to the kind of fat present.[73–75] During positive energy balance, energy overflow is associated with ectopic fat deposition in the liver and muscle (and possibly the heart, pancreas, and kidney) as well as higher levels of visceral adipose tissue. An increase in visceral fat correlates with rising epicardial adipose tissue (EAT), coronary atherosclerosis, and other forms of CVD, which is unsurprising given that visceral fat and EAT share the same mesodermal embryonic

origin.[42,46,47] Accumulation of EAT is linked with the presence and severity of AF, HFpEF and CAD and is predictive of poor outcomes following ablation of the pulmonary veins.[76,77] Atherogenic dyslipidaemia is linked with a wide range of lipoprotein abnormalities and pathways relating to insulin resistance, T2DM and atherosclerotic CVD (ASCVD).[77] Individuals with high blood triglyceride levels [even those with normal LDL cholesterol (LDL-C)] may therefore benefit from tests for common risk factors/abnormalities associated with ectopic fat, such as liver fat intermediates (alanine aminotransferase/gamma-glutamyl transferase), liver ultrasound or magnetic resonance imaging and HbA1c level, so that lifestyle interventions and support can be offered in an effort to lower CV and T2DM risks.[78]

Clinical interactions with other obesity complications

Table 3 summarizes key CVDs and adverse complications resulting from obesity-related pathophysiological mechanisms that lead to atherosclerotic dyslipidaemia, hypertension, and T2DM, and promote inflammation, oxidative stress, insulin resistance, endothelial disfunction and prothrombotic state.[42,46–48,52] Systemic inflammation is tightly linked with obesity/adiposity and the American Centers of Disease Control and Prevention (CDC) as well as American Heart Association (AHA) have recommended the use of high sensitivity C-reactive protein testing as an independent prognostic factor for CV outcomes in people with obesity and high CV risk.[79]

The term 'diabesity' was coined in recognition of the well-established relationship between central/abdominal obesity, insulin resistance and T2DM.[80] Systematic review data show that approximately one-third of people with T2DM will develop atherosclerosis, CHD, HF, angina, MI, or stroke.[81] People with OSA also have a higher risk of metabolic syndrome, which may contribute to their increased risk of developing CAD, AF and HF.[50] The heightened risk of CV complications in people with obesity and glomerulopathy or chronic kidney disease is thought to be mediated by inflammation, dyslipidaemia, hypertension, and endothelial dysfunction, but other pathways may also operate.[70] Metabolic-associated fatty liver disease (MAFLD; previously termed non-alcoholic fatty liver disease) is a common condition in patients with obesity, although it may not be an independent risk factor for CVD.[82,83] It is associated with insulin resistance, chronic systemic inflammation and oxidative stress, and diagnosis of T2DM is linked with the onset and progression of MAFLD.[82,83]

Hormonal diseases frequently occur alongside obesity and are correlated with CV risk.[84–87] Between 50 and 80% of women with PCOS have obesity, with 30–35% having impaired glucose tolerance, and up to 95% of women with obesity and PCOS have insulin resistance.[84] Hyperandrogenism and cardiometabolic abnormalities are associated with insulin resistance in women with PCOS (dyslipidaemia, hypertension, OSA and MAFLD), driving the threat of CVD upward.[85] Obesity, particularly in the presence of metabolic disorders, is causally related to functional hypogonadism in men and community-based studies show that up to 50% of men with T2DM also have hypogonadism.[85–87] These data may support the case for secondary prevention, given that those with established CVD have an elevated risk for future CHD death, MI, and stroke.[85–87]

Inflammatory arthropathy increases the risk of CHD and CV events, and musculoskeletal problems (e.g. inflammatory arthritis) are prevalent in people living with obesity (particularly those with T2DM).[88,89] Physical activity may be painful and systemic inflammation with microvascular changes (predominantly affecting the venous circulation) contribute to atherosclerotic risk.[88,89]

A reciprocal association exists between obesity and psychological disorders.[90] Depression, other mood disturbances, low self-esteem, and emotional eating may contribute to obesity development and hinder weight loss.[42,90,91] Eating disorders are prevalent in this group and the use of antipsychotic or antidepressant medicines can contribute to weight gain.[90,91] Depression and anxiety may exacerbate obesity, diabetes, and CVD, which may likewise worsen mood disorders, and increase the risk of morbidity and mortality.[90,91] Prevalence and attack frequency of neurological conditions, such as migraine, are higher in people living with obesity.[92,93] Individuals experiencing regular migraines are more likely to suffer MI, angina or ischaemic stroke.[92,93] Severe obesity is associated with idiopathic intracranial hypertension (IIH).[94] Although the underlying mechanism linking these conditions remains unknown, relatively modest weight loss (6–10%) can result in IIH remission among people living with obesity.[94]

Obesity and CVD are often concomitantly present with other chronic disorders (multimorbidity), such as periodontal disease, psoriasis, OSA, depression and rheumatoid arthritis, all of which appear to amplify CV risk.[95–98] It should be noted that direct causal pathways are uncertain and confounding dietary (e.g. high sugar intake) and socioeconomic factors may mean the associations are indirect, given the very strong relationship between socioeconomic class, obesity and its complications.[43,45,95–98] Pooled analysis of individual-level data from 16 cohort studies across the United States and Europe suggests that multimorbidity risk rises alongside BMI; the risk is doubled for people with overweight and

Table 3 A summary of key obesity-related cardiovascular diseases and adverse complications associated with cardiovascular risk[42,46–48,52]

Cardiovascular diseases	Adverse complications
Aortic valve stenosis	Type 2 diabetes
Heart failure	Atherogenic dyslipidaemia
Deep vein thrombosis	Hypertension
Peripheral artery disease	Obstructive sleep apnoea
Coronary artery disease	Kidney disease
Atrial fibrillation	Metabolic-associated fatty liver disease
Subarachnoid haemorrhage	Polycystic ovary syndrome
Abdominal aortic aneurysm	Hypogonadism
Intracerebral haemorrhage	Musculoskeletal conditions (e.g. arthritis)
Ischemic stroke	Psychological disorders (e.g. depression)
Transient ischemic attack	Migraine
Thoracic aortic aneurysm	

it is 10 times higher for those with class II/III obesity, vs. individuals considered to be in low risk weight categories.[98] This presents a significant challenge for HCPs in managing complex polypharmacy arrangements and prioritizing co-existing conditions according to their relative mortality risk. Treatment for obesity should be prioritized given that many comorbidities are likely to be improved with weight loss.[42,47,48]

Global clinical evaluation is important in the detection and treatment of obesity-related complications. Tools such as the King's Obesity Staging Criteria and Edmonton Obesity Staging System are useful in standardizing and facilitating practical assessment of obesity complications and mortality risk.[99,100] The value of multidisciplinary or cardiometabolic clinics has become increasingly clear, given the complex and multidimensional nature of obesity-related disease.[100] While appropriate referral for support relating to overweight/obesity traditionally sits with physicians outside of the cardiology setting (e.g. family physicians, obesity medicine specialists), the cardiologist is called to play a critical role in facilitating access to specialist multidisciplinary services for people with obesity and CVD.[101]

Clinical approaches and challenges of managing obesity and heart disease: a focus on heart failure, atrial fibrillation, and coronary heart disease

Heart failure

An unequivocal relationship exists between obesity and HF.[102] HFpEF diagnosis is typically complex and based upon symptoms such as exercise intolerance (e.g. inability to climb stairs) and lower extremity oedema.[102] Blood-based biomarkers include B-type natriuretic peptide (BNP), with abnormally high BNP levels being present in people with HF who have a BMI considered to be within the normal range.[103,104] Thresholds for BNP levels should be adapted/lowered for HF detection in people with obesity.[104] Weight loss is an important intervention for obesity-induced cardiomyopathy and HFpEF, and referral to weight management services should be considered.[102,105] Some medications used to treat HFrEF can make weight loss more challenging.[106–109] Use of beta-blocker therapies, such as metoprolol, is associated with weight gain in people who already have overweight/obesity, although carvedilol does not appear to have the same effect.[109] Proposed underlying mechanisms for beta-blocker related weight gain include reduction in resting and total energy expenditure as well as lowered diet-induced thermogenesis and fat oxidation rate.[107–109] Increased tiredness can accompany beta-blocker use and exercise tolerance may be diminished.[107–109] Surgical interventions (e.g. bariatric surgery) have been linked with reduced HF and AF risk in people with obesity, including those with T2DM, and are associated with reduced mortality in people with pre-existing HF.[105,110] Sodium glucose cotransporter-2 inhibitor (SGLT2i) treatments (originally approved for T2DM) have demonstrated benefits beyond blood glucose reduction, including lowering of body weight, blood pressure, and incidence of HF hospitalization in people who have pre-existing HF with or without diabetes, and some have recently been approved for treatment of HFrEF and HFpEF.[111–115]

Atrial fibrillation

AF is the most common sustained arrhythmia and a frequent cause of stroke and CV death.[116–118] AF and related comorbidities adversely impact QoL.[116–119] Other complications of obesity such as OSA, hypertension and HF are known causes of AF.[117,118] Available treatment options are generally considered inadequate; medications provide variable rates of control, and although ablation procedures may be helpful, relapse is common.[117] Severity of obesity can impact on drug pharmacokinetics and pharmacodynamics, resulting in further complications following AF ablation.[117]

Recent randomized controlled trials have revealed that lifestyle changes, including weight loss, reduce the recurrence and severity of AF.[120,121] Even relatively conservative levels of weight reduction provide benefit.[120,121] Data from the pREVEntion and regReSsive Effect of weight-loss and risk factor modification on Atrial Fibrillation (REVERSE-AF) trial show that weight reduction of 3–9%, achieved through physician-led support and lifestyle management, results in reversal from persistent to paroxysmal or no AF in around 49% of individuals.[121] Clinical outcomes are more profound with substantial weight loss; those achieving ≥10% reductions in body weight show an 88% reversal from persistent to paroxysmal or no AF.[121] Bariatric surgery has been associated with both a reduced incidence of new AF and the reversal of pre-existing AF.[122,123]

Coronary artery disease

Approximately 70–80% of people with CAD have overweight/obesity and yet most cardiac rehabilitation programmes do not include specific weight management interventions.[124] People with CAD usually have multiple obesity-related comorbidities and adverse complications (e.g. hypertension, T2DM, dyslipidaemia). Prevalence of depression, anxiety, and generalized anxiety disorder is high among people with CAD and often accompanied by a decrease in physical exercise.[125–127] People undertaking weight loss and physical activity programmes during cardiac rehabilitation may lose body fat but gain muscle mass and, consequently, their BMI will not change significantly.[128] Therefore, assessments of body fat, WHR or WC (which more accurately evaluate CV risk, compared with BMI) are recommended for those individuals.[128,129] Additional metrics include calculation of percentage body fat and body composition (e.g. muscle mass, total and visceral fat) via DEXA or bioelectrical impedance. If clinically meaningful changes in physical activity or physical exercise are anticipated, favourable changes in body composition analyses (e.g. DEXA) are likely to be accompanied by positive modifications to clinical parameters regarding cardiometabolic risk and mobility.[27]

Controversies and paradoxes

The concepts of normal weight obesity, the obesity paradox, and metabolically healthy obesity (MHO) are among the major controversies relating to treatment of CVD or cardiometabolic disease.[26,130–148] Debate in this area has caused confusion among clinicians, patients, healthcare funders and providers, which may

present a barrier to the success of obesity-focused health improvement programmes.

'Normal weight' obesity

BMI is the main diagnostic indicator of overweight/obesity used in clinical practice, but this measure cannot provide an accurate indication of fat mass or distribution.[9,27,129–131] Individuals with normal weight could have sarcopenia with decreased muscle mass and increased percentage body fat, yet be considered to have a healthy BMI.[130,131] This is especially misleading if they have central adiposity and are consequently at higher CVD risk.[9,130–132] Studies show that, among people with normal BMI, WHR provides a robust measure of adiposity and associated CV risk.[35,131] A study examining data from 15 184 people included in the Third National Health and Nutrition Examination Survey (NHANES III) in the United States showed that overall mortality was higher for individuals with normal BMI and central obesity, compared with those with the same BMI but no central adiposity [men: hazard ratio (HR), 1.87 (95% CI, 1.53–2.29); women: HR, 1.48 (95% CI, 1.35–1.62)], and CV mortality showed the same relationship [men: HR, 1.78 (95% CI, 1.23–2.57); women: HR, 2.25 (95% CI, 1.66–3.05)].[131] These data emphasize the increased risk for death and CV events among people with a normal BMI but central obesity and are supported further by studies in the community setting from various countries, including the PERU MIGRANT (PEru's Rural to Urban MIGRANTs) study and the CRONICAS Cohort study.[133–135] Complementary anthropometric measures, such as WC (and possibly body composition analyses), are helpful in identifying people with normal BMI and central obesity who are likely to benefit from further investigation regarding CV risk factors (e.g. lipid levels, diabetes).[9,13–15,35,130–132]

The obesity paradox

Conflicting opinion regarding the benefits of weight reduction in people with HF, CVD, and/or T2DM is based upon studies suggesting that lower BMI may be associated with higher rates of mortality in some high-risk groups.[136,138] This seems counterintuitive given the evidence (particularly from Mendelian randomization studies) supporting a causal role for obesity in the development of CVD and cardiometabolic diseases, although this might be confounded by factors such as the individual's habitual diet and physical activity.[39,136–140] It is also important to consider whether weight loss was intentional or unintentional in such studies, as the latter may represent undiagnosed disease (e.g. cancer, severe systemic inflammation), and confound interpretation. In general, studies that look at intentional weight loss have shown benefit.[21,149,150]

A landmark systematic review examining 40 studies, including 250 152 people with CAD, showed that overweight or mild obesity was not predictive of increased mortality or CV mortality, compared with normal BMI, while people with severe obesity (≥35 kg/m^2) were at greatest risk of CV mortality.[136] Subsequent research, including the Meta-Analysis Global Group in Chronic Heart Failure (MAGGIC) and ORIGIN studies, has revealed similarly controversial results.[137,138] The MAGGIC study included almost 40 000 people with chronic HF in 30 cohorts and showed that mortality rate was increased as ejection fraction reduced, whereas mortality rate was diminished with increasing BMI.[137] Low weight individuals or those losing more weight over time tended to demonstrate higher mortality.[137] The ORIGIN trial assessed the relationship between weight, change in weight, and outcomes in people with established CV risk factors and T2DM or prediabetes.[138] Once again, survival was greater with higher baseline BMI.[138] Confounding factors (e.g. smoking, chronic illness, lung disease, cancer) or reverse causality may account for this phenomenon.[139] The severity of a person's disease impacts their weight loss trajectory. For example, those with more severe HF will lose weight faster yet have higher outcome risks, and systemic inflammation in HF will lead to weight loss (*Figure 5*).[139] Such *unintentional* weight loss is often marked by relative reduction of muscle mass and peripheral fat, rather than central fat. Study results should therefore be interpreted with caution when it is unclear whether the weight loss observed was intentional or unintentional.[139] As discussed above regarding normal weight obesity, BMI alone cannot provide an indication of CV risk due to its inability to discriminate between adiposity and lean mass.[136] Evidence suggests that markers of central fat, even in people with illness, are better indicators of future risk compared with BMI alone and intentional weight reduction is usually beneficial for controlling CVD risk in those with central obesity.[128,144]

Clinical evaluation plays an important part in assessing a person's level of 'health', defined by the WHO as complete physical, mental, and social well-being, not merely the absence of disease or infirmity.[148,151] A person with overweight/obesity might not display overt risks for CVD while they are young, although their risk will increase as they age. The WOF advocates that a healthy lifestyle should be encouraged from the early stages of life to minimize future weight gain.[5,148] Certain diseases associated with increased adiposity are more common (e.g. T2DM), while causes of CVD that are not obesity-related can be more severe or have a poorer prognosis (e.g. familial hypercholesterolaemia).[148] Larger nutritional reserves and better/more healthful diet might provide a survival advantage once severe illness occurs, while malnourished/underweight individuals have poor prognoses.[140,148]

Metabolically healthy obesity

MHO describes those people with a BMI >30 kg/m^2, who do not have elevated risk factors for CVD, although different cut-offs have been used to define this.[152] The 12-year MESA study, examining the relationship between obesity, metabolic syndrome and CVD, concluded that people with MHO were not at increased risk of CV death when compared with metabolically healthy normal weight individuals.[139,147] However, these data also showed that 48% of those in the MHO group went on to develop metabolic syndrome over time.[116] MHO individuals who developed risk factors had a 60% higher chance of suffering a major CV event compared with healthy people without obesity.[145,147] More recently, UK biobank data from over 380 000 people demonstrated that, compared with participants without obesity, those with MHO were at higher risk of incident HF [HR, 1.60 (95% CI, 1.45–1.75)] and respiratory diseases [HR, 1.20 (95% CI, 1.16–1.25)], but not ASCVD.[153] Compared with people without obesity who were metabolically healthy, those with MHO were at a higher risk of all-cause mortality [HR, 1.22 (95% CI, 1.14–1.31)], incident ASCVD [HR, 1.18 (95% CI, 1.10–1.27)], HF [HR, 1.76 (95% CI, 1.61–1.92)], and respiratory disease [HR, 1.28 (95% CI, 1.24–1.33)].[153] These results provide two important messages. Firstly, even if ASCVD risk is not

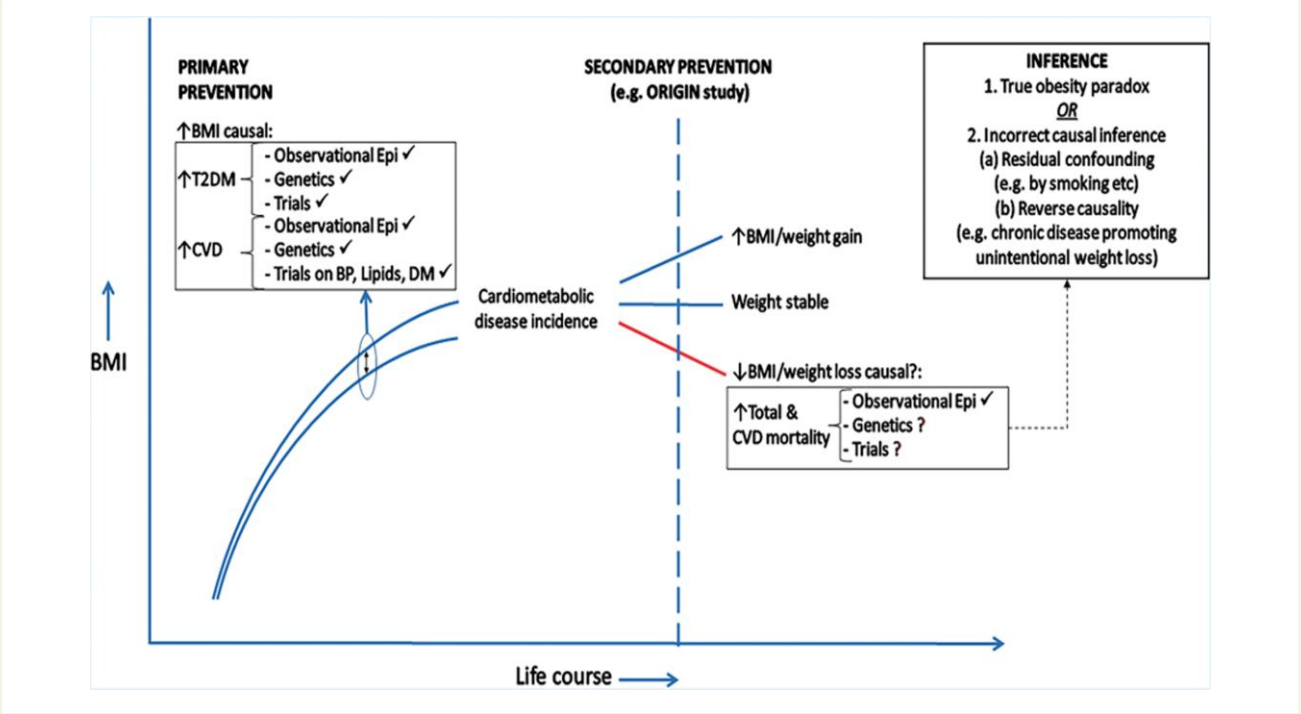


Figure 5 The differences in levels of evidence for weight loss in the primary and secondary prevention settings, using a life course model.[139] There is clear and consistent evidence from a variety of sources supporting a causal role for obesity in primary prevention of cardiovascular disease and of diabetes, as well as evidence that weight loss causes diabetes remission. In contrast, multiple observational studies suggest that people losing weight in the secondary prevention setting may be at greater risks of total and cardiovascular disease mortality, as seems to be the case in the ORIGIN trial. However, the interpretation of such findings is complicated by residual confounding and reverse causality. Future trials in this space would help improve the evidence base and help resolve the obesity paradox conundrum. BMI, body mass index; T2DM, type 2 diabetes mellitus. From Sattar N, Welsh P. The obesity paradox in secondary prevention: a weighty intervention or a wait for more evidence? Eur Heart J. 2020;41:2678–2680. doi:10.1093/eurheartj/ehaa398. Reprinted by permission of Oxford University Press on behalf of the European Society of Cardiology. https://academic.oup.com/journals/pages/open_access/funder_policies/chorus/standard_publication_model.

necessarily elevated at baseline, higher weight places such individuals closer to their threshold for ectopic fat gain and subsequent T2DM.[153] This means that people with MHO will develop ASCVD risk factors more rapidly, compared with lean individuals. Secondly, the consequences of elevated BMI will be different for some conditions (e.g. HF or chronic obstructive pulmonary disease) and other high-risk conditions are more prevalent in people with apparent MHO, irrespective of metabolic changes.[153] These data and perspectives lead us to suggest the term MHO is misleading and should be avoided.[153]

Treatments for obesity and effects on the heart: the benefits of weight loss

Weight loss beneficially affects traditional CVD risk factors (e.g. hypertension, atherogenic dyslipidaemia, and T2DM), but relapse is common without long-term treatment or support.[154–161] The broadening of health insurance policies to cover weight loss/management options would improve access to treatments with the potential to lower the burden of CVD. Recommended weight management interventions encompass lifestyle, behavioural, pharmacotherapy and surgical options.[55,159,162–165] Weight reduction through lifestyle interventions reduces progression to T2DM and long-term incidence of CV mortality in populations with prediabetes.[161] Studies also emphasize the importance of diet/food choices (e.g. Mediterranean diet) in maintaining health and primary prevention of CVD.[166] The Look AHEAD (Action for Health in Diabetes) trial, examining the impact of intensive lifestyle-based weight loss interventions in 5 145 people with T2DM, did not show any benefit for the primary outcome but a secondary post-hoc analysis demonstrated that incidence of CV death, non-fatal acute MI, non-fatal stroke, or admission to hospital for angina was 21% lower among people losing >10% of their body weight during the first year.[167] This suggests that a weight threshold needs to be reached before mortality benefit is achieved. The nutritional quality of the diet is also an important factor that should be considered when counselling on methods of weight loss.[140] Diets that are rich in vegetables, fruits and fibre, with lower amounts of red meat, are typically considered better for CV health.[45,140,166] The Prevención con Dieta Mediterránea (PREDIMED) study showed that focusing on diet quality, in this case a Mediterranean diet, was associated with a reduced risk of

CVD.[166] Short-term studies indicate that some improvement might be observed regarding cardiometabolic parameters with diets that restrict refined or total carbohydrates, but long-term efficacy is yet to be shown.[75] Much controversy surrounds different dietary interventions (including the use of intermittent fasting and very low energy diets) and the value of most approaches remains consistent, regardless of the chosen strategy.[168,169]

Approved pharmacological treatments for weight reduction offer variable levels of efficacy and are limited by cost and safety concerns.[170] For example, the drug phentermine is approved in combination with topiramate for use in weight management in the United States and Latin America, but requires heart rate monitoring in all recipients, especially those with cardiac or cerebrovascular disease.[171,172] Creatinine levels should also be monitored during treatment.[171,172] The glucagon-like peptide-1 receptor agonist (GLP-1 RA) liraglutide (3.0 mg) is approved for chronic weight management in individuals with overweight/obesity.[173,174] While not supported by dedicated CV outcomes trials (CVOTs), liraglutide 3.0 mg can improve CV risk factors and T2DM risk.[175]

CVOTs for anti-obesity drugs have historically faced multiple issues relating to study design, premature termination due to safety issues or failure to show CV benefit.[48] More recent and ongoing trials are anticipated to provide useful insights for future management of obesity-related CV risk.[176–180] The Phase 3 development programme for the GLP-1 RA drug semaglutide (2.4 mg subcutaneous injection; STEP trials 1–4) showed average weight loss of ≥15% and associated improvements in CV risk factors.[177–180] Semaglutide is approved for weight management in the United States and the UK, and it is under evaluation for use in Europe and elsewhere.[181,182] Ongoing CV outcome studies are evaluating oral semaglutide in patients with T2DM (the SOUL trial; Semaglutide Cardiovascular Outcomes Trial in Patients With Type 2 Diabetes) and semaglutide 2.4 mg subcutaneous weekly injection in people with obesity and established CVD (the SELECT trial; Semaglutide Effects on Cardiovascular Outcomes in People With Overweight or Obesity; due to complete in September 2023).[176,183] The Phase 3 SURPASS programme (tirzepatide clinical development programme) is also assessing the efficacy and safety of tirzepatide, a novel dual glucose-dependent insulinotropic polypeptide/GLP-1 RA therapy administered as a 5, 10 and 15 mg subcutaneous weekly injection, in people with T2DM.[184–186] In particular, the ongoing SURPASS CVOT may help to improve understanding regarding the impact of intentional weight loss and CV outcomes.[176–180]

SGLT2is have shown remarkable benefits in people with T2DM and established CVD or risk factors for CVD, predominantly in the prevention for HF.[111,187] In particular, improved HF outcomes were reduced more in absolute terms in people with higher BMI.[187] Some SGLT2i agents have recently been approved as treatments for HF in people without T2DM.[112,188] Although these drugs cause weight loss, it seems likely that their effect on CVD may be through multiple mechanisms (particularly haemodynamic), and they are not specifically recommended for the treatment of obesity, even in the presence of CVD.[111,187,188] Nonetheless, any weight loss achieved with their use is likely to be beneficial.

Given the proven links between T2DM and overweight/obesity, regular monitoring of blood glucose levels could aid early detection of T2DM and provide an opportunity for prompt intervention with treatments, such as GLP-1 RAs or SGLT2is, where evidence supports their effectiveness in slowing T2DM progression and lowering CVD burden.[111,176–188]

Observational data regarding surgical interventions show that bariatric procedures improve weight loss as well as incidence of T2DM (lowered by 78%), CV death, MI and stroke (reduced by 33%) over a 15-year follow-up.[156–159,189–195] There is also evidence for bariatric surgery being associated with larger potential reductions of cardiorenal complications (e.g. HF) than ASCVD outcomes in patients living with T2DM and obesity.[196] Although bariatric surgery is very effective for weight loss and the observational data summarized above provide 'proof of principle' that weight loss is likely to be beneficial for CVD prevention in those with severe obesity, the proportion of people currently able to access surgery is extremely low compared to the numbers of people living with obesity. It seems likely that it will continue to be an important option for those with severe obesity, but it is unlikely to be widely used in the general population, especially as the recent developments in pharmacotherapy are approaching the efficacy of bariatric surgery.

Current recommendations and future directions in the management of obesity and cardiovascular disease

European Society of Cardiology (ESC) guidelines highlight the importance of effective diagnosis and treatment of obesity in preventing CVD in clinical practice.[197] The ESC guidelines also recommend comprehensive assessment for people with overweight/obesity to examine the risk of adiposity-related sequelae, including hypertension, dyslipidaemia, insulin resistance, systemic inflammation, decline in kidney function, and the development of T2DM.[197]

New horizons in the management of adiposity and CV risk should see the emergence of combination therapies encompassing surgery, pharmacotherapy, and lifestyle interventions, delivered either face-to-face or via electronic media. Comprehensive structured programmes would be beneficial, drawing on expertise from multidisciplinary teams that include psychologists, dieticians, general practitioners/family doctors, cardiologists, obesity medicine specialists, and bariatric surgeons. Various guidelines and position statements have been published on the management of overweight/obesity by the European Association for the Study of Obesity, AHA, American College of Cardiology, The Obesity Society, Scottish Intercollegiate Guideline Network, the National Institute for Health and Care Excellence, and the Obesity Medicine Association.[12,42,55,159,162–164] A broad selection of multidisciplinary approaches are recommended.[12,55,159,162–165] A systematic overview of 19 international evidence-based guidelines concluded that adiposity should be treated as a chronic condition.[165] Comprehensive lifestyle programmes are favoured alongside behavioural support therapies and bariatric surgery should be offered to people with a BMI ≥35 kg/m^2 and additional CV risk

factors who have been unable to achieve significant weight loss through physical activity diet and/or pharmacotherapy.[165]

A recent scientific review from the AHA recommended investment in randomized controlled trials to evaluate the effectiveness of lifestyle and dietary interventions as well as the development of effective strategies to improve functional outcomes for people with overweight/obesity through primary prevention, weight maintenance, and treatment.[55] CVOTs assessing the effectiveness of various pharmacotherapies in reducing obesity-related cardiometabolic or cardiorenal complications are helping to identify potential mechanisms for disease and providing possible treatment options.[48,176,186,187] Importantly, to create an environment that truly supports people with overweight/obesity in addressing their CV risk, there needs to be fundamental change regarding public policy and the regulation of key industries (e.g. the food sector) that have been instrumental in driving and exacerbating the global obesity epidemic. In line with the Ottawa Charter of Health Promotion, building healthy public policies is an important pillar for primordial prevention of obesity.[198] An international treaty, carrying gravitas similar to that of the WHO Framework Convention on Tobacco Control, is recommended to address this major global public health issue that threatens both developed and developing countries.[199]

World Heart Federation and World Obesity Federation action plan for management of obesity-related and cardiovascular risk

The following action plan aims to help in identifying and reducing the risk of obesity-related CVD and mortality. The WOF and WHF recognize the diversity of healthcare systems across the globe and implementation of these recommendations should be adapted according to the availability of local resources and services.

(1) The growing evidence base suggests obesity to be a major contributor to CVD via direct and indirect mechanisms.[42,46–55] Therefore, effective strategies are needed to prevent obesity at a population level and to support people living with overweight/obesity and risk of CVD or existing CVD to lose weight and maintain a healthier weight.

(2) Given the wealth of evidence linking CVD with obesity, assessment of CV risk and aggressive strategies for risk reduction among those living with overweight/obesity should help to reduce the burden of CV morbidity and mortality in this group.[29–42,46–55]

(3) Although responses in individuals vary widely, lifestyle modifications (e.g. healthful nutrition, routine aerobic and resistance physical activity) generally provide modest weight loss and (even independent of weight loss) long-term CV benefits.[158–168] Referral to dietary or nutritional and/or physical activity counselling may be considered for those with overweight/obesity and CV risk or CVD who are interested or receptive to treatment.

(4) The potential benefits of pharmacological treatment options (e.g. GLP-1 RAs) may be discussed alongside lifestyle modifications with appropriate individuals, in line with current and emerging evidence in this rapidly evolving area.[170,173–186] In particular, evidence from ongoing CVOTs may be relevant in informing future prescribing and management approaches for people with overweight/obesity and CVD.[176–186]

(5) Bariatric surgery has been shown to promote weight loss, reduce CV risk factors, and lower overall CVD risk.[105,110,122,155–157,189–196] Health professionals should discuss referral to appropriate bariatric surgery services with people who have severe obesity (in general, people with BMI >35 kg/m^2 with established CVD or BMI >40 kg/m^2).

(6) Assessment of body fat, WHR or WC is recommended for people undergoing cardiac rehabilitation to identify those who have excess total or visceral adiposity and are likely to benefit from further investigation regarding CV risk (e.g. assessment of lipids). There are cases where total and central adiposity are undetected in individuals with a relatively low BMI.[9,13–15,35,130–132]

(7) Future treatment options for obesity have the potential to deliver substantial and sustained weight loss and provide an opportunity to clarify the impact of intentional weight reduction on CV risk and mortality. Clinicians should, in the meantime, diagnose obesity in people with CVD or at risk for CVD to better allow a patient-centred approach and to maximize the chances of attaining a healthful body weight and reduced CVD risk.

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All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this manuscript, take responsibility for the integrity of the work as a whole, and have given final approval for the version to be published.

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Data availability

No datasets were generated or analysed during the development of this review paper. All data discussed in this paper were published previously. Please refer to the original publications cited in the reference list for further details of individual datasets.

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