Evidence Review and Environmental Scan: Clinical Management of Obesity and Overweight in the Context of Cardiovascular Health

Report for the Heart Foundation

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Commissioning Body

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Use of Artificial Intelligence (AI)

AI was used in the following ways: i) ASReview, an open-source AI tool that utilises machine learning with human interaction, was used to facilitate literature searches (see Methods); ii) Adobe Acrobat AI Assistant was used to locate data for extraction within publications, with human verification ensuring accuracy; iii) Microsoft Co-Pilot was used for general grammatical recommendations of human written and human conceptualised text and, iv) also for initial explorations for the environmental scan, with human researchers completing the scan, information extraction and verification in duplicate.

Contents

Executive Summary

This report presents the findings of an evidence review and environmental scan undertaken to inform the management of obesity within the context of cardiovascular disease (CVD). The evidence review aimed to synthesise current scientific literature on the diagnosis, assessment, and treatment of overweight and obesity, with a particular focus on their relationship to CVD and associated cardiometabolic risk factors. Complementing this, the environmental scan examined the Australian health system to identify existing policies, programs, and structural enablers and barriers that influence the implementation and effectiveness of obesity and CVD-related interventions.

Summary of key findings:

- Evidence Review

Contemporary guidelines emphasise the need to move beyond BMI alone in diagnosing obesity, advocating for confirmation of excess adiposity. Individualised staging and assessment of cardiometabolic risk, alongside a holistic approach to health, are critical for accurate diagnosis and management. Obesity is a significant and independent risk factor for CVD, major adverse cardiovascular events (MACE), and mortality. However, this relationship is influenced by metabolic health, adipose tissue distribution, cardiorespiratory fitness and comorbidities such as type 2 diabetes. Behavioural interventions, particularly those involving dietary modification and structured exercise, remain foundational for the management of both obesity and CVD. Evidence supports the use of individualised prescriptions that consider sociocultural determinants, behavioural support, and long-term adherence strategies. Improvements in diet quality and exercise confer broad health benefits beyond weight loss and should be delivered through appropriately qualified professionals.

Pharmacological interventions, including GLP-1 receptor agonists, demonstrate broad cardiovascular benefits, though challenges related to adherence, cost, and equitable access limit uptake. Intentional weight loss, supported by multidisciplinary care, provides significant cardiovascular benefit, whereas unintentional weight loss may be a marker of poor outcomes in those with CVD. Preservation of lean mass through co-prescription of diet and resistance-based exercise is critical, with strategies that enhance anabolic responses, such as adequate protein intake and resistance training, central to long-term weight loss success. Importantly, weight regain following discontinuation of pharmacotherapy or other behavioural approaches is a recognised concern, particularly in the absence of sustained behavioural support.

Bariatric surgery is well supported by observational studies, demonstrating the greatest magnitude of weight loss and consistent reductions in cardiovascular morbidity and mortality among individuals with obesity. While more invasive than other approaches, short-term procedural risk is low, and current guidelines recommend its consideration following unsuccessful lifestyle and pharmacological interventions, particularly for individuals with a BMI ≥40 kg/m² or ≥35 kg/m² with obesity-related conditions.

- Environmental Scan

The environmental scan identified several systemic barriers to effective obesity and CVD management in Australia. Care for individuals with multimorbidities is often siloed and fragmented, with poor continuity between primary, secondary, tertiary, and community services. Long waitlists for specialist obesity services, limited integration of dietetics and exercise physiology in tertiary care, and workforce maldistribution especially in rural and remote regions further constrain service delivery. Funding models also present significant challenges, with low investment in preventive health, high out-of-pocket costs, and the absence of dedicated Medicare items for obesity treatment in general practice.

Despite these challenges, several enablers offer opportunities for improvement. Digital health innovations, including telehealth and remote monitoring, can extend workforce reach and improve access in underserved areas. Community-based care models, particularly those embedded in schools, workplaces, and faith-based organisations, have demonstrated potential for improving population health and advancing equity. State and NGO-led programs, such as “Wellness My Way” from Health and Wellbeing Queensland, are helping to fill service gaps, although awareness and referral pathways require further development. Importantly, investment in obesity prevention is economically justified, with potential to reduce long-term healthcare costs.

Weight stigma emerged as a pervasive issue, contributing to adverse mental and physical health outcomes, increased cardiometabolic risk, and premature mortality. Experiences of stigma, often beginning in childhood or adolescence, are associated with elevated cardiovascular disease risk and internalised bias, underscoring the need for inclusive, respectful care and public health messaging.

Achieving equitable cardiovascular risk reduction for Australians living with overweight or obesity requires a well-funded, integrated model of care as the default, embedding multidisciplinary support and scalable treatment options. Tailored delivery for priority populations, including First Nations peoples, culturally and linguistically diverse (CALD) communities, people with disability, those with mental illness, and residents of regional, remote, and low-SES areas, is essential to ensure access, engagement, and sustained outcomes.

In summary, the findings of this report highlight the need for a paradigm shift in the management of obesity and CVD toward integrated, patient-centred, and equity-led models of care. Clinical practice must evolve to incorporate comprehensive assessments, multidisciplinary support, and culturally safe service delivery tailored to priority populations. Policy reform is required to address funding gaps, improve access, and support long-term adherence to evidence-based interventions. Addressing weight stigma and embedding respectful, inclusive care practices will be essential to improving outcomes for Australians living with overweight or obesity both with and at risk of CVD.

1. Introduction

1.1. Obesity in Australia

According to the Australian Institute of Health and Welfare, in 2022, 66% of adults (18 years and over) were living with overweight or obesity as defined by BMI (~13 million Australians).[1] Of these, 34% were living with overweight but not obesity, 32% were living with obesity and 13% were living with severe obesity (defined as BMI ≥35kg/m^2).[1] Prevalence of overweight and obesity has increased from 56% in 1995 to 66% in 2022; obesity increased from 19% to 32% in this timeframe.[1] In 2022, 26% of children and adolescents (aged 2-17 years) were living with overweight or obesity (~1.3 million), with 18% living with overweight and 8.1% living with obesity. This has been relatively stable since 2017-2018 (25% vs 26% in 2022). In 2022, Australia was ranked 10th/21 OECD countries for the prevalence of overweight or obesity. The proportion of men living with obesity was the 4th highest (32%, equal with Mexico), following New Zealand (33%), Hungary (36%) and USA (44%). For women, Australia ranked 9th highest (33%). Perhaps more concerningly, 63% of adult men and 72% of adult women has a waist circumference indicative of an increased or substantially increased risk of metabolic complications; increasing from 2017-2018 (60% of men and 66% of women).[1]

Population Variations

Many Aboriginal and Torres Strait Islander peoples navigate experiences of overweight and obesity. This reflects broader systematic and environmental impacts on health and wellbeing for First Nations peoples. Recent evidence suggests that 74% of adults and 38% of children in the Aboriginal and Torres Strait Islander community live with overweight or obesity.[2] These patterns highlight the need to develop, implement and evaluate culturally safe, community-controlled approaches that promote holistic wellbeing and self-determination as well as empower First Nations individuals and families. Overweight/obesity health outcomes across geographic and socioeconomic contexts demonstrate higher rates in inner regional (68%), outer regional and remote areas (70%), and among also those living in areas with lower socioeconomic resources (68%). These findings reinforce the importance of understanding and addressing social and cultural determinants of health through equity-driven, place-based strategies that build on the strengths of First Nations communities.

Health impacts and burden of CVD attributable to overweight and obesity

In 2018, overweight and obesity was the second highest risk factor for ill health and death contributing to 51% of the burden of hypertensive heart disease and 28% of the burden of coronary heart disease.[3] It also contributed to the burden of several related conditions including type 2 diabetes (55%) and chronic kidney disease (42%). Overweight and obesity accounted for 10% of deaths in 2018 (16,400 deaths). Attributable disability-adjusted life years (DALYs) due to overweight and obesity in 2018 were 87,884 for coronary heart disease, 30,156 for stroke and 17,114 for atrial fibrillation and flutter.[3] Specifically in males aged 35-84 years and females aged 45-84 years, the greatest burden due to overweight and obesity was from coronary heart disease.[3]

1.2 Objectives

The objectives of this evidence review and environmental scan were:

Evidence Review

To conduct a comprehensive review of current scientific literature on the diagnosis, assessment, and management of overweight and obesity, with a specific focus on their relationship to cardiovascular disease (CVD) and associated cardiovascular risk factors. This includes evaluating:

- The role of overweight and obesity in the development and progression of CVD.
- The effectiveness of various clinical interventions (i.e., behavioural, pharmacological, surgical) in reducing cardiovascular risk among individuals with overweight or obesity.
- The utility and limitations of commonly used diagnostic tools such as BMI in predicting cardiovascular outcomes.

Environmental Scan

To undertake a structured environmental scan of the Australian health system to identify and assess:

- Existing national and state-level policies, strategies, and frameworks addressing obesity, overweight and cardiovascular health.
- Current services and programs available for the prevention, diagnosis, and management of overweight and obesity and CVD, including primary care, specialist services, and community-based initiatives.
- System-level enablers and barriers, including workforce capacity, funding models, infrastructure, and equity considerations, that influence the implementation and effectiveness of obesity and CVD-related interventions.

1.3 Definitions

1.3.1 Lancet Commission: Definition and diagnostic criteria of clinical obesity

In 2025, The Lancet Commission published new definitions and diagnostic criteria for clinical obesity.[4] The following terms and definitions are proposed from the 2025 Lancet Commission.

Obesity

"Obesity is characterised by excessive adiposity, with or without abnormal distribution or function of the adipose tissue." The causes of obesity are multifactorial and incompletely understood, involving genetic, environmental, psychological, nutritional, and metabolic factors.

Clinical Obesity

"A chronic, systemic illness characterized by alterations in the function of tissues, organs, or the individual, directly caused by excess adiposity."

Criteria for Diagnosis:

Anthropometric Criterion: Confirmation of excess body fat by at least one other anthropometric measure (e.g., waist circumference) or direct fat measurement, in addition to BMI. Excess adiposity can be pragmatically assumed for BMI >40 kg/m².

Clinical Criteria: Signs or symptoms of ongoing dysfunction of organ systems (e.g., cardiovascular, respiratory, musculoskeletal). Age-adjusted limitations of daily activities (e.g., bathing, dressing, toileting, eating).

Preclinical Obesity

"A physical phenotype characterized by excess adiposity with preserved function of other tissues and organs." Clinical Implications of pre-clinical obesity include the increased risk of developing clinical obesity or other non-communicable diseases (e.g., type 2 diabetes, cardiovascular disease). The statement suggests that preclinical obesity does not generally require treatment but may need monitoring and health counselling. The primary goal is to reduce the risk of developing clinical obesity and other obesity-related diseases or conditions. Management strategies should aim to prevent progression to clinical obesity or associated diseases. The statement also suggests people with preclinical obesity should receive evidence-based health counselling to promote healthy lifestyle choices alongside monitoring.

PRACTICAL CONSIDERATIONS FOR THE HEART FOUNDATION TASKFORCE

The construct of 'preclinical obesity' is akin to that of 'metabolically healthy obesity'. Given the Grade 1 Evidence that metabolically-healthy obesity is a transient state with increased risk for CVD long-term (see section **3.1.2**) the HF Australia could recommend a pro-active and intentional prevention approach for people with 'preclinical obesity' with appropriate referral to allied health professionals and linkage to community resources and services.

Remission of Clinical Obesity

"Partial or complete resolution of clinical and laboratory evidence of tissue/organ dysfunction associated with clinical obesity." Remission does not imply cure and requires sustained resolution (at least 6 months) without ongoing pharmacologic treatment.

Obesity-Related Diseases/Disorders

"Non-communicable diseases or disorders (e.g., type 2 diabetes, certain cancers, obstructive sleep apnoea, metabolic dysfunction-associated steatohepatitis, mental illness) that co-occur with obesity due to overlapping aetiology or pathophysiology."

Obesity-Related Complications

"Severe organ dysfunction and end-organ damage caused by clinical obesity, leading to life-altering or potentially life-threatening outcomes (e.g., heart attack, stroke, renal failure)."

1.3.2 European Association for the Study of Obesity (EASO) Framework for the diagnosis, staging and management of obesity in adults

In 2024, the EASO proposed a new framework based on the notion that obesity is an adiposity-based chronic disease (ABCD). It defined obesity as a "multifactorial, chronic, relapsing, non-communicable disease marked by abnormal and/or excessive accumulation of body fat that presents a risk to health".[5] In addition to highlighting the limitations of evaluating obesity based on BMI alone, it also advocates the need for comprehensive clinical evaluation rather than focusing on anthropometric measures alone. The Framework emphasises the following components:

Diagnosis should include both anthropometric and clinical components. Clinical components include medical, functional and psychological evaluation. Waist-to-height ratio (WtHR) is recommended as superior to waist circumference alone for assessing cardiometabolic risk.

Clinical Staging evaluates and describes an individual's health status. Staging is based on the severity and complications of overweight/obesity to provide guidance on prognostic implications and therapeutic approaches.

Management should be underpinned by behavioural modification that includes nutrition, physical activity, stress reduction, and sleep improvement. Psychological therapy, obesity management medications and metabolic or bariatric procedures should be considered as adjunct approaches and considered based on the comprehensive clinical evaluation, not just BMI alone.

PRACTICAL CONSIDERATIONS FOR THE HEART FOUNDATION TASKFORCE

Consistent across these new definitions and guidelines are:

i) The requirement that the diagnosis of obesity should extend beyond BMI alone and include confirmation of excess adiposity (e.g., via waist circumference, WtHR, or body fat %). Relying solely on BMI fails to account for adipose tissue distribution and function.
ii) Staging and assessment of obesity and related cardiometabolic disease risk should be individualised following clinical evaluation.
iii) Evaluation and management of obesity should have a greater focus on holistic health.

Collectively this emphasises the importance of patient-centred and multidisciplinary care for the management of obesity in the context of cardiovascular disease.

1.3.3 Australian National Obesity Prevention Strategy

The Australian National Obesity Prevention Strategy (2022-2032) sets aspirational targets for the prevention, and evidence-informed management of overweight and obesity in Australia.[6] While the focus of this strategy is to define ambitions, strategies, and targets to address obesity in Australia, it is important to note the more simplistic definition of obesity utilised.

In this document, obesity is defined as *"excessive fat accumulation that presents a risk to health. Body mass index (BMI) is a persons weight (in kilograms) divided by the square of his or her height (in metres). Which is a practical and accepted method used to monitor overweight and obese populations. An adult with a BMI equal to or more than 25 is considered overweight. An adult with a BMI of 30 or more is generally considered obese, with a BMI of 35 or more as an indicator of severe obesity. Cut-offs may be different for*

some ethnic populations. In individuals, BMI measurement does not necessarily reflect body fat distribution or describe the degree of fatness in different individuals. Overweight and obesity in children is classified using WHO growth charts and based on standard deviations above the median."[6]

1.3.4 How should clinical obesity and overweight be defined and characterised to support accurate diagnosis and risk assessment for the Australian population?

Factoring in the updated definitions for obesity and clinical frameworks, the definitions and characterisation of obesity should encompass a measure of excess adiposity and clinical staging based on the presence or absence of obesity-related comorbidities based on comprehensive individual medical evaluation. Table 1.3.1 provides information on commonly used anthropometric and body composition measures and considerations regarding use and limitations in the assessment of overweight and obesity.

Table 1.3.1 Common anthropometric and body composition measures and their use in assessment of overweight and obesity

Anthropometric and body composition measure	Definition	Notes

Body mass index (BMI, kg/m^2)	World Health Organisation classification of overweight and obesity in adults.[7]
	• Overweight: BMI 25 to <30 kg/m^2
	• Obesity: BMI ≥30 kg/m^2
	  ○ Obesity Class 1: BMI 30 to <35 kg/m^2
	  ○ Obesity Class 2: BMI 35 to <40 kg/m^2
	  ○ Obesity Class 3 (severe obesity): BMI ≥40 kg/m^2
		Does not differentiate fat versus muscle; ignores fat distribution; less accurate in some ethnic groups and older adults.
		BMI Is currently used in PBS and clinical trial entry criteria.
		'Severe' obesity is defined differently to Australian National Obesity Prevention Strategy.

Excess adiposity [4, 7-9]	Waist circumference
	  ○ Men: >94 cm (increased risk), >102 cm (high risk)
	  ○ Women: >80 cm (increased risk), >88 cm (high risk)
	Waist-to-hip ratio
	• Men: ≥0.90
	• Women: ≥0.85.
	• A ratio greater than 1.0 for either sex indicates a
		Single measure; risk classification can vary by ethnicity and measurement technique.
		Does not differentiate between subcutaneous adipose tissue and visceral adipose tissue (VAT); but is a good surrogate for VAT and liver fat.[10, 11]

	significantly increased risk of health complications. Waist-to-height ratio • Central fat distribution – 'apples' - >0.5 • Central obesity: >0.6	
Body roundness index (BRI)[12]	Calculated as $364.2 - 365.5 \times \sqrt{(1-[\text{waist circumference in centimeters} / 2\pi]^2 / [0.5 \times \text{height in centimeters}]^2)}$	A newer anthropometric measurement that incorporates body shape to estimate visceral fat and total body fat percentages using the concept of eccentricity. Aso includes waist circumference, allowing for a more comprehensive assessment of fat distribution, particularly visceral fat.[12]
Bioelectric impedance analysis (BIA)	Uses bioelectrical impedance to estimate total body water, fat mass and fat free mass. Population-specific prediction equations based on the resistance of these tissues to a small alternative electrical current.[13]	While more easily accessible than DEXA, BIA may underestimate fat mass and overestimate fat free mass in people with obesity.[14] BIA relies on a constant hydration factor and accuracy is influenced by hydration levels and body water distribution. People with obesity may have increased extracellular water and increased total body water.[14] Likely invalid in people with high levels of obesity (BMI >34 kg/m^2)[14] If there are high levels of adiposity in leg region, a non-conductive barrier should be placed between the legs. Accuracy at any level of BMI/adiposity depends on following stringent pre-test conditions.
Dual-energy X-Ray Absorptiometry (DEXA)	More commonly used clinically to evaluate bone mineral density, DEXA is considered the 'gold-standard' for assessing total body adiposity. Provides total and regional data for fat mass, lean mass and bone mineral content.	There are size restrictions (weight based) and many beds have a small region of interest that don't accommodate larger bodies. Positioning errors and challenges with larger bodies may provide inaccurate results.

	Some models provide an estimate of visceral adipose tissue.	Estimates of VAT with DXA may be overestimated compared with MRI at high VAT levels [15] and may underestimate longitudinal changes in VAT compared to MRI.[16] Accuracy at any level of BMI/adiposity depends on following stringent pre-test conditions.

1.3.5 Challenges for evaluation of cardiovascular disease risk in people with obesity

Obesity poses several structural and functional challenges to the accurate and reliable assessment and diagnosis of CVD. According to the American Heart Association (AHA),[17] several diagnostic procedures for coronary artery disease are affected by obesity (see Table 4.1.1). The AHA recommends that cardiovascular evaluation in individuals with obesity should be guided by local expertise and tailored to the patient's specific circumstances, weighing the relative strengths and limitations of each approach with careful consideration of the risk-benefit ratio.[17]

2. Methodology

2.1 Evidence Review

2.1.1. Approach

A systematic synthesis of peer-reviewed literature on the diagnosis and management of obesity and overweight in the context of CVD and cardiovascular risk was conducted. To provide a comprehensive overview of existing evidence, searches specifically targeted existing systematic reviews and meta-analyses. Databases searched were Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, Medline, Embase, and Cumulative Index to Nursing and Allied Health Literature (CINAHL) using key terms and MESH terms, developed in collaboration with a research librarian (Shell Clarke). Targeted searches were conducted separately for each relevant topic (1. connection between obesity/overweight and CVD, 2. current and emerging pharmacological therapies, 3. lifestyle modification strategies, 4. surgical management options) to ensure the identification of all relevant published evidence. Searches were undertaken between 25th June - 1st July 2025 and included studies were limited to the last 10 years (2015-2025). Details of the research questions and associated search strategies are in **Appendix 6.1.**

2.1.2. Screening

Title and abstract screening was conducted independently by two reviewers using ASReview, an open-source artificial intelligence (AI) tool designed to assist in systematic reviews. ASReview uses an *active* learning algorithm, which is a specific type of machine learning algorithm which interacts with a human to train and improve the model. The model is designed to order titles and abstracts based on their estimated relevance based on prior knowledge. The model is trained iteratively: as reviewers classify each record as relevant or irrelevant, the algorithm updates to better predict which remaining records are likely to be relevant. An overview of the ASReview screening process is shown in **Figure 2.1.1.** The model was retrained separately for each research question to maximise both sensitivity and specificity.

Before the full screening process began, a random sample of 200 records was screened for each research question. This sampling aimed to estimate the prevalence of relevant studies in the dataset. Based on this estimate, an upper threshold for the number of relevant studies was calculated using the following formula:

$$R = \mathrm{N}\left(\mathrm{p} + 1.96 \times \sqrt{\frac{(\mathrm{p} * (1 - \mathrm{p})}{n}}\right)$$

where N is the total number of articles identified in the literature search, p is the proportion of relevant articles identified in the random sample of articles, and n is the number of random titles and abstracts screened. To improve sensitivity and reduce the risk of missing relevant studies, a heuristic stopping rule of 50 consecutive irrelevant titles and abstracts was implemented. This approach has been shown to improve the sensitivity of machine learning-assisted screening.[18] Therefore, title and abstract screening was stopped once the upper threshold was reached and 50 consecutive titles and abstracts were marked as irrelevant. Any remaining records that had not been screened at the point the stopping criteria were met were excluded, as they were ranked below the relevance threshold by the machine learning model. All records deemed relevant by either reviewer during title and abstract screening were retrieved for full-text screening, which was conducted in Covidence. Two independent reviewers screened the full texts. In cases of disagreement, the reviewers discussed the study until a consensus was reached.

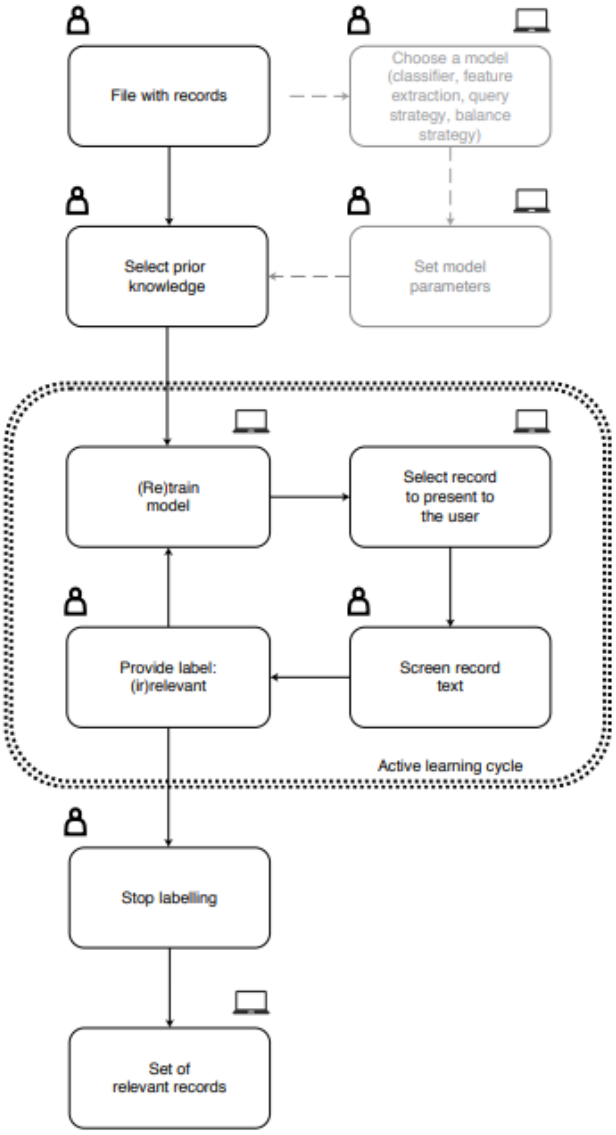

Figure 2.1.1– Schematic of the ASReview machine learning model. Reprinted from "An open source machine learning framework for efficient and transparent systematic reviews", by R. van de Schoot, et al., 2021, Nature Machine Intelligence, 3, p. 127. Copyright 2021 by Springer Nature.

2.1.3. Data Extraction

Data describing characteristics and outcomes were extracted into a standardised form for synthesis. Evidence profiles were created based on the identified literature to provide an overview of the latest evidence on each topic.

2.2 Environmental Scan

2.2.1 Approach

Primary Objective: To understand how overweight and obesity management is integrated into cardiovascular disease prevention and treatment in Australia.

Key Research Questions

- What national and state-level policies address overweight and obesity and CVD?
- What services currently exist for overweight and obesity management in the context of CVD?
- What are the economic implications of overweight and obesity-related CVD management?
- What are the key barriers and enablers for equity, access, and integration addressed across different population groups?

Special attention will be given to service availability and outcomes for:

- First Nations peoples
- CALD communities
- People in regional, rural, and remote areas
- People with mental health conditions
- People with disabilities
- Children and adolescents

Data Sources

- National and international position statements, consensus guidelines, and policy documents from cardiology and obesity societies.
- Government websites and Google searches for national and state-level obesity and CVD policies.
- Information from Australian obesity societies regarding their scope, supported populations, and service models.
- Health economic reports and service directories.

Data Collection Tools

A structured Excel spreadsheet was developed to catalogue:

- Policies
- Services
- Societies
- Web links and references

3. Evidence Review

3.1 Obesity and Cardiovascular Disease

A growing body of meta-analytic evidence confirms that obesity is a significant and independent risk factor for CVD, major adverse cardiovascular events (MACE), and both all-cause and cardiovascular mortality. However, the relationship is nuanced by factors such as metabolic health, adipose tissue distribution, cardiorespiratory fitness, and comorbid conditions like type 2 diabetes (T2D). The evidence supports that obesity, particularly when accompanied by metabolic dysfunction or low fitness, significantly increases the risk of cardiovascular morbidity and mortality.[19] The systematic search netted 54 meta-analyses between

2015-2025 evaluating the association of overweight and/or obesity with risk of CVD (**Figure 3.1.1**; **Appendix 6.2** for study details of pertinent literature).

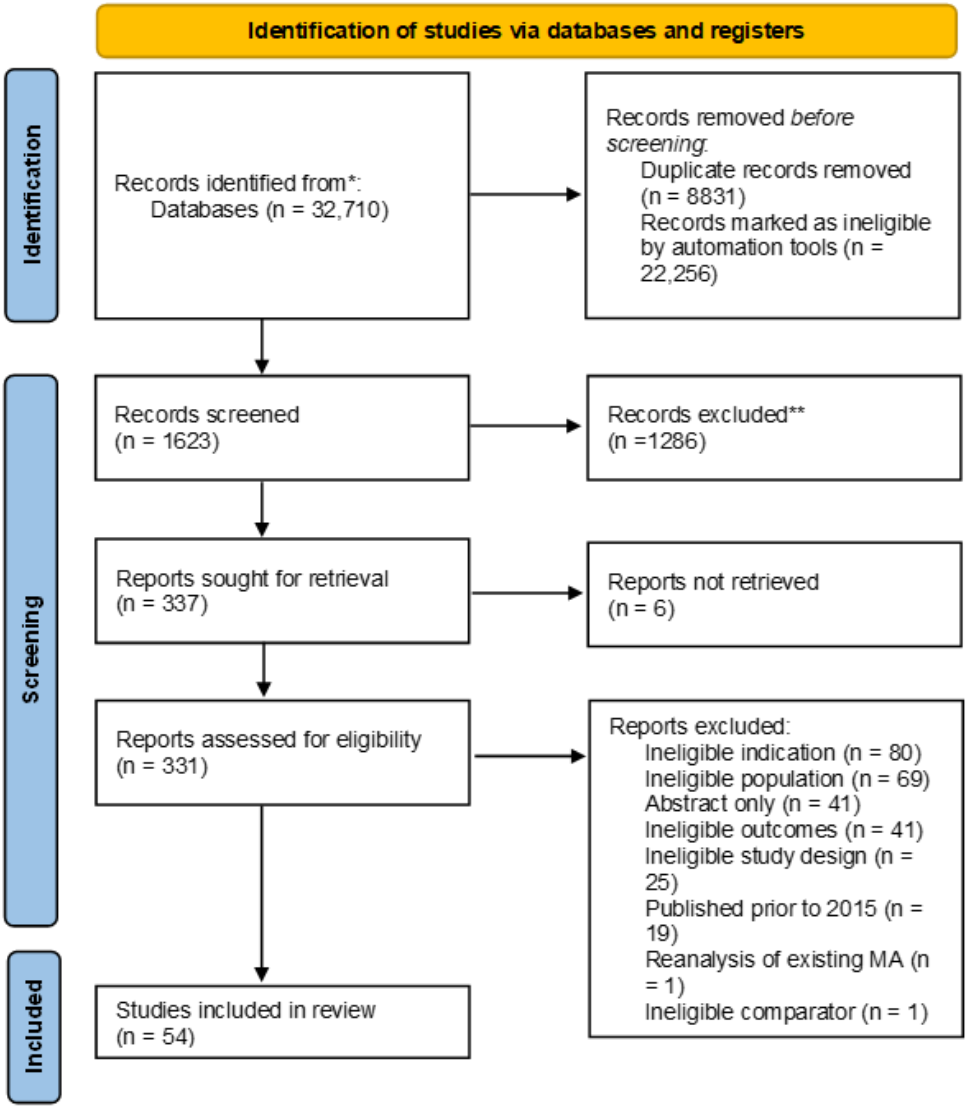

Figure 3.1.1- PRISMA search results – Risk of CVD in obesity

The majority of reviews examined the association of overweight/obesity on general CVD outcomes (21%) or mortality and/or MACE (25%) (**Figure 3.1.2**).

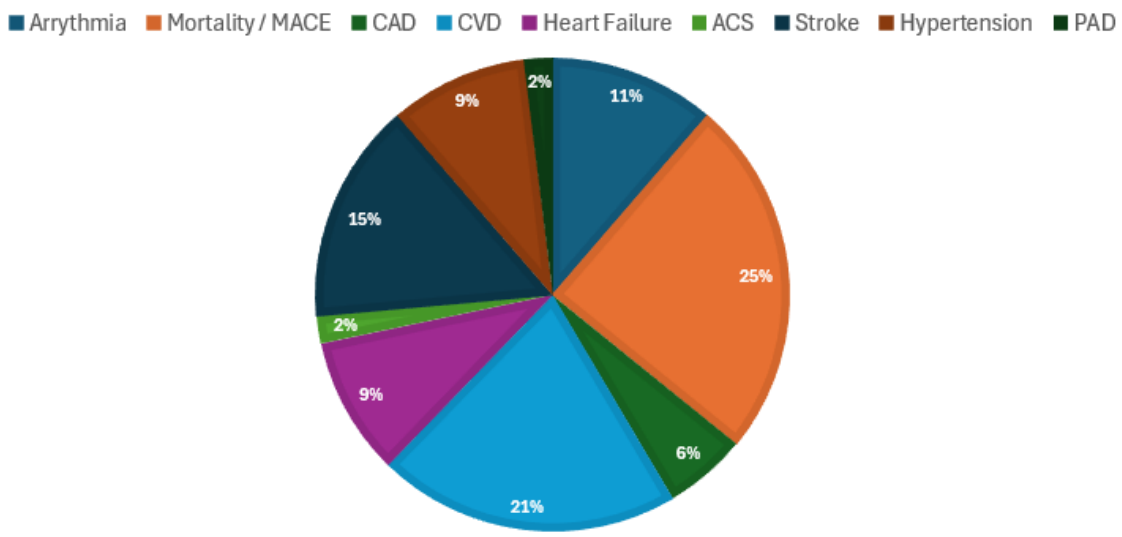

Figure 3.1.2. Breakdown of major topics of meta-analyses examining the association between overweight/obesity and CVD.

3.1.1. Obesity and CVD Risk

Most studies demonstrated a positive association between obesity (primarily defined by BMI category) and increased CVD risk. Longitudinal data show that lifetime BMI trajectories significantly influence cardiovascular outcomes.[20] For example, individuals with a persistently overweight trajectory from childhood to adulthood have a 149% higher risk of developing hypertension than those with a stable normal weight [RR 2.49; 95% CI: 1.9–3.28; I^2 69.5%].[20] Similarly, those who transition from normal weight in childhood to overweight in adulthood also face a substantially elevated risk [RR 2.38; 95% CI: 1.70–3.33; I^2 95%].[20] In populations with type 2 diabetes who are at heightened risk for CVD, data from 21 cohort studies involving over 1.3 million individuals show that each 5-unit increase in BMI was associated with a 12% increase in CVD incidence [RR 1.12; 95% CI: 1.04–1.20; I^2 98.2%].[21]

The impact of metabolic-dysfunction, central adiposity and cardiorespiratory fitness on CVD risk:

The extent to which obesity *per se*, as quantified by BMI, contributes to adverse health outcomes compared with metabolic dysregulation, reflected by individual components of the metabolic syndrome, remains unclear. Most studies included in this review suggested that BMI alone is an inadequate marker of cardiometabolic risk, as metabolic abnormalities can occur even in individuals with normal weight. Moreover, the location of excess adiposity is a more critical determinant of CVD risk than overall adiposity levels.[22] Specifically, abdominal (central) obesity, particularly the accumulation of visceral adipose tissue, and ectopic fat deposits such as hepatic fat, are more strongly associated with increased CV risk than general obesity.[22] This elevated risk is largely driven by adipose tissue dysfunction, which promotes systemic inflammation, insulin resistance, and endothelial dysfunction.[23]. In a meta-analysis of 31 prospective cohort studies involving 669,560 participants, Xue et al. (2021) found that each 10 cm increase in waist circumference was associated with a 4% increase in CVD risk in men and a 3.4% increase in women.[24] These findings underscore the importance of assessing abdominal fat distribution, rather than relying solely on BMI. Additionally, individuals with normal weight obesity (defined as having a normal BMI

but a high body fat percentage) are at significantly increased risk for both CVD [25] and several cardiometabolic risk factors.[26, 27] A systematic review and meta-analysis reported that normal weight obesity was associated with high triglycerides [OR 1.90 (95% CI: 1.44, 2.35)], hypertension [OR 1.40 (95% CI: 1.28, 1.51)] and metabolic syndrome [OR 1.92 (95% CI: 1.58, 2.26)].[26]

While metabolically-healthy obesity is associated with an increased risk of CVD,[28] change in metabolic health status had a stronger impact on risk of CVD and type 2 diabetes than change in BMI category.[29] Transitioning from metabolically-unhealthy obesity to metabolically-healthy obesity reduced CVD risk by 13% [HR 0.87 (95% CI 0.74–1.02)] and in those with normal weight, transitioning from metabolically unhealthy to metabolically healthy reduced CVD risk by 60% [HR 0.40 (95% CI 0.29–0.55].[29] Metabolically unhealthy phenotypes (of any BMI classification) were strongly associated with increased risk of CVD (RRs ranged from 1.86 to 2.16), myocardial infarction (RRs ranged from 1.44 to 1.82) and heart failure (RRs ranged from 1.78 to 2.11).[30] Notably, Ortega and colleagues (2018) demonstrated that metabolically-healthy obese individuals were more active and had a higher cardiorespiratory fitness than metabolically-unhealthy obese individuals, indicating that cardiorespiratory fitness might explain some differences in CV prognosis.[31] These findings suggest that effective obesity management should prioritise addressing metabolic dysfunction and improving cardiorespiratory fitness rather than focusing solely on weight reduction.

3.1.2 Obesity, CVD Mortality and Major Adverse Cardiac Events (MACE)

Across general populations, elevated BMI is consistently associated with increased risk of premature myocardial infarction, sudden cardiac death, and CVD mortality. CV event risk increases progressively with higher BMI notably when accompanied by low cardiorespiratory fitness and metabolic dysregulation.[19]

In meta-analyses of cohort and cross-sectional studies, overweight and obesity based on BMI criteria have been shown to be associated with a 46% and 64% higher risk of premature myocardial infarction, respectively,[32] and a 21% and 52% increased risk of sudden cardiac death, respectively.[32-34] A meta-analysis by Colpani and colleagues (2018), which included 59 prospective cohort studies in over 5.3 million middle age and elderly women, found that obesity was significantly associated with increased mortality risk.[35] Women with obesity had a 24% higher risk of all-cause mortality than those with normal weight (RR: 1.24, 95% CI 1.16–1.33). Among women with a BMI of 30-35 kg/m², the relative risk of cardiovascular mortality was more than double that of normal-weight women (RR 2.30; 95% CI: 1.56-3.40).[35]

In adults with type 2 diabetes, a non-linear association between BMI and CVD mortality has been consistently observed,[21, 36, 37] with the lowest mortality risk observed by Zhao *et al.* at BMI ~28.4 kg/m^2.[21] or between 29-31 kg/m^2, with increased risk at >31kg/m^2 in Kwon *et al*.[36] While higher BMI increases CVD incidence, the lowest mortality risk is often observed in the overweight or mildly obese range. Significant heterogeneity suggests these relationships are complex and potentially confounded by reverse causation or other unknown contributors, which are discussed in more detail in section 3.2, below.

The impact of metabolic-dysregulation and central adiposity on hard CVD outcomes:

Metabolic health status further modifies the obesity-CVD relationship. A meta-analysis of 41 prospective cohort studies involving over 4 million participants demonstrated that metabolically-unhealthy normal

weight (MUH-NW) individuals had significantly higher cardiovascular risks compared to those with metabolically healthy obesity (MH-O). Specifically, MUH-NW was associated with a 2.37-fold increased risk of cardiovascular mortality (RR: 2.37; 95% CI: 1.97-2.86) and a 1.73-fold increased risk of major adverse cardiovascular events (MACE) (RR: 1.73; 95% CI: 1.49-2.00).[38] These findings show that BMI did not adequately reflect obesity-related risk factors and underscore the importance of assessing metabolic health alongside body weight in cardiovascular risk stratification.[38] However, metabolically healthy obesity is not benign. While MUH-NW individuals are at significantly higher risk of CV events, earlier systematic reviews suggest that those with metabolically-healthy obesity are at a 45-50% increased risk of CV events than those who are metabolically-healthy and normal-weight.[39 40] Importantly, the risk of CV events increased with longer follow-up,[39] suggesting that metabolically-healthy obesity (related to the newer term of 'pre-clinical obesity') is likely a transient state of sub-clinical CVD that may progress if not actively managed with appropriate therapy (i.e., healthy diet and increased physical activity with targeted behavioural support).

The impact of cardiorespiratory fitness on hard CVD outcomes:

Cardiorespiratory fitness (CRF) is a potent and independent predictor of CVD-related mortality in people with overweight/obesity.[41 42] Fit individuals, irrespective of BMI did not show a significant increase in CVD or all-cause mortality compared with normal-weight fit individuals [HR, 95% CI (1.5, 0.82-2.76 for overweight-fit vs normal weight-fit), (1.62, 0.87-3.01 for obese-fit vs normal weight-fit)].[41] Consequently, there was a 2-3 fold greater CVD-related mortality in unfit individuals than normal weight-fit individuals [(for normal weight-unfit HR 2.04, 1.32-3.14), (for overweight-unfit HR 2.58, 1.48-4.52), (for obese-unfit HR 3.35, 1.17-9.61).[41] In Zheng (2016), the association between obesity (including metabolically-healthy obesity) and CV events were weakened, although still significant, when adjusted for cardiorespiratory fitness or physical activity (HR 1.33, 95% CI 1.06–1.68).[40] Thus, CRF is a critical modifier of obesity-related risk. Exercise interventions targeting CRF should be prioritised to reduce CVD mortality risk.[42]

3.1.3 Arrythmia

Obesity is associated with an increased risk of atrial fibrillation (AF),[43-47] with both general (i.e., elevated BMI and body weight) and abdominal adiposity measures (i.e., waist circumference, WtHR) posing significant risk for AF.[47] The meta-analysis by Wu *et al* (2023) including over 17 million participants demonstrated that obesity is associated with a 39% higher risk of AF [RR 1.39 (95% CI 1.30 to 1.49)], independent of other metabolic abnormalities.[44] Further, people with metabolically healthy obesity were at higher risk of AF than metabolically healthy people of healthy weight (HR 1.34) and a lower risk of AF than those with metabolically unhealthy obesity (RR 0.48).[43]

3.1.4 Heart Failure

A 'J-curve' relationship has been demonstrated between BMI and heart failure (HF) risk, with HF incidence increasing progressively with higher BMI categories: 0.99 cases per 100 person years for underweight, 0.34 cases per 100 person years for healthy weight, 0.59 cases per 100 person years for overweight, 1.05 cases per 100 person years for obesity and 2.79 cases per 100 person years for those with excessive obesity.[48] Mahajan and colleagues (2020) showed that while there was a non-significant 22% and 11% greater risk of HF in those with underweight and overweight respectively, the risk of developing HF was 62% higher for

those with obesity and 73% higher for those with excessive obesity.[48] Purported mechanisms include that obesity leads to increased cardiac output with subsequent left ventricular hypertrophy resulting in diastolic dysfunction as well as inflammation produced by epicardial adipose tissue.[48] Aune *et al.* (2016) demonstrated that both general (per BMI) and abdominal (per waist circumference) obesity independently increased the risk of HF.[49] For incident HF, the relative risk for a 5-unit increase in BMI was 1.41 and for a 10 cm increase in waist was 1.29.[49]

3.1.5 Coronary Heart Disease, Coronary Artery Disease & Peripheral Artery Disease

Obesity is associated with the development of atherosclerotic CVD and increases the odds of coronary artery disease (CAD) by 20% per 1 SD increase in BMI [OR 1:20 (95% CI 1.02 to1.41)].[50] The associations between elevated BMI and coronary heart disease (CHD) were similar between men and women: a one unit increase in BMI was associated with an age-adjusted increase of CHD of 4% [HR 1.04 (95% CI 1.03 to 1.05)] in women and 5% [OR 1.05 (95% CI 1.04 to 1.07)] in men.[51] Individuals with premature CHD were 59% more likely to have obesity than healthy-weight controls.[52] Those with metabolically healthy obesity had a higher odds for coronary artery calcification than those with metabolically healthy, normal-weight obesity [OR 1.36 (95% CI 1.11 to 1.66)] with age and smoking status potential modifiers.[53] Having obesity (BMI ≥30 kg/m^2) is also positively associated with peripheral artery disease.[54]

3.1.6 Stroke

Obesity, and notably obesity with metabolic dysregulation, significantly increases the risk of stroke.[55-59] In Liu *et al.* (2018) the risk of stroke was increased by 10% with each 5-unit increment in BMI.[58] Individuals with metabolically healthy obesity had a higher risk of stroke compared with metabolically healthy normal weight [RR 1.17 (95% CI 1.11 to 1.23).[57] Stroke risk was also increased in metabolically unhealthy phenotypes, regardless of BMI, while metabolically healthy phenotypes did not show a significant increase in stroke risk.[55] Those with metabolically unhealthy normal weight has a 63% higher likelihood of stroke than metabolically healthy normal weight individuals [HR 1.63 (95% CI 1.41 to 1.89)].[55] Wang and colleagues (2022) observed a higher risk of ischemic stroke with obesity particularly in men.[56]

3.17 Hypertension

The risk of hypertension increases continuously with general (i.e., BMI) and adiposity specific (e.g. waist circumference) measures of obesity.[60] The life course trajectory of BMI is also associated with varying risk of developing hypertension: those with stable 'high' BMI had an 80% higher risk of developing hypertension [RR 1.80 (95% CI 1.29 to 2.50)] than stable 'normal'.[61] The 'Fluctuated (sharp-increase)' trajectory (continued sharp increase of BMI >3kg/m^2) and the 'Fluctuated (elevated-decrease)' trajectory (initially elevated and then decreased BMI) were also associated with an increased risk of hypertension, with 'Stable low' (BMI ≤ 18.5 kg/m^2 and the range of change in BMI ≤ 1 kg/m^2) displaying lower risk.[61]

3.1.8 Ancillary health impacts

There are numerous comorbidities associated with obesity that significantly increase the risk of CVD. These notably include:

Metabolic dysfunction-associated fatty liver disease (MAFLD). Formerly termed non-alcoholic fatty liver disease (NAFLD) and also referred to globally as metabolic dysfunction-associated steatotic liver disease (MASLD, definitions and criteria vary slightly), MAFLD affects over 30% of adults globally and confers a significantly higher risk of CVD and CVD mortality than those without MAFLD.[62] People with MAFLD had an over two-fold risk of CVD incidence than those without MAFLD [RR 2.26 (95% CI, 2.00 to 2.54)] and 1.57 times higher risk of CVD mortality [RR 1.57 (95% CI 1.42 to 1.72)].[62] Given the common underlying metabolic dysregulation of MAFLD and CVD, management pathways and recommendations are similar including diet and exercise being foundational components,[63-65] with newer pharmacotherapy recently approved by the US Food and Drug Administration (FDA) for MAFLD. In August 2025, the FDA approved Semaglutide (Wegovy) for MAFLD (specifically metabolic dysfunction-associated steatohepatitis) following evidence that 63% of participants treated with Wegovy achieved resolution of steatohepatitis and no worsening of liver fibrosis compared with 35% in placebo. Liver fibrosis was also improved in 37% of participants compared to 22% in placebo.[66]

Obstructive Sleep Apnoea (OSA): Obesity, and especially central adiposity, is strongly associated with OSA,[67] which independently increases cardiovascular risk. In a cross sectional study of over 9K participants, neck circumference, WHR, body fat percentage and the visceral adiposity index were associated with a 9-14% increase in OSA.[67] Every 0.01-unit increase in WHR was associated with a 3% elevated risk.[67] OSA causes cycles of intermittent hypoxia, carbon-dioxide retention and negative intra-thoracic pressure and is associated with several CV outcomes.[68] Acute effects include oscillations in heart rate and increased blood pressure and chronically to left ventricular hypertrophy and autonomic dysfunction.[68 69] In a meta-analysis by Loke *et al.* (2012), OSA was significantly associated with increased risk of stroke [OR 2.24 (95% CI 1.57 to 4.31), ischemic heart disease in men only [OR men 1.91 95% CI 1.06 to 3.65) and CV mortality [OR 2.09 (95% CI 1.20 to 3.65).[69] Treatment with continuous positive airway pressure (CPAP) for ≥ 4 hours per day was associated with a significantly reduced the risk of MACE [HR 0.69 (95%CI 0.52 to 0.92) compared to those who used CPAP for <4 hours per day, with authors emphasising the importance of treatment compliance for secondary CVD prevention.[70] However, the Sleep Apnea Cardiovascular Endpoints (SAVE) study failed to demonstrate a reduction in cardiovascular events with continuous positive airways pressure in subjects with moderate-to-severe obstructive sleep apnoea and established CVD.[71]

Chronic Kidney Disease (CKD): The American Heart Association introduced the concept of the Cardiovascular-Kidney-Metabolic (CKM) syndrome, recognising the overlapping and synergistic effects of obesity, type 2 diabetes, CVD, and CKD.[72] These conditions have numerous mutual risk factors and pathophysiological mechanisms with obesity a major independent risk factor for both CVD and CKD.[73] Indeed, 65.4% of men and 77.9% of women who developed CKD had a BMI over 25 kg/m^2.[74] The hazard ratio (HR) for CKD increased with cumulative excess weight (CEW), with HRs of 1.155 for men and 1.105 for women per standard deviation increase in CEW.[74] Kidney disease promotes a persistent, systemic inflammatory environment that drives changes in both vascular and cardiac structures. These changes can lead to the development of atherosclerosis, vascular calcification, myocardial fibrosis, and calcification of the heart valves.[75] A meta-analysis reported that the risk of mortality increases as kidney function declines. Specifically, when compared to an estimated glomerular filtration rate (eGFR) of 95 mL/min/1.73 m², an eGFR of 60 mL/min/1.73 m² corresponds to a 1.18-fold increase in death risk (95% CI: 1.05–1.32),

while an eGFR of 45 mL/min/1.73 m² raises the risk to 1.57 (CI: 1.39–1.78), and an eGFR of 15 mL/min/1.73 m² is associated with a 3.14-fold increase (CI: 2.39–4.13).[76] Cardiovascular mortality mirrors these findings.

Screening and management of comorbidities related to obesity should be considered in the broader management of obesity and CVD. Multidisciplinary models of care including endocrinologists, hepatologists, gastroenterologists, nephrologists and other related healthcare providers should be integrated into cardiometabolic care pathways.

PRACTICAL CONSIDERATIONS FOR THE HEART FOUNDATION TASKFORCE

- Interventions targeting weight reduction, metabolic optimisation, and increased fitness should be prioritised for reducing the burden of CVD in populations with obesity.
- A comprehensive evaluation of body composition and metabolic health, beyond BMI, is essential for accurate CVD risk stratification. Ideally this should include measures, or a surrogate measure, of visceral adiposity, hepatic steatosis, and sarcopenia.
- According to Chartrand et al. (2022),[23] four 'lifestyle vital signs' should be considered in clinical practice to enhance risk discrimination in individuals with overweight or obesity:
    - Waist circumference (abdominal adiposity)
    - Cardiorespiratory fitness
    - Overall diet quality
    - Level of physical activity
- Waist circumference or waist-to-height ratio should be considered as a clinical vital sign, given their strong predictive value for cardiometabolic risk. A simple public health message- 'Keep your waist circumference less than half your height'- has been proposed to improve population-level awareness and prevention.[24]
- Cardiorespiratory fitness is an independent predictor of cardiovascular outcomes in individuals with overweight and obesity. Clinicians should consider incorporating CRF assessments into routine care. For those in general practice, consider using approaches, tools and resources as presented in Keating *et al.* 2024.[77]
- Further clarity is needed on how best to measure metabolic dysregulation in routine practice. Emerging biomarkers and composite indices may offer improved risk stratification beyond traditional measures.
- Screening and management of comorbidities related to obesity should be considered in the broader management of obesity and CVD. Multidisciplinary models of care including endocrinologists, hepatologists, gastroenterologists, nephrologists and other related healthcare providers should be integrated into cardiometabolic care pathways.

3.1.9 Impact of weight loss on CV outcomes in people with obesity and on outcomes in people with established CVD.

Broadly, weight control interventions including pharmacological, surgical, dietary and exercise reduce all-cause mortality and CV outcomes.[78] An umbrella review by Chen *et al.* (2025) evaluated the overall impact of weight control interventions on all-cause mortality and CV outcomes with the goal to clarify the

relative benefits and limitations of each approach. While not explicitly in populations living with obesity and/or CVD, systematic reviews and meta-analyses of observational studies and RCTs were included if they reported on outcomes of all-cause mortality and cardiovascular outcomes, including CVD mortality, MACE, stroke, myocardial infarction, heart failure, and atrial fibrillation.[78] Thirty-one meta-analyses were included (n=13 from RCTs, n=18 from cohort studies) with 21 (51%) evaluating pharmacological strategies, 12 (26%) bariatric surgery and 7 (15%) dietary interventions. In individuals with type 2 diabetes or overweight/obesity, glucagon-like peptide-1 receptor agonists (GLP-1 RAs) significantly reduced all-cause mortality, MACE, stroke, cardiovascular mortality, myocardial infarction, and heart failure.[78] Bariatric surgery was associated with reduced risk for all CV outcomes except atrial fibrillation. Low-fat diets were associated with reduced all-cause mortality and Mediterranean and Nordic diets reduced stroke and CV mortality, while physical activity was associated with reductions in both all-cause and CV mortality.[78] Interestingly, comprehensive lifestyle interventions showed no CV benefit with the authors proposing that these may be hindered by complexity and variability in adherence.[78] Across analyses, the certainty of evidence was mostly rated as low or moderate due to bias, imprecision and inconsistency.[78]

Intentional vs unintentional weight loss

Outcomes of weight loss in people with obesity and/or CVD have varied across the literature and are largely influenced by the nature of weight loss (intentional or unintentional) and specific CVD aetiology (see **Appendix 6.3** for select studies). De Stefani and co-workers (2018) defined unintentional weight loss as 'weight loss without self-reported action, e.g., diet, physical activity or medication use'.[79] In their meta-analysis of people with overweight or obesity, unintentional weight loss (n=24,995) was associated with increased all-cause mortality [RR 1.11 (95% CI 1.04 to 1.18)] but not MACE.[79] In people living with obesity, intentional weight loss was associated with improved indices of cardiac structure and myocardial function[48], improved haemodynamic effects [80], improved cardiovascular disease risk factors[81] and reduced cardiovascular mortality.[82] Across nine bariatric surgery studies achieving mean body weight reduction of 39 kg over a mean follow up of 18 months, there was a reduction in left ventricular mass index [SMD -0.49 (95% CI -0.73 to -0.26)] and left atrial size [SMD -0.39 (95% CI -0.72 to 0.07)] and improvement in diastolic function [SMD 0.65 (95% CI 0.38 to 0.91)].[48] In individuals with obesity but without heart failure, therapeutic weight loss (via dietetic intervention n=6 studies, or bariatric surgery n=3 studies) led to a median 43kg (~25%) reduction over 9.7 months and was associated with significant improvements in biventricular filling pressure and other haemodynamic indices.[80] This included reductions in resting heart rate [-9 bpm (95% CI -12 to -6)], mean arterial pressure [-7 mmHg (95% CI -11 to -3)], resting oxygen consumption [-85 mL/min (95% CI -111 to -60)], mean pulmonary artery pressure [-5 mmHg (95% CI -8 to -2)] and mean pulmonary capillary wedge pressure [-3 mmHg (95% CI -5 to -1)].[80]

Heart Failure

In a meta-analysis of >26K patients with heart failure weight loss was associated with significantly increased CV and all-cause mortality [HR 1.64 (95% CI 1.18 to 2.28) and HR 1.75 (95% CI 1.43 to 2.14), respectively].[83] These associations were higher in those without overweight or obesity [HR 1.90 (95% CI 1.14 to 3.14) than those with overweight or obesity [HR 1.76 (95% CI 1.41 to 2.20)].[83] While most included studies did not differentiate between intentional or unintentional weight loss, the authors concluded that assessing weight changes provides prognostic information in people with heart failure.[83]

However, an earlier systematic review evaluating outcomes following intentional weight loss in people with obesity and heart failure described improvements in exercise capacity, quality of life and NYHA classification.[84] The authors suggested that bariatric surgery may be safe and effective in people with heart failure with multidisciplinary management and oversight.[84] Overall, observational studies are compromised by methodological challenges including misclassification of weight loss intentionality,[79] and more research is needed to define the optimal methods to achieve weight loss in patients with obesity and heart failure.[80] Comprehensive guidance on the management of obesity in adults with heart failure can be found in the 2025 American College of Cardiology (ACC) scientific statement, which highlights the benefits of intentional weight loss via caloric restriction and other dietary approaches alongside physical activity and via medication or bariatric surgery.[85] It also emphasises that unintentional weight loss should be avoided given its association with adverse outcomes.[85]

Weight loss maintenance

Sustainability of intentional weight loss is imperative to sustaining long-term health benefits. While there is a general understanding that weight-loss maintenance is notoriously challenging, there is evidence to suggest that some degree of weight-loss maintenance can be achieved, and this is primarily driven by adherence to diet, physical activity and pharmacotherapy.[86] An earlier (2007) review of diet, exercise and pharmacological weight-loss interventions with a minimum 1-year follow-up (n=26,455, 69% 'completers') demonstrated that weight loss plateaued at ~6months (5-9% loss from baseline) and modest weight loss (3-6%) was sustained for 1-4 years.[87] Lamestra *et al.* (2015) showed that the overall adherence to weight loss interventions was 60.5% (95% CI 53%-76%), with greater adherence associated with supervised programs, interventions that offer social support and dietary-focused interventions.[86] Similarly, in a 10-year observational study of self-reported weight loss and behaviour change in the National Weight Control Registry, over 87% of participants maintained at least a 10% weight loss at Years 5 and 10.[88] Decreases in physical activity, dietary restraint, self-weighing frequency and increases in percent energy from fat were associated with greater weight regain.[88] For those taking GLP-1RAs, supervised exercise during pharmacotherapy enhanced long-term weight maintenance and body composition following treatment cessation.[89] In the year following 12 month treatment with liraglutide, weight regain was 6kg larger after termination of liraglutide compared with after termination of supervised exercise.[89] Combining supervised exercise with obesity medications was the most effective strategy for long-term weight and body composition maintenance.[89]

PRACTICAL CONSIDERATIONS FOR THE HEART FOUNDATION TASKFORCE

- Intentional weight loss via multidisciplinary methods provides broad CV benefit for people with or at risk of CVD. Unintentional weight loss should be monitored given its association with adverse outcomes.
- For people with or at risk of CVD who are actively pursuing weight loss and subsequent maintenance, consistent multidisciplinary support should be a priority.

3.2 Obesity and Outcomes in Cardiovascular Disease

The systematic search netted 61 meta-analyses between 2016-2025 evaluating the impact of overweight/obesity on outcomes in CVD (**Figure 3.2.1; Appendix 6.4** for select study details). Six meta-analyses published in 2015 were excluded due to duplication of research questions in later studies (i.e., redundancy).

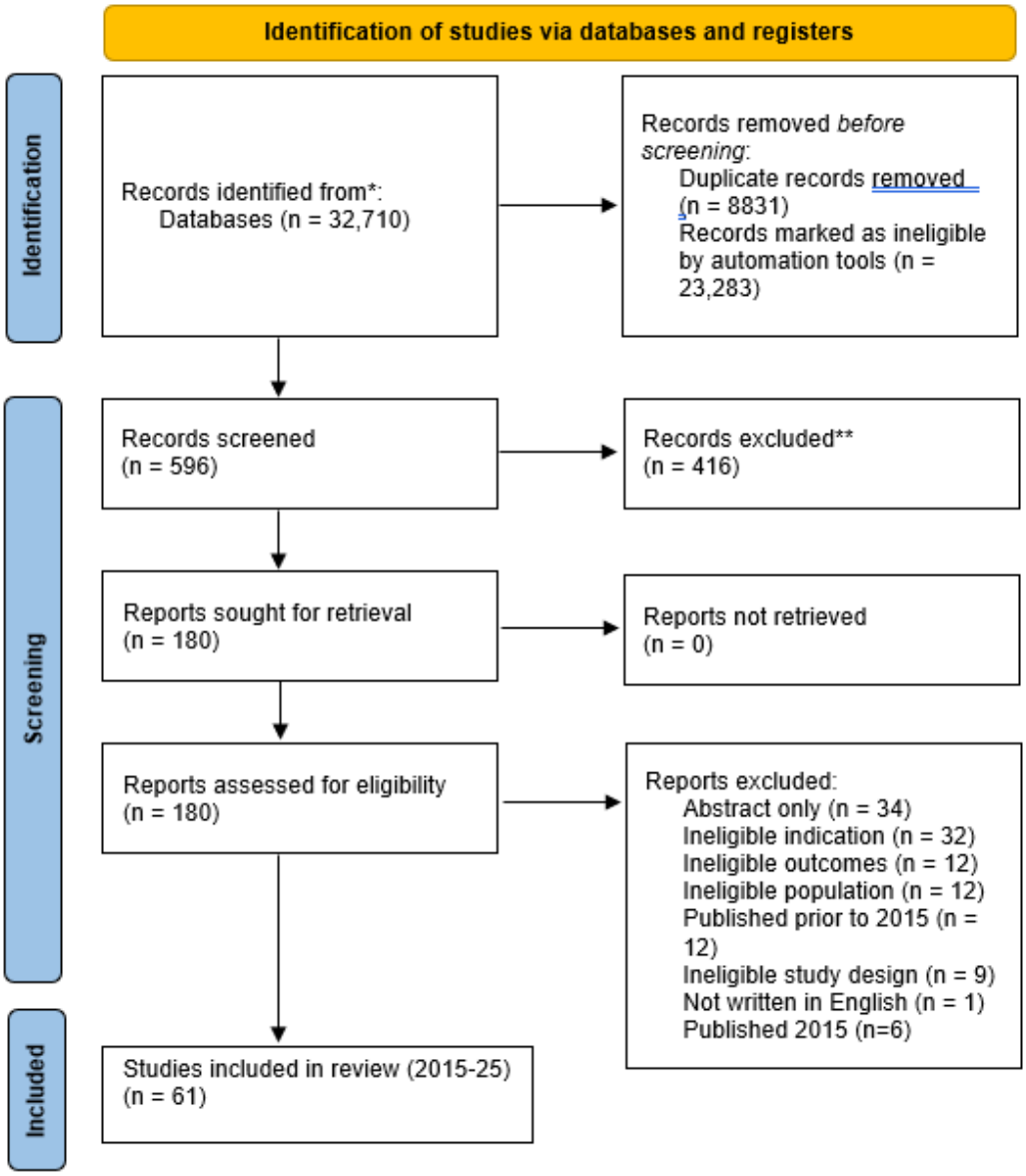

Figure 3.2.1- PRISMA search results – CVD outcomes/prognosis and obesity

The majority of reviews examined the association of overweight/obesity on mortality and/or MACE (29%) or on outcomes of CVD-related surgery (28%) (**Figure 3.2.2**).

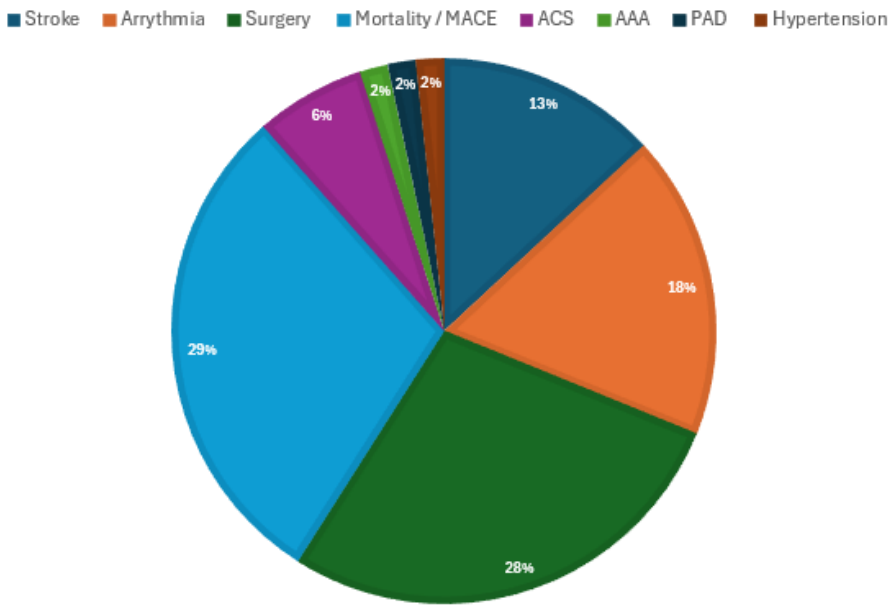

Figure 3.2.2. Breakdown of major topics of meta-analyses examining the association between overweight/obesity and outcomes of CVD.

3.2.1. Overweight/Obesity, Mortality and MACE in people with CVD.

Most studies observed a non-linear association between BMI and CVD mortality or CV event in people with CVD, with patients classified as overweight or obese having favourable outcomes compared to normal and underweight patients.[90-99] A meta-analysis by Nowark *et al.* (2024) involving 82 studies in adults with CVD showed that the risk for all-cause mortality increased with BMI <25 kg/m^2 with no significant change in mortality at other BMI values.[90] In patients who experienced cardiac arrest, BMI did not significantly impact short-term mortality or neurological outcomes; however, patients with overweight or obesity had reduced long-term mortality risk, particularly for in-hospital cardiac arrest cases.[94] Adults with previous myocardial infarction who were followed for up to 17 years had a ~15% lower post-MI mortality risk if they had overweight [adjusted (a) HR 0.85; 95% CI: 0.76–0.94] or obesity (aHR 0.86; 95% CI: 0.81–0.91).[95] Several meta-analyses have observed similar U-shaped relationships between BMI and all-cause mortality in patients with heart failure.[48, 100-102] However, the concept of the 'obesity paradox' in heart failure patients was challenged by Marcks and colleagues (2021) who conducted an individual patient data analysis in 5,819 patients with chronic heart failure on the same data set as a previous study.[103] While lower BMI (≤18.5 kg/m²) had a 2-fold risk of mortality, no significant protective effect of obesity was observed in patients less than 75 years of age or in patients without co-morbidities.[103] The authors challenged the notion of a direct protective effect of obesity in heart failure and suggested that the 'paradox' is likely explained by less advanced disease and fewer co-morbidities.[103] Moreover, a strong influence of age has been suggested, with the 'obesity paradox' more evident in older patients (>60 years),[99] which is potentially implicated by lean mass and functional capacity.

These observations are likely underpinned by the complex interplay of unassessed individual variables. For example, people with obesity are often identified and managed earlier in life, which can lead to more proactive surveillance and treatment.[17] They may be more likely to receive cardioprotective medications

contributing to improved outcomes. Additionally, the presence of excess energy stores may offer a metabolic reserve that becomes beneficial during the catabolic stress associated with advanced cardiovascular disease.[39] Lower BMI may indicate CVD-related cachexia and a more advanced disease state.[103] Ultimately, these complex and sometimes counterintuitive relationships underscore the need for a tailored, patient-centred approach that focuses on reducing excess adiposity and improving overall cardiometabolic health. Limitations in the present literature include lack of standard BMI classification in some studies, absence of central obesity measures, and exclusion of severe obesity (BMI ≥35 kg/m²),[91] as well as residual confounding and reliance on BMI as an imperfect measure of obesity.[100]

3.2.2 Overweight, obesity and surgical outcomes in people with CVD.

The 'obesity paradox' is similarly described in the literature examining the influence of obesity on surgical outcomes in CVD. Across various surgical interventions, mild to moderate obesity per BMI was consistently associated with improved survival, while extreme obesity and being underweight were linked to poorer outcomes[104-109] In general cardiac surgery (e.g., coronary artery bypass grafting, valve surgery, aortic surgery, and left ventricular assist device implantation), Liu *et al* 2020 found that higher BMI was not associated with increased post-surgery mortality (RR 0.93 for every 5-unit increase in BMI) with a mortality nadir at BMI 25-27.5 kg/m^2.[110] Underweight BMI and extreme obesity (BMI >53 kg/m^2) were associated with worse prognosis.[110]

In patients undergoing coronary artery bypass grafting, reduced graft failure was observed in patients with overweight (aOR 0.79) and obesity class one (aOR 0.81) and class two (aOR 0.61) but not class three (aOR 0.94).[106] In adults undergoing transcatheter aortic valve implantation, obesity was associated with reduced 30-day mortality [OR 0.71 (95%CI 0.60-0.84)] and improved long-term survival [HR 0.87 (95% CI 0.82 to 0.93)].[105] In Seo *et al* 2022 similar observations were observed in patients undergoing transcatheter aortic valve replacement, with overweight and obesity associated with lower mid- and long-term mortality than 'healthy wight' BMI.[107] However, obesity was linked to higher odds of major vascular complications and permanent pacemaker implantation.[107] The authors emphasised that the 'obesity paradox' may be influenced by confounders of age and frailty.[107] In adults with peripheral artery disease who underwent lower extremity revascularization, obesity was associated with a lower mortality (RR 0.78) and reduced MACE (RR 0.86) but a higher risk of surgical site infections (RR 1.69).[108] In adult patients who underwent percutaneous coronary intervention, a U-shaped mortality curve was observed with the lowest risk of mortality in those with BMI 27-32 kg/m^2.[109]

3.2.3 Overweight, obesity and stroke in people with CVD.

The 'obesity paradox' is also described in the literature evaluating the influence of obesity on outcomes in stroke survivors, notably for mortality [111, 112] and stroke recurrence.[113, 114] In patients with a stroke diagnosis, overweight (RR 0.91) and obesity (RR 0.89) had a decreased risk of stroke recurrence than 'healthy' weight BMI, while underweight increased risk (RR1.59).[113] The authors observed that each 1-unit increase in BMI was associated with a reduced stroke recurrence risk by 2% [RR 0.98 (95% CI 0.96 to 0.99)].[113] Qin *et al.* (2024) reported lower mortality and better functional outcomes in patients with overweight or obesity, with underweight status linked to worse outcomes.[111] Using the 90-day global functional outcome scale called modified Rankin Scale (mRS), that ranges from 0 (no functional deficits at

all) to 6 (death), the authors demonstrated better functional outcomes (mRS ≥3) for overweight (RR 0.92) and obesity (RR 0.89).[111] In Wei *et al.* (2025) the favourable associations between overweight and obesity and stroke recurrence were more pronounced in older adults (≥65 years) and during long term follow up ≥3 years).[114] Similar to CV risk more broadly, metabolic syndrome (including abdominal obesity) is a significant predictor of recurrent stroke.[59] In adult stroke or transient ischemic attack survivors, metabolic syndrome was a significant predictor of recurrent stroke [RR 1.52 (95% CI 1.17 to 1.97)] with elevated glycaemia being the strongest individual component predictor across metabolic syndrome components.[59]

3.2.4 Overweight, obesity and acute coronary syndrome (ACS) in people with CVD.

Individuals with overweight or obesity, defined by BMI, were also associated with lower mortality and complication rates in people with ACS.[115, 116] Şaylık *et al.* (2023) observed significantly reduced 30-day and long-term mortality in those with overweight (RR 0.69 and 0.73, respectively) and obesity (RR 0.61 and 0.68, respectively), while low-weight patients had increased mortality (RR 1.74 and 2.06, respectively).[115] Jelavic *et al.* (2023) reported that patients with overweight and obesity had lower odds of reinfarction, cardiac arrest, and death, despite higher prevalence of comorbidities like hypertension and diabetes.[116]

3.2.5 Overweight, obesity and arrythmia in people with CVD.

Unlike the outcomes reviewed above, obesity is a significant risk factor for the onset and post-ablation recurrence of atrial fibrillation (AF). In a meta-analysis of over 15 million participants across 50 cohort and case-control studies, Folli and coworkers observed a graded increase in newly diagnosed AF risk with BMI: overweight (OR 1.32), obesity (OR 1.71), excessive obesity (1.77) compared with underweight.[117] A smaller increased risk for recurrent post-ablation AF was observed in those with obesity (OR 1.36) and excessive obesity (1.40) but not overweight compared to 'healthy' weight.[117] Liu *et al* (2023) observed a 15% increased risk of post-ablation AF recurrence per 5 kg/m^2 increase in BMI in patients with AF undergoing radiofrequency ablation.[118] In patients undergoing mixed cardiac surgeries, obesity significantly increased the risk of postoperative AF [RR 1.39 (95% CI 1.21 to 1.61)], but overweight or underweight did not.[119]

3.3. Pharmacological Therapies

Pharmacotherapies are generally recommended for people living with obesity when first line lifestyle interventions are insufficient in isolation. Importantly, pharmacological treatments should only be considered as complementary therapy to lifestyle modification.[120] In the context of CVD, the European Society of Cardiology recommend some traditional obesity medications such as orlistat, naltrexone/bupropion be used with caution in those with known CVD.[120] In this context, GLP-1 receptor agonists (GLP-1RAs) have emerged as a cornerstone in pharmacological obesity management, demonstrating consistent efficacy across weight reduction, cardiometabolic improvement, and cardiovascular event prevention. Their role in primary and secondary prevention of cardiovascular disease is increasingly supported by high-quality evidence, positioning them as a key therapeutic option in cardiometabolic care. Meta-analyses examining the benefits of a wide range of agents including semaglutide, liraglutide, exenatide, dulaglutide, efpeglenatide, and newer agents like tirzepatide,

retatrutide, and orforglipron have shown clinically meaningful effects. Adherence challenges, cost, and access remain barriers to widespread implementation.[121]

Overall, the systematic review netted 77 meta-analyses examining obesity and CV-related outcomes with pharmacological intervention between 2015-2025 (**Figure 3.3.1**).

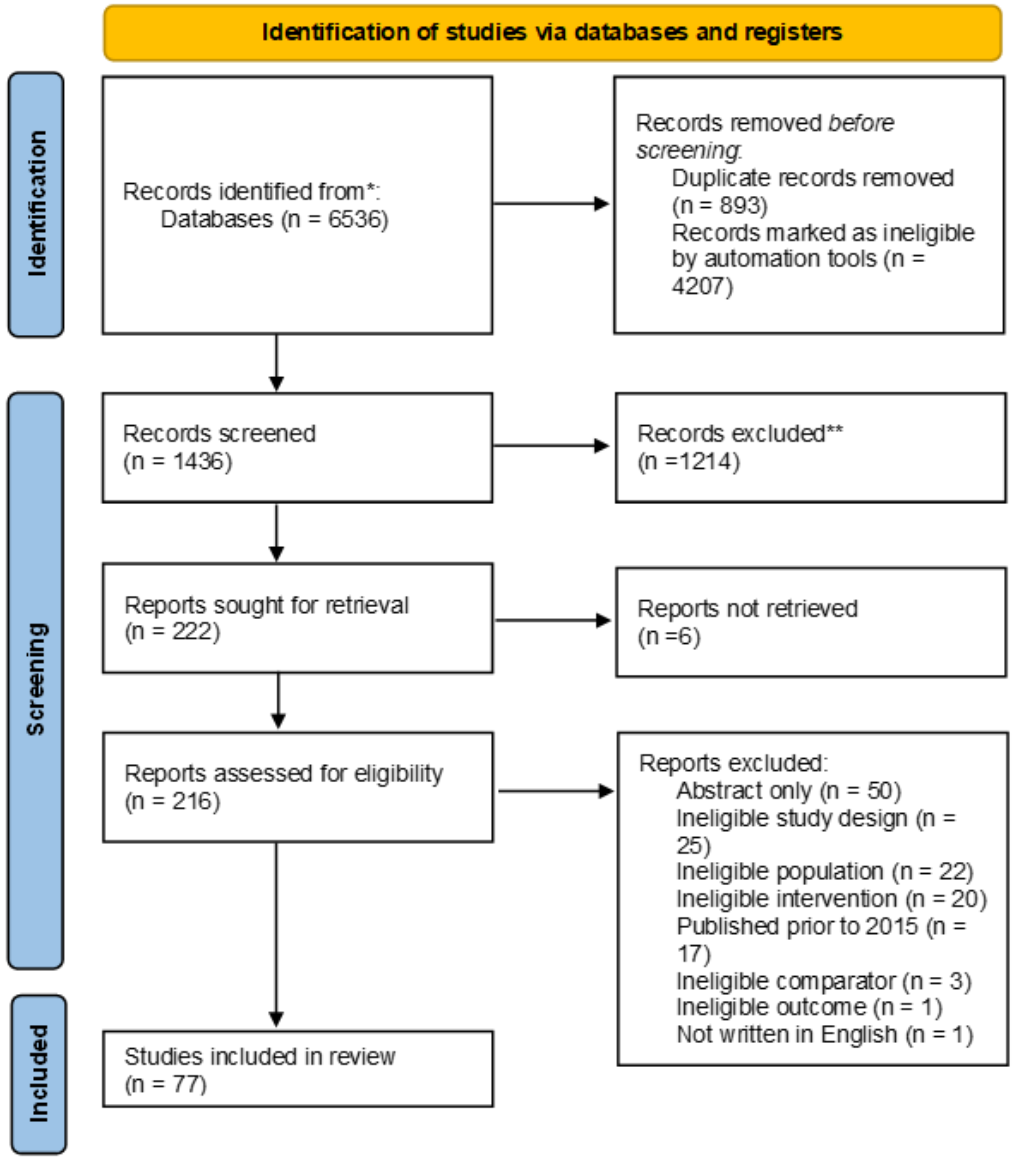

Figure 3.3.1 – PRISMA Pharmacological Therapies

In 2025, 22 meta-analyses were published evaluating the efficacy of pharmacotherapy on CVD and CVD-risk. The majority of these examined GLP-1 receptor agonists, and most within patients with type 2 diabetes where the primary entry criterion was not based on having either overweight or obesity**.** Due to primary study cross over and some limits to full text access, 17 meta-analyses were pooled for data extraction from 2025. Texts between 2015-2024 were reviewed for novelty and data from an additional

four meta-analyses were extracted. The total number studies included for data extraction was 21, with the majority focused on GLP-1Ras (79%) (**Figure 3.3.2; Appendix 6.5**).

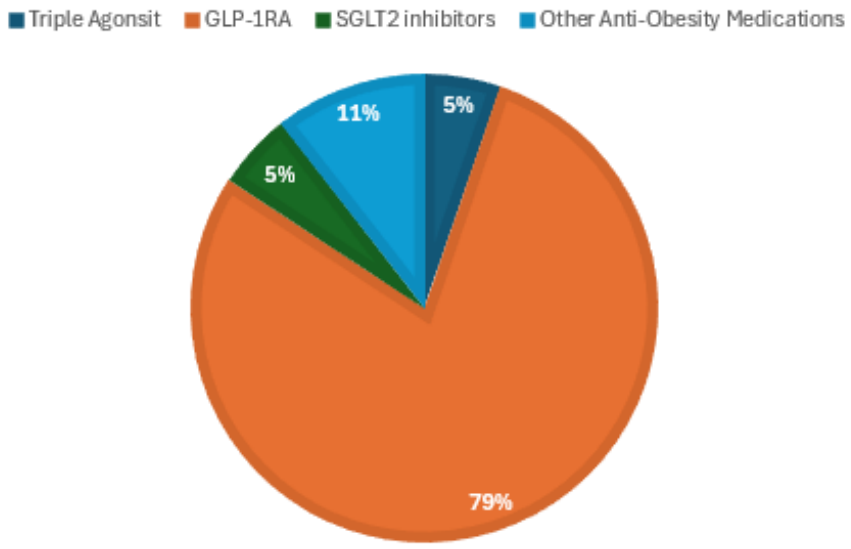

Figure 3.3.2 Breakdown of major topics of meta-analyses examining the efficacy of pharmacotherapy on CVD and CV risk.

3.3.1 GLP-1 Receptor Agonists and triple agonists

Body weight and composition

Across studies, GLP-1RAs consistently produced significant weight loss. Isolated GLP-1RAs (i.e., semaglutite) reduced body weight by pooled mean of -7.78 kg (-8.80 to -6.75)[122] and combination agents like retatrutide [123] and tirzepatide [124, 125] achieved mean reductions exceeding 10% of baseline body weight. These effects were accompanied by reductions in BMI and waist circumference,[123, 126-128] with greater weight loss efficacy frequently observed in patients without diabetes.[126] In a meta-analysis of 878 people with overweight or obesity, with or without T2D, the triple agonist retatrutide led to significant pooled reductions in body weight (MD -14.33% 95% CI: -18.27 to -10.39), BMI (MD -5.38 units 95% CI: -5.74 to -5.01) and waist circumference (MD -10.51 cm 95% CI: -11.67 to -9.35), although significant heterogeneity was observed.[123] An and colleagues (2025) evaluated 14 GLP-1RAs across 156 RCTs involving over 144K participants.[122] The network meta-analysis showed that six of the nine GLP-1RAs reduced body mass index, with orforglipron demonstrating the greatest reductions (-3.84 kg/m^2 95% CI: -5.43 to -2.25).[122] Six of 12 GLP-1RAs reduced body weight with orforglipron demonstrating the greatest reductions (-10.48 kg 95% CI: -13.92 to -7.03).[122] In adults with overweight or obesity without type 2 diabetes, GLP-1RA based therapy reduced BMI by a pooled mean of -6.50 kg/m^2 (95% CI: -7.90 to -5.10).[128]

Cardiovascular risk factors

GLP-1RAs also demonstrated favourable effects on cardiovascular risk factors in patients with type 2 diabetes reported by An and colleagues.[122] Systolic blood pressure was modestly but significantly reduced across multiple agents,[123, 124, 129, 130], with greater reductions associated with greater weight

loss.[130] Subgroup analyses highlighted differences in efficacy based on intervention duration, dosage, and mechanisms of action across different cardiometabolic risk factors highlighting the need for personalised prescriptions.[124 128] Retatrutide (triple agonist targeting GLP-1, GIP, and glucagon receptors) treatment led to a mean ~10 mmHg reduction in SBP [MD: −9.88 mm Hg (95% CI: −11.39 to −8.37)] and~21 mg/dL reduction in fasting plasma glucose [MD: -23.51 mg/dL (95% CI: −31.33 to -15.69) in adults with overweight or obesity, with or without T2D.[123] Improvements in HbA1c and fasting glucose were consistent across all agents, suggesting potent metabolic benefits beyond weight loss alone. Greater effect were observed with dual or triple agonist activity (e.g., tirzepatide, retatrutide); however, consistent effects are seen with isolated GLP-1RAs.[122 123] Improvements in total cholesterol and LDL- and HDL-cholesterol profiles were more modest and varied regarding specific agent.[122 124] Longer treatment durations (>1 year) were associated with greater reductions in cardiometabolic risk measures in people with overweight or obesity highlighting the importance of supporting long-term access and maintenance.[126] Specifically in adults with overweight or obesity without type 2 diabetes, GLP-1RA based therapy reduced systolic blood pressure by a pooled mean of -7.10 mmHg (95% CI -11.00 to -2.70).[128]

CV mortality and MACE

Several GLP-1RAs demonstrated reductions in MACE, cardiovascular mortality, and all-cause mortality. In a large network meta-analysis in people with type 2 diabetes, efpeglenatide was most effective in reducing MACE, while oral semaglutide demonstrated the greatest reduction in cardiovascular and all-cause mortality.[122] In adults with overweight or obesity without type 2 diabetes, GLP-1RA based therapy reduced the risk of all-cause mortality [RR 0.81 (95% CI 0.71 to 0.93)], CV events [RR 0.81 (95% CI 0.76 to 0.87)], MACE [RR 0.80 (95% CI 0.72 to 0.89)], and myocardial infarction [RR 0.72 (95% CI 0.61 to 0.85].[128] These findings were supported by consistent results across other reviews,[131 132], which also highlighted reductions in myocardial infarction and stroke risk.[133] The meta-analysis by Badve and colleagues (2025) which included 11 trials (n=85,373 participants) supported GLP-1RAs as both kidney- and heart-protective in people with T2D and without T2D but with CVD.[134] Key results of this study are below.

Per Badve *et al* (2025),[134] compared with placebo, treatment with GLP-1RAs resulted in:

Kidney Outcomes [134]

- 18% reduction in the risk of the composite kidney outcome (HR 0.82, 95% CI 0.73–0.93) in participants with type 2 diabetes
- 16% reduced the risk of kidney failure (HR 0.84 [95% CI 0.72–0.99] for participants with type 2 diabetes; HR 0.84 [0.72–0.98] for participants with or without diabetes.
- 31% reduced risk of worsening kidney function (HR 0.79 [95% CI 0.68–0.92] for participants with type 2 diabetes; HR 0.78 [0.68–0.91] for participants with or without diabetes.

CV Outcomes [134]

- 13% reduction in the risk of MACE (HR 0.87, 95% CI 0.81–0.93) in participants with type 2 diabetes and a 14% reduction when the SELECT trial was included in the analysis (HR 0.86, 95% CI 0.80–0.92). In people with CVD and no T2D risk of MACE was reduced by 20% [HR 0.80 (0.72–0.89)]

- 14% reduced risk of CV death (HR 0.86, 95% CI 0.80–0.92), 10% reduced risk of non-fatal myocardial infarction (HR 0.90, 0.82–0.99), and 13% reduced risk of non-fatal stroke (HR 0.87, 0.79–0.96) in people with T2D. In those without T2D but with CVD there was a 15% reduction in CV death [HR 0.85 (0.71–1.01)]
- 12% relative reduction in the risk of death due to any cause in participants with type 2 diabetes (HR 0.88, 95% CI 0.83–0.93), and a 13% reduction (HR 0.87, 0·82–0.91 when the SELECT trial was included.
- In those without T2D but with CVD there was a 28% reduction in non-fatal MI [HR 0.72 (0.61–0.85)].

Safety

Safety profiles across GLP-1RAs were generally favourable. Gastrointestinal side effects were the most common, particularly with agents like orforglipron and taspoglutide, but serious adverse events were not significantly increased compared to placebo.[122] However Neves and colleagues (2025) examined GLP-1RAs across 7 RCTs with 2,559 patients with heart failure with either reduced- or preserved-ejection fractions (HRrEF and HRpEF).[135] Findings demonstrated that GLP-1RAs were associated with a higher risk of worsening HF events in HFrEF patients [HR: 1.23 (95% CI: 1.00-1.51)], which the authors hypothesised to be linked with increased heart rate and intracellular cyclic adenosine monophosphate levels.[135] However, this observation was not consistent with the findings of Otamni et al (2025) who showed no significant change in the risk of HF events in either HFpEF (RR 0.37) or HFrEF (RR 0.66) groups and demonstrated improved CV mortality (RR 0.74) with subcutaneous semaglutide in people with HF and obesity.[131] Further RCTs are needed to understand and clarify the safety and efficacy of GLP-1RAs in those with HFrEF.[135]

3.3.2 Other pharmacotherapies

The network meta-analysis by Benedictus *et al.* evaluated a range of pharmacotherapies including phentermine/topiramate, phentermine, naltrexone/bupropion and orlistat across 18 RCTs (n=12,259).[136] Combined, all pharmacotherapies reduced BMI more than placebo (MD -2.12 kg/m^2 95% CI: -2.64 to -1.59), with phentermine/topiramate having the largest reductions (MD -3.28kg/m^2 95% CI: -3.96 to -2.60).[136] Collectively side effects were mild and mostly related to GI symptoms.[136] A pooled mean BMI reduction of -1.43 kg/m^2 was observed with the SGLT2 inhibitor dapagliflozin compared with placebo with modest benefits on body weight and waist circumference in people with obesity and pre-diabetes.[137] Modest reductions in BMI have been observed with fluoxetine (a selective serotonin reuptake inhibitor)[138] and acarbose monotherapy[139] in people with overweight or obesity. Regarding naltrexone/bupropion, Liu *et al* (2025) recommended caution for prescription due to potential risks of hypertension and palpitations, which may be particularly pertinent in the context of CVD.[125]

PRACTICAL CONSIDERATIONS FOR THE HEART FOUNDATION TASKFORCE

- Prior to GLP-1 RA's, obesity management medications failed to demonstrate CV outcome benefits either due to having only modest effects on weight loss or concerning side-effects. GLP-1 RA based therapies have been demonstrated to improve CV outcomes in patients with diabetes or who are overweight or obese with underlying CV disease.
- Adherence challenges, costs and access will need to be considered for widespread implementation and equitable access
- Considerations for the preservation/minimising loss of lean mass is paramount with co-prescription of diet and exercise imperative. While the optimal prescriptions for nutrition and exercise remain to be clearly established, strategies that enhance anabolic responses (e.g., adequate protein intake and resistance training) will be central.
- Weight regains following the discontinuation of pharmacotherapy remains a significant concern, particularly as the increase in body weight is likely to involve central adiposity in the absence of sustained behavioural interventions.

3.4 Surgical Management

The European Society of Cardiology (2023) indicates consideration of bariatric surgery for individuals with BMI ≥40 kg/m^2 or BMI ≥35 kg/m^2 with at least one obesity-related disease, and after lifestyle intervention combined with medications have failed to produce sustained weight loss.[120] Bariatric surgery has been shown to active the greatest level of weight loss compared with lifestyle intervention and currently available pharmacotherapies.[140] Bariatric surgery is consistently associated with significant reductions in cardiovascular morbidity and mortality among individuals with obesity, as demonstrated across multiple systematic reviews and meta-analyses of observational cohorts. While more invasive and carrying higher risk than other intervention, short-term (<30 day) all-cause mortality associated with bariatric surgery is low (0.18%).[141] The evidence spanned a range of surgical procedures including Roux-en-Y gastric bypass, sleeve gastrectomy, adjustable gastric banding, and biliopancreatic diversion and encompasses diverse study designs and populations. Taken together, the evidence strongly supports bariatric surgery as an intervention that facilitates weight loss and significantly reduces cardiovascular risk and improves survival. While heterogeneity was observed and study quality varied, findings were generally consistent underscoring the clinical utility of bariatric surgery in the management of obesity and related cardiovascular disease. The systematic search netted 24 meta-analyses between 2015-2025 evaluating the impact of surgery on CVD risk and outcomes (**Figure 3.4.1; Appendix 6.6** for study details).

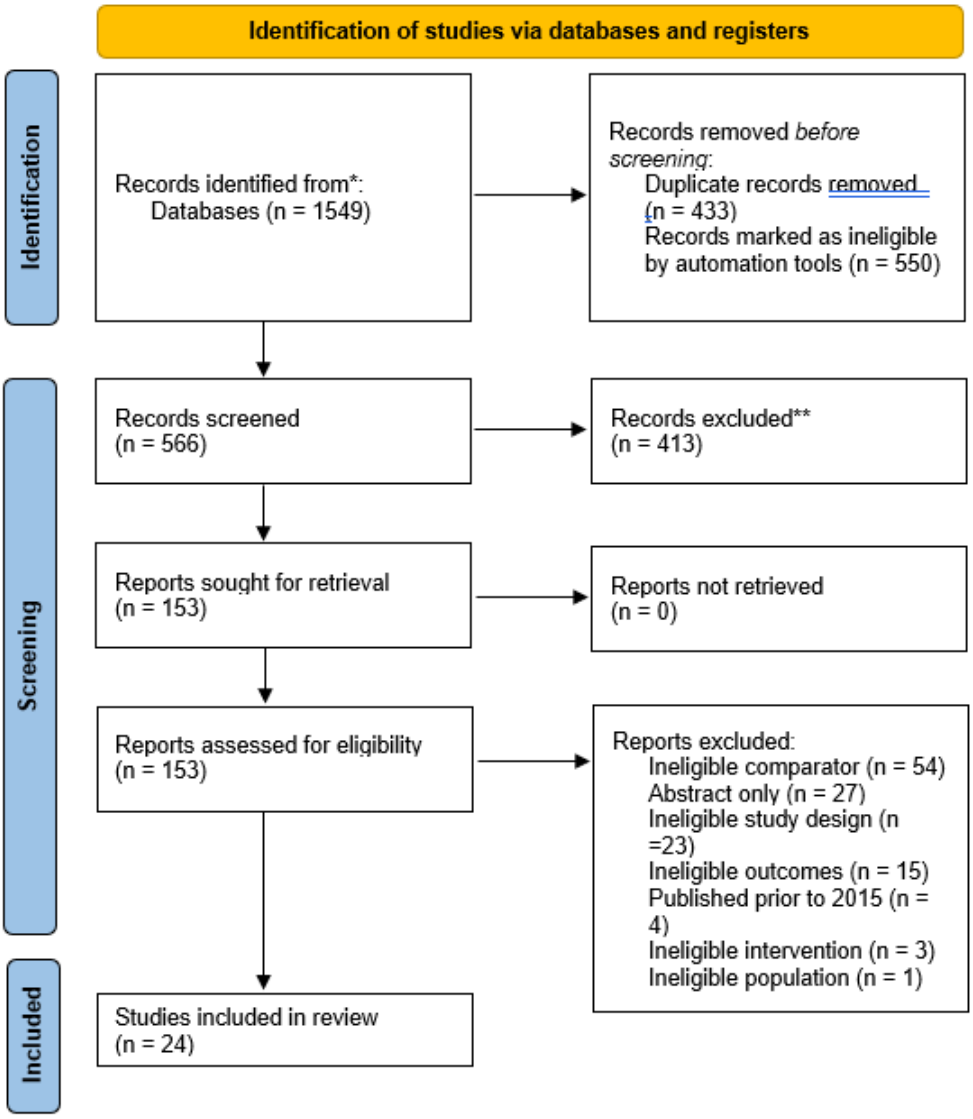

Figure 3.4.1- PRISMA Surgical Intervention

The majority of reviews examined the association between bariatric surgery and mortality and/or MACE (34%) or on outcomes of CVD (33%) (**Figure 3.4.2**).

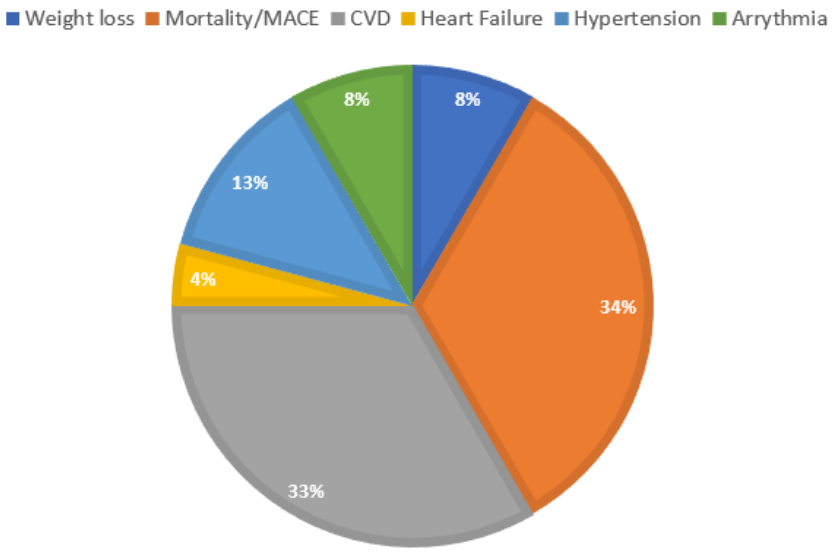

Figure 3.4.2 Breakdown of major topics of meta-analyses examining the efficacy of surgical intervention on CVD and CV risk

3.4.1 Outcomes of surgery- mortality, MACE, heart failure, stroke, atrial fibrillation

There is a substantial survival benefit of surgery on cardiovascular mortality with meta-analyses consistently showing a near-halving of risk (hazard and odds ratios consistently ~0.5) than those who were unoperated.[142-147] These effects were observed across both cohort and controlled clinical studies, with Pontiroli and colleagues (2020) noting stronger effects in older patients [OR 0.23 vs OR 0.62 for those below cohort median age].[143] Carsado *et al* (2017) and van Veldhuisen *et al* (2022) further corroborated these findings, showing significant reductions in all-cause mortality (HR 0.59 and HR 0.55, respectively) in those who underwent bariatric surgery than non-operated controls.[141 148]

Reductions in MACE was also consistently reported, with a 40-60% reduction in MACE risk following various bariatric surgeries (HR and RR ranging from 0.49 to 0.58).[142 146 149 150] Cui and colleagues (40 matched cohort studies encompassing over 626,000 individuals) showed a 42% risk reduction [HR 0.58 (95% CI 0.51 to 0.66)] for MACE following a broad range of procedures including Roux-en-Y gastric bypass, sleeve gastrectomy, adjustable gastric banding, vertical banded gastroplasty, biliopancreatic diversion, and duodenal switch.[22] In people with obesity and CVD (n >1.7 M) those who had bariatric surgery (n=74,042) had a 51% lower odds of MACE.[149] Several meta-analyses reported significant reductions in MACE-related endpoints, including myocardial infarction, stroke, and heart failure.[21 145 146 148 150] Patients with known HF who underwent bariatric surgery had a 72% reduced risk of heart failure exacerbations [RR 0.28 (95% CI 0.13 to 0.59] compared with those with known presurgical HF who had non-surgical treatment.[151]

In Chokesuwattanaskul *et al* (2020), the overall incidence of AF following bariatric surgery (n=7681) was 5.3% after median 7.9 years; with a 0.42-fold decrease in risk of AF following surgery [OR 0.42 (95%CI 0.22 to 0.83)].[152] This is consistent with findings by Pontiroli *et al* (2023) showing 34% reduced risk of incident AF [OR 0.66 (95% CI 0.48 to 0.93)], with stronger effects in those with higher percent weight loss following

surgery.[153] However, the lower risk of AF in van Veldhuisen (2022) was not statistically significant [HR 0.82 (95%CI 0.64 to 1.06), p=0.120].[148]

3.4.2 Outcomes of surgery- CVD risk

Beyond mortality and major cardiovascular events, bariatric surgery significantly improves CV risk factors. Meta-analyses by Goodarzi *et al* (2025), Yan *et al* (2016) and Pipek *et al* (2024) demonstrated superior reductions in blood pressure, lipid profiles, glycaemic indices (HbA1c, fasting glucose, HOMA-IR) and waist circumference compared to non-surgical interventions.[154-156] Intragastric balloon therapy also yielded meaningful improvements in glycaemic control (-0.6 to 1.1% HbA1c) and blood pressure (~3 to 9 mmHg reduction for SBP) in RCT and observational studies.[157] In Wiggins *et al* (2020) who observed CV-risk in >1.5M patients over at least 18 months showed those who underwent bariatric surgery (n=269,818) had a 61% lower likelihood of T2D and 67% lower likelihood of dyslipidaemia.[144] As expected, bariatric surgery consistently led to substantial reductions in BMI and body weight. BMI reductions to the magnitude of 6-8 units and weight losses of 15-20% were reported [156, 158, 159].

Hypertension outcomes were notably improved following bariatric surgery. Significant reductions in systolic and diastolic blood pressure was reported in several reviews.[160-162] Dastjerdi *et al* (2025) evaluated the utility of bariatric surgery in blood pressure control across 29 RCTs (n=2407).[160] The pooled mean difference was -4.5 / -3.0 (SBP/DBP) in bariatric surgery verses non-surgical treatment.[27] In the abovementioned study by Wiggins *et al.* similarly found that the those who had bariatric surgery had 64% lower likelihood of hypertension.[144] Longer-term benefits in hypertension have also been observed; Sebastian and colleagues (2025) demonstrated a nearly threefold increase in hypertension remission (RR = 2.77) following bariatric surgery compared with non-surgical intervention.[161].

3.5 Behavioural Interventions

The systematic search netted 104 meta-analyses between 2015-2025 evaluating the impact of diet and/or exercise interventions on CVD risk and outcomes in people with overweight or obesity (**Figure 3.5.1**)**.** These were reviewed by two individual researchers, and pertinent studies were selected for extraction based on recency and topic for broad coverage of interventions (**Appendix 6.7** for study details from select trials).

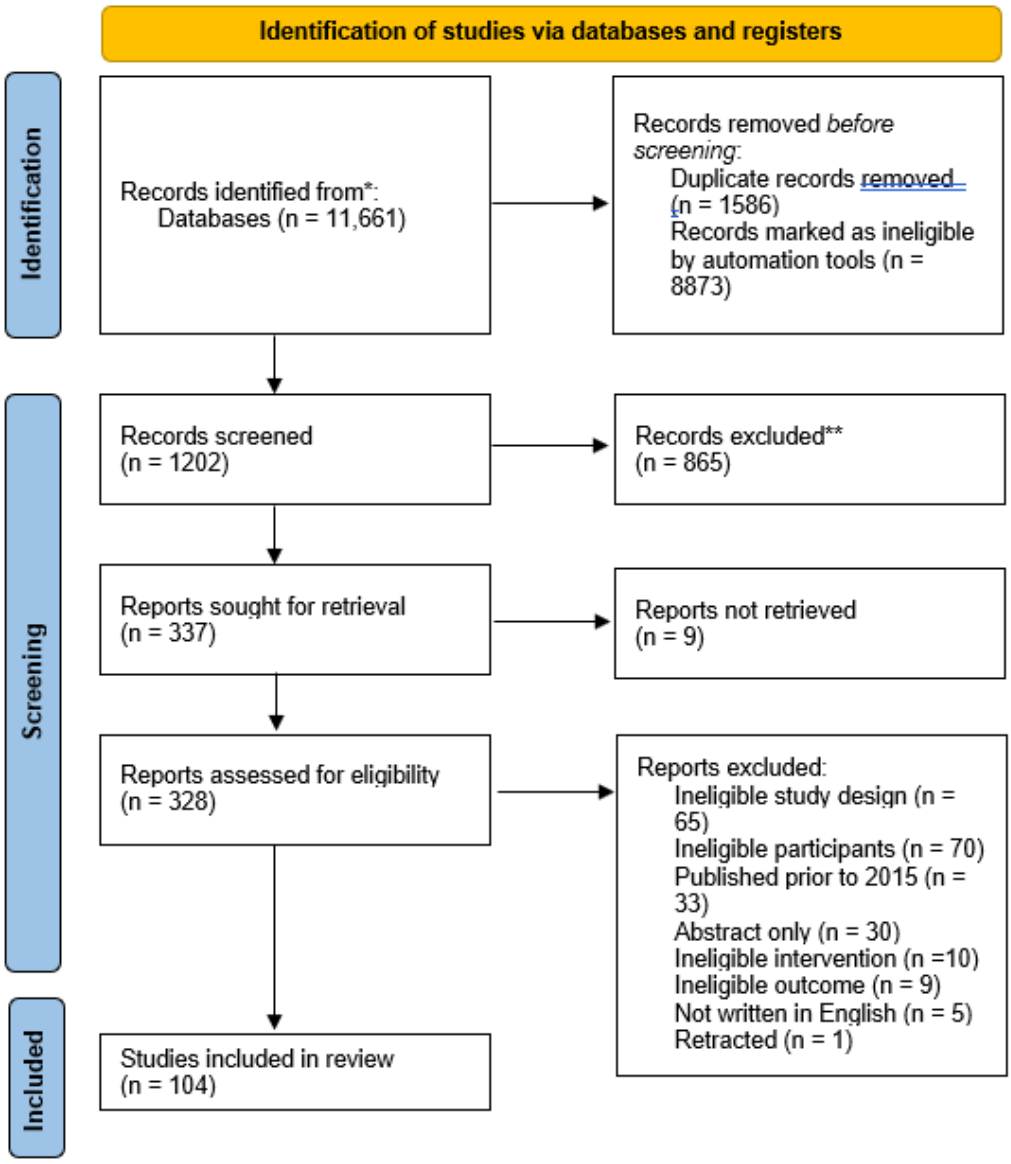

Figure 3.5.1- PRISMA Behavioural Interventions

There was an approximately equal distribution of reviews examining diet (36%) and exercise (37%) and 27% examined combined diet and exercise approaches for the management of overweight/obesity and risk of CVD/CVD outcomes (**Figure 3.5.2**).

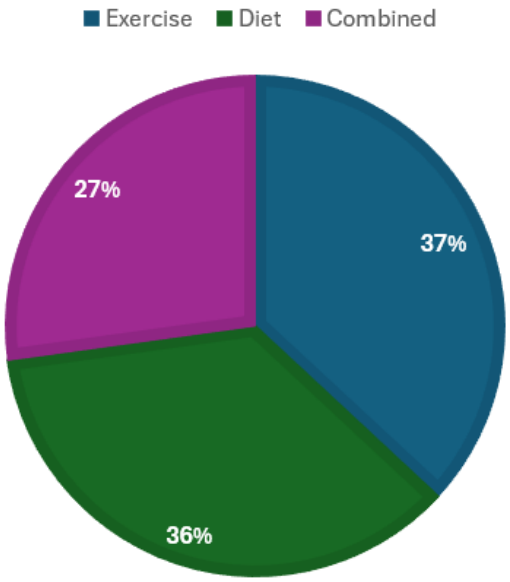

Figure 3.5.2 Breakdown of major topics of meta-analyses examining the efficacy of behavioural intervention on overweight/obesity and CVD and CV risk.

3.5.1 Diet interventions

Meta-analysis examined diverse dietary strategies including intermittent fasting, time-restricted eating, low-carbohydrate diets, low-fat diets, the DASH and Mediterranean diets, vegetarian diets, and meal replacements. Overall, the evidence from these meta-analyses demonstrates consistent, though variable, improvements in weight-related and cardiometabolic outcomes. A network meta-analysis comparing 14 popular named diets in adults with overweight or obesity demonstrated that most diets led to modest and comparable weight loss (~4kg) and CV risk improvements (SBP ~3-5 mmHg reductions; LDL-C ~5-7 mg/dL reductions; HDL-C ~2 mg/dL increase) at 6 months.[163] At 12 months most effects diminished, except for LDL-C reduction with Mediterranean diets.[163] These data suggest the need to prioritise individual preference and behavioural support for diet adherence for optimal dietary intervention outcomes. Evidence also indicates that for people with overweight or obesity with or at risk of CVD, dietary intervention should be supported by appropriately qualified dietitians. Dietary interventions provided by dietitians reduced the risk of hypertension incidence by 54% [RR 0.46 (95% CI 0.22 to 0.97)] and stroke by 66% [RR 0.34 (95% CI 0.14 to 0.81)] with improvements in blood pressure, body weight, and CVD risk factors.[164]

The Mediterranean diet (MedDiet)

The MedDiet is the most consistently promoted cardioprotective diet owing to pooled observational and clinical trial evidence demonstrating that adherence to the MedDiet reduced risk of overall mortality by 9% [RR 0.91 (95% CI 0.89 to 0.93)], CV mortality by 25% [RR 0.75 (95% CI 0.68 to 0.83)], incidence of CVD by 33% [RR 0.67 (0.58 to 0.77)], incidence of CHD by 28% [RR 0.72 (0.60 to 0.86)], incidence of MI by 33% [RR 0.67 (0.54 to 0.83)], and incidence of stroke by 24% [RR 0.76 (0.60 to 0.96).[165] In adults with overweight or obesity without CVD (n=10,352 across 26 RCTs), the MedDiet demonstrated reductions in BMI [-0.61 kg/m² (95% CI -1.14 to -0.09)], waist circumference [−2.48 cm (95% CI −3.99 to −0.96)], triglycerides [-7.93

mg/dL (95% CI -13.48 to -2.39)], and fatty liver index [-12.26 (95% CI −23.96 to −0.56)], though most outcomes were supported by very low certainty evidence.[166] Notably, one trial (PREDIMED) reported a 35% reduction in myocardial infarction, stroke, or cardiovascular death, suggesting potential long-term cardioprotective effects.[167]

The Dietary Approaches to Stop Hypertension (DASH diet)

The DASH diet emphasises nutrient-dense, whole foods such as fruits, vegetables, low-fat dairy, and whole grains while limiting foods high in sodium, saturated fat, and added sugars.[168] In the meta-analysis of 22 studies assessing DASH compared with usual diets by Zare *et al* (2025),[169] the DASH approach significantly reduced total cholesterol [-5.05 mg/dl (95% CI -8.78 to -1.31], LDL-C [-5.33 mg/dl (95% CI -8.54 to -2.11] and VLDL-C [-3.26 mg/dl (95% CI -6.19 to -0.34)], though effects on triglycerides and HDL-C were not significant. Benefits were more pronounced in shorter interventions (≤8 weeks), highlighting the importance of early dietary adherence.[169]

Low carbohydrate diets

Low carbohydrate diets are typically defined as carbohydrate intake ≤40-45% of total energy, with ≤50-130 g/day, or <26% of total intake for very low carbohydrate diets.[170 171] Compared with non-carbohydrate restricted diets, this approach led to significantly higher reduction in short-term (3-4mth) body weight [-2.59 kg (95% CI -3.93 to -1.25)] but not fasting glucose in people with obesity.[171] However, this approach showed no clear advantages long term (10-14 or 18-30 months) for weight loss. Low carbohydrate diets improved several CV risk factors long term (10-30 months) including HDL-C (2.38 to 4.94 mg/dL), and TG (-23.26 to -27.09 mg/dL) with no differences in blood pressure.[171]

Lei and colleagues (2022) compared low carbohydrate diets with low fat diets (fat intake <30% of total energy) across 22 RCTs (~2000 participants in each diet) in people with overweight or obesity.[170] They observed that low carbohydrate diets were more effective than low fat diets for reducing triglycerides, increasing HDL-C, lowering diastolic blood pressure, and promoting short-term weight loss. Conversely, low fat diets were superior for reducing total and LDL cholesterol.[95] Importantly the magnitude of differences in the variables between groups are unlikely clinically meaningful and there were no significant differences between the approaches at 24-months. Therefore, while findings suggest that macronutrient focusing dietary strategies may be tailored to individual metabolic profiles and lipid targets, personal preferences and acceptability leading to long term adherence should factor in decision making.

Vegetarian diets

Vegetarian diets are defined as excluding meat, poultry, and fish with some variations also excluding eggs and dairy. In a meta-analysis of 9 studies (n=1628), that examined a range of vegetarian dietary patterns including vegan and lacto-ovo-vegetarian patterns, there were modest reductions in weight [-3.60 kg (95% CI -4.75 to -2.46)], BMI [-0.87 kg/m² (95% CI -1.80 to 0.06)], waist circumference [-3.00 cm (95% CI -6.20 to 0.20)] and glucose levels [-10.64 mg/dL (95% CI -15.77 to -5.51)], but showed limited impact on blood pressure and lipid profiles across trials of 6-24 months in duration.[172]

Wholegrain dietary patterns

Dietary patterns rich in whole grains showed modest benefits in weight reduction and lipid profiles, with effects generally diminishing by 12 months.[173]

Eating Pattern Modifications (Intermittent Fasting and Time Restricted Eating)

Intermittent Fasting (IF) is an eating pattern that intersperses periods of eating with periods of fasting of variable durations. IF shows comparable efficacy to continuous caloric restriction in comparison with non-diet control for reducing body weight [2.84 kg (95% CI 4.37 to1.31)], fat mass [3.06 kg (95% CI 4.21 to 1.91)], and waist circumference [3.85 cm (95%CI 5.10 to 2.59] with modest advantages in lowering fasting glucose, triglycerides, and diastolic blood pressure.[174] IF may be superior to caloric restriction for fat mass and HDL-C, but adherence to the approach long-term remains a challenge.[174] The 5:2 IF mode also demonstrated reductions in BMI [-0.85kg/m^2 (95% CI -1.52 to -0.17)], waist circumference [-2.77cm (95% CI -3.48 to 2.06)], LDL-C [SMD -0.24 (-0.45 to -0.03)], and systolic blood pressure [-2.93 mmHg (95% CI-4.06 to -1.81), though effects on glycaemic markers and visceral fat were inconsistent.[175] In adults with overweight and obesity these dietary approaches are considered to be safe and feasible but require monitoring of physical and psychological conditions during fasting periods. However, these approaches have not been directly evaluated in those with established CVD, warranting caution and highlighting the need for medical and dietetic oversight.

Time-restricted eating (TRE) typically requires fasting for 14-16 hours daily, with food consumption permitted during a 4- to 12-hour window.[176] In adults with excess weight and obesity-related metabolic conditions, TRE significantly reduced body weight [2.26 kg (95% CI -3.10 to -1.43)], waist circumference [-2.35 cm (95%CI -4.43 to -0.27)], and fat mass [SMD -0.63 (95%CI -1.10 to -0.17)].[176] Generally, shorter eating windows (4-6 hours) resulted in more pronounced results across outcomes. However, effects on glycaemic control, lipid profiles, and blood pressure were mixed, and adherence to shorter windows may be difficult in real-world settings due to the restrictive nature.[176]

Meal replacement approaches

Meal replacement strategies include discrete foods, food products, or drinks replacing one or more meals daily.[177] When combined with behavioural support, meal-replacement approaches yielded consistent and sustained weight loss in adults with overweight or obesity. Notably in those assigned a meal replacement diet with an enhanced level of support, the mean weight loss was -6.13 kg (-7.35 to -4.91) compared with alternative diets and regular support.[177] The odds of achieving ≥5% weight loss was ~2 times higher with meal replacements than diet-only (OR 2.83) and ~4 times higher than minimal control when supported (OR 4.3).[177] The odds of achieving ≥10% weight loss was ~8 times higher with meal replacement and support than minimal contact.[177] In some of the included studies, these weight loss benefits persisted up to 4 years.

3.5.2 Exercise Interventions

Exercise interventions are a foundational component of lifestyle management for individuals with obesity and elevated cardiovascular risk, and for those with established CVD. Importantly, many of the benefits of

exercise occur irrespective of weight loss. Meta-analyses and network meta-analyses consistently demonstrate that structured physical activity, particularly aerobic exercise, resistance exercise, combined aerobic and resistance exercise, and high-intensity interval training (HIIT), can yield clinically meaningful improvements in anthropometric, metabolic, and vascular outcomes.[178] It is important to emphasise that weight loss induced by exercise interventions in isolation is modest, but improvements in cardiorespiratory fitness and metabolic health are significant.[178] Given the broad benefits associated with achieving the recommended physical activity guidelines, exercise prescription for people with overweight or obesity with our without CVD should be underpinned by individual preferences, capabilities, access and other sociocultural determinants to optimise long-term adherence.

Aerobic exercise

Across studies, aerobic exercise was most effective in reducing body weight and BMI, with reductions ranging from 2 to 4 kg and 0.9 to 1.4 kg/m², respectively.[179 180] Aerobic exercise reduced waist circumference (-3.4 cm), fasting glucose (-0.15 mmol/L), triglycerides (-0.3 mmol/L), and improved HDL-C (0.05mmol/L) and cardiorespiratory fitness (4.2 mL/kg/min) in adults with metabolic syndrome.[181] The meta-analysis by Armstrong *at al.* showed that vigorous intensity aerobic exercise led to greater reduction in WC than moderate intensity [-4.2 cm (95% CI -4.99 to -3.42) vs -2.50 cm (95% CI -3.22 to -1.79)], which was associated with visceral adipose tissue reduction.[182] In adults with obesity, moderate-to-vigorous intensity aerobic-based interventions led to a greater reduction in waist circumference than resistance-based interventions.[178] The highest likelihood of reducing body fat percentage was with a combination of high-intensity aerobic and high-load resistance training.[178]

Aerobic exercise significantly improves vascular function with improvements in flow-mediated dilation (small effect: SMD 0.46) and reduced central arterial stiffness (pulse wave velocity; large effect size: SMD 0.88) in older adults with overweight and obesity, with more pronounced improvements in females.[183] In populations with comorbidities such as type 2 diabetes, metabolic syndrome, and metabolic dysfunction-associated steatotic liver disease (formerly, non-alcoholic fatty liver disease), exercise interventions, especially HIIT and aerobic training, significantly reduced intrahepatic fat, HbA1c, and blood pressure.[181 184]

High-intensity interval training

HIIT involves one or more bouts of high intensity exercise interspersed with lower intensity recovery periods. HIIT is increasingly used in cardiac rehabilitation settings [185] and has been shown to be safe, effective and feasible in people with complex obesity-related conditions when supported by appropriately qualified exercise professionals.[186] In people with overweight or obesity, HIIT is particularly beneficial for reducing intrahepatic fat, and improving body composition and cardiorespiratory fitness.[179, 184, 187] HIIT is generally considered superior to moderate intensity continuous training for improving cardiorespiratory fitness,[178, 179, 184, 187] with pooled mean increases of 7.4 mL/kg/min observed in people with overweight or obesity.[179] This is clinically meaningful given that a 1 MET (3.5 mL/kg/min) improvement in cardiorespiratory fitness is associated with a 13% and 15% reduced risk of all-cause and CVD-mortality, respectively.[188] Meta-analyses have shown that HIIT also significantly improved fasting glucose, insulin resistance (HOMA-IR), and triglyceride levels, indicating broad metabolic benefits.[179, 180]

Resistance Training

Resistance training is an essential component of interventions targeting significant weight loss to preserve lean mass and bone content.[189] While generally considered less effective for reducing body adiposity and intrahepatic fat than aerobic training in people with obesity,[184] its inclusion in exercise programs for people with overweight or obesity and cardiovascular disease is important given the impact on lean mass and other cardiometabolic risk variables. In people with overweight or obesity, resistance training improved systolic blood pressure [-2.96 (95% CI -5.22 to -0.70) vs control].[180] In broad populations, resistance training and particularly isometric exercise training have demonstrated benefit, with pooled reductions in SBP/DBP of -4.55/-3.04 mmHg, p<0.001 for dynamic resistance training and -8.24/-4.00 mmHg, p<0.001 for isometric training.[190] Notably the relative importance of resistance training during active weight loss (e.g., via surgical or pharmacotherapeutic intervention) should be emphasised even in the absence of grade 1 evidence, due to its clinical relevance.

Combined aerobic and resistance training

In people with overweight or obesity, combined training is likely the most appropriate and effective modality for improving blood pressure (SBP -5.5 mmHg; DBP -4.7 mmHg), fasting glucose (-0.3 mmol/L) and body fat (-2.8 %), with reductions of ~2.5 kg in body weight and ~4 cm in waist circumference observed across interventions (mean 21 weeks duration).[180] Combined aerobic and resistance training interventions have also provided additional benefits beyond surgical weight loss following bariatric surgery. Compared with bariatric surgery alone, combined protocols were effective in reducing systolic blood pressure [-7.2 mmHg (95% CI -12.42 to -1.94)] and triglycerides [-17.6 mg/dL (95% CI -34.2 to -1.0)], with benefits observed even if commencing >6months post-surgery.[191] Those who exercised following surgery improved exercise capacity [six minute walk test (6MWT)] by ~30 metres more than those who did not.[192]

Emerging non-exercise approaches to physical activity (not obesity-specific)

Emerging evidence from epidemiological data have explored lifestyle-related physical activity (i.e., non 'structured exercise' approaches). A study using data from inactive people in the UK Biobank (n=103,684) with 7.9 yr follow up examined the association between physical activity and MACE events (n=824) and death from any cause (n=1111).[193] In people who report no exercise, short bouts of intermittent lifestyle physical activity reduced the risk of MACE: compared to activity bouts <1min, the risk of MACE was lower for physical activity bouts lasting 1 to <3 minutes [HR 0.71 (95% CI 0.54–0.93)], 3 to <5 minutes [HR 0.62 (95% CI 0.48–0.81)] and 5 to <10 minutes [HR 0.59 (95% CI 0.46–0.76)].[193] Shorter physical activity bouts (<1min) were associated with lower MACE risk only when at least 15% of the bout duration consisted of vigorous activity.[193] Interestingly, longer bouts (5-<10min) had similar associations with MACE risk, showing that the largest CV health benefits can be attained with relatively short bouts of vigorous physical activity.

Exercise recommendations for people with overweight and obesity and consideration for CV risk management.

Physical activity recommendations by Exercise and Sports Science Australia advocate for regular physical activity for preventing weight gain, supporting weight loss and preventing weight regain in people with overweight or obesity.[194] Aerobic exercise of at least moderate intensity is recommended for weight loss and health benefits. Specific recommendations for weight-related outcomes include:

- *Prevention of weight gain*: >150-300 minutes per week of moderate-vigorous intensity aerobic exercise.
- *Weight loss*: 300-420 minutes per week of moderate-vigorous intensity aerobic exercise.
- *Prevention of weight regain:* at least 60 minutes of moderate-vigorous intensity activity on most days of the week
- *Reduction in central adiposity:* Lower amounts (<300 min/week) may reduce visceral fat and waist circumference.

The statement highlights that the priority outcomes for exercise in weight management should be improvements in overall health and quality of life followed by reductions in ectopic fat and central adiposity.[194] It also encourages clinicians to de-emphasise weight-related goals until cardiovascular and metabolic health goals are achieved, which often occur with exercise irrespective of weight loss.[194]

PRACTICAL CONSIDERATIONS FOR THE HEART FOUNDATION TASKFORCE

- For optimal cardiovascular outcomes in people with overweight or obesity, diet and exercise should be the foundation of management. Given the holistic health benefits achieved with adherence to any evidence-based diet and exercise approach, an emphasis should be placed on individual preferences, sociocultural determinants, and behavioural support to facilitate long-term adherence.
- Individualised diet and exercise prescription, cognisant of individual health status and the above-mentioned factors should be provided through engagement with appropriately qualified diet and exercise professionals.
- The broad health benefits of improving diet quality and exercising regularly *beyond weight loss* should be highlighted.

3.6 High-Priority Populations

Management strategies to improve cardiovascular outcomes, weight reduction and overall health in diverse communities

Cardiovascular disease (CVD) remains Australia's leading cause of morbidity and mortality, with overweight and obesity amplifying risk and clustering in priority populations, including people in low socioeconomic areas, First Nations communities, culturally and linguistically diverse (CALD) groups, people with disability, and those living in regional and remote settings. Marked inequities persist whereby individuals in the most disadvantaged areas are substantially more likely to have obesity and carry a higher CVD burden than those in advantaged areas, underscoring the need for targeted action. To close these gaps, care should be integrated and tailored, linking dietetic care, adapted physical activity, behavioural support and medication review, while being delivered in culturally safe, co-designed models, supported by bilingual health workers

equipped with culturally adapted resources, and by accessible/assistive exercise and nutrition supports to suit abilities.

A synthesis of peer-reviewed evidence on tailored and integrated strategies, spanning behavioural interventions and, where indicated, escalation to pharmacotherapy and bariatric surgery is provided to guide recommendations that improve cardiovascular outcomes, promote healthy weight reduction, and enhance overall health in these priority populations. As part of the Environmental Scan, Table 4.2.1 maps pertinent policies, strategies and reports, programs and services and supportive infrastructure to these high-priority populations.

3.6.1 Low socioeconomic groups

People in the most disadvantaged communities are 57% more likely to have obesity than the most advantaged areas.[195] Among people living in the lowest socioeconomic areas, the burden of CVD is 1.8 times higher.[196] Tailored and integrated management strategies for cardiovascular health, particularly those that are community-informed and locally delivered, have been shown to improve outcomes, support healthy weight reduction, and enhance overall wellbeing.[197-199] Promising approaches have emerged that can be implemented on an individual, community, or population basis to reduce disparities in outcomes.[200] For example, structured physical activity has demonstrated effectiveness in the management of cardiovascular health in low-socioeconomic populations.[201 202]

Evidence suggests that the redistribution of healthcare management from physician to nonphysician providers improves health care access and is an important strategy in low socioeconomic areas.[203 204] Furthermore, programs that connect health care with community organisations, schools, housing and employment services, are more likely to engage individuals meaningfully and sustainably.[205] This aligns with the American Heart Association's recent statement emphasising the importance of evidence-based behavioural interventions for CVD prevention in community settings to improve population health and advance equity.[206] These approaches can foster trust, improve health literacy, and empower people to take charge of their health in ways that are realistic and relevant to their everyday lives. When health strategies are responsive to community priorities and lived experience, they not only reduce disease burden but also build a foundation for long-term health equity.

To add to this, Myers-Ingram et al., (2023) revealed short-term effects of eHealth interventions on weight loss and increased physical activity levels for low SES participants.[207] Evidence was limited to a small number of studies, with small to moderate sample sizes. Inter-study comparison was challenging because of considerable variability. Future work should prioritise how to utilise eHealth in the longer term either as a supportive public health measure or by determining its long-term efficacy in engendering volitional health behaviour changes.[207]

3.6.2 Culturally and linguistically diverse (CALD) communities

Obesity rates among CALD communities vary greatly between first-generation immigrants and children from CALD backgrounds. First-generation immigrants have relatively better health upon arriving in Australia ('healthy migrant effect') but this has been shown to worsen over time due to adoption of Western diet and lifestyle.[208] Children from CALD backgrounds face higher risks of obesity, partly due to barriers in

accessing preventative services with factors such as low health literacy, cultural differences, and limited engagement with health programs contributing to this disparity.[208] A protective factor for members of CALD communities can include a rich cultural knowledge, strong food traditions, and supportive community networks, all powerful drivers of cardiovascular health and wellbeing.[209] When these strengths are acknowledged and integrated into health care models, there is greater opportunity to engage communities in preventative care and chronic disease management in ways that are meaningful and effective.[210]

Tailored or integrated management strategies that embed cultural responsiveness, language support, and community partnership have been shown to improve cardiovascular outcomes and promote long-term health improvements in CALD communities.[211] For example, programs that involve bilingual health workers, culturally adapted education materials based on the needs of the CALD community, and community-based interventions within trusted localised settings create safer and more accessible environments for health engagement.[212] These approaches, build trust and improve health literacy, whilst enhancing adherence to healthy lifestyle behaviours. As an example, George and colleagues(2018) developed a Mediterranean Diet (MedDiet) model tailored for a multicultural Australian population to manage chronic diseases including CVD.[213] The study tailored to principles of the MedDiet (e.g., being predominantly plant based, high in monounsaturated fats, includes fruits, vegetables, grain, nuts, seeds and fish, with moderate amounts of diary and red wine and minimal red meat and processed foods), and created a two-week meal plan incorporating culturally diverse and locally available ingredients.[213] The approach retained the health benefits of the traditional MedDiet while being adaptable and sustainable for diverse populations.[213] Ultimately, such strategies can reduce disease risk and strengthen the capability of CALD communities to lead and sustain their own health outcomes.

Beyond this, Milam *et al.* (2024) highlighted the opportunity to improve cardiovascular outcomes in patients undergoing cardiac surgery by addressing systemic inequities in care.[214] Despite carrying a greater burden of cardiovascular disease, underrepresented racial and ethnic groups demonstrate resilience in the face of limited access to cardiovascular and surgical care.[214] By applying a health equity lens and implementing culturally responsive, multipronged interventions, health systems can enhance perioperative care and support better outcomes for all patients undergoing cardiac surgery.

3.6.3 Disability

Lifestyle programs can be adapted to disability. In a three-arm randomised controlled trial (RCT) of 102 adults with diverse physical disabilities (spinal cord injury, multiple sclerosis, spina bifida, cerebral palsy, stroke, lupus; mean BMI 32), a 9-month telehealth program tailored to each person's capabilities produced greater weight loss than control (-2.1 kg in physical activity coaching; -0.5 kg with added nutrition coaching) while the control group gained weight (+2.6 kg). This supports the value of integrated, accessible delivery models for this priority population.[215]

A 2024 systematic review of RCTs of behavioural weight-loss interventions specifically in people with physical disabilities concluded that tailored, multicomponent programs (diet, activity and behavioural support) achieved clinically significant weight loss in several trials, though effect sizes varied and longer follow-up was scarce.[216] In osteoarthritis, the 18-month IDEA RCT (n=454; BMI 27–41) found intensive diet (± exercise) achieved ~9–11 kg loss and lowered IL-6 (an inflammatory cardiometabolic risk marker),

alongside better pain, function and quality of life compared with exercise alone. This indicates the fundamental nature of weight reduction promoting and improvement in health status when nutrition is emphasised and exercise is adapted.[217] In adults with obesity and knee osteoarthritis, a 68-week RCT (STEP-9; n=407) showed once-weekly semaglutide 2.4 mg, given in addition to reduced-calorie diet and physical-activity counselling, produced a 13.7% mean weight loss vs 3.2% loss with placebo and yielded greater improvements in pain and SF-36 physical function, reinforcing that GLP-1 receptor agonists can both reduce weight and improve disability-related outcomes when integrated with lifestyle care.[218] For severe obesity in osteoarthritis, a randomised trial found bariatric surgery prior to total knee arthroplasty reduced postoperative complications compared with usual care, suggesting a surgical weight-loss pathway can improve overall outcomes in this population with physical disability when appropriately selected.[219]

In spinal cord injury (SCI), a systematic review concluded that exercise training improved cardiorespiratory fitness and certain health outcomes, while individual trials showed modality and intensity were important considerations. Early-rehabilitation higher-intensity training improved insulin sensitivity and lipid profile compared with lower intensity, and circuit resistance training favourably shifted atherogenic lipids.[220 221] Evidence on remote and behaviourally integrated approaches in SCI is emerging: a pilot RCT of telehealth counselling (adapted from Diabetes Prevention Program) in adults with SCI and cardiometabolic risk improved self-reported activity, depression and pain but showed limited short-term change in fitness/biomarkers, highlighting feasibility and the likely need for higher doses or assistive modalities (e.g., functional electrical stimulation) to shift cardiometabolic risk.[222]

Functional electrical stimulation cycling and neuromuscular electrical-stimulation–assisted training in SCI have been shown to improve body composition and insulin sensitivity/glucose disposal in controlled studies, supporting their inclusion in tailored programs where feasible.[223, 224] Nutrition-focused RCTs in spinal cord injury (e.g., behavioural intervention with nutrition education) have demonstrated improvements in serum lipids, body weight and blood pressure, underscoring that tailored dietary counselling can modify cardiovascular risk factors even when mobility is restricted.[225]

Post-stroke populations (many with excess weight) benefit from structured aerobic training that is adapted to deficits. A 2024 network meta-analysis found aerobic exercise improves peak $\dot{V}O_2$ and lowers systolic blood pressure versus control.[226] Moreover, RCTs comparing HIIT vs moderate-intensity training show comparable gains in cardiorespiratory fitness with acceptable safety.[227]

3.6.4 Mental Health

Deng et al., (2025) demonstrated through their systematic literature review that individuals with metabolically healthy obesity (MHO) have a modestly elevated risk of depression compared to those with metabolically healthy non-obesity [OR 1.08 (95% CI 1.04 to 1.12)].[228] The risk is even higher for those with metabolically unhealthy non-obesity [OR 1.15 (95% CI 1.04 to 1.28)] and highest among metabolically unhealthy individuals with obesity [OR =1.30 (95% CI 1.12 to 1.51)].[228] Notably, the association of MHO with depression is stronger among women [OR 1.14 (95% CI 1.08 to 1.20)] and those in North American [OR 1.26 (95% CI 1.01 to 1.58)] and European populations [OR 1.23 (1.07–1.41)].[228] The authors emphasised the need for standardised definitions of MHO to reduce heterogeneity across studies and highlighted that

high-risk groups (particularly women and populations in the West) may benefit from targeted interventions. They called for further prospective research, including in developing countries.[228]

Tailored lifestyle programs delivered in mental-health settings produce modest but clinically meaningful weight loss and better physical fitness in adults with serious mental illness, such as schizophrenia and schizoaffective disorder. In the 18-month ACHIEVE randomized trial (n=291), a tailored behavioural program for those living with the aforementioned conditions led to a 3.2 kg reduction between-group difference and a higher proportion achieving ≥5% weight loss versus control; the trial was not powered to detect changes in BP or lipids.[229] The In SHAPE program (weekly health-coach sessions, gym access, nutrition education) replicated benefits in community settings and demonstrated that ~51% achieved clinically significant cardiovascular risk reduction (defined as ≥5% weight loss or >50 m improvement on 6-minute walk) at 12 months, sustained to 18 months.[230] The STRIDE RCT in people taking antipsychotics also demonstrated greater weight loss and improvements in diabetes risk markers versus usual care.[231]

Integrated/collaborative care models that treat mental and cardiometabolic conditions together improve key cardiovascular risk factors. In TEAMcare, adults with depression plus poorly controlled diabetes and/or coronary disease receiving nurse-led, treat-to-target collaborative care had better control of HbA1c, systolic BP and LDL cholesterol at 12 months than usual care, alongside improved depression.[232] In primary care patients with obesity and depression, the RAINBOW collaborative-care intervention (behavioural weight management, problem-solving therapy and stepped antidepressant management) produced modest but significant BMI reduction and improved depressive symptoms at 12 months.[233]. Related analyses show gains in patient-centred quality-of-life measures.[234]

Adjunct pharmacotherapy can amplify weight and metabolic benefits when tailored to psychiatric treatment. In antipsychotic-treated adults with schizophrenia-spectrum disorders and prediabetes, liraglutide (16 weeks) normalised glucose tolerance in 63.8% vs 16.0% on placebo and produced ~5.3 kg placebo-subtracted weight loss, demonstrating improvements in cardiometabolic risk beyond weight alone.[235] Meta-analyses of randomised, placebo-controlled trials show adjunct metformin reduces antipsychotic-associated weight gain and improves insulin resistance/HOMA-IR (with mean reductions in body weight and BMI vs placebo), supporting use when lifestyle measures are insufficient.[236]

Metabolic/bariatric surgery with appropriate psychiatric assessment and follow-up is also effective in selected patients with mental health conditions. A recent systematic review reported weight-loss and remission of obesity-related comorbidities after surgery in patients with bipolar or schizophrenia comparable to other populations, without worsening psychiatric status; evidence is largely observational but consistently reassuring.[237]

3.6.5 Regional and remote areas

Coronary heart disease is the leading cause of disease burden in all remote areas, with its burden in remote and very remote areas being 2.2 times that of major cities. Almost 70% of adults in remote areas (compared with 64.4% in major cities) experience overweight or obesity.[238] Adults in regional and remote areas are often closely connected to their communities and place.[239] This connection can support stronger cardiovascular outcomes but access to health care is limited, and specialist services are scarce.[240 241] As a result, travel distances are often long for vital health care and cardiovascular

management programs.[241] To add to this, stigma around mental health and obesity can compound issues relating to access and intervention engagement.[242] These challenges are greater for people living concurrently with both mental health issues and overweight or obesity and seeking to access health and wellbeing services in regional and remote areas. Notably, care that reflects local needs and treats the whole person, can improve cardiovascular health outcomes for people living in these important areas of Australia.[240]

A systematic review conducted by Summers, Lea & East (2024) found from the thirteen studies reviewed that obesity is especially prevalent in geographically isolated areas, where factors like gender, culture, and poor mental health contribute to negative trends.[243] The authors also found that generalised weight loss advice often fails in these communities.[243] It instead demonstrated that tailored, locally grounded weight-loss support, particularly for women, using affordable, traditional food options and community-based models may be more effective.[243]

Extending on this, cardiovascular integrated care and management strategies work best when implemented locally and are easily accessible.[244] Evidence has demonstrated that when physical and mental health are treated together then health and wellbeing outcomes improve.[245] However, as per Table 4.2.1, below mental health is rarely acknowledged or addressed in strategies or services dedicated to the management of obesity and/or cardiometabolic disease. Cardiovascular health services that are embedded across a broad range of health factors reduce gaps in health care and make this approach more accessible. Recent evidence has pointed toward telehealth and team-based models offering strong continuity of care, and this points to a viable direction forward for many regional and remote health teams.[246]

Central to this integrated management strategy must be that programs reflect local values and build trust in the community as a result.[247] Research has demonstrated consistently that people from regional and remote areas engage with health and wellbeing services more when they feel understood and heard by health professionals.[248, 249] For adults living in regional and remote areas with overweight and obesity and who have a co-occurring mental health condition, then it is fundamental that mental and physical health are treated together, and that cardiovascular programs are embedded within this treatment or management strategy.

3.6.6 Children, adolescents and young adults

Young people in regional and remote areas face unique challenges when it comes to maintaining a healthy weight and cardiovascular health.[250] Health services are often limited, and few are designed specifically for young people.[251] Long travel distances, workforce shortages and limited after-hours care reduce access at critical times. Without early intervention, risk factors such as poor nutrition, low physical activity and excess weight can follow young people into adulthood.[252] It is clear from this work that challenges for young people in regional and remote areas often emerge alongside key life transitions. Adolescents and young adults are navigating school, identity and social pressure.[253] Outreach and fly-in services may be offered in some more remote areas, but these services are time-limited, rarely tailored to specific local needs, and lack sufficient knowledge of the environmental, economic and cultural context in which people live.[254] Health support during this developmental time period must be flexible, developmentally appropriate and easy to access.[255 256] A one-size-fits-all approach will be unlikely to work for young

people living in regional and remote areas of Australia.[257] Young people need integrated management strategies that fits their lives.[258]

Cardiovascular programs that are fun, practical and built with youth leadership are more likely to succeed and this is particularly evident in regional and remote areas.[259] Sport, school and online spaces are powerful platforms in management strategies co-designed with young people to improve cardiovascular outcomes, reduce excess weight and promote overall health outcomes.[259] Important in this are trusted adults, such as teachers, sport coaches and local health workers, who can help bridge the gap between health advice and real-world action for young people.[260] When young people living in regional and remote areas feel safe and heard, they are more likely to stay engaged and make lasting changes in their life and the lives of family and friends. Management strategies that are co-designed with young people do more than reduce weight and improve cardiovascular health, they build resilience, confidence and belonging in developmentally specific and responsive ways.[261] Investing in youth-centred, locally led approaches creates lifelong benefits for the young person and the various stakeholders, with the resounding feature being that regional and remote area values are embedded in strategies. This sets young people up for healthier futures and strengthens the regional and remote communities they grow up in. Young people in regional and remote areas need co-developed solutions built in partnership with responsive care teams.

3.6.7 First Nations communities

For First Nations peoples living with overweight or obesity, effective care must reflect cultural identity, community priorities and connection to Country.[262] To add to this, it is vital to have a dedicated focus on the First Nations population, widespread community involvement within the First Nations community (often through the use of Aboriginal and Torres Strait Islander community health workers) and a focus on high-risk individuals within the population, together with regularly scheduled contact between the program and participants.[263] Health is understood as a balance of physical, emotional, spiritual and cultural wellbeing for First Nations peoples.[264] When programs are co-designed in partnership with First Nations communities, then they are more likely to meet local needs by building genuine and meaningful engagement.[265-267] This improves health care access and increases long-term engagement with management strategies which will improve cardiovascular outcomes.

Integrated strategies that link physical health, nutrition and mental wellbeing can lead to stronger cardiovascular outcomes and healthy weight reduction for First Nations peoples.[268] These approaches are most effective when co-delivered through culturally safe settings and involving culturally responsive health professionals.[250, 269] Community-led services positioned in co-created spaces where people feel respected and understood are the gold standard.[269] This strengthens participation and supports sustained health improvements for community. The most impactful strategies are led by Aboriginal and Torres Strait Islander peoples and controlled by Aboriginal and Torres Strait Islander community organisations.[267, 268, 270]

Features of successful programs in other health and wellbeing areas centre around culture as both a protective factor and enabler of engagement, offering the foundation for health care.[271] For First Nations peoples, this improves outcomes and restores agency. At the same time, embedding culture as a

determinant of health promotes empowerment and increases longevity of programs in Aboriginal and Torres Strait Islander communities.[272] Tailored management strategies that improve cardiovascular outcomes, weight reduction and overall health outcomes that privilege Aboriginal and Torres Strait Islander cultures and that are community-controlled and co-designed will promote healing and strengthen communities for improvement to a broad range of health outcomes.[273]

Indigenous patients seeking bariatric surgery demonstrated a strong commitment to improving their health and quality of life, with many motivated by their roles within family and community.[274] Family plays a central role as a source of support and inspiration throughout the surgical journey. While weight loss outcomes are comparable to those of non-Indigenous patients, there is an opportunity to strengthen the cultural responsiveness and continuity of care across the bariatric pathway. Enhanced engagement and support before and after surgery, particularly from non-surgical services, can further enable Indigenous patients to achieve their health goals in ways that align with their values and aspirations. To add to this, providing background community-based lifestyle programs may facilitate the conduct of randomised trials of newer, effective anti-obesity pharmacotherapy in this high priority population.[275]

PRACTICAL CONSIDERATIONS FOR THE HEART FOUNDATION TASKFORCE

- Reducing cardiovascular risk for Australians living with overweight or obesity with or at risk of CVD, requires an equity-led, integrated model of care as the default. This includes embedding dietetics, exercise physiology, behavioural support, and medication review with step-up options to GLP-1–based pharmacotherapy and bariatric surgery when indicated.
- The delivery of this integrated care should be tailored to priority populations. For example: Remove access and engagement barriers through co-designed, culturally safe models in Aboriginal Community Controlled Health Services/Aboriginal Community-Controlled Organisations for First Nations peoples; bilingual peoples and adapted resources for CALD communities; accessible/assistive exercise modalities and nutrition support for people with disability; integrated metabolic-mental health care for those with mental illness; and tele-enabled, locally delivered teams for regional/remote and low-SES communities.
- Health systems need to be appropriately funded. For example, reimburse multidisciplinary packages (dietitian, exercise physiology, psychology), equip patients with home BP/weight devices and tele-monitoring, invest in community navigators and bilingual/First Nations health workers, and formalise partnerships with community organisations to sustain engagement and outcomes.

4. Environmental Scan

4.1 Prominent Global Heart Association Position Statements on Obesity and Cardiovascular Disease

4.1.1 Several societies and associations from around the world have sought to provide evidence-supported guidance on the management of obesity in the context of cardiovascular disease via consensus statements or similar evidence reviews (Table 4.1.1).

Common features across these statements included:

1. Recognising obesity as a chronic disease with multifactorial aetiology
2. Multidisciplinary management is required to achieve long-term outcomes
3. Diagnosis of obesity and emphasis for management should move beyond BMI classifications and focus on excess adiposity and metabolic health status (i.e., presence or absence of metabolic dysregulation). *This includes emphasising waist circumference related measures as a proxy for visceral adiposity.*
4. Diet- and exercise-based behavioural interventions are the foundation of obesity care and first-line approach.
5. Pharmacotherapy is generally safe and effective for both obesity management and cardiovascular disease outcomes when tailored for individual risk, with an emphasis on long-term adherence. Most statements recommend pharmacotherapy for those who do not adhere to or respond to behavioural intervention. Surgery is more invasive and carries higher risk than pharmacotherapy; however, with appropriate medical oversight is an effective approach for significant weight loss with additional cardiovascular and survival benefits. *Considerations for access and costs varied depending on geographical location.*

The following considerations for obesity management in the context of CVD were less consistently reported:

1. Reducing weight stigma and using person-first language is imperative. *Particularly emphasised as an explicit focus in the North American associations [140, 276] and the World Health Federation[277], but less emphasised in the European Association, Asia-Pacific and Middle-East statements [120, 278, 279].*
2. The role of cardiologists and other medical and healthcare clinicians in obesity management. *Despite consistently advocating for multidisciplinary care, there was no consistent recommendation for the most appropriate model of care for obesity and CVD management.*
3. Recognition of sleep and psychological intervention as a core component of care alongside dietary and exercise interventions to achieve sustainable outcomes for individuals with obesity and CVD.
4. Cultural and regional adaptation to address diagnosis and management in under-represented populations
5. Approaches to address the evidence-implementation gap for obesity management were only provided in the AHA statement on the implementation of obesity science into clinical practice,[276] despite many of the barriers being raised across global statements.

6. The importance of co-prescription of anabolic exercise (i.e., that which builds or maintains muscle mass) and diet to promote retention of lean mass with obesity management medications.

Table 4.1.1. Key global position and consensus statements from major heart and cardiovascular organisations regarding the management of obesity or obesity-related conditions in the context of CVD.

Organisation **Date** ***Name of publication*** **[link]**	**Specific Recommendations** **Lifestyle (behavioural interventions)**	**Pharmacotherapy**	**Surgery**	**Other Clinical Considerations**
American College of Cardiology (ACC) 2025 *Concise Clinical Guidance: Medical Weight Management for Cardiovascular Health[140]* https://www.portailvasculaire.fr/sites/default/files/docs/gilbert-et-al-2025-concise-clinical-guidance-an-acc-expert-consensus-statement-on-medical-weight-management-for.pdf	<u>No specific lifestyle advice provided.</u> **Key Points:** Insufficient to achieve long-term weight loss; cannot reverse complications and comorbidities associated with obesity Should be offered alongside pharmacotherapy (such as Nutrient-stimulated hormone therapy) to optimize outcomes Lifestyle + pharmacotherapy intervention have shown minimal additional effect on weight loss than pharmacotherapy alone Advises against asking patients to trial lifestyle intervention first, before pharmacotherapy- i.e., should not wait until lifestyle intervention fails before considering pharmacotherapy. Lifestyle therapy should be integrated into a multidisciplinary care approach, including health coaching with registered dietitians	<u>Focus on Nutrient-stimulated hormone (NuSH) therapies</u> **Key Points:** Includes: glucagon-like peptide-1 (GLP-1) receptor agonists (e.g., liraglutide, semaglutide) and dual GLP-1/glucose-dependent insulinotropic polypeptide (GIP) receptor agonists (e.g., tirzepatide) GLP-1 and GIP receptor agonists: liraglutide (~8% weight loss), semaglutide (~15% weight loss), tirzepatide (~21% weight loss),with good safety profiles and CVD benefit NuSH therapies fill the gap between lifestyle interventions (often insufficient) and bariatric surgery (effective but invasive). Dosing titratable to minimise side effects and maximise weight loss	<u>No specific advice for surgery</u> **Key Points:** Highly effective in weight reduction compared with lifestyle therapies, but may be less desired by patient due to invasiveness Achieve the greatest magnitude of weight loss (up to 25%), compared with both lifestyle and pharmacotherapy GLP-1 receptor agonist therapy may be preoperatively continued in patients without elevated risk of delayed gastric emptying and aspiration. If the decision to discontinue prior, the recommended duration is one week prior to surgery; but evidence to inform this is limited.	Emphasises obesity as a chronic disease with multifactorial causes. Key Challenges 1. Access and affordability: Depending on the national health system, high costs and limited insurance coverage are major barriers. 2. Supply shortages 3. Discontinuation of therapy leads to weight regain. Other considerations: - Caution in geriatric populations due to higher risk of frailty and sarcopenia - Tirzepatide may reduce efficacy of some contraceptives - May need to review other medications (e.g. anti-hypertensives, anti-hyperglycemic agents) to prevent complications. - Strategies to reduce weight stigma including space and equipment, medical devices and procedures are outlined

	and exercise physiologists, which has been shown to improve weight loss, physical activity, and metabolic markers. Especially important with pharmacotherapy discontinuation.	outcomes. GI side effects and intolerances that can be managed through appropriate dosing and behavioural modification. GLP-1 and GIP receptor agonists should not be used in those with personal/family history of medullary thyroid carcinoma, or hypersensitivity to the individual product/excipients Avoid compound NuSH therapies NuSH therapy should be adopted long-term and should not be discontinued to avoid weight regained.		
American Heart Association *Implementation of Obesity Science into Clinical Practice: A Scientific Statement from the American Heart Association[276]* 2025 https://pmc.ncbi.nlm.nih.gov/articles/PMC11416804/	**Key Points:** **<u>Implementation gaps in lifestyle interventions</u>** Only 16% of healthcare practitioners can identify evidence-based lifestyle treatments for obesity. Low referral rates to clinical weight management programs due to lack of clinician knowledge, comfort, and structural barriers. 23% of patients never discuss weight or lifestyle interventions with clinicians. When discussions do occur, many patients report clinicians do not ask for permission	**Key Points:** **<u>Implementation gaps in pharmacotherapy</u>** Despite >50% of adults being eligible for obesity pharmacotherapy, only a small fraction receives these treatments, this contrasts with prescription patterns for diabetes and hypertension medications. Under-prescribed in healthcare settings despite their efficacy potentially due to clinicians' knowledge gap about anti-obesity medications, safety concerns, and	**Key Points:** **<u>Implementation gaps in bariatric surgery</u>** Bariatric surgery is considered as the last-line therapy for obesity that cannot be managed through lifestyle intervention or pharmacotherapy alone, and its safety and efficacy are continuously being improved overtime. However, social and economic access is highly limited among underrepresented populations,	Advancements in obesity science and obesity care (lifestyle modification programs, new pharmacotherapies, robust outcomes for bariatric surgery) are not being effectively translated into routine clinical practice hindering effective management. Gaps are sustained by structural, societal and cultural barriers Implementation of obesity science is crucial for better and contextually appropriate care, specifically in underrepresented populations with obesity. This requires multi-level action at the clinician, community, system and policy levels.

	before discussing obesity, leading to discomfort and avoidance Even though intensive lifestyle interventions are more effective than brief lifestyle advice, physicians are much more likely to provide the latter Recommendations to empower patients to ask questions about weight management and provide resources for lifestyle changes are provided Other barriers to providing obesity counselling were discussed (e.g. lack of reimbursement) Lifestyle interventions are more likely to succeed if implemented at a couple, family, or household level. Digital tools, and telemedicine can improve access to lifestyle therapy, especially in underserved areas. Address socioeconomic and racial disparities in access to lifestyle interventions.	limited healthcare coverage in the US (high out-of-pocket cost) Health policies play a major role in improving the access of these medications High costs and limited coverage disproportionately affect underrepresented and low-income populations, who have the highest obesity burden	e.g., Black, Hispanic/Latino, and low-income populations are less likely to undergo surgery despite higher obesity prevalence. Patients need to have high levels of health literacy to enact the behavioural modifications necessary for long-term weight loss and maintenance Availability of high-volume bariatric surgery centres are limited to certain geographical regions Limited coverage from public insurance companies for post-operative care. Costs, travel expenses, and lost wages for follow-up care hinder access for underprivileged groups.	Sustainable clinic-community linkages are necessary to facilitate implementation of obesity and weight management programs Emphasis on obesity education for healthcare professionals (e.g. via offering certification programs in obesity science), effective behavioural counselling strategies (5As framework) Limitations of weight-centric approach of assessing and treating obesity (e.g. via BMIs) were discussed, and it is important to stop using weight as the sole indication of health in clinical practice. Instead, the focus should be on addressing obesity-related complications and adverse health outcomes Social support should be the emphasis for all obesity interventions Clinicians need to be trained to communicate in a transparent, stigma-free and sensitive manner with patients about weight
World Heart Federation (WHF) 2025	**Key Points:** Structured lifestyle modifications, including diet and physical activity, are essential for managing obesity and reducing CVD risks	**Key Points:** Pharmacotherapy, when combined with lifestyle interventions, can effectively promote weight loss and help maintain it long-term	**Key Points:** Minimally invasive surgery can be an effective long term treatment, with about 90% of patients achieving at least 15-40% weight loss.	Recognises obesity as a disease/disease process attributed to a combination of social, biological, environmental, and commercial determinants. Strategies should therefore address determinants upstream to the individual (e.g. commercial

World Heart Report on Obesity and Cardiovascular Disease[277] https://world-heart-federation.org/wp-content/uploads/World_Heart_Report_2025_Online-Version.pdf	Modest weight loss (5 to 10%) can significantly improve CV risk factors like hypertension, dyslipidaemia, and insulin resistance; greater weight loss, more profound benefits including reduced incidence of myocardial infarction and stroke Lifestyle interventions should be integrated into clinical management plans, including cardiac rehabilitation programs, to improve outcomes for patients with obesity and CVD. **Diet:** Conflicting dietary recommendations for patients with multiple conditions (e.g., diabetes, kidney disease, and heart disease) should be clarified by clinicians-guidance must be clear and personalized to avoid confusion. **Physical Activity:** Regular exercise can be hindered by physical limitations such as joint pain, deconditioning and OSA. Urban planning and community initiatives, such as creating walkable neighbourhoods and green spaces, can encourage physical activity. Long-term care:	GLP-1RAs can achieve modest weight loss (<5-10%) but can have side effects and some categories may be harmful for CV conditions. GLP-1RAs have been shown to reduce major adverse cardiovascular events (MACE), including heart failure hospitalizations and myocardial infarction, in people with and without Type 2 diabetes. The impact of having obesity on pharmacological treatment is discussed in the context of change in pharmacokinetics, pharmacodynamics, and medication absorption, distribution, metabolism and elimination). The impact of other pharmacological treatments that are not targeted at obesity progression are outlined (beta-blockers, anti-depressants). Governmental effort to increase availability and affordability of anti-obesity medications is required	The impact of obesity on surgical treatment is outlined, given obesity poses technical difficulties such as challenges with vascular access, higher risks of stent thrombosis, surgical wound infections, prolonged ventilation and renal failure.	determinants), improve equitable access to intervention options through policy and advocacy. Obesity prevention should begin during/before childhood, through addressing maternal obesity/diabetes, promoting breastfeeding Regular screening for overweight/obesity and related biomarkers among both adults and children are recommended *Weight stigma:* Defined as “individual’s social devaluation and denigration due to their excess body weight, leading to negative attitudes, stereotypes, prejudice and discrimination” Can result in long-lasting psychological and physical consequences. Children and young adults are particularly vulnerable, with obesity being the leading cause of bullying I schools, affecting their education and mental health. People with obesity can be perceived as lazy, gluttonous, and lacking self-discipline. Weight stigma occurs in workplaces, healthcare settings, and media. Weight stigma and discrimination should be addressed as part of public health policies/campaigns. Recommendations to address stigma are outlined.

Recommend behavioural/lifestyle interventions for improving psychological health of people living with obesity, even if weight loss is minimal

Intervention should embed a mental health component to address the psychological impact associated with obesity

Public health and policy support:

Policies that promote access to nutritious foods, regulate food marketing, and create environments conducive to physical activity are vital for supporting individual lifestyle changes

Governments should take initiative to spread public awareness, increase availability and accessibility of lifestyle intervention programs.

Equity-focused approaches by governments and local authorities can reduce the disproportionate burden of obesity and CVD on vulnerable groups

Public health policies to encourage healthier lifestyle behaviors (e.g., restriction of marketing, SSB tax)

School-based/workplace-based programs needed to help establish lifelong healthy lifestyle habits and incentivise healthy lifestyle habits

	Integrate overweight and obesity prevention in primary care settings			
Asian Pacific Society of Cardiology (APSC) 2024 *Obesity in the Asia-Pacific Region: Current Perspectives* https://www.japscjournal.com/articles/obesity-asia-pacific-region-current-perspectives?language_content_entity=en	**Key Points:** **<u>Diet</u>** Caloric deficit of 500kcal/day is recommended **<u>Physical activity</u>** Recommend current physical activity guidelines for general population (150–300 min of moderate intensity physical activity or 75–150 min of vigorous intensity physical activity with two days of resistance training per week). Recommend combining physical activity intervention with dietary modification for greater benefit. **<u>Behavioural change</u>** Recommendations to support behaviour change include education, goal setting, self-monitoring (weight, food intake and exercise), stimulus control and stress reduction. Address any concurrent eating disorders Encourage smoking cessation & alcohol cessation	**Key Points:** Pharmacotherapy should only be used after lifestyle intervention has failed to achieve weight-loss targets Long term treatment is required for sustained weight loss Efficacy of common anti-obesity pharmacotherapy options available in Asia Pacific regions were outlined including: phentermine, topiramate, orlistat, naltrexone/bupropion, GLP-1 Ras. Barriers to accessing pharmacological treatment in different Asia-Pacific regions were discussed, including cost and reimbursements	**Key Points:** Support the use of bariatric surgery for achieving sustained weight loss, improving obesity-related comorbidities and mortality. Referred to the 'Asia-Pacific Metabolic and Bariatric Surgery Society' on the BMI thresholds, safety and efficacy of bariatric surgery in different Asia Pacific regions Emphasis on multidisciplinary postoperative surveillance to monitor and address potential remission and side-effects (e.g. psychiatric disorders) Barriers to accessing surgical treatment in Asia-Pacific regions were discussed	**Key Points:** Highlighted the rising obesity burden in Asia-Pacific Discussed diagnostic criteria, treatment access, and disparities between different Asia-Pacific regions Highlighted the diagnostic difference of overweight and obesity between different populations within Asia-Pacific regions, as well as difference in fat distribution and prevalence of abdominal obesity Discussed the 'obesity paradox' and the importance of factoring in anthropometric measurements rather than BMI alone when estimating CVD risk Emphasis on obesity prevention, multidisciplinary management and shared decision making between patient and healthcare professionals Important to address weight stigma at a multinational level through political and social advocacy Special considerations should be given to low-income households experiencing obesity, and efforts are warranted to make treatment options more accessible and affordable (e.g. government subsidies)

ANMCO (Italian Association of Hospital Cardiologists) *ANMCO (Italian Association of Hospital Cardiologists) scientific statement: obesity in adults—an approach for cardiologists[279]* 2024 https://pmc.ncbi.nlm.nih.gov/articles/PMC10761446/	**Key Points:** Minimal specific recommendations. A multidisciplinary approach is promoted in both diagnostic and therapeutic phases of management with curative diet therapy and adequate physical activity promoted alongside pharmacotherapy, psychological and social support and bariatric surgery if indicated. A team of professionals, including dietitians, clinical psychologists, and exercise trainers, is recommended to provide comprehensive support	**Key Points:** Although effective, pharmacological interventions alone are inadequate and should be supplemented with other strategies (unspecified). Obesity may affect the pharmacokinetics and pharmacodynamics of anticoagulant drug. In patients with severe obesity anticoagulant treatment must be individualised	No specific recommendations	Recognises obesity as a chronic disease caused by multitude of factors besides personal choices, and thus mandating a multidisciplinary approach. Limitation of BMI, and the strengths and limitations of existing adiposity assessment tools were discussed (CT and MRI are the gold standards) Emphasis on stigma-free communication (5As framework recommended) in healthcare settings *Diagnosing/Treating CVD in patients with obesity (in general)* Obesity can change the specificity and sensitivity of non-invasive and invasive diagnostic tools for CVD (e.g., change in platelet reactivity) Obesity can change the treatment outcomes of percutaneous coronary intervention (PCI), cardiac surgery *Diagnosing/assessing CAD in patients with OB* Obesity complicates the results of evaluative tools used CAD (electrocardiography, exercise stress test nuclear medicine tests, stress MRI, coronary artery calcium (CAC) scan screening, CT, and coronary angiography)
Saudi Heart Association *A Saudi Heart Association Position Statement on Obesity and Cardiovascular Disease[278]*	**Key Points:** Lifestyle interventions are recommended as the first-line approach for managing obesity or overweight in adults.	**Key Points:** Pharmacotherapy is recommended as an adjunct to lifestyle interventions when lifestyle changes alone result in insufficient weight loss.	**Key Points:** It should only be considered if the patient meets any of the following criteria and can tolerate bariatric surgery:	Overweight and obesity (especially excess central/visceral adiposity, epicardial fat, independent of BMI) is key risk factor for CVD and CV mortality (inc. CAD, HF, AF, SCD). Also a risk factor for OSA, which is associated with increased risk of AF and HF

2024 https://pmc.ncbi.nlm.nih.gov/articles/PMC11518015/	Multidisciplinary lifestyle management can improve CV risk factors, and lower CV mortality and incidence if weight loss is achieved **Diet** Emphasis on Mediterranean, low-fat, or low-carbohydrate diets for better CV health. Very little evidence to support the CV benefits of ketogenic, intermittent fasting, or very low-calorie diet despite their weight loss efficacy. **Physical Activity** Both aerobic and resistance exercise reduce visceral adiposity even without weight loss 150 min/wk is adequate to reduce visceral fat (moderate intensity is just as effective as vigorous) Physical activity improves cardiorespiratory fitness, which is linked to reduced CVD risk, CV outcomes and CV mortality Exercise should be included in any weight management program given its association with improve CV function, reduce CVD risk, CV outcome and CV mortality	Selection of medications should consider patient profiles, comorbidities, preferences, cost, and drug access Certain earlier weight-loss medications have CV risk and adverse side effects No clinical data to support the use of traditional herbal medicine Potential efficacy of medications not approved for weight loss were also discussed (Metformin; SGLT-2 inhibitors; cagrilintide; Retatrutide) Potential efficacy of oral-route anti-obesity medications were discussed	1) BMI ≥ 30 kg/m^2, lifestyle and/or pharmacological interventions fail 2) BMI ≥ 40 kg/m^2 3) BMI ≥ 35 kg/m^2 AND has concurrent weight-related complications Among those without CVD, bariatric surgery is associated with reduced CV/all-cause mortality, and obesity-related comorbidities Among those with CVD (limited data exist), bariatric surgery is associated with reduced MACE, incident HF, compared to non-surgical interventions Limited accessibility to bariatric surgeries despite the number of people living with obesity	Emphasis on managing obesity among younger population, and especially in those with pre-established CVD Weight loss among those with obesity is important for the primary and secondary prevention of CVD Important to identify and address underlying eating/psychological factors contributing to obesity via psychological/ behavioural therapies (e.g. mindfulness intervention, CBT) Diagnosing/predicting HF outcomes in patients with obesity: Natriuretic peptides are reduced among people with obesity, which could confound assessment of HF via natriuretic peptides (different threshold values exist) Impact of obesity on CV screening CV screening should be regularly conducted in patients with obesity even if asymptomatic. However, obesity often confounds results of CV assessment tools (these are discussed in the statement) Impact of obesity on CV treatment/management Obesity can change the pharmacokinetics and properties of CVD drugs and can affect the response to rhythm control strategies (pharmacological/surgical); e.g. patients with obesity have lower response to antiarrhythmic medications.

European Society of Cardiology (ESC) 2023 *Obesity and Cardiovascular Disease: Clinical Consensus Statement[120]* https://academic.oup.com/eurheartj/article/45/38/4063/7738070	**Key Points:** Lifestyle intervention should aim to facilitate weight loss through a combination of physical activity, diet and psychological interventions, with pharmacotherapy and bariatric procedures as potential complementary therapies. Weight losses of 5-10% can be achieved but weight-loss maintenance is a key issue. Intensive, multidisciplinary and multicomponent interventions (e.g. group or individual, technology-based delivery, education, peer support, self-monitoring, coaching, cognitive restructuring and goal setting) with holistic objectives (i.e., including patient education, addressing mental health, sleep behaviour and chronic stress) Cost-effectiveness of lifestyle interventions were discussed: Lifestyle interventions are generally cost-effective, especially for individuals with higher BMI and comorbidities, and can lead to long-term health benefits. **<u>Physical Activity/Exercise</u>** Exercise is essential for weight loss maintenance and overall cardiovascular risk reduction. Recommendations include 150 to 300 minutes of moderate intensity or 75 to 150 minutes of vigorous intensity	**Key Points:** Pharmacological treatments should only be considered as complementary therapy to lifestyle modification if sufficient weight reduction cannot be achieved with lifestyle modification alone. Anti-obesity medications are typically indicated for patients with a BMI ≥30 kg/m² or BMI ≥27 kg/m² with at least one weight-related comorbidity. Orlistat and bupropion/naltrexone should be used with caution as weight loss medications, particularly in patients with known CVD Semaglutide (2.4 mg/weekly) is the only option to have demonstrated cardiovascular benefits in patients with obesity and pre-existing CVD. Weight loss effects are limited to the duration of treatment, with significant weight regain observed after cessation- this has implications for addressing the cost-effectiveness of drug therapies. Whether drugs should be used life-long or as intermittent treatment over decades is not yet determined.	**Key Points:** Bariatric surgery should only be considered for individuals with BMI ≥40 kg/m^2 or BMI ≥35 kg/m^2 with at least one obesity-related disease, and after lifestyle intervention combined with medications have failed to produce sustained weight loss. Average weight loss at 12 months following laparoscopic sleeve gastrectomy is 25% and following laparoscopic Roux-en-Y Gastric Bypass is 30%. These losses can be sustained for at least 5 years. Cardiometabolic benefits include T2D remission (~10 years), improved blood pressure, lipid profiles and reduced MASH as well as reduced all-cause and CV-mortality. Pre-surgical requirements, early post-procedural and long-term complications are outlined.	Defines obesity as a chronic disease Emphasis on multidisciplinary, person-centred approach Emphasis on primary prevention of obesity at an environmental level through public health policies In patients with obesity and co-occurring T2D/hypertension/ dyslipidaemia/OSA, weight reduction should be the main goal of treatment Addressing emotional coping mechanisms and stigma associated with obesity is crucial. Psychological interventions and behavioural counselling (especially family-based, multi-component weight management interventions) are recommended for effective and long-term lifestyle change. Emphasis on training health professionals to interact with patients living with overweight and obesity in non-stigmatised manner to facilitate weight loss motivation (e.g. 5As framework: Assess, Advise, Agree, Assist, Arrange) Comparisons between bariatric surgery and newer anti-obesity medications are lacking.

physical activity weekly, along with muscle strengthening exercises 2-3 times per week.

Individuals who cannot achieve these recommendations should be encouraged to stay as active as their ability allows and reduce sedentary time.

Combined aerobic and resistance training combined with dietary modification can achieve sustained loss of fat mass (especially VAT) while maintaining fat-free mass as first-line treatment for obesity.

Diet

Caloric deficit of 500–750 kcal/day is generally recommended, with adjustments to individual body weight and activity levels.

Dietary intervention should be tailored to individual preference, be culturally appropriate, effective and affordable for long-term adherence regardless of body size

Common hypocaloric dietary interventions (e.g. Mediterranean diet, plant-based diets) result in similar weight loss and CVD risk reduction; however, Mediterranean diet is superior in terms of long-term maintenance of weight loss benefits and CV risk reduction

	Caloric restriction should not be recommended in patients with diseases with established catabolic dominance, such as cancer, to prevent weight loss Promoting lifelong healthy diet adaptation is crucial after initial weight reduction			
American Heart Association *Weight-Loss Strategies for Prevention and Treatment of Hypertension: A Scientific Statement from the American Heart Association[280]* 2021 https://www.ahajournals.org/doi/10.1161/HYP.0000000000000202	**Key Points:** A 5 to 10% reduction in body weight over six months is recommended for significant improvements in blood pressure and CV factors. **Diet** Heart-health diets like the Mediterranean diet and DASH diets are recommended for effective hypertension control, weight management and CVD risk reduction. Low sodium intake alone (independent of diet) also reduces blood pressure, especially among older & Black populations and those with hypertension. Increased potassium intake may help lower blood pressure, but excessive intake may have adverse outcomes. Intermittent fasting may lead to modest weight loss, but the effect on blood pressure is relatively weak and require further research **Physical Activity**	**Key Points:** Pharmacotherapy (in conjunction to lifestyle) is especially recommended for individuals with limited treatment response to lifestyle modifications alone and have a BMI ≥30 kg/m^2 or a BMI ≥27 kg/m^2 in the presence of weight-related comorbidities (e.g. hypertension) Efficacy & safety of FDA-approved drugs on weight loss and blood pressure management were discussed (orlistat, phentermine/ topiramate, naltrexone/bupropion, liraglutide, semaglutide) Patients with sustained weight loss and in whom these drugs are well tolerated may benefit from long-term use of anti-obesity pharmacotherapy Long-term effect of these drugs on blood pressure requires further research	**Key Points:** Bariatric surgery effectively reduces adiposity in individuals with severe obesity in the long-term, and has short-term and long-term blood pressure reductions in individuals with obesity. Early blood pressure reduction (as early as 1-week postoperative) may be due to neuroendocrine changes (e.g., increased GLP-1, reduced SNS activity, normalised RAAS). A 63% resolution of hypertension was observed in one study, reducing reliance on medication. Individuals with following criteria may be recommended for metabolic surgeries: - BMI ≥40 kg/m^2 - BMI ≥35 kg/m^2 with comorbidity - Psychologically stable	Obesity (especially visceral adiposity) is a major risk factor for primary hypertension, which in turn heightens the risk for CV and renal disease. Lifestyle interventions can result in clinically-significant blood pressure reductions if weight loss is sustained, which is difficult to do with lifestyle interventions alone due to high rate of recidivism. Combined lifestyle with pharmacological and/or surgical interventions for those with both obesity and hypertension should be considered. Critical research gaps in current interventions for treating obesity-related hypertension were discussed Prevention strategies of obesity-related hypertension were discussed, with emphasis on multi-disciplinary efforts

Physical activity and exercise training can reduce weight, blood pressure and improve obesity and hypertension, with the greatest improvement in CVD risk factors resulting from 5%-10% weight loss through PA (150 min. or more/week):

<150 min/wk produces no to minimal weight loss

150 to 225 min/wk produces 2- to 3-kg weight loss

225 to 420 min/wk produces 5- to 7.5-kg weight loss

200 to 300 min/wk of PA is needed for long-term weight maintenance.

Timelines for weight loss are not reported but primary studies are generally between 8-20 weeks.

Exercise reduces blood pressure independent of weight loss.

Given that exercise can improve cardiorespiratory fitness (strong predictor of CVD risk), exercise should be incorporated into all antihypertension and weight-loss interventions

Resistance training can improve blood pressure and lower CVD mortality independent of weight loss and change in cardiorespiratory fitness.

- No active substance abuse.

- Has T2D and BMI ≥30 kg/m^2 (≥27.5 kg/m^2 in Asian population) and are not achieving good glycaemic control

	Reducing sedentary time can reduce blood pressure, although no specific recommendations exist.			
American Heart Association (AHA) 2021 *Obesity and Cardiovascular Disease: A Scientific Statement From the American Heart Association[17]* https://www.ahajournals.org/doi/10.1161/CIR.0000000000000973	**Key Points:** Lifestyle intervention (e.g. Diabetes Prevention Program) is equally as effective as pharmacotherapy Focus on reducing visceral adiposity (VAT) Emphasis on multidisciplinary obesity management to achieve lifestyle change **<u>Exercise</u>** Regular *aerobic exercise* (3 to 5 sessions per week for 12 to 52 weeks) is effective in reducing VAT, even without weight loss. Moderate-intensity exercise is generally sufficient to reduce VAT, with high-intensity exercise showing mixed results. Walking and meeting physical activity recommendations (150 minutes per week) are beneficial. While resistance training alone has shown equivocal results for VAT reduction, it can complement aerobic exercise for overall health benefits. Exercise also reduces hepatic (liver) & pericardial fat	**Key Points:** *Liraglutide:* reduced MACEs and CV mortality *Lorcaserin:* (now removed from shelf by FDA) lacked efficacy for reducing CV mortality and CVD events. *Orlistat:* limited efficacy and safety for treating HF patients with obesity. *SGLT2:* demonstrated efficacy for weight loss and reduced hospitalisation for HF and CV death	**Key Points:** Bariatric surgery achieves greater weight loss (10-40 kg) compared to medical weight loss (5-10 kg), reduces risk of fatal & non-fatal coronary artery disease (CAD) events May be used in addition to lifestyle intervention caloric restriction for greater weight loss and develop greater capacity to perform physical activity Class 3 obesity is a relative contraindication for heart transplants due to higher rates of rejection and greater 5yr mortality. Severe obesity (class 3) is a relative contraindication for heart transplantation due to higher acute rejection rates and 5-year mortality. Bariatric surgery may help reduce weight and improve candidacy for transplantation. Obesity is not universally considered a contraindication for	*Other considerations* Highlights the importance of assessing obesity-related risk based on abdominal fat (e.g., WC, WHR), fat distribution, and ectopic fat rather than BMI alone since these are stronger predictors of CVD, mortality and cardiometabolic disease. It is important to distinguish metabolic health status (linked to levels of visceral adiposity) in those classified with overweight or obesity based on BMI classifications; this will modify associations with CV risk. There are differences in treatment outcomes in people with obesity compared with those without PCI, antiplatelet therapy, and surgical revascularization. Discussed the 'obesity paradox' in the context of HF, percutaneous coronary intervention. Management of obesity among older adults at risk of HF should focus on maintaining weight and improving functional outcomes rather than weight loss *Considerations for diagnosis of CAD in those with obesity:* Challenges due to obesity including:

The improved fitness from exercise training help improve prognosis in heart failure (HF) patients regardless of BMI

Diet:

Caloric restriction reduces VAT, hepatic and ectopic fat including epicardial and pericardial fat

Mediterranean diet has been shown to reduce MACEs in high CV risk patients

Combined (physical activity + diet)

Effectively reduce VAT and ectopic fat independent of weight loss.

Programs like the Diabetes Prevention Program and Look AHEAD Trial have demonstrated greater VAT reductions when combining dietary changes with physical activity.

left ventricular assist device implantation

Patients with obesity (notably central obesity) undergoing surgery may have an increased risk of post-operative complications (e.g., wound infection)

- Differences in baseline ECG due to change in heart position and increased distance between heart and electrodes affecting ECG accuracy
- Changes in ECG related with obesity including increased heart rate, increased QRS interval, Increased QTc interval, ST segment depression.
- Reduced exercise capacity due to pulmonary dysfunction, orthopaedic limitations and left ventricular diastolic dysfunction
- Higher likelihood of test terminating prior to achieving 80-85% of age-predicted heart rate due to fatigue, leg pain or dyspnoea
- Reduced image quality for single photon emission CT (SPECT) due to attenuation artefact (e.g., by diaphragm or breast)
- Weight-based limitations of imaging technologies
- Stress cardiac MRI may be limited by weight limits, bore diameter and claustrophobia with higher waist circumference restricting access.
- In cardiac CT coronary angiography, image quality degrades as BMI increases due to reduced signal-to-noise ratio

Vascular access may be more difficult for coronary angiography

4.2 Policies, Strategies, Reports, Services and Societies - National, State and Territory

4.2.1 The following are presented in **Table 4.2.1**:

- Existing national and state-level policies, strategies, and frameworks addressing obesity, overweight and/or cardiovascular health.
- Current services, programs and societies available for the prevention, diagnosis, and management of obesity and CVD, with a focus on community-based initiatives.

Figure 4.2.1 provides a summary of key national and state level polices, programs and services and supportive infrastructure for the management of obesity and CVD in Australia.

A comprehensive living Obesity Activity Map is provided by the Obesity Collective: https://airtable.com/appysqyCvYWTzvGjJ/shrniQIcMv1fryqA2/tblePiEx9rAlE7F8g

The Obesity Activity Map (last updated 2021) includes information and links to over 2000 entries of the following specific to obesity care: i) advocacy/networks/statements; ii) information/education/training; iii) services/programs; iv) research trials; v) events/challenges; vi) funding/incentives; vii) government/policy regulation and viii) products.

Overall, there is comprehensive coverage of policies, guidelines and services for general health and wellbeing, and obesity-related and CVD care. However, few of these explicitly integrate both obesity and CVD management, or specifically address high-priority groups, with a dearth of information and resourcing for mental health in the context of obesity and CVD care. There are no clear models of integrated and multidisciplinary care.

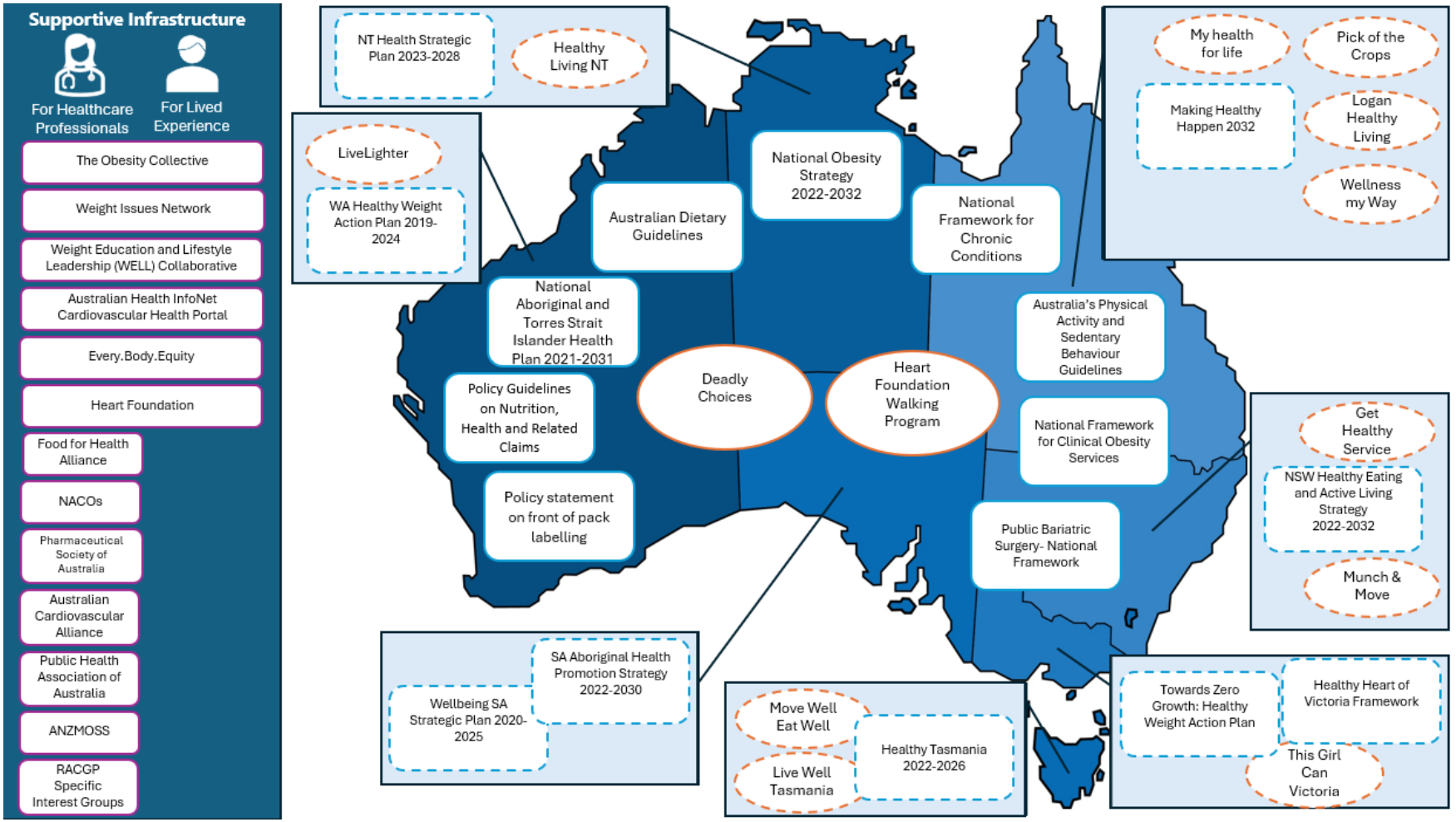

Figure 4.2.1 Summary of key National (solid outline) and State/Territory (dashed outline) policies/strategies/reports (blue outline) and programs/services (orange outline) relevant to obesity and CVD management in Australia. Supportive infrastructure relevant to healthcare professionals and lived experienced people with obesity and CVD are shown in the left panel (purple solid outline). Background image of Australia downloaded from Vecteezy.com.

Table 4.2.1 Existing national and state/territory-level policies, strategies, frameworks, services, programs and supportive infrastructure addressing obesity, overweight and/or cardiovascular health.

Policies, Strategies and Reports										
Name/Title [link]	**Description/Purpose**	**Jurisdiction**	**Specific to primary population**		**Relevant to High Priority Populations#**					
			Overweight and Obesity	**CVD**	**Youth**	**CALD**	**First Nations**	**Rural, Regional and Remote**	**Disability**	**Mental Health**
National Obesity Strategy 2022-2032 https://www.health.gov.au/resources/publications/national-obesity-strategy-2022-2032?language=en	Prevent and reduce overweight and obesity in Australia. Aim to promote healthy weight maintenance in people without overweight or obesity; prevent further weight gain and reduce weight in people with overweight or obesity; halt the rise and reverse the trend in the prevalence of obesity in adults by 2030; and reduce overweight or obesity in children and adolescents aged 2-17 years by at least 5% by 2030.	National (Department of Health, Disability and Ageing).								
National Preventive Health Strategy 2021–2030 https://www.health.gov.au/resources/publications/national-preventive-health-strategy-2021-2030?language=en	Improve the health and wellbeing of all Australians at all stages of life through prevention. Aims to prevent ill-health from preconception period through to the early years of life; to help ensure all Australians live with good health and wellbeing for as long as possible; to achieve health equity for priority populations; to increase investment in prevention.	National (Department of Health, Disability and Ageing).	*Prevention of overweight and obesity discussed*	*Prevention of CVD discussed*						

National Strategic Framework for Chronic Conditions https://www.health.gov.au/resources/publications/national-strategic-framework-for-chronic-conditions?language=en	Prevention and management of chronic conditions in Australia Aims to provide guidance for the development and implementation of policies, strategies, actions and services to address chronic conditions and improve health outcomes.	National (Department of Health, Disability and Ageing)	*Overweight and obesity discussed as chronic condition and risk factors for targeted prevention*	*CVD discussed as chronic condition and risk factors for targeted prevention*
Australian Dietary Guidelines https://www.health.gov.au/resources/publications/the-australian-dietary-guidelines?language=en	Provide evidence-based dietary guidelines to promote healthier eating patterns among Australians, reduce the risk of diet-related chronic diseases, and improve overall health and wellbeing. Designed for the general healthy population and aim to support informed food choices, public health strategies, and nutrition education.	National (Department of Health, Disability and Ageing).		
Australia's Physical Activity and Sedentary Behaviour Guidelines https://www.health.gov.au/topics/physical-activity-and-exercise/physical-activity-and-exercise-guidelines-for-all-australians	Provide Australians with physical activity and sedentary behaviour guidelines tailored to different age groups and life stages. Designed to help individuals incorporate more activity into their daily lives and improve overall health outcomes.	National (Department of Health, Disability and Ageing).		
Policy Guidelines on Nutrition, Health and Related Claims	Outlines the policy guidelines for nutrition, health, and related claims in Australia and New Zealand.	National		

https://www.foodregulation.gov.au/resources/publications/policy-guideline-nutrition-health-and-related-claims	Aims to protect and improve public health by ensuring responsible use of scientifically valid claims; support healthy food choices through government, community, and industry initiatives; ensure compliance with national policies, legislation, and international trade obligations; Enable monitoring and enforcement to prevent misleading claims and protect consumer	Australian Government	
Policy statement on front of pack labelling https://www.foodregulation.gov.au/resources/publications/policy-statement-front-pack-labelling	Outlines the policy statement for Front of Pack Labelling (FOPL) in Australia and New Zealand. Provides nutrition information on packaged foods to help consumers make healthier choices.	National Australian Government	
National Framework for Clinical Obesity Services chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://www.nacos.org.au/wp-content/uploads/2023/04/NACOS-Framework-combined-25022020.pdf	Provide practical guidance for designing, delivering, and accessing clinical obesity services in Australia. Aims to address the challenges of obesity care by defining principles, standards, and referral pathways for healthcare professionals, consumers, policymakers, and other stakeholders.	National National Association of Clinical Obesity Services (NACOS)	
Public Bariatric Surgery – A National Framework	Provides a National Framework for implementing bariatric-metabolic surgery in Australia's public hospital	National Australian & New Zealand	*Mentions obesity-related cardiomyop*

chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://anzmoss.com.au/wp-content/uploads/Public-Bariatric-Surgery-Framework_full-report.pdf	system to address the unmet clinical need for effective obesity treatment. Aims to standardise care, improve access and ensure sustainable delivery of bariatric services. Outlines eligibility criteria, prioritisation, preoperative education, procedures, postoperative care, and emphasises patient-centred care, multidisciplinary team involvement.	Metabolic and Obesity Surgery Society (ANZMOSS) and Collaborative Public Bariatric Surgery Taskforce	*athy as prioritisation criteria for bariatric surgery*
The National Aboriginal and Torres Strait Islander Health Plan 2021-2031 The National Aboriginal and Torres Strait Islander Health Plan 2021–2031 | Australian Government Department of Health, Disability and Ageing	Aims to improve health outcomes for Aboriginal and Torres Strait Islander people by setting the policy direction for health and wellbeing over the next decade. Focuses on 12 key priorities and emphasises prevention-focused, culturally safe, responsive, equitable, and racism-free care. The plan aligns with the National Agreement on Closing the Gap. The plan is centred in culture and embeds self-determination, partnership, and shared decision-making as essential strategies to close the gap in health outcomes.	National (Department of Health, Disability and Ageing).	
NSW Healthy Eating and Active Living Strategy 2022-2032 https://www.health.nsw.gov.au/heal/Pages/nsw-	Overweight & Obesity prevention in NSW Aims to align with the National Preventative Health Strategy 2021-2030 to reduce overweight and obesity in	State NSW Ministry of Health, NSW Government	

healthy-eating-strategy.aspx	children and young people, and halt the rise and reverse the trend of obesity in adults by 2030								
A Healthier Start for Victorians: A consensus statement on obesity prevention https://www.vichealth.vic.gov.au/sites/default/files/Obesity-Consensus-Full-Report.pdf	Obesity prevention in VIC Aims to provide practical recommendations to the Victorian government to address obesity, with a key focus on children and young people.	State Healthy Eating and Active Living Roundtable, VicHealth, VIC Government							
Healthy Heart of Victoria Framework https://www.healthyloddoncampaspe.au/sites/default/files/2023-05/Healthy-Heart-of-Victoria-Framework.pdf	Physical activity promotion in Loddon Campaspe to improve health outcomes Aims to understand current physical activity participation in the Loddon Campaspe region, create environments that encourage physical activity, and engage health and wellbeing brokers to drive systematic change that promote active living.	State Loddon Campaspe Regional Partnership, VIC Government	*Region has higher rate of overweight and obesity but did not specifically target*						
Making Healthy Happen 2032 https://hw.qld.gov.au/making-healthy-happen/	Obesity prevention and intervention in QLD Aims to reduce the number of Queenslanders whose health and wellbeing are impacted by overweight and obesity through promoting environments that encourage healthy living, improving healthcare access to overweight and obesity intervention, and reducing weight-stigma.	State Health and Wellbeing Queensland, QLD Government							

WA Healthy Weight Action Plan 2019-2024 https://www.health.wa.gov.au/~/media/Files/Corporate/general-documents/Health-Networks/WA-Healthy-Weight-Action-Plan/PDF/Healthy-Weight-Action-Plan-2019-2024.pdf	Early intervention of people identified as at-risk of becoming overweight and management of people who currently live with obesity Aims to coordinate action across government and organisations to halt the rise of overweight and obesity in WA; reduce weight stigma; improve access to weight management services; develop a healthcare workforce more equipped for overweight and obesity care; create a culture and environment that encourages and supports continuous quality improvement; encourage innovations; empower actions from community.	State WA Department of Health	
Healthy Tasmania Five-Year Strategic Plan 2022–2026 https://www.health.tas.gov.au/publications/healthy-tasmania-five-year-strategic-plan-2022-2026	Guide preventive health activity across government and communities in TAS. Aims to improve population health outcomes, health equity, promote a healthier environment and greater social connections in TAS communities	State Government of TAS	
SA Aboriginal Health Promotion Strategy 2022-2030 https://www.preventivehealth.sa.gov.au/assets/downloads/AHP0005-AHStrategy-Final-Art.pdf	Strengthening and promotion of the cultural determinants of health and wellbeing in SA's First Nations communities Aims to strengthen and promote cultural determinants of health; inform the development and implementation of culturally appropriate policy and practice, guide culturally-appropriate and respectful interactions between Wellbeing SA and First Nations	State Government of SA	

	communities; identify opportunities for partnership with First Nations communities organisations in a culturally appropriate and respectful way		
Towards Zero Growth: Healthy Weight Action Plan https://www.parliament.act.gov.au/__data/assets/pdf_file/0007/2548033/QON-208-Answer-Att-B-Towards-Zero-Growth-Healthy-Weight-Action-Plan.pdf	Address the rising levels of overweight and obesity in the ACT. Aims to achieve 'zero growth' in obesity rated by increasing physical activity and improving nutrition both within the government and across the ACT through food environment, schools, workplaces, urban planning, social inclusion and evaluation.	Territory Government of ACT	
NT Health Strategic Plan 2023-2028 https://health.nt.gov.au/__data/assets/pdf_file/0015/1206510/nt-health-strategic-plan-2023-2028.pdf	Preventive health and primary healthcare service improvement in NT. Aims to target workforce development; promote wellbeing and prevent illness; provide high quality health care that reflects personal and community needs; improve sustainability of service delivery and support systems.	Territory Government of NT	
Wellbeing SA Strategic Plan 2020-2025 https://www.wellbeingsa.sa.gov.au/assets/images/20090.1-WellbeingSA-StrategicPlan-2020update-WEB.pdf	Primary, secondary and tertiary prevention of diseases in SA Aims to lead system change required to support health and wellbeing and embed prevention across the life course, with key focus on prevention in the early years, mental health, and chronic disease prevention	State Government of SA	

Programs and Services

Name/Title [link]	Description/Purpose	Jurisdiction	Specific to primary population			Relevant to High Priority Populations#			
			Overweight and Obesity	CVD	Youth	CALD	First Nations	Rural, Regional and Remote	Disability	Mental Health
My health for life https://hw.qld.gov.au/initiatives/my-health-for-life/	Foster healthy lifestyle habits among QLD populations to reduce risk of T2D and CVD Involves free health coaching sessions (online/in-person), including goal setting, ongoing support, resources and group-based sessions to support healthy lifestyle habits across Queenslanders of all backgrounds and health status	State Health and Wellbeing Queensland, Queensland Government.								
Get Healthy Service https://www.gethealthynsw.com.au/	Help NSW residents achieve and maintain health goals via lifestyle changes Involves free phone/online health coaching sessions on healthy lifestyle habits, weight management, alcohol reduction, pregnancy weight management; post-cancer treatment physical activity promotion, for people > 16 years	State NSW Government								
Munch & Move https://www.nsw.gov.au/health-and-wellbeing/healthy-living/munch-and-move	Improve physical activity & diet among children attending early childhood education and care services (ECECs) in NSW Aims to provide ECECs in NSW with resources, tools and staff training to encourage early lifestyle habits in ECEC	State NSW Government								

	children, with goals like planning healthy menus, fostering ECEC environment that encourage healthy behaviours and meet national standards for ECECs.	
Deadly Choices https://deadlychoices.com.au/	Preventative health in First Nations communities Aims to encourage First Nations peoples to regularly access local health services, complete annual health checks, make healthier lifestyle choices and cease smoking/vaping.	National Institute for Urban Indigenous Health, QLD
Heart Foundation Walking program https://walking.heartfoundation.org.au/?gad_source=1&gad_campaignid=22735445433&gbraid=0AAAAAqw2-o-k-zIHmhFiRpL68BjL_SMsR&gclid=CjwKCAjwg7PDBhBxEiwAf1CVu-RJgrzQidBBTem9xxSwZMOYp4L6KakEBfisvRJ0p8Gv7Y26T9n2IBoCq4oQAvD_BwE	Reduce CVD risk through encouraging more people to walk Provides free personally-tailored walking plans, and connect participants with local walking communities.	National Australian Government
LiveLighter https://livelighter.com.au/	Public health education to encourage physical activity, healthy eating and prevent excess weight gain in people from WA. Provide resources for communities and health professionals on ways to be active and eat well, via mass media,	State Government of WA

	social media, online tools, printed resources.		
Pick of the Crops https://hw.qld.gov.au/pick-of-the-crop/	Improve fruit/vegetable consumption in school-aged children in QLD Aims to increase opportunities for QLD primary school children to learn about and eat more vegetables and fruit via school-based initiatives	State Health and Wellbeing Queensland, Queensland Government	
Logan Healthy Living https://hw.qld.gov.au/logan-healthy-living/	Chronic disease prevention and management in QLD Aims to deliver lifestyle management program via allied health led services.	State Health and Wellbeing Queensland, Queensland Government	
This Girl Can Victoria https://www.vichealth.vic.gov.au/programs-projects/campaigns-initiatives/this-girl-can-a-vichealth-campaign	Physical promotion in women Aims to provide resources on ways for women in Victoria to be more active, and resources for supporters from the physical activity sector to encourage physical activity in women within their communities.	State VicHealth, VIC Government	
Move Well Eat Well https://www.health.tas.gov.au/move-well-eat-well	Support children's health and wellbeing in primary schools and early childhood services in TAS. Aims to provide guidance, resources and opportunities for schools and services to promote physical activity and healthy diet in Tasmania.	State TAS Government	
Live Well Tasmania https://lwt.org.au/	Empower individual health and wellbeing, community capacity, resilience and sustainability.	Non-government	

	Aims to conduct research, provide evidence-based programs, projects, workshops and events in relation to its aims, with emphasis on youth living in poverty, and environmental sustainability of healthy living	Live Well Tasmania
Healthy Living NT https://www.healthylivingnt.org.au/about-us/healthy-living-nt	Support people diagnosed with diabetes, CVD and related chronic conditions in NT Aims to advocate on behalf of people with diabetes, CVD and related chronic on policy development and service provision.	Non-government Diabetes Association of the NT
Wellness my Way https://hw.qld.gov.au/wellnessmyway/	Chronic disease prevention and early intervention Provides free digital health assessment, followed by telephone consultation to develop health action plan aimed at improving healthy lifestyle behaviours, along with connecting the consumer with free/low-cost programs suited to their needs.	State Health and Wellbeing Queensland; South West Hospital and Health

Supportive Infrastructure – Societies, Organisations and Hubs

Name/Title [link]	Description/Purpose	Specific to primary population		Relevant to High Priority Populations#					
		Healthcare Stakeholders	Lived Experience	Youth	CALD	First Nations	Rural, Regional and Remote	Disability	Mental Health

The Obesity Collective https://theobesitycollective.org.au/	Reduce the health and wellbeing impacts of obesity in Australia, especially around weight stigma. Aims to raise awareness for obesity, reduce weight stigma, promote evidence-based prevention and treatment	
Food for Health Alliance https://www.foodforhealthalliance.org.au/	Advocate for policy to improve food environment and prevent overweight and obesity in Australia Aims to advocate for laws and policies that improve food labelling, protect children from food marketing, pricing measure that support healthier diets, and improve healthfulness of infant/toddler foods	
National Association of Clinical Obesity Services (NACOs) https://nacos.org.au/	Improve the quality of care for people with overweight or obesity. Aims to promote high-quality care according to National Framework for Clinical Obesity Services; reduce weight stigma; engage stakeholders; raise awareness; enhance equitable access to specialist/surgical obesity services in poorly resourced areas; improve quality of obesity care by implementing and evaluating new evidence-based policies and practices in Australia's health system.	*Primarily for health service providers; but does have a 'find a service' feature*
Pharmaceutical Society of Australia	Improve access to safe, quality and effective healthcare through optimising	

https://www.psa.org.au/	the role of pharmacists in the Australian healthcare system. Aims to provide resources, professional development and network for pharmacists,
Australian Cardiovascular Alliance https://ozheart.org/	Aims to improve prevention, treatment and recovery outcomes of CVD through advocacy, driving strategic initiatives in research, advocacy, community engagement and capacity building to improve CVD outcomes in Australia.
Australian and New Zealand Obesity Society (ANZOS) https://www.anzos.com/	Aims to advance research, treatment, and public health initiatives related to obesity prevention and management, while promoting a holistic approach and addressing weight stigma
Australian and New Zealand Paediatric Obesity Network (ANZPON) https://www.anzos.com/about-us-anzpon	Aims to provide professional support and a collaborative space for individuals working in the area of childhood obesity across Australia and New Zealand. It aims to facilitate communication, share topics of interest, and address questions in a supportive environment.
Weight Issue Network https://weightissuesnetwork.org/	Represent and advocate people living with overweight or obesity Aims to reduce weight stigma, promote person-centred care, raise awareness, provide evidence-based education on obesity and facilitate community for people with overweight or obesity to share experiences.

Public Health Association of Australia https://www.phaa.net.au/	Reduce burden of disease in Australia through prevention. Aims to draft and shape public health policies through campaigns to improve health and wellbeing across Australia, with emphasis on chronic disease prevention, children, First Nations peoples, and sustainability.					
Australian & New Zealand Metabolic and Obesity Surgery Society (ANZMOSS) https://anzmoss.com.au/	Aims to advance diagnosis and treatment of obesity with specific emphasis on surgical interventions. Promotes research in treatment for overweight and obesity, provides guidelines on practice and trainings surrounding surgical interventions for obesity.		*Primarily for health service providers; but does have a 'find a service' feature*			
Weight Education and Lifestyle Leadership (WELL) Collaborative https://thewellcollaborative.org.au/about/	Bring together practitioners, consumers, and community members in Western Australia to change the way overweight and obesity are discussed and addressed. It serves as a central hub for resources and education, fostering dialogue between healthcare practitioners, consumers, and the community.					
Australian Health InfoNet Cardiovascular Health Portal https://healthinfonet.ecu.edu.au/learn/health-topics/cardiovascular-health/	Provides information on CVD and its impact on Aboriginal and Torres Strait Islander communities, highlighting risk factors, health challenges, and proposed actions for improvement. Provides information and resources for health workers, policy makers and					

	anyone working in Aboriginal and Torres Strait Islander Health				
Every.Body.Equity https://www.everybodyequity.com/	Advocates for improved access to bariatric surgery within the Australian public health system. Aim is to ensure that every person has access to necessary medical treatment for obesity, reducing stigma and improving equity in healthcare.				
RACGP Specific Interest Group for Obesity / RACGP Specific Interest Group for Cardiology https://www.racgp.org.au/the-racgp/faculties/specific-interests	For RACGP members with specific interests in obesity or cardiology. Provides the opportunity to share information and knowledge by regular contact.				

# Indicates that the document mentions this high-priority population.

4.2.2 Primary care models and guidelines

In 2022, The Australian Obesity Management Algorithm was published to provide a practical tool for primary care physicians to manage obesity in non-pregnant adults.[281] The document provides guiding principles on the benefits of weight loss, the role of primary care, addressing weight bias and adopting a person-centred approach as well as treatment options aligned to a management algorithm.[281] Regarding implementation, primary care physicians are encouraged to regularly monitor weight and complications, use chronic disease management systems for follow-up and develop referral networks for specialist care.[281] However, the integration of care for those with CVD is not detailed. In primary care, general practitioners manage CV risk factors and refer to CVD specialists as needed. Notably, the Medicare Benefits Schedule (MBS) does not currently include items that are explicitly designated for obesity management in general practice and therefore GPs cannot bill Medicare for services only focused on obesity treatment unless it is part of a broader chronic condition (i.e., through GP Chronic Condition Management Plans). These plans include items for preparation and reviews and up to five allied health services per year (such as dietetics or exercise physiology).

4.2.3 Specialist services and integrated care

Specialist obesity and metabolic clinics are based in tertiary hospitals or private settings (e.g., Royal Prince Alfred Hospital, NSW). These services provide multidisciplinary care including endocrinologists, bariatric surgeons, psychologists and dietitians. Rarely are exercise physiologists integrated. Complex CVD is often managed within specialist cardiology services within hospitals. Most tertiary care settings host cardiac rehabilitation which includes education on diet and exercise.

4.2.4 Economic implications

In 2022-2023 spending on CVD in Australia was $16.2 billion, making it the second highest spending category after cancer.[282] According to the World Obesity Atlas (2023), the projected impact of overweight (including obesity) for 2025 is US$12,917 million for healthcare impact and estimated US$1,631 billion (2.2%) of GDP.[283] This is anticipated to increase to US$15,249 million for healthcare impact and estimated US$1,873 billion (2.3%) of GDP by 2030 and US$17,914 million for healthcare impact and estimated US$2,170 billion (2.5%) of GDP by 2035; which is classified as ‘very high’.[283] A recent forecast estimated that by 2029, 1,061,756 Australians will be living with CVD with the total healthcare costs of CVD projected to exceed AUD $61.89 billion and chronic costs accounting for 75% of this amount.[284] Indirect costs from lost productivity was estimated at $78.75 billion.[284] It was estimated that a 10% decrease in CV risk within the primary prevention population would result in a 4% reduction in healthcare costs and 5% reduction in productivity losses.[284] There are no available data of the economic impact of addressing obesity on the costs of CVD in Australia.

4.2.5 Weight stigma

Weight stigma involves the negative attitudes, stereotypes and discrimination against individuals living with excess body weight.[285] Weight stigma is associated with adverse mental and physical health outcomes, social inequities,[286] increased risk of CVD,[287] and premature mortality beyond risk posed by elevated BMI.[288] Weight bias internalisation contributed to heightened cardiometabolic risk, particularly through elevated triglycerides.[287] According to a multi-national survey of adults who engaged with WW

International (formerly Weight Watchers), in Australia 56% of respondents (n=698) experienced weight stigma, 50.5% had been teased about weight, 38% reported being treated unfairly because of their weight and 31% reported discrimination because of their weight.[289] The onset of weight stigma was largely in childhood (≤10 years) and adolescents (11-19 years).[289]

Weight stigma reduction in clinical settings

In their expert consensus statement on medical weight management for the optimisation of cardiovascular health, the American College of Cardiology emphasise the importance of the clinical setting for the patient experience.[140] Clinicians are encouraged to use person-first language and validate the lifelong journey that patients face with obesity as a chronic disease.[140] Clinical spaces should be designed to accommodate people with larger bodies such as providing armless chairs or wide chairs with arms, having high-capacity exam tables and scales as well as large size patient gowns and medical equipment.[140] It is also encouraged to focus on health outcomes rather than weight alone and to address psychosocial health, quality of life and functional status as part of holistic management.[77]

Weight stigma reduction in physical activity and dietetic settings

A recent call for action by Alberga, Nagpal and Patton highlighted that weight stigma challenges occur in physical activity settings,[285] which can extend to all healthcare settings. Those with higher weight face inequitable access and opportunities in exercise settings. The authors proposed several recommendations including: i) to incorporate lived experience perspectives in the development of physical activity interventions and guidelines; ii) to adopt person-centred goals, shifting from weight loss to overall health and wellbeing; iii) apply upstream strategies including mandatory training on weight stigma for exercise professionals and facility owners, modifying exercise environments to accommodate individuals of all body sizes (including equipment and clothing) and depicting positive imagery of people with higher body weights engaging in physical activity in media and promotional materials.[285] Similarly, dietetic education often emphasises weight-centric approaches which can perpetuate weight stigma, and nutrition and dietetic education, polices and professional standards should align with weight-inclusive principles to ensure equitable care.[290]

4.2.6 Equity considerations

As identified in section 1.1 and reviewed in section 3.6, there are several underserved priority groups who have higher rates of obesity and CVD and face greater barriers to care. As addressed above, weight stigma in healthcare settings also may discourage people with obesity and CVD to seek help. The National Obesity Strategy (2022-2032) emphasises equity and culturally safe care and stigma awareness, which is being further led by groups like The Obesity Collective and the Weight Issues Network (see **Table 4.2.1**) to shift attitudes and change the quality of care for people living with larger bodies. Regarding the currently available polices and services, mental health is rarely addressed which highlights a gap for implementation given the associations between mental health, obesity, CVD and stigma.

4.2.7 System-level enablers and barriers in Australia – a snapshot

Barriers

Workforce capacity and infrastructure

- Siloed and fragmented care for those living with multi-morbidities (e.g., obesity alongside CVD, MAFLD, CKD). Poor continuation of care due to lack of referral pathways between primary, secondary, tertiary and community care.[291]
- Long wait lists for specialist obesity services.[291]
- Lack of integration of diet and (more so) exercise physiology within tertiary care (e.g.,[292]) results in insufficient specialist staff with many services relying on generalists.
- Workforce maldistribution, notably those in rural and remote regions facing shortages of specialist care and limit access to multidisciplinary teams.

Funding models

- Low investment in preventative health. Just 0.1% of the federal health budget was allocated to obesity prevention in Australia between 2013 and 2022.[293]
- High out-of-pocket costs for people seeking specialist obesity services and medications which limits access especially in low socioeconomic status regions.[291]
- No specific Medicare item for obesity treatment in isolation in general practice.

Enablers

Workforce capacity and infrastructure

- Digital health including telehealth and remote monitoring can extend workforce reach in underserved areas.
- Community-based care: The American Heart Association emphasises the importance of implementing evidence-based behavioural interventions for CVD prevention into community settings to improve population health and advance equity.[206] Community settings such as faith-based, schools, workplaces and social service settings have strong potential for reaching populations often excluded by healthcare systems.[206] The statement highlights community leadership and by-in as critical enablers of successful interventions.[206]
- State and local government and NGO-led programs (e.g., 'Wellness my Way' from Health and Wellbeing Queensland, see Table 4.2.1) are helping to fill service gaps especially in prevention; although awareness of, and referral to, these services are not well evaluated.

Funding models

- Investment in obesity prevention can reduce long-term health costs.[293]

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6. Appendices

6.1 Search Strategy

Research Question/s	Search Strategy (e.g. for Pubmed)	PICO/PCC
1. What is the association between overweight or obesity and the risk of experiencing a cardiovascular event (primary or secondary) in adults? 2. What is the impact of overweight or obesity on the diagnosis, clinical management and outcomes for people living with CVD? 3. In adults living with overweight or obesity, how do structured weight management interventions – compared to standard care or no intervention – impact cardiovascular outcomes?	**SEARCH 1** “Overweight”[MeSH] OR “Body composition”[MeSH] OR “body weight”[MeSH] OR “Body Mass Index”[MeSH] OR Obesity[tiab] OR Obese[tiab] OR corpulence[tiab] OR overweight[tiab] OR adiposity[tiab] OR “body composition”[tiab] OR adipose[tiab] OR “body weight”[tiab] OR “body mass index”[tiab] OR BMI[tiab] **AND** "cardiovascular diseases"[MeSH] OR "Heart disease risk factors"[MeSH] OR CVD[tiab] OR "hypertension"[tiab] OR “blood pressure”[tiab] OR "stroke"[tiab] OR "peripheral arterial disease"[tiab] OR cardiovascular*[tiab] OR cardia*[tiab] OR coronary[tiab] OR angina*[tiab] OR ventric*[tiab] OR myocard*[tiab] OR pericard*[tiab] OR isch?em*[tiab] OR emboli*[tiab] OR arrhythmi*[tiab] OR thrombo*[tiab] OR "atrial fibrillat*"[tiab] OR tachycardi*[tiab] OR endocardi*[tiab] OR "risk factor*"[tiab] **AND** ("systematic reviews as topic"[MeSH Terms]) OR (systematic review* [ti] or meta-analysis [ti] or metaanalysis [ti] or systematic literature review [ti] OR systematic scoping review [ti] OR systematic narrative review [ti] OR systematic qualitative review [ti] OR systematic evidence review [ti] OR systematic quantitative review [ti] OR systematic meta-review [ti] OR systematic critical review [ti] OR systematic mixed studies review [ti] OR systematic mapping review [ti] OR systematic cochrane review [ti] OR systematic search and review [ti] OR systematic integrative review [ti] or systematic review [pt])	P: people with overweight and/or obesity O: CV risk or CV event - P: people with overweight and/or obesity O: CV diagnosis or management or cardiometabolic outcomes *Clinic Scope: Coronary artery disease, heart failure, arrythmias, stroke, peripheral arterial disease, hypertension, cholesterol* - P: people with overweight and/or obesity I: weight management interventions C: standard care/no intervention O: CV risk or CV event

4.	In adults living with overweight or obesity and CVD, which pharmacological therapies are effective in achieving weight loss and improving cardiovascular outcomes (and cardiovascular risk factors)?	**Search 1 AND** "Anti-obesity agents"[MeSH] OR "drug therapy"[MeSH] OR orlistat[MeSH] OR phentermine[MeSH] OR liraglutide[MeSH] OR "Anti-obesity agents"[tiab] OR "anti-obesity drug*"[tiab] OR "appetite depressant*"[tiab] OR medication*[tiab] OR pharmacotherapy[tiab] OR "drug therapy"[tiab] OR "drug treatment*"[tiab] OR pharmacological[tiab] OR orlistat[tiab] OR phentermine[tiab] OR naltrexone–bupropion[tiab] OR liraglutide[tiab] OR semaglutide[tiab] OR tirzepatide[tiab] OR topiramate[tiab] OR "off-label prescribing"[tiab]"	P: in people with overweight/obesity with or at risk of CVD I: Pharmacological therapies: *Clinic Scope: Consider medicines available in Australia (orlistat, naltrexone/bupropion, phentermine/topiramate, liraglutide, tirzepatide and semaglutide), novel medicines in Phase 3 clinical trials, off-label prescribing* C: standard care or no intervention O: CV outcomes & CV risk outcomes
5.	What is the impact of bariatric surgery (focusing on the common techniques in Australia: gastric bypass, gastric sleeve, lap band or gastric banding) on cardiovascular morbidity and mortality and long-term or sustained improvements in complications of obesity?	**Search 1 AND** "Bariatric surgery"[MeSH] OR "gastrectomy"[MeSH] OR "Bariatric surgery"[tiab] OR "bariatric operation*"[tiab] OR "gastric bypass"[tiab] OR gastroplasty[tiab] OR "jejunoileal bypass"[tiab] OR Lipectomy[tiab] OR "gastric sleeve"[tiab] OR "gastric banding"[tiab] OR "Weight loss surgery"[tiab] OR gastrectomy[tiab]	P: in people with overweight/obesity with or at risk of CVD I: Bariatric/metabolic surgery C: Non-surgical intervention O: CV morbidity and mortality; CV risk including obesity

6.	In adults living with overweight or obesity and CVD, which nutritional interventions are most effective in supporting weight loss and improving CV outcomes.	**Search 1 AND** "healthy lifestyle"[MeSH] OR "recommended dietary allowances"[MeSH] OR "diet therapy"[MeSH] OR "nutrition therapy"[MeSH] OR "exercise"[MeSH] OR "exercise therapy"[MeSH] OR "Physical exertion"[MeSH] OR "fasting"[MeSH] OR "Dietary patterns"[MeSH] OR "body weight maintenance"[MeSH] OR "healthy lifestyle"[tiab] OR "recommended dietary allowance*"[tiab] OR "healthy eating"[tiab] OR diet[tiab] OR Diets[tiab] OR dietary[tiab] OR nutrition[tiab] OR exercise[tiab] OR "Physical exertion"[tiab] OR "physical activit*"[tiab] OR "dietary patterns"[tiab] OR "intermittent fasting"[tiab] OR "time restricted eating"[tiab] OR "eating patterns"[tiab] OR walking[tiab] OR “high intensity interval training”[tiab] OR "energy intake"[tiab] OR "calor* restriction*"[tiab] OR "dietary pattern*"[tiab]	P: in people with overweight/obesity with or at risk of CVD I: Diet/Nutrition or Exercise C: Non-diet or non-exercise intervention or standard care control O: CV morbidity and mortality; CV risk including obesity *Clinic Scope: Consider dietary patterns, energy intake goals, intermittent fasting.*
7.	In adults living with overweight or obesity and CVD, which physical activity types (type, time and intensity) are most effective in supporting weight loss and improving CV outcomes?		

6.2 Systematic review and meta-analyses for the impact of overweight and obesity on the risk of CVD

Table 6.2 Systematic review and meta-analyses for the impact of overweight and obesity on the risk of CVD

CVD and CVD Risk Factors								
Study	**n studies/ participants**	**Population**	**Databases Searched & Year/Range/ Countries**	**Study Designs**	**Obesity Measure**	**Effect Estimate**	**Results ES (95%CI), heterogeneity**	**Quality & Key points**
Kibret *et al.* 2024	N=17 studies, 370,689 participants.	Focus: Life-course BMI trajectories from childhood to adulthood and their association with cardiovascular disease (CVD) risks and outcomes. Age range: Childhood (5–18 years) to adulthood (over 19).	MEDLINE, EMBASE, Scopus, CINAHL, Cochrane Library, Web of Science, and Global Health. From inception to September 2022, updated in September 2023.	Prospective and retrospective cohort studies.	BMI	RR	<u>Persistently overweight trajectory</u> Hypertension: RR 2.49 (95% CI: 1.9, 3.28). I2 = 69.5%, p = 0.0001 Type 2 diabetes: RR 4.62 (95% CI: 2.36, 9.04). <u>Normal-to-overweight trajectory</u> Hypertension: RR 2.38 (95% CI: 1.70, 3.33). I2 = 90.8%, p = 0.0001 Type 2 diabetes: RR 3.66 (95% CI: 2.57, 5.19).	Findings were generally robust in sensitivity analyses restricted to objectively measured BMI, the follow-up of ≥20 years, or to good quality studies. Lifetime BMI trajectories influence health outcomes. Persistently overweight and normal-to-overweight trajectories are associated with higher risks of hypertension and type 2 diabetes. Preventive strategies should be implemented at all life stages to reduce CVD risks and adverse outcomes later in life
Re *et al.* 2023	N=30 studies. Participants: Varied between	South Asian populations, primarily from India (83.3%), Bangladesh	MEDLINE and Embase, between 1990–2023	Prospective cohort, case-control, and	BMI, WC, WHR, WHtR, HC	OR	<u>Blood Pressure:</u> SBP per 5 kg/m² higher BMI: Mean difference 3 mmHg (95% CI 1.30–4.50).	Mean score of 6.5/9 for cohort studies, 5.2/9 for case-control studies, and

	140 and 59,037 across studies.	(10%), Mauritius, and Pakistan	Countries: Afghanistan, Bangladesh, Bhutan, India, Maldives, Nepal, Pakistan, and Sri Lanka.	cross-sectional studies			SBP per 13 cm larger WC: Mean difference 6 mmHg (95% CI 4.81–7.81). WHR associations were not statistically significant. <u>Hypertension (HTN):</u> OR per 5 kg/m² higher BMI: 1.33 (95% CI 1.18–1.51). OR per 13 cm larger WC: 1.45 (95% CI 1.05–1.98). OR per 0.1-unit larger WHR: 1.22 (95% CI 1.04–1.41). <u>Cardiovascular Disease (CVD):</u> Overweight vs normal BMI: OR 1.65 (95% CI 1.55–1.75). Large vs normal WC: OR 1.48 (95% CI 1.21–1.80). Large vs normal WHR: OR 2.51 (95% CI 0.94–6.69).	7/10 for cross-sectional studies. Limitations: Reverse causality, publication bias, lack of adjustment for confounders like physical activity and diet. Key Points: BMI and WC are strongly associated with CVD and HTN risk in South Asians. WC showed stronger associations with blood pressure and HTN than BMI. WHR was weaker in predicting CVD and HTN compared to BMI and WC. Ethnic-specific mechanisms and fat distribution differences may explain variations in CVD risk.
Zhang *et al.* 2023	17 studies included. Mean sample size: 486,419 participants (range: 2,692 to 7,148,763)	Included studies that investigated the association between transitions of metabolic health and adiposity phenotype (MH-NW, MU-NW, MH-O, MU-O) to another phenotype with the risks of: (1) incident type 2 diabetes,	Databases: MEDLINE and EMBASE. Search conducted through August 2022. Countries: China, South Korea, Japan,	Prospective cohort studies	BMI Overweight/obesity defined as: BMI ≥24 kg/m² in five studies. BMI ≥30 kg/m² in two studies.	HR, OR, RR	<u>Type 2 Diabetes Mellitus (T2DM)</u> Transition from metabolically healthy normal weight (MH-NW) to metabolically unhealthy normal weight (MU-NW): HR 2.87 (95% CI 2.43–3.38), I^2 = 49.2%. Transition from metabolically healthy obesity (MH-O) to metabolically unhealthy obesity (MU-O):	12 studies rated as high quality (Newcastle–Ottawa Scale score: 7–8). 5 studies rated as moderate quality (score: 4–6). Key Points: Transitions in metabolic health and adiposity status significantly alter risks of

(2) incident events of composite cardiovascular disease outcomes and (3) all-cause mortality. Individuals of stable/persistent phenotype were considered the referent group in all comparisons. Majority of studies conducted in Asia (China, South Korea, Japan, Iran). Two studies in the United States and two in Europe. Mean age ranged from 42.8 to 61.1 years.	Iran, United States, Europe.	BMI ≥25 kg/m² in remaining studies.	HR 2.68 (95% CI 2.07–3.47), I^2 = 72.0%. Transition from metabolically unhealthy normal weight (MU-NW) to metabolically healthy normal weight (MH-NW): HR 0.40 (95% CI 0.29–0.55), I^2 = 36.1%. Transition from metabolically unhealthy obesity (MU-O) to metabolically healthy obesity (MH-O): HR 0.34 (95% CI 0.18–0.64), I^2 = 78.0%. Transition from metabolically healthy normal weight (MH-NW) to metabolically unhealthy obesity (MU-O): HR 4.76 (95% CI 3.12–7.26), I^2 = 57.6%. <u>Cardiovascular Diseases:</u> Transition from metabolically healthy normal weight (MH-NW) to metabolically unhealthy normal weight (MU-NW): HR 1.40 (95% CI 1.31–1.49), I^2 = 68.8%. Transition from metabolically healthy obesity (MH-O) to metabolically unhealthy obesity (MU-O): HR 1.46 (95% CI 1.32–1.62), I^2 = 79.9%. Transition from metabolically unhealthy normal weight (MU-NW) to metabolically healthy normal weight (MH-NW): HR 0.71 (95% CI 0.63–0.80), I^2 = 67.9%.	type 2 diabetes and cardiovascular diseases. Change in metabolic health has a stronger impact on risks than change in BMI category. Obesity treatment should prioritise improving metabolic health parameters over focusing solely on weight loss.

							Transition from metabolically unhealthy obesity (MU-O) to metabolically healthy obesity (MH-O): HR 0.87 (95% CI 0.74–1.02), I^2 = 61.3%. Transition from metabolically healthy normal weight (MH-NW) to metabolically unhealthy obesity (MU-O): HR 1.44 (95% CI 1.18–1.74), I^2 = 78.9%.	
Mohammadian *et al.* 2022	N=25 studies, total participants: 177,792.	General population (mostly adults). All studies had to represent the target population and compare them with the normal-weight non-obese (NWNOs).	Scopus, Web of Science, EMBASE, PubMed. Search conducted until October 2021. Majority of studies conducted in China (5 studies) and Korea (4 studies). Other countries: United States, Sweden, Colombia, West Indies, India, Iran, Japan, Iceland, Malaysia, Switzerland, Brazil, and Finland Age range: 13 to 75 years	Observational (case-controlled and cohort studies)	BMI, WC, WHR, WHtR, body fat mass. Normal Weight Obesity (NWO): Defined as normal BMI (18.5–24.9 kg/m²) with high body fat %	OR, SMD	Sex stratified relationship between NWO and cardiometabolic risk factors: Hyperglycaemia OR: 1.50 (95% CI: 1.23, 1.76). High Triglycerides OR: 1.90 (95% CI: 1.44, 2.35). Low HDL OR: 1.28 (95% CI: 1.06, 1.49). Diabetes OR: 1.39 (95% CI: 1.30, 1.49). Dyslipidaemia OR: 1.83 (95% CI: 1.61, 2.04). Hypertension OR: 1.40 (95% CI: 1.28, 1.51). Metabolic Syndrome OR: 1.92 (95% CI: 1.58, 2.26)	Newcastle-Ottawa Scale used; scores ranged from satisfactory to good quality (5–9) Key points: NWO increases odds of cardiometabolic risk factors (CMRFs). BMI is inadequate for assessing obesity risk; body fat percentage is essential. Preventive measures for NWO are critical to avoid future obesity-related comorbidities.
Rakhmat *et al.* 2021	N=24 cross-sectional studies, total of 75,201 subjects.	Adults aged ≥18 years old with normal weight obesity (NWO) compared to adults with normal weight lean	PubMed, ProQuest, EBSCO Host, Europe PMC.	Observational studies (cross-sectional)	BMI Normal BMI defined using WHO criteria	OR	Metabolic Syndrome OR = 2.24 [1.74, 2.89]; p < .001; I^2 = 76%, P heterogeneity < 0.001. Hypertension	NOS scoring used Key points:

		(NWL). NWO is defined as normal BMI with high body fat percentage. NWL is defined as normal BMI with normal or low body fat percentage.	Inception until September 21, 2021. Studies included diverse regions, with the highest prevalence of NWO in South Asia		(Asia Pacific: 18.5–22.9 kg/m²; Caucasian: 18.5–24.9 kg/m²; China: 18.5–23.9 kg/m²; Thailand: male <27 kg/m², female <25 kg/m²). High body fat percentage (cut-off points varied across studies).		OR = 1.60 [1.36, 1.89]; p < .001; I² = 76%, P heterogeneity < 0.001. <u>Diabetes</u> OR = 1.72 [1.54, 1.92]; p < .001; I² = 47%, P heterogeneity < 0.001. <u>Dyslipidaemia</u> OR = 1.50 [1.03, 2.18]; p = .03; I² = 94%, P heterogeneity < 0.001.	NWO is significantly associated with cardiometabolic risk factors. Traditional BMI criteria should be challenged as it may mask risks in NWO individuals. Further prospective cohort studies are needed to better understand NWO.
Xue *et al.* 2021	N=31 prospective cohort studies, total 669,560 participants and 25,214 cases.	General population aged 18 years or older. Studies included men, women, and both sexes, with mean ages ranging from 34 to 75 years.	PubMed, Embase, and Web of Science. Up to September 28, 2019. Studies from Europe, USA, Asia, and Australia.	Prospective cohort studies with follow-up durations of more than 3 years.	WC, WHR, WHtR	RR	<u>WC</u> RR = 1.43 (95% CI: 1.30, 1.56), heterogeneity I² = 58.6%. Risk of CVD increased by 4.0% per 10 cm increase in men and 3.4% in women. <u>WHR</u> RR = 1.43 (95% CI: 1.33, 1.54), heterogeneity I² = 30.6%. Risk of CVD increased by 4.0% per 0.1 unit increase in men and 3.5% in women. <u>WHtR</u> RR = 1.57 (95% CI: 1.37, 1.79), heterogeneity I² = 37.6%	NOS used Abdominal obesity (WC, WHR, WHtR) is significantly associated with increased CVD risk. WHtR is considered the best predictor among the three measures. Recommended cut-off points: WC < 90 cm and WHR < 0.9 for men; WC < 80 cm and WHR < 0.85 for women; WHtR < 0.5 for both sexes.

							Risk of CVD increased by 8.6% per 0.1 unit increase in men and 6.0% in women.	"Keep your waist circumference to less than half your height" is a simple public health message for CVD prevention.
Opio *et al.* 2020	N= 23 prospective cohort studies, 4,492,723 participants	Adult men and women aged 18 years and older Excluded individuals with pre-existing cardiovascular disease (CVD), diabetes mellitus, cancer, or chronic kidney disease Included outcomes consisting of fatal and nonfatal cardiovascular events and all-cause mortality. Fatal and nonfatal CV events were defined as death due to CVD or one of the following: myocardial infarction, acute coronary syndrome, angina, coronary revascularization, coronary artery bypass surgery, congestive heart failure, stroke and transient ischaemic attack.	Medline, EMBASE, SCOPUS, Cochrane Library From inception up to 31st October 2019	Prospective cohort studies	BMI Body Mass Index (BMI) categories Normal weight: BMI = 18.5–24.9 kg/m² Overweight: BMI = 25–29.9 kg/m² Obese: BMI ≥ 30 kg/m² Exposure groups stratified according to metabolic health status and weight classification as follows: metabolically healthy normal weight (MHNW),	RR	<u>Cardiovascular disease risk</u> There was an increased risk of CVD in the group with MHOW compared with the group with MHNW: RR = 1.34 (95% CI: 1.23–1.46, n = 20, I^2 = 90.3%) There was a significantly increased risk of all-cause mortality (RR = 1.22, CI: 1.02–1.46, n = 5, I2 = 48.8%) and CVD mortality (RR = 1.34, CI: 1.12–1.61 n = 4, I2 = 0.0%) in the group with MHOW compared with the group with MHNW There was an increased risk of CVD in the group with MHO compared with the group with MHNW RR = 1.58 (95% CI: 1.34–1.85, n = 21, I^2 = 92.2%) There was a significantly increased risk of all-cause mortality (RR = 1.59, CI: 1.02–2.47, n = 6, I2 = 86.2%) but not of cardiovascular mortality (RR = 2.22, CI: 0.96–5.11, n = 4, I2 = 81.9) in the group with MHO compared with the group with MHNW	Key Points: Cardiovascular disease risk is increased in metabolically healthy overweight and obesity groups, even in the absence of metabolic risk factors. The risk was consistent regardless of the number of risk factors used to define metabolic health

					metabolically healthy overweight (MHOW), metabolically healthy obese (MHO), metabolically unhealthy normal weight (MUNW), metabolically unhealthy overweight (MUOW) and metabolically unhealthy obesity (MUO)			
Mirzababaei *at al.* 2019	N=21 studies , 778,401 participants	General population aged over 18 years Studies conducted in Asia, America, Europe, and Australia	PubMed and Scopus, Up to May 29, 2018 Countries: Asian, American, European, and Australian populations	Prospective cohort studies	BMI based on WHO criteria: Normal weight (NW): 18.5–24.9 kg/m² Overweight (OW): 25–29.9 kg/m² Obese (OB): ≥30.0 kg/m² Body fat percentage (BF%), WC	RR	<u>MUHNW phenotype</u> CVDs: RR = 1.86 (95% CI: 1.58–2.18), I^2 = 63.3% MI: RR = 1.44 (95% CI: 1.22–1.70), I^2 = 31.6% HF: RR = 2.11 (95% CI: 1.18–3.77), I^2 = 0% <u>MUHOW phenotype:</u> CVDs: RR = 2.04 (95% CI: 1.73–2.41), I^2 = 76.3% MI: RR = 1.69 (95% CI: 1.53–1.88), I^2 = 0% HF: RR = 1.88 (95% CI: 1.00–3.51), I^2 = 85%	NOS used Key Points: Metabolically unhealthy phenotypes (MUHNW, MUHOW, MUHO) are strongly associated with increased risk of CVDs, MI, and HF. Metabolically healthy overweight/obese (MHOW/MHO) phenotypes are associated with increased risk of CVDs but not MI or HF. Screening for obesity and metabolic abnormalities is

								essential for preventive measures.
							MUHO phenotype: CVDs: RR = 2.16 (95% CI: 1.87–2.50), I^2 = 66.3% MI: RR = 1.82 (95% CI: 1.50–2.22), I^2 = 66.5% HF: RR = 1.78 (95% CI: 1.45–2.18), I^2 = 0% MHOW phenotype: CVDs: RR = 1.20 (95% CI: 1.12–1.27), I^2 = 14% MI: RR = 1.19 (95% CI: 0.96–1.48), I^2 = 50.3% HF: RR = 1.10 (95% CI: 0.60–2.00), I^2 = 0% MHO phenotype: CVDs: RR = 1.46 (95% CI: 1.27–1.67), I^2 = 42.6% MI: RR = 1.26 (95% CI: 0.87–1.82), I^2 = 67% HF: RR = 0.96 (95% CI: 0.25–3.77), I^2 = 77%	
Yeh *et al.* 2019	N=43 cohort studies. Participants: 4,822,205 individuals	Adults aged 18 years or older. Median age: 49.9 years (range: 30.3–74.0 years).	PubMed/Medline, EMBASE, CINAHL, Cochrane database. From inception to May 2019.	Cohort studies	BMI, WC, Body Fat Metabolic health defined by insulin resistance,	OR	Compared to individuals with a metabolically healthy normal weight, individuals with MHO had higher adjusted risk of CVD and all-cause mortality. CVD Risk:	Mean Newcastle-Ottawa Scale score: 7.9 ± 1.0 (out of 9). Key Points: Metabolically healthy obesity (MHO) is associated with

		Median proportion of women: 52%. Median smoking rate: 20%. Median follow-up duration: 10.6 years (range: 1.0–30.0 years).	Countries: Most studies conducted in the United States or Europe.		metabolic syndrome, or metabolic disease diagnosed by blood glucose, blood pressure, or lipid profiles.		OR = 1.52 (95% CI: 1.38–1.66), I^2 = 61%. All-Cause Mortality: OR = 1.23 (95% CI: 1.05–1.43), I^2 = 62%. Subgroup analysis showed significant heterogeneity based on definitions of metabolic health and obesity.	increased risk of CVD and all-cause mortality. BMI, sex, age, and smoking habits influence the risk. Long-term weight loss is recommended for individuals with obesity.
Ortega *et al.* 2018	Aim 1: 67 cross-sectional studies (N = varied, up to 342,442 participants). Aim 2: 11 longitudinal studies (N = varied, up to 65,175 participants)	Adults and adolescents from various countries, including Europe, the United States, Korea, and others. Age range: 11.8–72 years.	PubMed and Web of Science. From inception to March 21, 2018. Countries: Studies from multiple countries, including the United States, European nations, Korea, and others	Aim 1: Cross-sectional studies. Aim 2: Longitudinal cohort studies with follow-up durations ranging from 8 to 14 years.	BMI (BMI ≥ 30 kg/m²). Metabolically Healthy Obesity (MHO) defined as having 0 metabolic syndrome (MetS) criteria (waist circumference excluded). Metabolically Unhealthy Obesity (MUO) defined as meeting ≥1 MetS criteria.	SMD, HR	Aim 1: PA: SMD = 0.267 (95% CI: 0.090, 0.444), I^2 = 48.3%. SB: SMD = -0.199 (95% CI: -0.317, -0.081), I^2 = 44.6%. CRF: SMD = 0.317 (95% CI: 0.232, 0.402), I^2 = 49.1%. MST: SMD = -0.049 (95% CI: -0.241, 0.143), I^2 = 0%. Aim 2: All-cause mortality: HR = 1.32 (95% CI: 0.833, 2.108), I^2 = 73.0%. CVD mortality/morbidity: HR = 1.24 (95% CI: 1.071, 1.444), I^2 = 0%. ria.	80% of cross-sectional studies and 100% of longitudinal studies were rated as high-quality (low risk of bias). Tools used: Joanna Briggs Institute checklist (cross-sectional) and Newcastle Ottawa Scale (longitudinal) Key points: MHO individuals are more active, spend less time in sedentary behaviours, and have higher cardiorespiratory fitness compared to MUO individuals. MHO individuals have a 24–33% higher risk of all-cause mortality and CVD mortality/morbidity compared to MHNW individuals, but this risk is

								borderline significant/non-significant. CRF plays a critical role in explaining the differences in prognosis between M**H**O and MHNW.
Riaz *et al.* 2018	5 included in meta-analysis (7 in systematic review). Participants: 881,692 total participants in meta-analysis	Mean age: 60 years (range: 50–64 years). Participants from various studies, primarily adults.	MEDLINE and Scopus. From database inception to January 2018. Countries: Not explicitly listed, but studies included data from large-scale genetic and epidemiological cohorts (e.g., UK Biobank)	Mendelian randomization studies. Systematic review and meta-analysis following MOOSE and American Heart Association guidelines.	BMI	OR	Type 2 Diabetes Significant association with obesity (67% increased odds per 1-SD increase in BMI). OR= 1.67 (95% CI: 1.30–2.14), P < .001, I^2 = 93%. Coronary Artery Disease: Significant association with obesity (20% increased odds per 1-SD increase in BMI). OR = 1.20 (95% CI: 1.02–1.41), P = .03, I^2 = 87%. Stroke No significant association with obesity. OR = 1.02 (95% CI: 0.95–1.09), P = .65, I^2 = 0%	Mendelian randomization assumptions: Assumption 1 (genotype associated with phenotype): Validated in 4 studies. Assumptions 2 and 3 (absence of pleiotropy): Verified in 3 studies. Funnel plot suggested low publication bias. Limitations: Lack of individual patient data, inability to assess mortality outcomes, and assumption dependency of Mendelian randomization. Key Points Obesity is significantly associated with increased risk of T2D and CAD but not stroke. Mendelian randomization minimises confounding, providing less biased estimates.

								Limitations include heterogeneity, lack of mortality data, and reliance on assumptions.
Colpani *et al.* 2018	N=59 studies involving 5,358,902 women 20 articles evaluated BMI, comprising 5,173,769 women	Middle-aged and elderly women (mean age >40 years, perimenopausal and postmenopausal women). Women without cardiovascular disease (CVD) at baseline.	PubMed, Embase, Medline, WoS, Lilacs, Scielo, PsycInfo, Popline, Google Scholar. Up to February 29, 2016. Countries: 15 studies from North America, 1 from South America, 11 from Europe, 3 from the Western Pacific region	Prospective cohort studies. Follow-up duration: 3.2 to 32 years.	BMI Categories: BMI <25 kg/m² (normal weight), 25–30 kg/m² (overweight), 30–35 kg/m² (obesity class I). Dose-response relation analysed (per 5 kg/m² increase in BMI).	RR	Each 5 kg/m² increase in BMI was associated with a 24% higher risk for all-cause mortality (RR: 1.24, 95% CI 1.16–1.33). Compared to a BMI < 25 kg/m2, the risk increased from 1.47 (95% CI 1.20–1.81) for BMI 25–30 kg/m2 to 1.67 (95% CI 1.24–2.25) for BMI 30–35 kg/m2 for CHD; and from 1.46 (95% CI 1.31–1.63) for BMI 25–30 kg/m2 category, 2.3 (95% CI 1.56–3.40) for BMI 30–35 kg/m2 category for CVD mortality. For each 5 kg/m2 higher in BMI the risk of mortality increased by 1.24 (95% CI 1.16–1.33) BMI 30–35 kg/m²: RR for CHD incidence = 1.67 (95% CI 1.24–2.25), RR for CVD mortality = 2.3 (95% CI 1.56–3.40). Physical Activity: RR for overall CVD = 0.74 (95% CI 0.67–0.80), CHD = 0.71 (95% CI 0.67–0.75), stroke = 0.77 (95% CI 0.70–0.85), CVD mortality = 0.70 (95% CI 0.58–0.84), all-cause mortality = 0.71 (95% CI 0.65–0.78).	Most studies scored high methodological quality; three studies scored moderate quality. Lack of standardized methods for assessing lifestyle factors and menopause status noted as limitations. Smoking and higher BMI increase CVD and mortality risk. Physical activity and moderate alcohol intake reduce CVD and mortality risk. Combined healthy lifestyle factors significantly lower CVD and mortality risk

Mortality / MACE

Study	n studies/ participants	Population	Databases Searched & Year/Range/ Countries	Study Designs	Obesity Measure	Effect Estimate	Results ES (95%CI), heterogeneity	Quality & Key points
Weeldreyer *et al.* 2024	N=20 Total observations: 398,716	Adults with varying BMI and CRF levels, including individuals with CVD, diabetes, renal disease, asthma, hormone replacement therapy, smokers, and chronic respiratory diseases. Excluded populations: cancer, liver failure/cirrhosis, psychological/psychiatric problems, substance abuse, eating disorders, neurological degenerative problems, and pregnant females. 67% male, 33% female	PubMed/MEDLINE, Web of Science, SportDiscus January 1980 to February 2023 USA, Sweden, Finland, Norway, UK	Prospective cohort studies Joint impact of CRF and BMI on all-cause and CVD mortality, with CRF assessed using maximal or $\dot{V}O_2$peak exercise tests and BMI	BMI categorized into normal weight (<25 kg/m²), overweight (25–29.9 kg/m²), and obese (≥30 kg/m²).	HR	<u>FIT</u> Compared with the reference group, overweight- fit (CVD HR (95% CI): 1.50 (0.82–2.76), all- cause HR: 0.96 (0.61–1.50)) and obese- fit (CVD: 1.62 (0.87–3.01), all- cause: 1.11 (0.88–1.40)) did not have a statistically different risk of mortality. <u>UNFIT</u> Normal weight- unfit (CVD: 2.04 (1.32–3.14), all- cause: 1.92 (1.43–2.57)), overweight- unfit (CVD: 2.58 (1.48–4.52), all- cause: 1.82 (1.47–2.24)) and obese-unfit (CVD: 3.35 (1.17–9.61), all- cause: 2.04 (1.54–2.71)) demonstrated 2–3-fold greater mortality risks. Moderate to high heterogeneity observed in analyses. I² values ranged from low (<25%) to considerable (>75%) depending on the subgroup analysis.	Fit individuals, regardless of BMI, showed no statistically significant increase in CVD or all-cause mortality risk compared with normal weight-fit individuals. Unfit individuals across all BMI categories demonstrated 2–3-fold greater mortality risks compared with normal weight-fit individuals.
Putra *et al.* 2022	N= 41 studies, 4,028,750 participants	Adults aged ≥18 years Metabolically unhealthy normal weight (MUH-NW) and metabolically unhealthy obesity (MUH-O) phenotypes	PubMed, ProQuest, EBSCOhost, Europe PMC Inception to June 20, 2022 Studies conducted in well-developed	Prospective cohort studies	Body Mass Index (BMI): Normal weight: BMI 18.5–24.9 kg/m² Obesity: BMI ≥30 kg/m²	RR	<u>MUH-NW vs MH-O:</u> All-Cause Mortality (ACM): RR = 1.47 (95% CI: 1.32–1.64), I² = 89.8% Cardiovascular Mortality (CVM): RR = 2.37 (95% CI: 1.97–2.86), I² = 83.7%	Average Newcastle-Ottawa Scale (NOS) score: 8.95 ± 0.22 (low risk of bias) Key Points: MUH-NW is associated with significantly higher risks of ACM, CVM, and MACE compared to MH-O.

			countries predominantly				Major Adverse Cardiac Events (MACE): RR = 1.73 (95% CI: 1.49–2.00), I^2 = 74.3% MUH-O vs MUH-NW: ACM: RR = 0.97 (95% CI: 0.82–1.15), I^2 = 98.3% CVM: RR = 0.96 (95% CI: 0.88–1.05), I^2 = 77.0% MACE: RR = 0.95 (95% CI: 0.80–1.13), I^2 = 92.2%	MUH-O does not significantly increase risks compared to MUH-NW. BMI alone may not adequately reflect obesity-related risks; metabolic screening is recommended for normal weight populations. High heterogeneity observed; sources include diabetes mellitus status, metabolic criteria, and follow-up duration.
Dugani *et al.* 2021	N=77 studies, 12.7 million participants	Men aged 18-55 years; women aged 18-65 years across 58 countries.	MEDLINE (Ovid), AMED (Ovid), Embase (Ovid), EBSCO CINAHL Plus, ClinicalTrials.gov, Cochrane Central Register of Controlled Trials. Inception through April 30, 2020. 58 countries globally, with 24% of studies conducted in the United States	Case-control, cohort, and cross-sectional studies	Body Mass Index (BMI): BMI ≥30 kg/m² vs <30 kg/m² BMI ≥25 kg/m² vs <25 kg/m² Waist-to-hip ratio: Men: Waist-to-hip ratio >0.90 vs ≤0.90	OR	BMI ≥30 kg/m² vs <30 kg/m²: OR = 1.64 (95% CI, 1.31-2.06), heterogeneity I^2 = 94.9%. BMI ≥25 kg/m² vs <25 kg/m² OR = 1.46 (95% CI, 1.24-1.71), heterogeneity I^2 = 84.4%. Waist-to-hip ratio OR = 9.57 (95% CI, 5.52-16.6), heterogeneity not reported.	Using the Newcastle-Ottawa Scale- most studies had low risk of selection and comparability bias but high risk of exposure bias. Key Points: Obesity (BMI ≥25 kg/m²) is associated with a higher risk of premature MI. Mild elevations in BMI and triglyceride levels are concerning due to their increasing global prevalence. Findings highlight the need for interventions targeting modifiable risk factors like obesity.

Zhao *et al.* 2021	N= 21 cohort studies 1,349,075 individuals Cases: 57,725 (49,354 CVD incidence and 8,371 CVD mortality)	Focus: Patients with type 2 diabetes mellitus (T2DM) Regions: America (7 studies), Europe (7 studies), Asia (7 studies)	PubMed and Embase Up to June 8, 2020 US, Poland, Italy, UK, Sweden, Ukraine, Singapore, China, Korea	Cohort studies Follow-up Duration: Average of 8.0 years (range: 2.7–20 years)	BMI	RR	<u>CVD Incidence</u> RR = 1.12 (95% CI, 1.04–1.20) per 5-unit increase in BMI; I^2 = 98.2%, P heterogeneity < 0.001 <u>CVD Mortality</u> Lowest risk at BMI ~28.4 kg/m² BMI ≤28.4 kg/m²: RR = 0.87 (95% CI, 0.79–0.96), I^2 = 66.2%, P heterogeneity = 0.001 BMI >28.4 kg/m²: RR = 1.11 (95% CI, 1.04–1.18), I^2 = 0.0%, P heterogeneity = 0.760	Newcastle-Ottawa Scale: 16 of 17 articles rated as high quality Key Points: BMI has a linear association with CVD incidence and a nonlinear association with CVD mortality in T2DM patients. Lowest mortality risk observed at BMI ~28.4 kg/m². Obesity increases CVD risk due to clustering of cardiovascular risk factors and adipose tissue-related bioactive mediators. Subgroup analyses showed stable results across regions, sexes, and confounding factors.
Sergi *et al.* 2020	N=12 studies, All-cause mortality: 103,859 individuals (48,830 men, 55,029 women). Cardiovascular mortality: 94,965 individuals	Majority of participants aged ≥65 years, with mean/median age over 70 years. Studies conducted in Europe (6), Asia (3), USA (2), and Australia (1). Community-based studies with ≥60% participants aged ≥65	From inception to June 5, 2019. Italy, Sweden, Finland, China, Taiwan, USA, Australia.	Longitudinal cohort studies	WC, BMI	RR	<u>Abdominal Obesity</u> No significant association with all-cause or cardiovascular mortality in men or women. <u>High Triglycerides</u> Marginal association with reduced all-cause mortality in women; no significant results for men. <u>Low HDL Cholesterol</u> Increased all-cause mortality (RR = 1.16, 95% CI: 1.02–1.32) and cardiovascular	Studies scored ≥7 on the Newcastle-Ottawa Scale (NOS), indicating high quality. Key points: Gender differences observed in the impact of MetS components on mortality. Low HDL cholesterol, hyperglycaemia, and

	(44,699 men, 50,266 women).	years, comparing individuals with and without metabolic syndrome (MetS) components. Exclusion criteria: Studies conducted in hospitals/nursing homes or involving individuals with specific diseases (e.g., diabetes).				mortality (RR = 1.34, 95% CI: 1.03–1.74) in women; weaker results for men. <u>High Fasting Glycemia</u> Associated with higher all-cause mortality in women (RR = 1.35, 95% CI: 1.22–1.50) and men (RR = 1.21, 95% CI: 1.13–1.30); cardiovascular mortality only in women (RR = 1.36, 95% CI: 1.04–1.78). <u>Elevated Blood Pressure</u> Increased all-cause mortality (RR = 1.16, 95% CI: 1.03–1.32) and marginally significant cardiovascular mortality (RR = 1.39, 95% CI: 1.00–1.94) in women; no significant results for men. Moderate heterogeneity for most analyses (I^2 values between 25–75%).	elevated blood pressure were stronger predictors of mortality in women. Abdominal obesity and high triglycerides showed weaker associations with mortality in older populations. Personalised approaches are recommended for evaluating metabolic health in older adults, focusing on individual MetS components rather than the overall syndrome
Chen *et al.* 2019	10 studies 1,381,445 participants	Community-based studies and patients with heart failure	PubMed, Embase and Cochrane Library databases up to February 2018. USA, Canada, Israel, Japan, Spain, Finland	Prospective cohort studies	BMI categories: <u>Underweight:</u> BMI < 18.5 kg/m² <u>Normal weight:</u> BMI 18.5–24.9 kg/m² <u>Overweight:</u> BMI 25.0–29.9 kg/m² Obesity: BMI ≥ 30 kg/m²	RR	For Sudden Cardiac Death <u>Underweight vs. Normal Weight</u> RR = 1.20 (95% CI, 0.95–1.51); P = 0.13. No heterogeneity (I^2 = 0%, P = 0.83). <u>Overweight vs. Normal Weight</u> RR = 1.21 (95% CI, 1.08–1.35); P = 0.0008. Low heterogeneity (I^2 = 8%, P = 0.37). <u>Obesity vs. Normal Weight</u> RR = 1.52 (95% CI, 1.31–1.77); P < 0.00001. Moderate heterogeneity (I^2 = 30%, P = 0.17). Findings are robust across sensitivity analyses.	Quality assessed using Newcastle-Ottawa Scale (NOS)- all studies scored between 7–9 stars (moderate to high quality). Key Points: Obesity and being overweight are associated with an increased risk of sudden cardiac death. Underweight is not significantly associated with SCD risk.

								Further research is needed to explore mechanisms and other measures like waist circumference or fat distribution
Aune *et al.* 2018	14 prospective studies	Prospective and retrospective cohort studies and nested case–control studies of the association between adiposity measures (BMI, waist circumference, waist-to-hip ratio, hip circumference, and weight gain) and risk of sudden cardiac death published in English. Studies in high-risk populations (patient populations were excluded.	PubMed and Embase databases up to July 20th 2017	Prospective and retrospective cohort studies and nested case–control	BMI, W:H, WC	RR	The summary RR was 1.16 (95% CI 1.05–1.28, I2 = 68%, n = 14) per 5 unit increment in BMI, and 1.82 (95% CI 1.61–2.07, I2 = 0%, n = 3) per 0.1 unit increase in waist-to-hip ratio, and 1.03 (95% CI 0.93–1.15, I2 = 0%, n = 2) per 10 cm increase in waist circumference. The heterogeneity in the analysis of BMI and sudden cardiac death persisted across most subgroup analyses. The association was stronger among studies with longer follow-up compared to short follow-up and was observed in the European and American studies, but not in the Asian studies. There was a J-shaped association between BMI and sudden cardiac death and the lowest risk was observed in the normal weight range, however, the increased risk with a low BMI was attenuated among studies with a longer duration of follow-up.	Study quality was assessed using the Newcastle–Ottawa scale. Mean (median) score of 7.6 out of 9 points. Key Points: Increased risk of sudden cardiac death with increasing BMI and waist-to-hip ratio, however, further studies with adjustment for confounding factors and with stratified analyses by smoking status are needed of waist circumference, weight changes and adiposity at younger ages.
Barry *et al.* 2018	N=8 articles included in the meta-analysis. Participants: Tens of thousands of individuals, with	Adult humans, primarily men (~89–100% male in most studies). Mean ages varied across studies (e.g., 43.9–64.4 years).	PubMed and CINAHL. Articles published between January 1989 and December 2017.	Prospective longitudinal studies. Objective assessments of cardiorespiratory	BMI, per: Normal weight: 18.5–24.9 kg/m². Overweight: 25–29.9 kg/m².	HR	<u>Unfit individuals</u> 2–3 times higher risk of CVD mortality across all BMI levels. <u>Overweight fit individuals</u>	All studies scored ≥6 on the Newcastle-Ottawa Scale (NOS), indicating moderate to high quality. Key Points:

	specific numbers provided for each study (e.g., 44,674 participants in Farrell et al. 2013, 25,714 in Wei et al. 1999, etc.)	Baseline health status included specific conditions like diabetes, hypertension, and pre-diabetes in some studies.	Countries: United States and Russia (e.g., Aerobic Center Longitudinal Study [ACLS], Cooper Clinic Longitudinal Study [CCLS], Lipids Research Clinics Study [LRCS])	fitness (CRF) via maximal exercise tests and BMI via stadiometer and scale. Follow-up periods ranged from 8.1 to 19.8 years.	Obese: ≥30 kg/m² (with some variations across studies).		25% increased mortality risk compared to normal weight fit individuals (HR = 1.25, 95% CI: 1.07–1.46, I^2 = 38.7%). <u>Obese fit individuals</u> 42% increased mortality risk (HR = 1.42, 95% CI: 1.01–1.98, I^2 = 63.6%), but sensitivity analysis reduced this to non-significant levels in some cases. <u>Obese unfit individuals:</u> Tripled mortality risk (HR = 3.10, 95% CI: 2.36–4.07, I^2 = 74.0%)	CRF is a stronger predictor of CVD mortality risk than BMI. Unfit individuals have significantly higher mortality risk regardless of BMI. Fitness interventions should be prioritized to reduce CVD mortality risk. Age inversely related to CVD mortality risk in unfit and overweight/obese groups, possibly due to survivor bias.
Kwon *et al.* 2017	All-cause mortality: 16 cohort studies, 445,125 participants. Cardiovascular mortality: 2 cohort studies, 92,841 participants.	Patients with type 2 diabetes. Studies conducted in Europe, the United States, and East Asia.	MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials. Published between January 1, 1950, and January 31, 2016. Europe, United States, East Asia.	Prospective and retrospective cohort studies.	BMI- BMI categories varied across studies, with some using WHO recommendations and others using region-specific cutoffs (e.g., >23 kg/m² for Asian populations	HR	<u>All-cause mortality</u> Non-linear association observed. BMI nadir at 28–30 kg/m², with a U-shaped increase in risk. HR for every 5 kg/m² increase in BMI: 0.99 (95% CI: 0.97–1.00, P = 0.04). I^2 = 97.1%, P < 0.0001. <u>Cardiovascular mortality</u> Non-linear association observed. BMI nadir at 29–31 kg/m², with increased risk at BMI > 31 kg/m². HR for every 5 kg/m² increase in BMI: 0.98 (95% CI: 0.85–1.13, P = 0.79). I^2 = 1.4%, P < 0.0001.	Risk of bias assessed using the Newcastle-Ottawa Scale. Key points: 'Obesity paradox' observed in type 2 diabetes patients. Study location, diabetes duration, and smoking history contributed to heterogeneity. BMI nadir for lowest mortality risk: 28–30 kg/m² (all-cause) and 29–31 kg/m² (cardiovascular). Reverse causation and smoking history are potential confounders.

								Management strategies for normal-weight diabetes patients may differ from those for overweight/obese patients
Zaccardi *et al.* 2017	N=21 studies, N=24 cohorts 414,587 participants	Individuals with type 2 diabetes mellitus Mean baseline age ranged from 40 to 77 years Participants from USA, UK, Europe, Asia (Iran, South Korea, Taiwan)	PubMed, Web of Science, Scopus Articles published before March 1, 2016 Countries: USA, UK, Europe, Asia	Prospective cohort studies Follow-up duration ranged from 2.7 to 15.9 years	BMI	RR	<u>All-cause mortality:</u> Nonlinear relationship with BMI- lowest risk at BMI 31–35 kg/m² for men and 28–31 kg/m² for women. Increased risk for BMI <25 kg/m² in both sexes No significant heterogeneity (p = 0.376) <u>Cardiovascular mortality:</u> Possible inverse linear association with BMI (higher risk for BMI <27 kg/m²) RR per unit increase in BMI: 0.98 (95% CI: 0.96, 0.99; p = 0.013) Limited data availability	Most studies scored 8 or higher on the Newcastle–Ottawa Scale (NOS) Key Points: BMI is nonlinearly associated with all-cause mortality in type 2 diabetes. Lowest mortality risk observed in overweight BMI ranges. Sex differences in BMI-mortality association (lower nadir for women). Limited data for cardiovascular mortality; further research needed.
Eckel *et al.* 2016	N=22 included in the meta-analysis. Sample sizes ranged from 550 to 71,527 participants.	Predominantly Caucasian populations: USA n=7 studies, Australia n=1, Canada n=1, Iran n=1, Japan n=1, Europe n=10. Included studies reported RR for CVD mortality/incidence. Stratified by BMI categories and metabolic health.	PubMed and Web of Science. From inception to April 7, 2014. Limited to English and German.	Prospective cohort studies	BMI – obesity BMI ≥30 kg/m², WC, WHR	RR	Risk for Cardiac Events <u>Metabolically Healthy Obesity (MHO)</u> RR 1.45 (95% CI 1.20–1.70). I^2 = 74.5% <u>Metabolically Unhealthy Normal Weight (MUH-NW)</u> RR 2.07 (95% CI 1.62–2.65). <u>Metabolically Unhealthy Obesity (MUHO)</u> RR 2.31 (95% CI 1.99–2.69). I^2 = 58.6%. I^2 = 62.3%	Studies scored ≥6 stars on the Newcastle Ottawa Scale, indicating high quality. MHO participants are at an increased risk for cardiovascular events compared to MHNW participants. No clear definition of MHO identifies a subgroup without increased risk.

		Reference group: normal-weight healthy participants. Two studies were restricted to women, and five studies were restricted to men						Risk increases with longer follow-up times. More research is needed to define MHO and assess sex and ethnicity differences.
Zheng *et al.* 2016	22 prospective cohort studies 584,799 individuals	Adults aged ≥20 years at baseline. Geographically diverse populations: 10 cohorts from Europe, 7 from North America, and 5 from Asia	Medline, EMBASE, Web of Science, Cochrane Library Up to September 30, 2015 Countries: Europe, North America, Asia (specific ethnic composition not reported in most studies)	Prospective cohort studies	BMI and EC cut-offs. Stratified participants by metabolic status and weight classification	RR	<u>Cardiovascular (CV) Events</u> MHO phenotype RR: 1.50 (95% CI 1.27–1.77) HR: 1.60 (95% CI 1.38–1.84) Heterogeneity: Moderate (I^2 = 66.2% for unadjusted data; I^2 = 45.6% for adjusted data) <u>All-Cause Mortality</u> MHO phenotype RR: 1.18 (95% CI 0.83–1.66) HR: 1.07 (95% CI 0.92–1.25) Heterogeneity: High for unadjusted data (I^2 = 84.5%), low for adjusted data (I^2 = 17.6%) <u>Role of CRF</u> When regression models were adjusted for CRF or physical activity, the association between obesity (including MHO) and cardiovascular (CV) events weakened but remained statistically significant (HR 1.33, 95% CI 1.06–1.68). This indicates that CRF plays a central role in reducing the adverse effects of obesity on CV morbidity.	Cardiovascular Events: MHO individuals had a significantly higher risk compared to metabolically healthy normal-weight individuals. All-Cause Mortality: No significant association observed for MHO individuals. MHO is associated with increased risk of CV events but not all-cause mortality. Cardiorespiratory fitness plays a critical role in mitigating risks. The term "healthy" may not be appropriate for MHO individuals due to long-term risks. Weight reduction and fitness improvements are recommended for MHO individuals.
Liu *et al.* 2015	9 studies including 13	Included patients with T2D	PubMed and Embase.	Prospective cohort studies	BMI. <u>Categories</u>	RR	Overweight: RR 0.81 (95% CI 0.74–0.90) for all-cause mortality.	Quality Assessment: Studies scored between 6 and 9 stars

	cohorts with 161,984 participants.		Up to October 19, 2014. Countries: United States, Israel, Taiwan, Europe, Sweden, Britain, and Italy.	Underweight: BMI < 18.5 kg/m². Normal weight: BMI 18.5–24.9 kg/m² (18.5–22.9 kg/m² for Asian populations). Overweight: BMI 25–29.9 kg/m² (23–24.9 kg/m² for Asian populations). Obesity: BMI ≥ 30 kg/m² (≥ 25 kg/m² for Asian populations).		Obesity: RR 0.72 (95% CI 0.63–0.81) for all-cause mortality. Cardiovascular mortality: No significant association (RR 0.89; 95% CI 0.66–1.20 for overweight and RR 0.77; 95% CI 0.54–1.10 for obesity).	on the Newcastle-Ottawa Scale, indicating moderate to high quality Key Points: Overweight and obesity were associated with reduced risks of all-cause mortality in type 2 diabetes patients. No significant association was found between excess body weight and cardiovascular mortality. Authors suggested reconsideration of weight reduction recommendations for obese diabetic patients. Limitations include potential survivor bias, reliance on baseline BMI, and unmeasured confounders.
ARRYTHMIA							
Study	**n studies/ participants**	**Population**	**Databases Searched & Year/Range/ Countries**	**Study Designs**	**Obesity Measure**	**Effect Estimate**	**Results ES (95%CI), heterogeneity**	**Quality & Key points**
Liu *et al.* 2025	N=9 studies, 4,250,557 participants	General population from Asia (4 studies) and Europe (5 studies). Mean age ranged from 43 to 60 years, with 54% women	PubMed, EMBASE, Web of Science, Cochrane Library. Inception to January 22, 2025.	Cohort studies.	BMI	HR, RR	Pooled results revealed that individuals with MHO were associated with a greater incidence of AF than those with a metabolically healthy normal weight (HR: 1.34, 95 % CI: 1.26 to 1.42) with moderate certainty	Moderate to high (Newcastle-Ottawa Scale scores: 6–8) Key Points: MHO is associated with a higher risk of atrial fibrillation compared to

		Population/community-based (65 studies), occupational populations (22 studies), and others	Countries: Sweden, South Korea, Norway, France, Japan, Taiwan, Finland, Britain, China.				MHO vs. Metabolically Unhealthy Obesity: RR = 0.48 (95% CI: 0.36–0.64). MHO vs. Metabolically Unhealthy Normal Weight: HR = 1.04 (95% CI: 0.89–1.22).	metabolically healthy normal weight Individuals with MHO have a lower risk of AF than are those with metabolically unhealthy obesity. Previous studies and findings suggest that regular physical activity lowers the incidence of AF and mitigates obesity-related risks
Wu *et al.* 2023	N= 101 studies, 17,098,955 participants 738,843 incident cases of atrial fibrillation (AF)	Mean age: 56.6 years (range: 18.2–75.8 years) Studies conducted in North America (31), Europe (49), Asia (17), and Oceania (4)	MEDLINE, Web of Science, EMBASE From initiation until January 15, 2022 Countries: Studies from North America, Europe, Asia, and Oceania	Prospective cohort studies	BMI	RR	In all, the risk of AF was 1.39 (95% CI, 1.30–1.49) for obesity, 1.27 (95% CI, 1.22–1.32) per 5 kg/m^2 for increase in body mass index,	91% of studies were of high quality (Newcastle-Ottawa Scale score ≥6) Key Points: Obesity is associated with a 39% increased risk of AF, independent of other metabolic abnormalities.
Zheng *et al.* 2021	N=6 studies, 30,810,460 total participants	Korean, Japanese, American, and Stockholmer populations.	Cochrane Library, PubMed, and Embase. Search conducted through May 2020. Countries: Korea, Japan, USA, Sweden.	Cohort studies	Abdominal obesity measured using waist circumference	HR	Metabolic Syndrome (MetS) and Atrial Fibrillation (AF): HR 1.57 (95% CI 1.40–1.77). I^2 = 97% Components of MetS and AF: Abdominal obesity: HR 1.37 (95% CI 1.36–1.38). I^2 = 0% Elevated blood pressure: HR 1.56 (95% CI 1.46–1.66). I^2 = 71% Elevated fasting glucose: HR 1.18 (95% CI 1.15–1.21). I^2 = 25%	Quality assessed using Newcastle–Ottawa Scale (NOS); all studies scored >6, indicating acceptable quality. Key findings: MetS and its components (except high triglycerides) are associated with increased AF risk. Limitations: High heterogeneity, population bias (overrepresentation of

							Low HDL cholesterol: HR 1.18 (95% CI 1.06–1.32). I^2 = 87% High triglycerides: HR 0.99 (95% CI 0.87–1.11). I^2 = 91%	Korean studies), and varying MetS definitions.
Asad *et al.* 2018	N=16 trials, with 587, 372 participants: 91,031 participants with obesity and 496,341 participants without obesity	General population, stratified by obesity group (BMI >30 kg/m²) and gender.	MEDLINE and EMBASE databases were searched. Through July 2017.	Prospective cohort studies	Obesity was defined as BMI >30 kg/m² in the majority of studies	RR	AF during follow-up developed in 5,751 of 91,031 (6.3%) obese subjects and in 15,346 of 496,341 (3.1%) nonobese subjects (RR = 1.51, 95% CI 1.35 to 1.68; P < 0.00001). Based on the pooled estimate across the studies, the effect of obesity on incident AF was similar in men (RR = 1.41, 95% 1.24 to 1.62; P < 0.00001) and women (RR = 1.53, 95% CI 1.19 to 1.97; P < 0.00001). Significant heterogeneity across studies (I^2 = 89%; P < 0.00001).	Overall, the included studies were of good quality, assessed using the Newcastle–Ottawa Quality Assessment Scale. Key points: Obesity is associated with a 51% increased risk of new-onset atrial fibrillation (AF). The effect is consistent across genders. Obesity contributes to AF risk through mechanisms such as atrial remodelling, inflammation, and oxidative stress
Aune *et al.* 2017	29 prospective studies (32 publications). 83,006 atrial fibrillation cases among 2,405,381 participants.	Studies included populations from Europe (14 studies), USA (8 studies), Asia (4 studies), and Australia (3 studies)	PubMed and Embase. Search conducted up to October 24, 2016. Countries: Europe, USA, Asia, Australia	Cohort studies, and nested case–control studies.	BMI, waist circumference, hip circumference, waist-to-hip ratio, body fat mass, body fat percentage, weight, and weight gain	RR	BMI: RR = 1.28 (95% CI: 1.20–1.38), I^2 = 97%. Waist circumference: RR = 1.18 (95% CI: 1.12–1.25), I^2 = 73%. Hip circumference: RR = 1.32 (95% CI: 1.16–1.51), I^2 = 91%. Waist-to-hip ratio: RR = 1.09 (95% CI: 1.02–1.16), I^2 = 44%.	Study quality assessed using the Newcastle–Ottawa scale, with a mean score of 7.7/9 Key Points: Consistent findings across geographic locations and ethnic groups. Results suggest that general and abdominal adiposity

							Fat mass: RR = 1.09 (95% CI: 1.02–1.16), I^2 = 94%. Weight: RR = 1.10 (95% CI: 1.08–1.13), I^2 = 74%. Weight gain: RR = 1.08 (95% CI: 0.97–1.19), I^2 = 86%.	measures are significant risk factors for atrial fibrillation.
HEART FAILURE								
Study	**n studies/ participants**	**Population**	**Databases Searched & Year/Range/ Countries**	**Study Designs**	**Obesity Measure**	**Effect Estimate**	**Results ES (95%CI), heterogeneity**	**Quality & Key points**
Mahjan *et al.* 2019	N=29 studies. 375,056 participants for obesity and HF incidence; 41,019 participants for obesity and HF prognosis; 9 studies for intentional weight loss and cardiac structure/function.	General population, including obese individuals and those undergoing bariatric surgery. Mean age: 53 ± 8 years for HF incidence studies; 67 ± 4 years for HF prognosis studies. Follow-up: 12 ± 6 years for HF incidence; 4.8 ± 3.4 years for HF prognosis.	MEDLINE, Embase, Web of Science. Search period: January 1950 to April 3, 2018.	Observational studies	BMI	HR	<u>HF Incidence:</u> Underweight: HR 1.22 (95% CI 0.95–1.58, p=0.12) Overweight: HR 1.11 (95% CI 0.97–1.27, p=0.13) Obese: HR 1.62 (95% CI 1.32–1.99, p<0.001) Morbidly obese: HR 1.73 (95% CI 1.30–2.31, p<0.001) <u>HF Prognosis (CV Mortality):</u> Overweight: OR 0.86 (95% CI 0.79–0.94, p=0.001) Obese: OR 0.97 (95% CI 0.72–1.33, p=0.87) <u>Intentional Weight Loss:</u>	Newcastle-Ottawa Scale, indicating low risk of bias. Key findings: Obesity increases HF risk, but overweight individuals have the lowest CV mortality. Intentional weight loss improves cardiac structure and function. The "obesity paradox" (lower mortality in obese HF patients) remains controversial.

							Reduction in left ventricular mass index: SMD −0.49 (95% CI −0.73 to −0.26, p<0.0001) Improvement in diastolic function: SMD 0.65 (95% CI 0.38–0.91, p<0.0001) Reduction in left atrial size: SMD −0.39 (95% CI −0.72 to −0.07, p=0.02).	
Aune *et al.* 2016	23 studies for BMI and heart failure incidence (>15,905 cases among 647,388 participants)	Studies included participants from Europe (16 studies), the United States (10 studies), Asia (1 study from Japan), and Australia (1 study)	PubMed and Embase databases were searched up to October 10, 2014. Studies were conducted in Europe, the United States, Japan, and Australia.	Prospective cohort studies, retrospective cohort studies, and nested case-control studies.	BMI, WC, W:H	RR	BMI: Summary relative risk for a 5-unit increment was 1.41 (95% CI, 1.34–1.47; I^2 = 83%) for heart failure incidence and 1.25 (95% CI, 0.85–1.87; I^2 = 95%) for heart failure mortality Waist circumference: RR for a 10-cm increase was 1.29 (95% CI, 1.21–1.37; I^2 = 89%) Waist-to-hip ratio: RR for a 0.1-unit increase was 1.28 (95% CI, 1.12–1.47; I^2 = 85%	Study quality was high, with mean scores of 8.2–8.4 out of 9 (Newcastle-Ottawa Scale). Findings suggest that both general and abdominal adiposity independently increase the risk of heart failure.
CHD, CAD, PAD								
Study	**n studies/ participants**	**Population**	**Databases Searched & Year/Range/ Countries**	**Study Designs**	**Obesity Measure**	**Effect Estimate**	**Results ES (95%CI), heterogeneity**	**Quality & Key points**
Khoja *et al.* 2024	N=27 studies with 153,025 participants with premature CHD and 1,172,474 healthy controls.	Individuals diagnosed with premature coronary heart disease (PCHD) compared to healthy controls	PubMed, CINAHL, Embase, Web of Science, Google Scholar, ClinicalTrials.gov, WHO, CDC, American Heart	13 prospective/retrospective cohort studies, 171 case-control studies, and 24 cross-sectional studies.	BMI	OR	Individuals with PCHD were 59% more likely to be obese compared to healthy controls. OR 1.59 (95% CI 1.32, 1.91) i^2 95%.	Quality: Studies rated as high, moderate, and poor quality based on the National Heart, Lung, and Blood Institute (NHLBI) tool. Key Points:

			Association, American College of Cardiology. : Last search conducted on June 30, 2023. Countries: Studies included from high-income countries and low–middle-income countries					Obesity is a significant modifiable risk factor for PCHD. Obesity and higher BMI are more prevalent among individuals with PCHD compared with healthy controls.
Hsueh *et al.* 2020	N=9 studies, 6 for MA with 23,543 participants	General Mean age: 42.2 years. Female 46.6%. Obesity prevalence: 16.8% metabolically healthy obesity (MHO).	Cochrane, PubMed, Embase. Search range: Up to April 19, 2019. Countries: Korea, USA, Germany.	Cohort and cross sectional	BMI, WC	OR	Compared with MHNO subjects, MHO had a higher odds of CAC (OR 1.36, 95% CI [1.11 to 1.66]; I2 = 39%).	Quality assessed using Newcastle-Ottawa Scale (NOS): Cohort studies: ≥8/9 stars. Cross-sectional studies: 7–9/10 stars. Key Points: MHO is associated with elevated CAC risk, reflecting coronary atherosclerosis. Age and smoking status are possible effect modifiers.
Song *et al.* 2019	N=118 articles	General	PubMed, MEDLINE, Embase, Global Health database, CINAHL, Global Health Library, Allied and Complementary Medicine Database, ProQuest	Population based studies	BMI, WC	OR	Overweight (BMI 25–30 kg/m²): OR = 0.96 (95% CI 0.82–1.13). Obesity (BMI ≥30 kg/m²): OR = 1.55 (95% CI 1.23–1.96). BMI (per 1 kg/m² increase): OR = 0.92 (95% CI 0.87–0.97).	Key findings: Obesity (BMI ≥30 kg/m²) is positively associated with peripheral artery disease (PAD).

			Dissertations and Theses Global. Studies published between Jan 1, 2011, and April 30, 2019. Countries: 33 countries, including HICs (e.g., USA, UK, Japan) and LMICs (e.g., India, Brazil, China).				Waist circumference (per 1 cm increase): OR = 1.03 (95% CI 1.00–1.06).	
Riaz *et al.* 2018	5 included in meta-analysis (7 in systematic review). Participants: 881,692 total participants in meta-analysis	Mean age: 60 years (range: 50–64 years). Participants from various studies, primarily adults.	MEDLINE and Scopus. From database inception to January 2018. Countries: Not explicitly listed, but studies included data from large-scale genetic and epidemiological cohorts (e.g., UK Biobank)	Mendelian randomization studies. Systematic review and meta-analysis following MOOSE and American Heart Association guidelines.	BMI	OR	Type 2 Diabetes Significant association with obesity (67% increased odds per 1-SD increase in BMI). OR= 1.67 (95% CI: 1.30–2.14), P < .001, I^2 = 93%. Coronary Artery Disease: Significant association with obesity (20% increased odds per 1-SD increase in BMI). OR = 1.20 (95% CI: 1.02–1.41), P = .03, I^2 = 87%. Stroke No significant association with obesity. OR = 1.02 (95% CI: 0.95–1.09), P = .65, I^2 = 0%	Mendelian randomization assumptions: Assumption 1 (genotype associated with phenotype): Validated in 4 studies. Assumptions 2 and 3 (absence of pleiotropy): Verified in 3 studies. Funnel plot suggested low publication bias. Limitations: Lack of individual patient data, inability to assess mortality outcomes, and assumption dependency of Mendelian randomization. Key Points

								Obesity is significantly associated with increased risk of T2D and CAD but not stroke. Mendelian randomization minimises confounding, providing less biased estimates. Limitations include heterogeneity, lack of mortality data, and reliance on assumptions.
Mongraw-Chaffin *et al.* 2015	N=95 studies, 1,219,187 participants, 37,488 coronary heart disease cases	General	PubMed and Embase Up to February 20, 2015 Countries: Studies from multiple countries, including the USA, Japan, Norway, Denmark, Finland, Scotland, and others.	Prospective cohort studies Individual participant data from four large studies (ARIC, APCSC, NHANES III, SHHEC)	BMI	HR (age adjusted)	When measured continuously, a one-unit (kg/m 2) increment in BMI was associated with an age-adjusted increase in risk of coronary heart disease of 4% (HR 1·04, 95% CI 1·03–1·05) in women and 5% (HR 1·05, 1·04–1·07) in men Compared with people of a normal weight, the age-adjusted HR of coronary heart disease for the underweight group was 1·25 (1·05–1·49) in women and 1·09 (0·91–1·23) in men; for the overweight group 1·20 (1·12–1·29) in women and 1·22 (1·12–1·32) in men; and for the obese group 1·61 (1·42–1·82) in women and 1·60 (1·43–1·79) in men.	Quality Assessment: Studies were generally of good quality, assessed using the Newcastle-Ottawa Scale. Key Points: The association between BMI and coronary heart disease is similar for women and men
STROKE								
Study	**n studies/ participants**	**Population**	**Databases Searched & Year/Range/ Countries**	**Study Designs**	**Obesity Measure**	**Effect Estimate**	**Results ES (95%CI), heterogeneity**	**Quality & Key points**

Meng *et al.* 2022	N=11 prospective cohort studies with a total of 5,609,945 participants.	The population consisted of adults aged 18 years or older without preexisting stroke.	PubMed, Embase, and Cochrane Library. Search range: From inception to March 7, 2021. Geographic locations: Studies conducted in Europe (4), North America (2), and Asia (5)	Prospective cohort	BMI	HR	Metabolically Unhealthy Phenotypes (MUNW, MUOW, MUO) showed significantly higher stroke risk compared to metabolically healthy normal weight (MHNW): MUNW: HR = 1.63 (95% CI: 1.41–1.89), I^2 = 89.74%. MUOW: HR = 1.94 (95% CI: 1.58–2.40), I^2 = 91.17%. MUO: HR = 1.99 (95% CI: 1.66–2.40), I^2 = 93.49%. Metabolically Healthy Phenotypes (MHOW, MHO) did not show a significant increase in stroke risk: MHOW: HR = 1.07 (95% CI: 1.00–1.14), I^2 = 69.50%. MHO: HR = 1.07 (95% CI: 0.99–1.16), I^2 = 54.82%.	Methodological quality was assessed using the Newcastle–Ottawa Scale (NOS). Most studies scored 7 or more stars, indicating moderate to high quality. Key point Stroke risk is significantly elevated in metabolically unhealthy phenotypes, regardless of BMI
Wang *et al.* 2022	N=24 studies involving 5,798,826 participants	Participants aged 18–90 years from 8 countries: United States, Sweden, Denmark, China, Japan, South Korea, Britain, and Finland.	PubMed, EMBASE, Web of Science, Cochrane Library, WanFang Database, China National Knowledge Infrastructure (CNKI), CQVIP, and Chinese Biomedical Literature (CBM). From inception to December 1, 2021	11 prospective cohort studies, 7 longitudinal studies, 2 case–control studies, 2 cross-sectional studies, 1 retrospective cohort study, and 1 retrospective observational study.	BMI	RR	Underweight vs. Normal BMI: RR = 0.93 (95% CI 0.82–1.06), I^2 = 88.8%. Overweight vs. Normal BMI: RR = 1.25 (95% CI 1.16–1.34), I^2 = 84.8%. Obese vs. Normal BMI: RR = 1.47 (95% CI 1.02–2.11), I^2 = 99.4%.	All studies were of moderate to high quality based on the Newcastle–Ottawa Scale (NOS). Key points: Key findings: Higher BMI (overweight or obese) is positively associated with stroke risk, particularly ischemic stroke and in males. Lower BMI was not significantly associated with stroke risk.
Ma *et al.* 2021	N= 8 studies involving	Adults who were stroke-free at baseline,	PubMed, Embase, Cochrane Library	Prospective cohort studies	BMI	RR	MHO vs MH-NW: RR = 1.17 (95% CI: 1.11–1.23), I^2 = 0%	Quality assessed using the Newcastle-Ottawa Scale

	4,256,888 participants	categorized by BMI and metabolic status into six subtypes: Metabolically Healthy Normal Weight (MH-NW) Metabolically Healthy Overweight (MH-OW) Metabolically Healthy Obese (MHO) Metabolically Unhealthy Normal Weight (MU-NW) Metabolically Unhealthy Overweight (MU-OW) Metabolically Unhealthy Obese (MUO)	December 1946 to January 2019 Countries: USA, UK, Denmark, Korea, China				MH-OW vs MH-NW: RR = 1.02 (95% CI: 0.84–1.23), I^2 = 57% MU-NW vs MH-NW: RR = 1.83 (95% CI: 1.57–2.14), I^2 = 86% MU-OW vs MH-NW: RR = 1.93 (95% CI: 1.44–2.58), I^2 = 88% MUO vs MH-NW: RR = 2.00 (95% CI: 1.40–2.87), I^2 = 91%	(NOS); all studies scored at least 7 stars, indicating acceptable quality Key Points: MHO individuals have a higher risk of stroke compared to MH-NW individuals. All metabolically unhealthy groups (MU-NW, MU-OW, MUO) showed significantly elevated stroke risks, irrespective of weight status. No evidence supports the concept of "healthy obesity" as a harmless condition.
Liu *et al.* 2018	N=44 studies, 4,432,475 participants	General adult population	PubMed and Embase : Up to May 11, 2018 Countries: Studies from Asia, Europe, North America, Australia, and one study including participants from 9 countries.	Prospective cohort studies	BMI	RR	Summary relative risk (RR) for stroke incidence per 5-unit increment in BMI: 1.10 (95% CI, 1.06–1.13)	Quality: Most studies were high quality, with an average Newcastle–Ottawa Scale score of 8.2 Key points: The risk of stroke was increased by 10% with each 5-unit increment in BMI. Both overweight and obesity increase the stroke risk with a J-shaped dose–response relation.

								The nadir of the dose–response curve was observed at BMI 23–24 kg/m^2. Stronger association observed in men than women
Li *et al.* 2017	N=16 studies, 116,496 participants	Participants initially free of cardiovascular diseases	Databases: PubMed, EMBASE, Google Scholar. Year/Range: From inception to June 2016. Countries: USA (3 studies), Europe (3 studies), Asia (10 studies).	Prospective cohort studies	Central obesity defined by waist circumference, as per the NCEP criteria	RR	Comparing the persons without MetS, those with MetS Pooled relative risk (RR) for stroke: 1.70 (95% CI: 1.49–1.95). Subgroup analyses: Women: RR = 1.83 (95% CI: 1.31–2.56). Men: RR = 1.47 (95% CI: 1.22–1.78). Ischemic stroke: RR = 2.12 (95% CI: 1.46–3.08). Hemorrhagic stroke: RR = 1.48 (95% CI: 0.98–2.24).	Scores ranged from 6 to 9 points, indicating high-quality studies on NOS Key points: Metabolic syndrome might be an important risk factor of stroke, particularly among women and those with ischemic stroke.
HYPERTENSION								
Study	**n studies/ participants**	**Population**	**Databases Searched & Year/Range/ Countries**	**Study Designs**	**Obesity Measure**	**Effect Estimate**	**Results ES (95%CI), heterogeneity**	**Quality & Key points**
Tan *et al.* 2023	N=18 studies, 89,094 participants	General population of any age group, excluding individuals with hypertension at baseline	PubMed, Embase, Cochrane, Scopus, Web of Science.	Cohort studies	BMI	RR	BMI trajectories in relation to the risk of developing hypertension.	Quality assessed using the Newcastle–Ottawa Scale (NOS), scores ranged from 7

		Participants ranged in age from newborn to 101 years, with a median age of 42.5 years. Geographical areas included Asia (n = 14), North America (n = 2), Australia (n = 1), and South Africa (n = 1).	From inception to January 31, 2022. Countries: Studies conducted in China, Japan, Australia, South Africa, Canada, Singapore, Iran, and the USA.				Stable high: RR = 1.80 (95% CI: 1.29–2.50), p < 0.001, I^2 = 98.4%. Stable low: RR = 0.83 (95% CI: 0.79–0.87), p = 0.994, I^2 = 0.0%. Fluctuated (elevated-decrease): RR = 1.30 (95% CI: 1.24–1.37), p = 0.001, I^2 = 13.8%. Fluctuated (sharp-increase): RR = 1.53 (95% CI: 1.27–1.83), p < 0.001, I^2 = 86.8%.	to 9, indicating high overall quality Key Points: Compared with the "Stable normal" trajectory, the "Stable high" trajectory had the highest increased risk of hypertension. The "Fluctuated (sharp-increase)" trajectory and the "Fluctuated (elevated-decrease)" trajectory were also associated with an increased risk of hypertension. The "Stable low" trajectory displayed a lower risk of hypertension Age and baseline BMI were identified as significant contributors to heterogeneity
Jayedi *et al.* 2018	N=57 studies 2,343,466 participants 216,182 incident cases of hypertension	General population aged over 18 years	PubMed and Scopus Search range: From inception to January 25, 2017 Countries: USA, Europe, Asia, Africa, Mexico, Brazi	Prospective cohort studies	BMI, EC, WHR, WHtR	RR	BMI: Summary RR: 1.49 (95% CI: 1.41, 1.58) per 5-unit increment I^2 = 97.4% WC: Summary RR: 1.27 (95% CI: 1.15, 1.39) per 10-cm increment I^2 = 95.0% Summary RR: 1.37 (95% CI: 1.24, 1.51) per 0.1-unit increment I^2 = 76.4%	Studies with more than seven stars on the Newcastle–Ottawa scale were considered high quality Key points: Risk of hypertension increases continuously with all anthropometric measures.

Summary RR: 1.74 (95% CI: 1.35, 2.13) per 0.1-unit increment I^2 = 58.9%	Being lean within the normal BMI range is suggested for primary prevention of hypertension. Adjustment for baseline blood pressure attenuated the associations but did not eliminate them.

6.3 Systematic review and meta-analyses for the impact of weight loss in general on CV risk and CVD outcomes in people with or at risk of CVD

Table 6.3 Systematic review and meta-analyses for the impact of overweight and obesity on the risk of CVD

Study	n studies/ participants	Population	Databases Searched & Year/Range/ Countries	Study Designs	Obesity Measure	Effect Estimate	Results ES (95%CI), heterogeneity	Quality & Key points
Wu *et al.* 2024	13 studies reporting on 12 articles involving 26,164	Patients with heart failure	PubMed and Embase. Year/Range: Articles indexed up to May 7, 2023.	Post hoc analysis of randomised controlled trials or observational studies	Weight loss was compared with stable weight. Subgroup analysis included overweight/obese and non-overweight/obese patients.	HR	Pooled adjusted hazard ratio (HR) for all-cause mortality: 1.75 (95% CI 1.43-2.14). HR for cardiovascular mortality: 1.64 (95% CI 1.18-2.28). Subgroup analysis: Overweight/obese: HR 1.76 (95% CI 1.41-2.20). Non-overweight/obese: HR 1.90 (95% CI 1.14-3.14). Weight loss was associated with a pooled adjusted HR of 1.75 (95% CI 1.43–2.14) compared to stable weight, indicating a 75% increased risk of all-cause mortality. Weight loss was associated with a pooled adjusted HR of 1.64 (95% CI 1.18–2.28), indicating a 64% increased risk of cardiovascular mortality. Significant heterogeneity was observed across studies due to varying definitions of weight loss, study designs, and patient characteristics.	Quality: The included studies were classified as moderate to high quality based on the Newcastle–Ottawa Scale (NOS), with scores ranging from 6 to 9 points. Key Points Most studies did not differentiate between intentional and unintentional weight loss. Weight loss is a significant risk factor for increased cardiovascular and all-cause mortality in HF patients. Assessing weight changes provides prognostic information for HF patients. Authors conclude- Weight loss, whether intentional or unintentional, is associated with increased risks of cardiovascular and all-cause mortality in patients with heart failure

								Unintentional weight loss often reflects cardiac cachexia and is particularly detrimental to survival outcomes. Monitoring weight changes can enhance risk stratification and guide therapeutic strategies for HF patients, emphasizing the need to prevent unintentional weight loss
Mahjan *et al.* 2019	N=29 studies. 375,056 participants for obesity and HF incidence; 41,019 participants for obesity and HF prognosis; 9 studies for intentional weight loss and cardiac structure/function.	General population, including obese individuals and those undergoing bariatric surgery. Mean age: 53 ± 8 years for HF incidence studies; 67 ± 4 years for HF prognosis studies. Follow-up: 12 ± 6 years for HF incidence; 4.8 ± 3.4 years for HF prognosis.	MEDLINE, Embase, Web of Science. Search period: January 1950 to April 3, 2018.	Observational studies	BMI	HR	<u>HF Incidence:</u> Underweight: HR 1.22 (95% CI 0.95–1.58, p=0.12) Overweight: HR 1.11 (95% CI 0.97–1.27, p=0.13) Obese: HR 1.62 (95% CI 1.32–1.99, p<0.001) Morbidly obese: HR 1.73 (95% CI 1.30–2.31, p<0.001) <u>HF Prognosis (CV Mortality):</u> Overweight: OR 0.86 (95% CI 0.79–0.94, p=0.001) Obese: OR 0.97 (95% CI 0.72–1.33, p=0.87) <u>Intentional Weight Loss:</u> Reduction in left ventricular mass index: SMD −0.49 (95% CI −0.73 to −0.26, p<0.0001) Improvement in diastolic function: SMD 0.65 (95% CI 0.38–0.91, p<0.0001) Reduction in left atrial size: SMD −0.39 (95% CI −0.72 to −0.07, p=0.02).	Newcastle-Ottawa Scale, indicating low risk of bias. Key findings: Obesity increases HF risk, but overweight individuals have the lowest CV mortality. Intentional weight loss improves cardiac structure and function. The "obesity paradox" (lower mortality in obese HF patients) remains controversial.

Reddy *et al.* 2019	9 studies, 110 participants	Adults (age >18 years) with obesity without clinically overt heart failure	Relevant databases were systematically searched from inception to May 2018.	Prospective observational studies	Body weight	MD	Baseline weight ranged from 96 to 166 kg, with a median weight loss of 43 kg (range 10 to 58 kg), representing approximately 25% weight loss (range 9% to 42%) Heart Rate: −9 beats/min (95% CI: −12 to −6; p < 0.001; heterogeneity I^2 = 57%). Mean Arterial Pressure: −7 mm Hg (95% CI: −11 to −3; p < 0.001; heterogeneity I^2 = 41%). Resting Oxygen Consumption (VO2): −85 ml/min (95% CI: −111 to −60; p < 0.001; heterogeneity I^2 = 0%). Pulmonary Capillary Wedge Pressure: −3 mm Hg (95% CI: −5 to −1; p < 0.001; heterogeneity I^2 = 40%). Mean Pulmonary Artery Pressure: −5 mm Hg (95% CI: −8 to −2; p = 0.001; heterogeneity I^2 = 45%). no change in stroke volume (−1 ml, 95% CI: −9 to +6; p = 0.70).	Studies demonstrated high quality with low risk of bias, assessed using the New Castle Ottawa Scale Therapeutic weight loss may improve hemodynamic derangements in obesity, but randomized controlled trials are needed for confirmation. weight loss is associated with significant reductions in biventricular filling pressures and pulmonary artery pressure, heart rate, cardiac output, systemic blood pressure, and whole-body oxygen consumption
Le Blanc *et al.* 2019	122 randomized clinical trials (RCTs) and 2 observational studies. Participants: 62,533 in RCTs and 209,993 in observational studies.	Adults aged 18 years or older who had overweight or had obesity (BMI ≥25 or other weight-related measures)	MEDLINE, PubMed Publisher-Supplied Records, PsycINFO, Cochrane Central Register of Controlled Trials, ClinicalTrials.gov , WHO International	RCTs and observational studies	BMI	MD	Behaviour-Based Weight Loss: Pooled mean weight loss at 12–18 months: −2.39 kg (95% CI, -2.86 to -1.93). Behaviour-Based Weight Loss Maintenance: Pooled mean weight regain: −1.59 kg (95% CI, -2.38 to -0.79). Medication-Based Weight Loss: Weight loss ranged from -0.6 to -5.8 kg compared to placebo.	Quality: Studies rated as fair or good; poor-quality studies excluded. Key Points: Behaviour-based interventions were associated with moderate weight loss and reduced risk of diabetes. Medication-based interventions showed greater weight loss but higher rates of adverse events. Long-term health outcomes and subgroup data were limited.

			Clinical Trials Registry Platform. January 1, 2010 – June 6, 2017 (with ongoing surveillance through March 23, 2018).				Risk Reduction for Diabetes: Relative risk (RR): 0.67 (95% CI, 0.51 to 0.89). statistical heterogeneity was significant in pooled analyses, indicating variability in interventions and populations.	High attrition rates in medication trials were noted
De Stefani *et al.* 2018	N=15 studies, 178,644 participants; unintentional weight loss reported in 24,995 participants	Adults 50.3% women, mean age ranging from 42.2 to 75.3 years. Subgroups: older adults (≥65 years), overweight/obese populations (BMI ≥25 kg/m²), and participants with comorbidities (diabetes, cardiovascular disease, cancer, hypertension)	Medline/PubMed, Web of Science, SciELO, LILACS. Studies published up to October 2016. Countries: United States (9 studies), Australia, Finland, Israel, Netherlands, Norway, United Kingdom.	Observational cohort studies	BMI, weight loss, unintentional weight loss (WI without self-reported action e.g., diet, physical activity, medication use).	RR	For unintentional weight loss: Adjusted RR for all-cause mortality: 1.38 (95% CI: 1.23, 1.53). Subgroup analysis: Older adults: RR = 1.81 (95% CI: 1.59, 2.03). Overweight/obese: RR = 1.11 (95% CI: 1.04, 1.18). Participants without comorbidities: RR = 1.08 (95% CI: 0.95, 1.20). Adjusted RR for major cardiovascular events (MACE): 1.17 (95% CI: 0.98, 1.37).	Quality assessment: Newcastle-Ottawa Scale (NOS) for cohort studies. Studies with <4 stars excluded. Key Points: Unintentional weight loss significantly associated with increased all-cause mortality, especially in older adults and overweight/obese populations. No protective effect of unintentional weight loss for MACE. Methodological challenges include misclassification of weight loss categories and lack of dose-response analysis A lack of information on the intentionality of weight loss could explain part of the disagreements found among studies of weight loss, obesity, and mortality.

								Careful attention should be given to individuals with suspected unintended weight loss, particularly in overweight and obese, older adult, or unhealthy populations.
McDowell *et al.* 2018	N=11 (4 RCTs, 7 observational studies)	Patients with heart failure (HF) (either reduced ejection fraction [HFrEF] or preserved ejection fraction [HFpEF]) and obesity. Mean BMI ranged from 29.2 to 55 kg/m² across studies. Mean age ranged from 38 to 68.2 years.	PubMed, Embase, and CENTRAL. Search Year: November 2017.Publication Range: 1946–2017.	RCTs or observational studies	BMI	Nil	Weight Loss: RCTs reported weight loss ranging from -1.2 kg to -9.9 kg in intervention groups. Exercise Capacity: VO2max improvements ranged from +1.2 to +3.1 mL/kg/min in RCTs. Quality of Life: Significant improvements in MLHFQ and KCCQ scores in some studies. NYHA Classification: Improvements were significant in HFpEF populations but not consistently in HFrEF populations. Heterogeneity: High heterogeneity was noted due to differences in study designs, interventions, and populations.	Key Points Significant weight loss was achieved in most studies, particularly with bariatric surgery and lifestyle interventions. Improvements in VO2max and 6-min walk test were reported in some studies. Improvements were noted in Minnesota Living with Heart Failure Questionnaire (MLHFQ) and Kansas City Cardiomyopathy Questionnaire (KCCQ) scores. NYHA Classification: Improvements were observed in some studies Weight loss interventions were generally safe and showed trends toward improved cardiac function, exercise capacity, and quality of life. Bariatric surgery may be safe in HF patients through intensive optimization of pre-operative state and a multidisciplinary approach.
Ma *et al.* 2017	54 RCTs, 30,206 total participants	Adults with obesity (mean BMI ≥30 at baseline).	Medline, Embase, Cochrane	RCTs with a minimum follow-up of one year.	BMI	RR	Moderate quality evidence for an effect on cardiovascular mortality (n=8 trials, 134 events; risk ratio 0.93, 95% confidence interval 0.67 to	High-quality evidence for all-cause mortality reduction.

			Central Register of Controlled Trials, and full texts from the authors' trial registry. From 1966 to December 2015, with an updated search from August 2015 to December 2016. Countries: Trials were conducted in North America (57.4%), Europe (29.6%), Australia (3.7%), Brazil (1.9%), and Asian countries (9.3%).	Trials focused on dietary interventions targeting weight loss, with or without exercise advice or programs	Post hoc analyses included Asian populations with BMI ≥25	1.31; I2=0%) and very low quality evidence for an effect on cancer mortality (n=8 trials, 34 events; risk ratio 0.58, 95% confidence interval 0.30 to 1.11; I2=0%) (figs 3 and 4⇓). Limiting cardiovascular mortality to ACC/AHA defined events did not influence this result, as the data were identical (n=8 trials, 134 events; risk ratio 0.93, 95% confidence interval 0.67 to 1.31; I2=0%). Twenty four trials (15 176 participants) reported high quality evidence on participants developing new cardiovascular events (n=24, 1043 events; risk ratio 0.93, 95% confidence interval 0.83 to 1.04; I^2=0%) Weight change: After 1 year: Mean difference (MD) −3.42 kg (95% CI: −4.09 to −2.75 kg), I^2 = 92%. After 2 years: MD −2.51 kg (95% CI: −3.42 to −1.60 kg), I^2 = 89%. After ≥3 years: MD −2.56 kg (95% CI: −3.50 to −1.62 kg), I^2 = 87%.	Moderate-quality evidence for cardiovascular mortality. Very low-quality evidence for cancer mortality and new cancer events. All but one trial evaluated low fat, weight reducing diets. Weight-reducing diets, typically low in fat and saturated fat, may reduce premature all-cause mortality in people with obesity Limited evidence on cardiovascular and cancer outcomes highlights the need for further research
Zomer *et al.* 2016	98 studies assessing cardiovascular risk factors were included in the meta-analysis. At least 50 participants per trial arm were	Adults aged 18+ years. Studies included overweight and obese individuals (BMI ≥25 kg/m²). Excluded populations: pregnant/lactating	PubMed, Embase, Cochrane Library. Search Year/Range: Up to May 2013	RCTs Inclusion criteria: therapeutic weight loss interventions (diet, exercise, pharmacotherapy)- not bariatric surgery	BMI Mild (<5% weight loss). Moderate (5–10% weight loss).	Interventions that caused any weight loss: SBP: -2.68 mmHg (95% CI -3.37, -2.11). DBP: -1.34 mmHg (95% CI -1.71, -0.97). LDL Cholesterol: -0.20 mmol/L (95% CI -0.29, -0.10). Triglycerides: -0.13 mmol/L (95% CI -0.22, -0.03).	Publication bias detected, especially at shorter time points. Key points: interventions that cause weight loss contribute to reducing cardiovascular risk factors at least for the first two years and that these effects are seen with both mild

required for inclusion.	individuals, those with compromised systems (e.g., cancer, organ failure, mental illness, etc.	Fasting Plasma Glucose: -0.32 mmol/L (95% CI -0.43, -0.22). HbA1c: -0.40% (95% CI -0.52, -0.28).	(<5%) and moderate (5–<10%) weight loss Benefits were more pronounced in individuals aged ≥40 years.

6.4 Systematic review and meta-analyses for the impact of overweight and obesity on the risk of CVD

Table 6.4 Systematic review and meta-analyses for the impact of overweight and obesity on CVD outcomes/prognosis in people with CVD

Mortality / MACE **Study**	**n studies/ participants**	**Population**	**Databases Searched & Year/Range/ Countries**	**Study Designs**	**Obesity Measure**	**Effect Estimate**	**Results ES (95%CI), heterogeneity**	**Study Quality & Key points**
Nowark *et al.* 2024	82 studies (97 cohorts) included in the broader review. Specific participant numbers for cardiovascular disease (CVD) subgroup are not explicitly mentioned.	Specific to this: Adults with cardiovascular disease.	Pubmed, May 2000 – May 2023	Real-world cohorts with adjusted hazard ratios (HR) for all-cause mortality over at least 12 months.	BMI	HR	Among patients with cardiovascular diseases, the risk for all-cause mortality increased with BMI values below 25 kg/m2 but did not change noticeably for BMI values above that value (Table 1 in paper) ($p < 0.001$ for non-linearity,$I2 = 91.5\%$, $p < 0.001$).	Moderate quality, assessed using the Newcastle-Ottawa Scale (NOS). Key Points: BMI below 25 kg/m² increases mortality risk in CVD patients. No significant change in mortality risk for BMI above 25 kg/m². Results highlight the complexity of BMI's impact on mortality and suggest individualized clinical recommendations.
Wang *et al.* 2024	N=9, Participants: 25,798	Elderly patients (≥65 years) undergoing percutaneous coronary intervention (PCI).	PubMed, Cochrane, Embase. From inception to November 2022. Countries: Italy, China, USA,	Meta-analysis of observational studies.	BMI Underweight (<18.5 or <20 kg/m²) Normal weight (18.5–24.9 kg/m²)	RR	Underweight vs Normal Weight: RR: 1.52 (95% CI: 1.01–2.29), $I^2 = 59.4\%$, $p = 0.043$. Overweight vs Normal Weight: RR: 0.86 (95% CI: 0.77–0.95), $I^2 = 8.5\%$, $p = 0.384$. Obesity vs Normal Weight: RR: 0.57 (95% CI: 0.40–0.80), $I^2 = 61.2\%$, $p = 0.017$.	Articles scored ≥6 points on the Newcastle-Ottawa Scale (NOS), with most scoring >7 points, indicating high quality. Key Points: Demonstrates the 'obesity paradox' in elderly patients undergoing PCI. Overweight and obesity groups had decreased all-cause mortality

			Japan, Germany, Korea, Slovenia.		Overweight (25–29.9 kg/m²) Obesity (30–34.9 kg/m²).			compared to normal weight, while underweight had increased mortality. Limitations include lack of standard BMI classification in some studies, absence of central obesity measures, and exclusion of severe obesity (BMI ≥35 kg/m²). This meta-analysis provides evidence supporting the 'obesity paradox' in elderly PCI patients, suggesting further research is needed to explore underlying mechanisms.
Wattanachayakul *et al.* 2024	12 cohort studies included in the meta-analysis.	Patients with cardiac resynchronization therapy (CRT) devices, categorized as overweight, obese, underweight, or normal weight.	MEDLINE and EMBASE. From inception to January 2024.	Cohort studies.	BMI	RR	Overweight and obesity were associated with reduced all-cause mortality. Overweight: Pooled Risk Ratio (RR) = 0.77 (95% CI 0.69–0.87, I^2 = 47%). Obesity: Pooled RR = 0.81 (95% CI 0.67–0.97, I^2 = 59%). Underweight was associated with increased all-cause mortality. Underweight: Pooled RR = 1.37 (95% CI 1.14–1.64, I^2 = 0%). BMI as continuous data: Pooled Hazard Ratio (HR) = 0.94 (95% CI 0.89–0.98, I^2 = 72%). Higher BMI as continuous data was linked to decreased all-cause mortality.	NOS used Key Points: Observed an obesity paradox in CRT patients. Overweight and obesity were linked to reduced all-cause mortality. Underweight individuals had higher all-cause mortality. Further research is needed to understand underlying mechanisms and clinical implications

						Heterogeneity ranged from low to high (I^2 = 0%–72%).	
Liu *et al.* 2023	N=12, Participants: 54,397	ST-segment elevation myocardial infarction (STEMI) patients undergoing percutaneous coronary intervention (PCI).	PubMed, Web of Science, Embase, CNKI, Wanfang. From database inception to 2022. Countries: Israel, Korea, Portugal, USA, Netherlands, Spain, Switzerland, Taiwan, Italy, Germany, Japan, China.	Non-randomized controlled trials (Non-RCTs)	BMI Healthy-weight (18.5–24.9 kg/m²), Overweight (25.0–29.9 kg/m²), Obese (>30 kg/m²).	<u>In-hospital mortality</u> Overweight vs. Healthy-weight: OR = 0.66, 95% CI (0.58, 0.76), p < .001. I^2 = 40.9%, p = 0.118. Obese vs. Healthy-weight: OR = 0.60, 95% CI (0.51, 0.72), p < .001. I^2 = 0.0%, p = 0.718. Overweight vs. Obese: OR = 1.06, 95% CI (0.89, 1.27), p > .05. I^2 = 0.7%, p = 0.419. <u>Short-term mortality (30 days):</u> Overweight vs. Healthy-weight: OR = 0.66, 95% CI (0.58, 0.74), p < .001. I^2 = 42.1%, p = 0.141. Obese vs. Healthy-weight: OR = 0.62, 95% CI (0.53, 0.72), p < .001. I^2 = 0.0%, p = 0.636. Overweight vs. Obese: OR = 1.04, 95% CI (0.89, 1.22), p > .05. I^2 = 0.0%, p = 0.605. <u>Long-term mortality (≥1 year):</u> Overweight vs. Healthy-weight: OR = 0.63, 95% CI (0.58, 0.69), p < .001. I^2 = 6.3%, p = 0.377. Obese vs. Healthy-weight: OR = 0.59, 95% CI (0.52, 0.66), p < .001. I^2 = 0.0%, p = 0.955.	NOS used Key Points: The 'obesity paradox' exists in STEMI patients treated with PCI, showing lower mortality rates for overweight and obese patients compared to healthy-weight patients. No significant difference in mortality between overweight and obese patients. High BMI exhibits a protective effect on in-hospital, short-term, and long-term prognosis

							Overweight vs. Obese: OR = 1.07, 95% CI (0.95, 1.20), p > .05. I^2 = 0.0%, p = 0.762.	
Xie *et al.* 2023	N=20 studies, total participants NR	Patients experiencing cardiac arrest (CA) categorized by BMI: underweight, normal BMI, overweight, and obese. Includes both in-hospital and out-of-hospital cardiac arrest cases	PubMed, EMBASE, Scopus. Studies published until May 15, 2023. Countries: USA (7 studies), Republic of Korea (4 studies), Australia (2 studies), Taiwan (2 studies), Poland (1 study), Japan (1 study), Greece (1 study), Austria (1 study), France (1 study).	Retrospective: 17 studies. Prospective: 3 studies.	BMI Underweight (<18.5 kg/m²). Normal BMI (18.5–24.9 kg/m²). Overweight (25–29.9 kg/m²). Obese (≥30 kg/m²). Some studies used "nonobese" (<30 kg/m²) as a comparator group.	OR	<u>Overweight</u> In-hospital mortality: OR 0.96 (95% CI, 0.71–1.29), I^2 = 53.4%. Mortality within 6 months: OR 0.82 (95% CI, 0.64–1.06), I^2 = 31.6%. Mortality after 1 year: OR 0.57 (95% CI, 0.35–0.92), I^2 = 35.7%. Favourable neurological outcomes: OR 1.10 (95% CI, 0.86–1.42), I^2 = 31.7%. <u>Obese:</u> In-hospital mortality: OR 1.02 (95% CI, 0.88–1.18), I^2 = 73.1%. Mortality within 6 months: OR 1.07 (95% CI, 0.62–1.83), I^2 = 71.8%. Mortality after 1 year: OR 0.67 (95% CI, 0.51–0.89), I^2 = 0.0%. Favourable neurological outcomes: OR 0.95 (95% CI, 0.58–1.55), I^2 = 65.0%.	Newcastle-Ottawa Scale scores ranged from 6 to 8 (mean score: 7.4). Most studies were retrospective, introducing potential biases. Key Points: BMI does not significantly impact short-term mortality or neurological outcomes. Overweight and obese individuals show reduced long-term mortality risk, particularly for in-hospital cardiac arrest cases. Findings suggest the "obesity paradox" may apply to cardiac arrest outcomes. Place of arrest (in-hospital vs. out-of-hospital) significantly affects survival outcomes.
De Paola *et al.* 2022	27 studies included in the qualitative synthesis.	Adult patients aged 18 and older with a previous myocardial infarction (MI).	Medline (Ovid), EMBASE (Ovid), Web of Science.	Prospective cohort studies	BMI Underweight: BMI < 18.5 kg/m².	Adjusted Hazard Ratio (aHR)	<u>Mortality</u> Underweight: Adjusted Hazard Ratio (aHR): 1.42 (95% CI: 1.24–1.62). heterogeneity I^2 = 79%.	Moderate to high methodological quality. High heterogeneity in mortality outcomes.

	24 studies included in the meta-analysis. Total participants: 308,430 (132,759 women and 175,671 men)	Mean follow-up ranged from 6 months to 17 years. Majority of studies focused on older patients (mean age >65 years).	Search conducted on January 11, 2021, and updated on June 6, 2021. Countries: USA (13 studies), Germany (3), Japan (3), South Korea (2), Australia (1), Croatia (1), China (1), Denmark (1), France (1), Israel (1).		Normal weight: BMI 18.5–24.9 kg/m². Overweight: BMI 25–29.9 kg/m². Obese: BMI ≥ 30 kg/m². Morbidly obese: BMI ≥ 35 kg/m²		Overweight: aHR: 0.85 (95% CI: 0.76–0.94). heterogeneity I^2 = 86%. Obese: aHR: 0.86 (95% CI: 0.81–0.91). heterogeneity I^2 = 88%. Morbidly obese: HR: 0.89 (95% CI: 0.78–1.01). <u>Recurrence:</u> No statistically significant associations between BMI categories. <u>Hospital readmission:</u> No statistically significant associations between BMI categories.	Key Points: Overweight and obese patients had lower post-MI mortality risk (~15% reduction). Underweight patients had a significantly higher mortality risk (42% increase). No significant associations for recurrence or readmission outcomes.
Jiang *et al.* 2022	15 cohort studies with a total of 127,215 participants, out of which 73,999 were reported dead.	Pulmonary Hypertension patients.	PubMed, Scopus, Google Scholar. Studies published up to June 2021. Countries: United States (n = 8), China (n = 2), Kenya (n = 1), France (n = 1), Italy (n = 1), Israel (n = 1), Australia/New Zealand (n = 1).	Cohort studies	BMI	RR	Summary Relative Risk for mortality per 5-unit increment in BMI: 0.83 (95% CI: 0.77–0.89; I2 = 75.6%). Non-linear dose-response relation observed (P-non-linearity < 0.001), with the lowest risk at BMI 32–38 kg/m².	Six studies had high methodological quality (score ≥7), nine had low quality (<7) based on the Newcastle-Ottawa Scale. Key Points: Higher BMI is associated with decreased mortality among PH patients, supporting the "obesity paradox." The lowest mortality risk was observed at BMI 32–38 kg/m². Results should be interpreted cautiously, as they do not suggest causation or promote weight gain.

								Limitations include referral bias, residual confounders, and heterogeneity among studies.
Li *et al.* 2022	11 studies involving 69,273 participants.	Patients with heart failure with preserved ejection fraction (HFpEF). Mean age: 64 years; 52.4% female	PubMed and Embase. Up to February 2022. Countries: Studies conducted in the US (n = 4), Europe (n = 3), Asia (n = 2), Australia (n = 1), and one based on international cohorts.	2 post-hoc analyses of RCTs. 8 observational cohort studies. 1 individual patient data meta-analysis.	BMI Categorised into multiple ranges (e.g., <18.5, 18.5–24.9, 25–29.9, 30–34.9, ≥35 kg/m²). BMI analysed as both continuous and categorical variables.	HR	<u>All-cause mortality</u> Adjusted HR per 5-unit increase in BMI = 0.90 (95% CI: 0.84–0.95). U-shaped relationship with the lowest risk at BMI of 32–34 kg/m² <u>HF hospitalization</u> HR per 5-unit increase in BMI = 1.12 (95% CI: 1.05–1.19). Positive linear association. Moderate to high heterogeneity across studies ($I^2 > 50\%$).	Studies scored ≥6 on the Newcastle-Ottawa Scale (NOS), indicating moderate to high quality. Key Points: U-shaped relationship between BMI and all-cause mortality in HFpEF. Positive linear association between BMI and HF hospitalization. The 'obesity paradox' reconfirmed, suggesting potential protective effects of higher BMI in HFpEF patients. Limitations include residual confounding and reliance on BMI as an imperfect measure of obesity.
Lee *et al.* 2021	6 studies 2,427 participants	Adult patients with return of spontaneous circulation (ROSC) after out-of-hospital cardiac arrest (OHCA).	MEDLINE, EMBASE, Cochrane Library Up to July 16, 2021 Countries: USA, Japan, Korea, France, Greece	5 multicentre observational studies 1 single-centre observational study	BMI Underweight (<18.5 kg/m²) Normal weight (18.5–24.9 kg/m²) Overweight (25.0–29.9 kg/m²) Obese (≥30 kg/m²)	RR	<u>Neurological Outcomes</u> Overweight Patients: No significant difference in neurological outcomes compared to normal-weight patients (p = 0.72). Obese Patients: No significant difference in neurological outcomes compared to normal-weight patients (p = 0.31). <u>In-Hospital Mortality:</u> Overweight Patients:	Obese patients had higher in-hospital mortality compared to normal-weight patients but lower mortality compared to underweight patients. Overweight patients showed no significant differences in neurological outcomes or mortality compared to normal-weight patients

							No significant difference in in-hospital mortality compared to normal-weight patients (p = 0.50). Obese Patients: Higher in-hospital mortality compared to normal-weight patients (RR = 1.25; 95% CI = 1.12–1.39; p < 0.001; I^2 = 0%). Lower in-hospital mortality compared to underweight-to-normal-weight patients (RR = 0.87; 95% CI = 0.76–1.00; p = 0.04; I^2 = 38%).	
Marcks *et al.* 2021	Individual patient data analysis: included data from 5,819 participants with chronic heart failure (HF)	Patients with chronic HF, predominantly male (78%), with a mean age of 65 ± 12 years. Most had ischemic HF and HF with reduced ejection fraction (HFrEF). Co-morbidities such as hypertension, diabetes, COPD, and renal failure were common.	Medline, EMBASE, Cochrane Library, and Scopus in April 2017. (range not reported) Included cohorts from multiple countries, including the USA, Italy, Norway, Spain, Japan, Denmark, Sweden, Austria, and the Netherlands.	Individual patient data meta-analysis from pooled cohorts.	BMI Underweight (≤18.5 kg/m²) Normal weight (18.5–25.0 kg/m²) Overweight (25.0–30.0 kg/m²) Obese (>30.0 kg/m²)	HR	Lower BMI (≤18.5 kg/m²) was associated with worse outcomes (HR for mortality: 2.037, 95% CI: 1.366–3.039, p < 0.001). No significant protective effect of obesity was observed in younger patients (<75 years) without co-morbidities. Heterogeneity: Results varied significantly based on age and presence of co-morbidities. The obesity paradox was only observed in patients aged >75 years or with co-morbidities. After adjusting for biomarkers (NT-proBNP, hs-cTnT) and medications, BMI was no longer independently associated with outcomes.	Key points: The obesity paradox in HF is likely explained by less advanced disease and fewer co-morbidities in obese patients rather than a direct protective effect of obesity. Lower BMI may indicate cardiac cachexia and advanced disease. NT-proBNP levels were inversely correlated with BMI, while hs-cTnT and sST2 showed minimal or no association with BMI. This study challenges the notion of a direct protective effect of obesity in HF and highlights the importance of considering disease severity and co-morbidities in interpreting the obesity paradox.
Mahajan *et al.* 2020	N=29 studies 9 studies on obesity and HF:	General population across various BMI categories.	PubMed, Embase, Web of Science.	Meta-analysis of observational studies.	BMI: Underweight: <18.5 kg/m².	OR, HR	<u>Incidence of HF</u> J-curve relationship observed Underweight: OR 1.22 (95% CI 0.95–1.58).	Quality assessed using the Newcastle-Ottawa Scale. Low risk of detection and information biases.

375,056 participants. 11 studies on obesity and HF prognosis: 41,019 participants. 9 studies on intentional weight loss: Not specified.	Subgroups: Underweight, normal BMI, overweight, obese, and morbidly obese. Specific cohorts: Diabetic cohorts (3 studies)	January 1950 to April 3, 2018. Countries: Not explicitly mentioned, but studies included global populations.	Included RCTs, cohort studies, and registry-based studies.	Normal: 18.5–24.9 kg/m². Overweight: 25.0–29.9 kg/m². Obese: ≥30 kg/m². Severe obesity: >35 kg/m². Morbid obesity: >40 kg/m²	Overweight: OR 1.11 (95% CI 0.97–1.27). Obese: OR 1.62 (95% CI 1.32–1.99). Morbidly obese: OR 1.73 (95% CI 1.30–2.31). <u>CV Mortality</u> U-shaped curve observed. Overweight group had the least CV mortality. Substantial heterogeneity (I^2 ≥79%, p≤0.03). Underweight: HR 1.20 (95% CI 0.61–2.39). Overweight: HR 0.86 (95% CI 0.79–0.94). Obese: HR 0.97 (95% CI 0.72–1.33). <u>All-Cause Mortality:</u> Underweight: HR 1.40 (95% CI 1.25–1.57). Overweight: HR 0.88 (95% CI 0.79–0.98). Obese: HR 0.80 (95% CI 0.69–0.91). Morbidly obese: HR 0.80 (95% CI 0.77–0.83). <u>Intentional Weight Loss:</u> Reduction in left ventricular mass index: SMD −0.49 (95% CI −0.73 to −0.26; p<0.0001). Improvement in diastolic function: SMD 0.65 (95% CI 0.38 to 0.91; p<0.0001).	Key Points: Obesity increases HF risk but shows a paradoxical decline in all-cause mortality. Intentional weight loss improves cardiac structure and function. Further studies are needed to evaluate clinical outcomes of weight loss in HF patients.

							Reduction in left atrial size: SMD −0.39 (95% CI −0.72 to −0.07; p=0.02). Non-significant improvement in LVEF: SMD 0.43 (95% CI 0.00 to 0.86; p=0.05).	
Zhang J *et al.* 2019	N=10 studies Participants: 96,424 HFpEF: 59,263 participants HFrEF: 37,161 participants	HFpEF: Patients with preserved left ventricular ejection fraction (LVEF ≥ 50%). Mean age: 68 years Women: 38% HFrEF: Patients with reduced left ventricular ejection fraction (LVEF < 40%). Mean age: 60 years Women: 17%	PubMed and Embase June 1980 to April 2017 Countries: Most studies conducted in the USA, with additional studies from Canada, Israel, and MAGGIC meta-analysis data.	Prospective cohort studies Individual patient-data meta-analysis included	BMI	HR	<u>HFpEF:</u> U-shaped relationship between BMI and all-cause mortality. Hazard Ratio (HR) per 5-unit increase in BMI: 0.93 (95% CI: 0.89-0.97) Lowest mortality at BMI 32-33 kg/m². Heterogeneity: I^2 = 75.8%, p = 0.01. <u>HFrEF:</u> U-shaped relationship, flatter than HFpEF. Hazard Ratio (HR) per 5-unit increase in BMI: 0.96 (95% CI: 0.92-0.99) Lowest mortality at BMI 32 kg/m². Heterogeneity: I^2 = 95%, p < 0.001.	Key Points: Confirms the obesity paradox in heart failure patients. U-shaped relationship observed for both HFpEF and HFrEF. Nadir of risk at BMI 32-33 kg/m². Whether interventions to alter BMI affect risk remains unknown.
Zhang, K *et al.* 2019	N=72 studies (40 in meta-analysis)	Adult patients undergoing coronary artery bypass grafting (CABG)	PubMed, Web of Science, CINAHL, and Cochrane Library. Articles published before June 30, 2018.	Experimental studies (e.g., randomized controlled trials, pre-post studies). Observational studies (e.g., longitudinal	BMI	OR	Odds of post-CABG readmission among patients with overweight were 30% lower than normal-weight counterparts. [OR 0.70 (0.58, 0.85)] Odds of mid-to-long-term post-CABG mortality among patients with overweight were 20% lower than normal-weight counterparts.[OR 0.80 (0.67, 0.94)]	Study findings suggest that patients with overweight, but not obesity, had lower readmission and mid-to-long-term mortality rates following CABG compared to normal-weight counterparts.

				studies, case-control studies, cross-sectional studies).			No significant differences in readmission or mortality rates were found between patients with obesity and their normal-weight counterparts. See Table 2 in study for each comparison.	
Jayedi *et al.* 2018	N=14 studies with a total of 489,222 hypertensive patients. 41,872 cases of all-cause mortality and 2,123 cases of cardiovascular mortality	Patients with established hypertension (HTN). Studies included participants from Asia, the US, Europe, and multinational studies in Europe and the US. Mean follow-up duration: 7 years (range: 2–18.6 years). Predominantly older participants (mean age >50 years in most studies).	PubMed and Scopus. Search conducted up to January 25, 2017. Studies from Asia, the US, Europe, and multinational studies.	13 prospective cohort studies and 1 retrospective cohort study. Seven studies were prospective evaluations within RCTs	BMI (continuous and categories)	RR and HR	<u>CVD Mortality</u> RR = 0.95 (95% CI: 0.88, 1.02), P = 0.15, I^2 = 90.3% <u>All-cause mortality</u> RR = 0.92 (95% CI: 0.87, 0.97), P = 0.003, I^2 = 95.7% Nonlinear dose-response analysis suggested a reverse J-shaped association, with a nadir at BMI of 27.5–30 kg/m² Extreme heterogeneity observed in analyses (I^2 > 90%).	Evidence of the 'obesity paradox' in hypertensive patients, with lower mortality risk at BMI 27.5–30 kg/m². Strong influence of age on the BMI-mortality association, with the obesity paradox more evident in older patients (>60 years). Results should be interpreted cautiously due to the observational nature of included studies. Limited data for BMI >35 kg/m² in Western countries and >30 kg/m² in Asian countries
Ma *et al.* 2018	N=7 studies with 25,035 participants	Adult patients who suffered cardiac arrest (CA) of any aetiology. Included both out-of-hospital cardiac	PubMed, Embase, Ovid/Medline, and EBM Reviews.	Observational studies: 4 prospective and 3 retrospective.	BMI Underweight: BMI < 18.5 Normal weight: BMI 18.5–24.9	OR	<u>Underweight vs. Normal Weight</u> Higher mortality in underweight patients: OR 1.35 (95% CI 1.10–1.66), P = 0.004, I^2 = 17%. <u>Overweight vs. Normal Weight</u> Increased hospital survival: OR 0.80 (95% CI 0.65–0.98), P = 0.03, I^2 = 62%.	Quality assessed using Newcastle-Ottawa Scale (NOS): 6 studies scored >6 (high quality). 1 study scored 6 (intermediate quality). Key Points:

		arrest (OHCA) and in-hospital cardiac arrest (IHCA) patients. Some studies included patients treated with targeted temperature management (TTM) or extracorporeal cardiopulmonary resuscitation (ECPR).	Search conducted by the end of September 2017. Studies conducted between 1990 and 2015. Countries: USA, France, Italy, Korea, and Australia.		Overweight: BMI 25–29.9 Obese: BMI ≥ 30 One study used WHO classification for Asian populations, and another included severe obesity (BMI ≥ 35).		Better neurological recovery: OR 0.72 (95% C 0.61–0.85), P < 0.001, I^2 = 0%. <u>Obese vs. Normal Weight:</u> No significant difference in survival or neurological outcomes: OR 0.90 (95% CI 0.74–1.10), P = 0.31, I^2 = 67%.	Low BMI was associated with lower survival rates. Overweight patients had better survival and neurological outcomes. No significant difference in outcomes between obese and normal weight patients. High heterogeneity observed in survival outcomes due to differences in study populations, sample sizes, and follow-up periods. Limited data on severe obesity (BMI ≥ 35). Observational nature of studies limits causal inference.
Qin *et al.* 2017	N=14 prospective cohort studies. 46,794 heart failure (HF) patients with 13,508 death cases.	Subjects diagnosed with HF Stratified analyses conducted for patients aged over 60 years.	PubMed and EMBASE. Search conducted through March 2016.	Prospective cohort studies	BMI	HR	Patients with BMI >28 kg/m² had better survival, while underweight and severe obesity (BMI >37 kg/m²) were associated with higher mortality. HR per 5 kg/m² increase in BMI: 0.95 (95% CI = 0.92–0.97). High heterogeneity observed (I^2 = 90.10%, Pheterogeneity < 0.00001). Stratified analyses reduced heterogeneity in patients aged >60 years.	Quality assessed using the Newcastle-Ottawa scale. Studies ranked as low (below 3 stars), moderate (4–6 stars), or high quality (7–9 stars). Key points: U-shaped association between BMI and mortality in HF patients. Higher BMI (>28 kg/m²) linked to better survival. Underweight and severe obesity associated with increased mortality.

							U-shaped nonlinear relationship between BMI and all-cause mortality risk (Pnonlinearity = 0.0025)	
Wang *et al.* 2016	N=20 prospective studies Total participants: 82,076 Total deaths: 17,751	Patients who experienced acute myocardial infarction (AMI). Subgroups included STEMI, NSTEMI, and those who underwent PCI.	PubMed and Embase Year/Range: Studies published in English prior to March 2015	Prospective observational studies.	BMI Healthy weight: BMI < 25 kg/m² Overweight: BMI 25–30 kg/m² Obesity: BMI > 30 kg/m²	RR	<u>Healthy weight vs. Overweight/Obese</u> In-hospital mortality: RR = 0.72 (95% CI: 0.57–0.90), P = 0.0044, I² = 78% Short-term mortality: RR = 0.39 (95% CI: 0.28–0.55), P < 0.01, I² = 0% Medium-term mortality: RR = 0.66 (95% CI: 0.55–0.78), P < 0.01, I² = 64% Long-term mortality: RR = 0.68 (95% CI: 0.57–0.81), P < 0.01, I² = 95% <u>Obesity vs. Overweight</u> In-hospital mortality: RR = 0.82 (95% CI: 0.64–1.06), P = 0.1343, I² = 47% Short-term mortality: RR = 0.94 (95% CI: 0.55–1.58), P > 0.05, I² = Not significant Medium-term mortality: RR = 0.82 (95% CI: 0.65–1.04), P > 0.05, I² = Not significant Long-term mortality: RR = 0.98 (95% CI: 0.88–1.09), P > 0.05, I² = Not significant	Quality assessed using the Newcastle–Ottawa Scale. Studies with scores ≥7 were included. Key findings: Overweight and obesity were inversely associated with all-cause mortality compared to healthy weight, supporting the 'obesity paradox ' No significant difference in mortality risk between obese and overweight patients. Heterogeneity was observed in some analyses, but sensitivity analyses confirmed robustness of results.

Outcomes of/following SURGERY

Study	n studies/ participants	Population	Databases Searched & Year/Range/ Countries	Study Designs	Obesity Measure	Effect Estimate	Results ES (95%CI), heterogeneity	Study Quality & Key points

Yasmin *et al.* 2025	N=24 studies, 38,743 participants	Patients with aortic stenosis (AS) aged ≥18 years undergoing transcatheter aortic valve implantation (TAVI)	PubMed (MEDLINE) and Scopus. Studies published from inception to January 2023. Countries: Studies conducted in the USA, Netherlands, Italy, Canada, Germany, France, Spain, Israel, Korea, Belgium, and others.	Observational studies	BMI	HR, OR	Long-term overall survival between pt with obesity vs healthy weight: pooled estimates based on a random-effects model: HR 0.87, 95% CI 0.82-0.93, P<0.00001; I2=5% Significant improvement could be seen for long-term overall survival with every 1 kg/m2 increase in BMI HR 0.96, 95% CI 0.94-0.98, P<0.0001; I2=45% 30-day mortality: OR 0.71 (95% CI 0.60–0.84, P<0.0001). No significant difference was observed between pt with obesity healthy weight patients in MI OR 0.84, 95% CI 0.52-1.34, P=0.66; I^2=0% Or major bleeding (OR 0.94, 95% CI 0.72-1.21, P=0.02; I^2=54%) and major vascular events (OR 1.18, 95% CI 0.97-1.43, P=0.51; I^2=0%)	High quality; Newcastle-Ottawa Scale (NOS) scores ranged from 7 to 9 Key points: Obesity was associated with reduced 30-day mortality and improved long-term survival. No significant differences in procedural complications (MI, major bleeding, vascular events)
An *et al.* 2024	N=6 studies comprising 3928 patients and 12,048 grafts.	Patients undergoing coronary artery bypass grafting (CABG) with systematic postoperative coronary imaging.	Ovid MEDLINE, Ovid Embase, Cochrane Library (Wiley). From database inception to July 18, 2022. Countries: USA, Canada, Netherlands, and 33 nations (COMPASS trial).	RCTs	BMI	OR	Obesity was associated with reduced graft failure at the individual graft level [adjusted odds ratio 0.98 (95% CI 0.97–0.99), P = 0.01], but not at the patient level [adjusted odds ratio 0.99 (95% CI 0.97–1.01), P = 0.25]. Adjusted Odds Ratio (aOR) for graft failure at the individual graft level: BMI (continuous): aOR 0.98 (95% CI 0.97–0.99), p = 0.01. Overweight: aOR 0.79 (95% CI 0.64–0.96), p = 0.02.	Strengths: Systematic imaging follow-up at 1 year, individual graft-level analysis, adjustment for confounders. Limitations: Heterogeneity in surgical/postoperative protocols, missing BMI data for 11% of imaged patients, inability to assess timing of silent graft failure. Key Point: Findings suggest an 'obesity paradox' with reduced graft failure in overweight and mild-to-moderately obese patients.

							Obesity class 1: aOR 0.81 (95% CI 0.64–1.01), p = 0.06. Obesity class 2: aOR 0.61 (95% CI 0.45–0.83), p = 0.001. Obesity class 3: aOR 0.94 (95% CI 0.62–1.42), p = 0.75.	
Hoffman *et al.* 2024	3 studies identified in the systematic review, comprising 1,348 patients. Combined with institutional data, total participants = 1,738	Adults undergoing mechanical thrombectomy (MT) for anterior circulation large vessel occlusion (LVO).	PubMed, Scopus, Embase. Search performed: October 10, 2022. Institutional data: January 2015 to December 2021.	Institutional cohort: Retrospective analysis. Systematic review: Original data studies evaluating BMI and MT outcome	BMI		When analyzing BMI ordinally, obesity was associated with lower odds of favorable 90-day mRS (OR 0.42, 95% CI 0.20–0.86) compared with normal weight. Meta-analysis: OR 0.89 (95% CI 0.63–1.24). (no association) Favorable 90-day mRS: Institutional cohort: Obesity associated with worse outcomes. Meta-analysis: No significant association (OR 0.89, 95% CI 0.63–1.24, I^2 = 40.5%). Mortality: Meta-analysis: No significant association (OR 0.95, 95% CI 0.62–1.48, I^2 = 59.9%).	Quality—high- NOS scores 8/9, and two 9/9. Key Points: Institutional analysis showed obesity associated with worse functional outcomes. Meta-analysis eliminated associations with 90-day mRS and mortality. Limited by small number of studies, heterogeneity in BMI Suggests obesity paradox may not apply to MT for LVO.
Abi-Jaoude *et al.* 2023	N=8 studies with a total of 171,648 participants.	Adult patients with peripheral arterial disease (PAD) who underwent lower extremity revascularization (endovascular, open, or hybrid techniques)	MEDLINE, EMBASE, Web of Science), CINAHL, Cochrane Library Inception to November 16, 2021.	Cohort studies	BMI	RR	Mortality: RR = 0.78 (95% CI: 0.71–0.85), P < .001, I^2 = 0%. Major Adverse Cardiovascular Events: RR = 0.86 (95% CI: 0.77–0.97), P = .01, I^2 = 0%. Major Adverse Limb Events: RR = 1.02 (95% CI: 0.93–1.11), P = .73, I^2 = 15%.	Quality: 2 studies (25%) rated high quality (low risk of bias). 6 studies (75%) rated fair quality (moderate risk of bias). Median NOS score: 6 stars (moderate risk of bias) GRADE: All outcomes rated as "very low quality" due to serious risk of bias,

			Countries: USA, Hungary, Poland, South Korea, UK				Surgical Site Infections: RR = 1.69 (95% CI: 1.34–2.14), P < .001, I^2 = 78%. Endovascular Access Site Complications: RR = 1.11 (95% CI: 0.76–1.63), P = .58, I^2 = 86%. Perioperative Complications: RR = 1.04 (95% CI: 0.84–1.28), P = .73, I^2 = 92%	inconsistency, imprecision, and suspected publication bias. Key points: Obesity associated with more medical comorbidities, including diabetes, coronary artery disease, and congestive heart failure, but not PAD severity at presentation. Obesity was associated with an overall 22% reduced risk in mortality, and this reduced risk persisted with both endovascular and open surgery. Obesity was associated with a 14% reduced risk for MACE in open surgery only, with an increased risk of surgical site infections across all revascularization procedures.
Seo *et al.* 2022	N=26 studies, 74,163 participants	Patients undergoing transcatheter aortic valve replacement (TAVR) with varying BMI categories (normal, overweight, obesity).	PubMed and Embase Up to June 26, 2022 Countries: Studies were conducted in multiple countries, including the USA, Italy, Netherlands, Canada, Germany,	Retrospective observational	BMI	OR	Overweight was associated with lower risk of short-term mortality (HR: 0.77; 95% CI: 0.60–0.98) and mid-/long-term mortality (HR: 0.79; 95% CI: 0.70–0.89). Obesity was associated with lower risk for mid-/long-term mortality (HR: 0.79; 95% CI: 0.73–0.86), but no difference was observed in short-term mortality, although a trend was noted (HR: 0.87l 95% CI: 0.74–1.01) Major Vascular Complications: Obesity: OR 1.33 (95% CI: 1.05–1.68), I^2 = 40.85% Permanent Pacemaker Insertion:	Studies were assessed using the Newcastle–Ottawa Scale (NOS). Mean score of 7.9, indicating high quality. Overweight and obesity were associated with lower mid-/long-term mortality risk compared to normal BMI. Obesity was linked to higher odds of major vascular complications and permanent pacemaker implantation. The "obesity paradox" may be influenced by confounding factors such as age and frailty.

			France, China, Sweden, Poland, and others.				Overweight: OR 1.16 (95% CI: 1.03–1.30), I^2 = 0% Obesity: OR 1.26 (95% CI: 1.06–1.50), I^2 = 37.33%	Standardized BMI classification and prospective studies are needed for further validation
Mei *et al.* 2021	N=15 studies with a total of 138,592 participants.	Adult patients who underwent percutaneous coronary intervention (PCI).	PubMed, Embase, and Cochrane. Up to April 2020. Countries: USA, Switzerland, Netherlands, Japan, Italy, Korea, China, and Australia.	Meta-analysis of observational studies, including cohort studies.	BMI	HR	Pooled HR for all-cause mortality: 0.60 (95% CI: 0.45–0.82) comparing the highest BMI category (mean = 33.32 kg/m²) with the lowest category (mean = 18.89 kg/m²).*I^2 = 86.6* A U-shaped dose-response curve was observed, with higher mortality at BMI <27 kg/m² and >32 kg/m². The nadir of risk was at BMI 27–32 kg/m²	Quality Assessment: All included studies scored ≥7 points on the Newcastle–Ottawa Scale (NOS), indicating high quality. Key Points: The 'obesity paradox' observed in patients undergoing PCI, with the lowest mortality risk observed in overweight and obese patients (BMI 27–32 kg/m²). Underweight patients had the highest risk of all-cause mortality. The findings provide guidance for prognostic management post-PCI. Limitations include variability in BMI categories across studies and the inability to assess other prognostic indicators beyond all-cause mortality.
Liu *et al.* 2020	41 studies with 54,300 cases/1,774,387 postcardiac surgery patients.	Adult patients undergoing various cardiac surgeries, including coronary artery bypass grafting (CABG), valve surgery, aortic surgery, and left ventricular	PubMed and Embase. Through April 2019. Countries: Studies conducted in America (21), Europe (13),	Randomized clinical trials, cohort studies, and case-control studies	BMI	RR	Pooled RR for all-cause mortality was 0.93 (95% CI 0.89–0.97) for every 5-unit increment in BMI, indicating that higher BMI did not increase the risk of all-cause mortality in patients after cardiac surgery. A U-shaped association with the nadir of risk at a BMI of 25–27.5 kg/m2 was observed, as well as a higher mortality risk for the	Quality assessed using the Newcastle-Ottawa Scale (NOS); studies with NOS score ≥7 points were considered acceptable. Key findings: Slightly higher BMI (25–27.5 kg/m²) may improve survival.

		assist device (LVAD) implantation.	Oceania (4), Asia (2), and 1 multi-country study.				underweight and the extremely obese patients **E**RR = 0.95 (95% CI 0.92–0.98) for every 5-unit BMI increment. (I^2 = *96%*). U-shaped dose-response curve with increased mortality risk for BMI <21.5 kg/m² and BMI >53 kg/m².	Underweight and extreme obesity (BMI >53 kg/m²) are associated with worse prognosis. Limitations include reliance on BMI as a measure of adiposity, retrospective study designs, and significant heterogeneity across studies.
ARRYTHMIA								
Study	**n studies/ participants**	**Population**	**Databases Searched & Year/Range/ Countries**	**Study Designs**	**Obesity Measure**	**Effect Estimate**	**Results ES (95%CI), heterogeneity**	**Study Quality & Key points**
Folli *et al.* 2024	N=50 studies, Total participants: 15,134,939 (15,115,181 for newly diagnosed AF; 19,758 for recurrent post-ablation AF)	Participants with newly diagnosed AF and recurrent post-ablation AF.	PubMed, Embase, Cochrane Library. Search range: From inception to January 31, 2023.	Prospective and retrospective cohort studies, case-control studies.	BMI	OR	Newly diagnosed AF: Significant increase in AF risk for overweight OR 1.32 (95% Ci 1.26, 1.38) Obesity OR 1.71 (1.59, 1.84) excessive obesity OR 1.77 (1.48, 2.12) compared to normal weight (p < 0.01). Recurrent post-ablation AF: Significant increase in AF risk for obesity 1.36 (1.14, 1.68) and excessive obesity OR 1.40 (1.09, 1.81) but not overweight 1.11 (0.97, 1.26) compared to normal weight (p < 0.01).	Mean NOS score: 7.1 ± 1.40 for recurrent post-ablation AF studies; 5.6 ± 1.04 for newly diagnosed AF studies. Key findings: Obesity is a stronger risk factor for newly diagnosed AF than recurrent post-ablation AF. Obese women are more affected than men. Underweight has no significant effect on AF risk. Maintaining normal BMI is critical for prevention and better ablation outcomes.
Liu *et al.* 2023	N=26 studies, 7,878 cases / 26,450 individuals	Patients with atrial fibrillation (AF) undergoing radiofrequency ablation.	PubMed, EMBASE, Cochrane Library Until October 5, 2021	Cohort studies	BMI	RR	For every 5 kg/m² increase in BMI, the risk of AF recurrence increased by 15% (RR = 1.15, 95% CI: 1.08–1.22).	Quality: Majority of studies scored ≥7 points on the Newcastle-Ottawa Scale, Key Points: Positive linear association between BMI and AF recurrence post-ablation.

			Countries: North America (USA and Canada), Asia, Europe					Overweight and obesity (BMI > 28 kg/m²) are significantly associated with AF recurrence. Obesity is an independent risk factor for AF recurrence, even after adjusting for confounders like obstructive sleep apnoea, hypertension, and left atrial diameter.
Liu *et al.* 2021	35 cohorts involving 33,271 cases and 141,442 patients	Patients undergoing cardiac surgery, including coronary artery bypass grafting (CABG), valve surgery, and mixed cardiac surgeries.	PubMed, Cochrane Library, and EMBASE. Search conducted through December 2019. North America (17 cohorts), Europe (12 studies), Asia (5 studies), and Oceania (1 study).	Included randomized controlled trials (RCTs), cohort studies, and nested case-control studies. Most studies were cohort studies.	BMI	RR	Summary risk ratio (RR) for a 5-unit increase in BMI: 1.09 (95% CI [1.06–1.12]). Obesity (BMI ≥30) significantly increased the risk of postoperative atrial fibrillation (RR: 1.39, 95% CI [1.21–1.61]). Being overweight (BMI 25–29.9) or underweight (BMI <18.5) did not significantly increase POAF risk Overweight: RR 1.03 (95% CI [0.95–1.11], P = 0.48). Underweight: RR 1.44 (95% CI [0.90–2.30], P = 0.13). Significant heterogeneity observed (I^2 = 82%).	All included studies had a Newcastle-Ottawa Scale (NOS) score ≥6, indicating acceptable quality. Strengths: Large sample size, robust statistical analysis, and subgroup analyses confirming findings. Limitations: Observational study designs, significant heterogeneity, and lack of long-term POAF incidence data. Key finding: High BMI independently increased POAF risk, while being overweight or underweight did not significantly affect risk.
STROKE								
Study	**n studies/ participants**	**Population**	**Databases Searched & Year/Range/ Countries**	**Study Designs**	**Obesity Measure**	**Effect Estimate**	**Results ES (95%CI), heterogeneity**	**Quality & Key points**
Qian *et al.* 2025	18 studies included, involving	Patients with a definite diagnosis of stroke.	Web of Science, Cochrane Library, Embase, PubMed,	11 prospective cohort studies, 4 longitudinal studies, and 3	BMI	RR	Underweight: Increased recurrence risk of stroke (RR = 1.59, 95% CI 1.33–1.90).	Quality: 13 studies were high quality, and 5 were moderate quality based on the Newcastle-Ottawa Scale (NOS).

	165,366 participants.		Chinese Biomedical Literature (CBM), CQVIP, WanFang Database, and China National Knowledge Infrastructure (CNKI). From inception to February 2025. Countries: United States, Denmark, China, Japan, Korea, Greece, Turkey, and Germany.	case–control studies.			Overweight: Decreased recurrence risk of stroke (RR = 0.91, 95% CI 0.86–0.96). Obesity: Decreased recurrence risk of stroke (RR = 0.89, 95% CI 0.84–0.94). Dose–response analysis: Each 1-unit increase in BMI reduces stroke recurrence risk by 2% (RR = 0.98, 95% CI 0.96–0.99).	Key Points: Underweight is a risk factor for stroke recurrence. Overweight and obesity were 'protective factors', supporting the 'obesity paradox'
Wei *et al.* 2025	14 studies included in the systematic review (136,581 participants) [12 in the MA]	Adult stroke or transient ischemic attack (TIA) survivors.	PubMed, EMBASE, Cochrane CENTRAL. up to January 20, 2025. Countries: United Kingdom, United States, Denmark, Germany, Turkey, China, Japan, Australia, Canada, Israel,	1 randomized controlled trial (RCT). 6 retrospective studies. 7 prospective studies	BMI	RR, HR	Obese vs. Non-Obese: RR = 0.89 (95% CI: 0.71–1.13), P = 0.34, I^2 = 97%. HR = 0.85 (95% CI: 0.75–0.97), P = 0.01, I^2 = 85%. Protective effect observed in older adults (≥ 65 years): HR = 0.82 (95% CI: 0.70–0.96), P = 0.01, I^2 = 88%. Overweight vs. Normal Weight: HR = 0.89 (95% CI: 0.80–1.00), P = 0.05, I^2 = 86%.	Quality assessed using Newcastle-Ottawa Scale (NOS): Scores ranged from 6 to 8 (moderate quality). Key Points: Overweight and obesity may be associated with a lower risk of stroke recurrence, particularly in older adults and during long-term follow-up (≥ 3 years). Particularly in older adults and long-term follow-up.

			Italy, Czech Republic.				Protective effect in long-term follow-up (≥ 3 years): HR = 0.91 (95% CI: 0.84–0.98), P = 0.01, I^2 = 17%. Underweight vs. Normal Weight: HR = 1.14 (95% CI: 0.95–1.36), P = 0.16, I^2 = 63%	
Qin *et al.* 2024	N=32 cohort studies, 330,353 participants	Patients with stroke	PubMed, Web of Science, Embase, The Cochrane Library, CNKI, CBM, Wanfang Database, and VIP Database From database inception to January 1, 2023 Studies conducted in China, Korea, America, Germany, Denmark, The Czech Republic, Greece, Singapore, Canada, Switzerland, and Japan	Cohort studies	BMI	HR	Mortality: Underweight vs. Normal: RR = 1.78 (95% CI: 1.60–1.96) I^2 43.7% Overweight vs. Normal: RR = 0.81 (95% CI: 0.74–0.89) I^2 53.1% Obesity vs. Normal: RR = 0.76 (95% CI: 0.72–0.81) I^2 47.2% Functional Outcomes (mRs ≥3): Underweight vs. Normal: RR = 1.33 (95% CI: 1.22–1.45) I^2 38.7% Overweight vs. Normal: RR = 0.92 (95% CI: 0.89–0.96) I^2 0% Obesity vs. Normal: RR = 0.89 (95% CI: 0.84–0.94) I^2 19.3% Stroke Recurrence: Underweight vs. Normal: RR = 1.19 (95% CI: 1.04–1.37) I^2 0% Overweight vs. Normal: RR = 1.03 (95% CI: 0.90–1.17) I^2 69.1% Obesity vs. Normal: RR = 0.93 (95% CI: 0.87–1.00) I^2 0%	Studies scored using the Newcastle-Ottawa Scale (NOS) 2 studies scored 9 points, 16 studies scored 8 points, 11 studies scored 7 points, and 3 studies scored 6 points (high quality overall) Key points: Underweight BMI is associated with increased mortality, poor functional outcomes, and stroke recurrence. Overweight and obesity are associated with reduced mortality and better functional outcomes, supporting the "obesity paradox."

							High heterogeneity	
Li *et al.* 2017	N=5 studies, 7752 participants.	Stroke patients with a history of stroke or transient ischemic attack (TIA).	PubMed, EMBASE, Google Scholar, and conference proceedings of the International Stroke Conference. From inception until July 2016. Countries: 2 studies from the United States, 3 studies from China	Prospective cohort studies.	NR (abdominal obesity as part of MetS(	RR	Pooled relative risk (RR) for recurrent stroke associated with MetS: 1.52 (95% CI: 1.17-1.97). $I^2 = 0\%$ Elevated glycemia had the highest RR: 1.70 (95% CI: 1.12-2.56). Other components (elevated blood pressure, triglycerides, low HDL cholesterol, obesity) showed weaker associations.	Quality scores ranged from 7 to 9 points (moderate to high quality). Key points: MetS is a significant predictor of recurrent stroke. Elevated glycemia is the strongest individual predictor among MetS components.
Huang *et al.* 2016	15 studies with 122,472 stroke patients.	Stroke patients at baseline (ischemic or haemorrhagic stroke)	PubMed (1966–December 15, 2015), EMBASE (1947–December 15, 2015), Cochrane Library Database (Issue 11, 2015). Manual search of abstracts from AHA, ASA, and AAN scientific meetings.	Prospective cohort studies. Follow-up duration ranged from 3 to 60 months (median: 31.2 months).	BMI	RR, HR	Total Mortality: Underweight: RR = 1.54 (95% CI: 1.31–1.82, p = 3.66×10^{-7}, $I^2 = 82.9\%$). Overweight: RR = 0.89 (95% CI: 0.78–1.01, p = 0.068, $I^2 = 84.8\%$). Obesity: RR = 0.83 (95% CI: 0.73–0.93, p = 0.002, $I^2 = 77.8\%$). Recurrent Stroke Events: Underweight: RR = 1.03 (95% CI: 0.81–1.32, p = 0.797, $I^2 = 0.0\%$). Overweight: RR = 0.96 (95% CI: 0.90–1.04, p = 0.315, $I^2 = 0.0\%$).	Quality assessed using Newcastle-Ottawa Scale (NOS): Median score: 8.0 (IQR: 1.5). 13 studies rated as high quality, 2 as moderate quality. Key points: Obesity associated with lower total mortality and recurrent stroke events. Underweight associated with higher total mortality. Results consistent across subgroup and sensitivity analyses.

			Studies conducted in Europe, Asia, North America, and globally.				Obesity: RR = 0.89 (95% CI: 0.77–1.02, p = 0.096, I^2 = 40.0%).	Dose-response analysis showed nonlinear trend for total mortality and linear trend for recurrent stroke events.
ACUTE CORONARY SYNDROME								
Study	**n studies/ participants**	**Population**	**Databases Searched & Year/Range/ Countries**	**Study Designs**	**Obesity Measure**	**Effect Estimate**	**Results ES (95%CI), heterogeneity**	**Quality & Key points**
Şaylık *et al.* 2023	54 studies with 534,903 participants	Patients with acute coronary syndrome (ACS).	PubMed, Google Scholar, Cochrane Library. Timeline NR	Not explicitly reported	BMI	RR	Overweight 30-day mortality: RR = 0.69 (0.62–0.76), p < 0.01, I^2 = 65%. Long-term mortality: RR = 0.73 (0.70–0.77), p < 0.01, I^2 = 47%. Obesity: 30-day mortality: RR = 0.61 (0.52–0.70), p < 0.01, I^2 = 81%. Long-term mortality: RR = 0.68 (0.62–0.74), p < 0.01, I^2 = 76%. Low-weight patients: 30-day mortality: RR = 1.74 (1.39–2.18), p < 0.01, I^2 = 40%. Long-term mortality: RR = 2.06 (1.61–2.65), p < 0.01, I^2 = 92%.	Quality Assessment: Studies scored 6–9 on the Newcastle-Ottawa scale, indicating excellent quality. Dose-response meta-analysis: U-shaped association between BMI and mortality risk, with lowest risk at approximately 30 kg/m². Patients with overweight or obesity had lower mortality risks compared to normal-weight patients. Low-weight patients had higher mortality risks. BMI < 21.5 kg/m² and > 40 kg/m² were associated with higher mortality risk
Jelavic *et al.* 2023	N=24 studies, 585,919 participants	Patients with acute coronary syndrome (ACS),	PubMed and ScienceDirect.	23 cohorts, 1 RCT	BMU	OR	<u>Overweight (BMI 25.0–29.9 kg/m²) vs. Healthy Weight:</u>	Key points: Overweight and obesity are associated with lower risks of adverse outcomes

including unstable angina (UA), non-ST-elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarction (STEMI).	Studies enrolled between 1989–2020. Countries: USA (8), Europe (6), China (3), New Zealand (1), Australia (1), Japan (1), Israel (2), International (2).	Hypertension: OR = 1.28, CI [1.22–1.33], p = 0.000 Hyperlipidaemia: OR = 1.34, CI [1.27–1.42], p = 0.000 Diabetes: OR = 1.37, CI [1.31–1.44], p = 0.000 Peripheral Arterial Disease (PAD): OR = 0.80, CI [0.74–0.86], p = 0.000 Heart Failure (HF): OR = 0.84, CI [0.79–0.89], p = 0.000 Cardiogenic Shock: OR = 0.82, CI [0.78–0.87], p = 0.000 Cardiac Arrest: OR = 0.90, CI [0.84–0.96], p = 0.002 Reinfarction: OR = 0.87, CI [0.79–0.95], p = 0.001 Overall Death: OR = 0.64, CI [0.59–0.69], p = 0.000 Total In-Hospital Complications: OR = 0.77, CI [0.73–0.82], p = 0.000 Cardiovascular Death (Follow-Up): OR = 0.78, CI [0.69–0.89], p = 0.000 Overall Death (Follow-Up): OR = 0.62, CI [0.56–0.67], p = 0.000 Total MACE (Follow-Up): OR = 0.67, CI [0.62–0.73], p = 0.000	(e.g., death, complications, MACE) compared to normal weight. Severe obesity shows a less pronounced protective effect, with some outcomes not reaching statistical significance. Obesity paradox is evident, with mildly obese individuals showing the most favourable outcomes.

Obesity (BMI ≥30.0 kg/m²) vs. Normal Weight:

Hypertension: OR = 1.86, CI [1.75–1.98], p = 0.000

Hyperlipidaemia: OR = 1.68, CI [1.57–1.79], p = 0.000

Diabetes: OR = 2.40, CI [2.17–2.64], p = 0.000

Smoking: OR = 1.14, CI [1.12–1.16], p = 0.000

PAD: OR = 0.73, CI [0.66–0.81], p = 0.000

Reinfarction: OR = 0.83, CI [0.76–0.91], p = 0.000

Stroke: OR = 0.67, CI [0.54–0.85], p = 0.001

Overall Death: OR = 0.55, CI [0.49–0.63], p = 0.000

Total In-Hospital Complications: OR = 0.81, CI [0.70–0.93], p = 0.002

Cardiovascular Death (Follow-Up): OR = 0.77, CI [0.66–0.88], p = 0.000

Overall Death (Follow-Up): OR = 0.62, CI [0.53–0.72], p = 0.000

Total MACE (Follow-Up): OR = 0.63, CI [0.60–0.77], p = 0.000

Severe Obesity (BMI ≥35.0 kg/m²) vs. Normal Weight:

Hypertension: OR = 2.00, CI [1.95–2.06], p = 0.000

Hyperlipidaemia: OR = 1.70, CI [1.65–1.77], p = 0.000

Diabetes: OR = 3.75, CI [3.63–4.17], p = 0.000

Smoking: OR = 0.80, CI [0.70–0.91], p = 0.000
PAD: OR = 0.70, CI [0.61–0.82], p = 0.000

Cardiogenic Shock: OR = 0.76, CI [0.69–0.82], p = 0.000

Overall Death: OR = 0.65, CI [0.53–0.81], p = 0.000
Total In-Hospital Complications: OR = 0.87, CI [0.71–1.07], p = 0.185 (not significant)

Cardiovascular Death (Follow-Up): OR = 0.87, CI [0.69–1.09], p = 0.234 (not significant)

Overall Death (Follow-Up): OR = 0.81, CI [0.55–1.19], p = 0.277 (not significant)

Total MACE (Follow-Up): OR = 0.82, CI [0.59–1.14], p = 0.241 (not significant)

6.5 Systematic review and meta-analyses for the impact of pharmacotherapy on weight loss, CV risk and CVD outcomes in people with or at risk of CVD

Table 6.5 Systematic review and meta-analyses for the impact of pharmacotherapy on weight loss, CV risk and CVD outcomes in people with or at risk of CVD

Study	n studies/ participants	Specific drug/s and Population	Databases Searched & Year/Range/ Countries	Study Designs	Obesity Measure	Effect Estimate	Results ES (95%CI), heterogeneity	Quality & Key points
Abouelmagd, *et al.* 2025	N=3 randomised controlled trials (RCTs) Participants: 878 total (748 received retatrutide, 130 received placebo)	Drug: Retatrutide (triple agonist targeting GLP-1, GIP, and glucagon receptors) Population: Obese or overweight adults, with or without type 2 diabetes	PubMed, Scopus, Web of Science, Cochrane Library From inception to May 1, 2024 Countries: USA (all included studies conducted in the USA)	Randomized controlled trials (RCTs) Phase 1b, Phase 2 trials	Body weight, BMI, WC, percentage weight loss (≥5%, ≥10%, ≥15%)	Mean Difference and OR	<u>Body Weight (n=3 studies)</u> Mean difference (MD): −14.33% (95% CI: −18.27 to −10.39, P < 0.00001). I^2= 95% <u>BMI (n=3 studies)</u> MD: −5.38 (95% CI: −5.74 to −5.01, P < 0.00001). I^2= 75% <u>Waist Circumference (n=3 studies)</u> MD: −10.51 cm (95% CI: −11.67 to −9.35, P < 0.00001). I^2= 27% <u>HbA1c (n=2 studies)</u> MD: −0.91% (95% CI: −1.16 to −0.66, P < 0.00001). I^2= 95% <u>Fasting Plasma Glucose (n=2 studies)</u> MD: −23.51 mg/dL (95% CI: −31.33 to −15.69, P < 0.00001). I^2= 90% <u>Systolic Blood Pressure (n=2 studies)</u> MD: −9.88 mm Hg (95% CI: −11.39 to −8.37, P < 0.00001) I^2= 0% <u>Diastolic Blood Pressure (n=2 studies)</u>	Two studies had a low risk of bias; one study had "some concerns" regarding randomisation. Key Points: Retatrutide demonstrated significant weight loss and metabolic improvements. Safety profile consistent with GLP-1 receptor agonists, with gastrointestinal side effects being the most common. Results suggest retatrutide could become a leading option for obesity management, with superior efficacy compared to other antiobesity drugs. Long-term trials are needed to confirm findings and assess sustainability of weight loss.

							MD: −3.88 mm Hg (95% CI: −5.57 to −2.20, P < 0.00001). I^2= 60%	
Ali *et al.* 2025	N=35 RCTs in the meta-analysis [21 RCTs containing 10 997 patients with diabetes; 14 RCTs containing 11 699 patients without diabetes].	Drugs: Semaglutide, Liraglutide, Exenatide, Efpeglenatide Population: Patients with obesity, with or without diabetes	MEDLINE and Cochrane Until January 2022	RCTs	Weight change	Mean Difference	<u>Overall SBP reduction</u> MD = −3.14 [−3.60; −2.68] I^2 = 86.2%; p < .01 <u>Patients without diabetes</u> MD = −3.80 [−4.24; −3.37] I^2 = 83%; p < .01 <u>Patients with diabetes</u> MD = −2.13 [−3.27; −1.00] I^2 = 86%; p < .01	Moderate to low certainty of evidence Key Points: GLP-1RAs mildly lower SBP in overweight or obese patients, especially in those without diabetes, with effects linked to weight loss. The extent of this reduction in SBP varies only slightly with the specific drug–dose combination used Effect was more pronounced in patients without diabetes, who experienced a greater SBP reduction than those with diabetes.
An *et al.* 2025	N=156 RCTs, 144,782 patients	Drugs: 14 GLP-1 receptor agonists including SC-semaglutide, oral semaglutide, liraglutide, taspoglutide, reg-exenatide, LAR-exenatide, dulaglutide, albiglutide, lixisenatide, orforglipron, danuglipron, efpeglenatide,	PubMed, Embase, Cochrane Library, and Web of Science. From inception to December 15, 2024	RCTs of at least 24 week	BMI and body weight	MD	<u>Major Adverse Cardiovascular Events (12 studies, 85 672 patients)</u> Compared with placebo, all 9 different GLP-1RAs included significantly reduced the incidence rate of MACEs. Efpeglenatide showed the most significant effect (mean difference −0.30 [95% CI −0.54 to −0.07], SUCRA 85.8%). <u>All-Cause Mortality (14 studies, 86 777 patients)</u> Compared with placebo, all 9 different GLP-1RAs included significantly reduced the incidence rate of all-cause mortality.	Safety: A total of 108 studies involving 81 435 patients were included in the analysis of serious adverse events. Compared with placebo, 13 different GLP-1RAs did not significantly increase the incidence of serious adverse events. On the contrary, 10 GLP-1RAs, including efpeglenatide, showed a lower probability of serious adverse events than placebo A total of 108 studies involving 75 764 patients were included in the analysis of adverse events. Compared with placebo, 13 different GLP-1RAs

visepegenatide, and noiiglutide. Population: Adults aged ≥18 years, primarily patients with type 2 diabetes, overweight/obese individuals (BMI ≥25), and those with follow-up durations exceeding 52 weeks.

Oral semaglutide demonstrated the greatest reduction (mean difference −0.68 [95% CI −1.19 to −0.18], SUCRA 97.8%).

CV Mortality (12 studies, comprising 85 989 patients)

Compared with placebo, all 9 different GLP-1RAs included significantly reduced the incidence rate of cardiovascular mortality.

Oral semaglutide (mean difference −0.70 (95% CI −1.33 to −0.08), SUCRA 95.3%) showed the most significant effect.

Also compared results for stroke, myocardial infarction and hospitalization for heart failure, where efpeglenatide, SC-semaglutide, efpeglenatide, respectively, showed the most significant effect in terms of medication efficacy ranking.

HbA1c Reduction (129 studies, 67 944 patients)
Compared with placebo, 10 different GLP-1RAs, except efpeglenatide, visepegenatide and noiiglutide, significantly reduced HbA1c.

Orforglipron showed the most significant reduction (mean difference −2.14% [95% CI −3.60 to −0.68], SUCRA 92.8%).

Fasting blood glucose (97 studies, 38 932 patients)

Compared with placebo, all 13 different GLP-1RAs included, except efpeglenatide, did not significantly increase the incidence of adverse events, whereas 9 GLP-1RAs, including albiglutide, demonstrated a lower probability of adverse events compared with placebo.

A total of 85 studies involving 66 209 patients were included in the analysis of gastrointestinal adverse events. Compared with placebo, only orforglipron and taspoglutide significantly increased the incidence of gastrointestinal adverse events

High-quality studies assessed using the Cochrane Risk of Bias tool and CINeMA (Confidence in Network Meta-Analysis).

Key Points:
Efpeglenatide was most effective in reducing MACEs. Also demonstrated significant benefits
for stroke and hospitalization due to heart failure
Orforglipron excelled in glycemic control and weight reduction.

Oral semaglutide showed significant advantages in reducing all-cause and cardiovascular mortality.

SC-semaglutide was most effective in lowering systolic and diastolic blood pressure.

visepegenatide, noiiglutide and lixisenatide, significantly reduced fasting blood glucose.

Orforglipron (mean difference −2.53 mmol/L (95% CI −3.75 to −1.30), SUCRA 96.3%) showed the most significant effect

BMI (69 studies, 24 188 patients)
Compared with placebo, all 9 different GLP-1RAs, except noiiglutide, lixisenatide and LAR-exenatide, significantly reduced body mass index.

Orforglipron (mean difference −3.84 kg/m^2 (95% CI −5.43 to −2.25), SUCRA 96.2%) showed the most significant effect i

Body Weight Reduction (128 studies, i69 391 patients)

Compared with placebo, 6 of the 12 different GLP-1RAs included significantly reduced body weight.

Orforglipron (mean difference −10.48 kg (95% CI −13.92 to −7.03), SUCRA 98.8%) showed the most significant effect

SBP (75 studies, 52 976 patients)
Compared with placebo, only 4 out of the 9 different GLP-1RAs included (SC-semaglutide, oral semaglutide, liraglutide and dulaglutide) significantly reduced systolic blood pressure.

SC-Semaglutide (mean difference −4.48 mmHg (95% CI −5.60 to −3.35), SUCRA 94.9%) showed the most significant effect

No significant increase in serious adverse events or hypoglycemic events was observed for any GLP-1RAs.

DBP (70 studies, 52 055 patients),

Compared with placebo, only SC-Semaglutide (mean difference −1.90 mmHg (95% CI −2.58 to −1.23), SUCRA 90.5%) significantly reduced DBP.

Total Cholesterol (32 studies, 8546 patients)

Compared with placebo, only liraglutide (mean difference −0.23 mmol/L (95% CI −0.43 to −0.04), SUCRA 69.9%) significantly reduced total cholesterol.

Triglyceride (33 studies, 8045 patients)

Compared with placebo, noiiglutide and taspoglutide significantly reduced triglycerides among the 9 different GLP-1RAs included.

Noiiglutide (mean difference −0.40 mmol/L (95% CI −0.56 to −0.24), SUCRA 93.4%) showed the most significant effect.

HDL-C (34 studies, 8536 patients)
Compared with placebo, none of the 8 different GLP-1RAs included significantly increased high-density lipoprotein cholesterol.

LDL-C (35 studies, 9075 patients)
Compared with placebo, only Taspoglutide (mean difference −0.37 mmol/L (95% CI −0.61 to −0.13), SUCRA 96.8%) significantly reduced low-density lipoprotein cholesterol among the 9 different GLP-1RAs included.

Heterogeneity: Low heterogeneity observed, ensuring reliability of results

Benedictus *et al.* 2025	N=18 RCTS, total population of 12,259 patients aged 31 to 57 years	Drugs: Phentermine/topiramate, semaglutide, phentermine, naltrexone/bupropion, topiramate, and orlistat. Population: Overweight and obese patients, including those with comorbidities such as diabetes mellitus, hypertension, dyslipidaemia, and others.	PubMed, ScienceDirect, and Scopus. No year limit; studies published until August 2023.	RCTs and open-label trials	BMI	MD	In the meta-analysis assessment of the effect of interventions on BMI reduction all intervention groups provided better results than placebo (MD, − 2.12; 95% CI, − 2.64 to − 1.59; P ≤ 0.00001). Naltrexone/bupropion (MD, − 1.68; 95% CI, − 2.16 to − 1.19; P ≤ 0.00001) Orlistat (MD, − 1.46; 95% CI, − 2.05 to − 0.87; P ≤ 0. 00001) Phentermine (MD, − 2.31; 95% CI, − 2.69 to − 1.93; P ≤ 0.00001) Phentermine/topiramate (MD, − 3.28; 95% CI, − 3.96 to − 2.60; P ≤ 0.00001) Semaglutide (MD, − 2.92; 95% CI, − 6.41 to 0.57; P = 0.10), topiramate (MD, − 1.92; 95% CI, − 2.51 to − 1.33; P ≤ 0.00001) Further analysis assessed which therapy provided the best BMI re duction effect using the network meta-analysis method- BMI reduction was obtained in the intervention group with the following results: phentermine/topiramate (MD, − 3.28; 95% CI, − 4.47 to − 2.09), semaglutide (MD, − 2.92; 95% CI, − 4.38 to − 1.46), phentermine (MD, − 2.31; 95% CI, − 3.82 to − 0.81), naltrexone/bupropion (MD, − 1.68; 95% CI,− 2.87 to− 0.49), topiramate (MD, − 1.67; 95% CI, − 2.86 to − 0.48), and orlistat (MD, − 1.44; 95% CI, − 2.32 to − 0.55).	Most studies had a low risk of bias. Some studies showed unclear or high risk due to incomplete data or funder involvement. Phentermine/topiramate and semaglutide were most effective for BMI reduction. Side effects were mostly mild and related to the gastrointestinal system. Drug combinations (e.g., phentermine/topiramate) showed synergistic effects. Special populations (e.g., pregnant women, renal impairment) require tailored approaches. Adjunct dietary interventions enhance drug efficacy.
Kamrul-Hasan *et al.* 2025	N=6 RCTs, 800 participants	Drug: Beinaglutide (0.1-0.2 mg	MEDLINE (via PubMed),	RCTs 12-24 weeks	Body Weight, BMI, WC	MD, OR	<u>Body weight reduction</u>	Certainty of evidence ranged from very low (body weight reduction) to

		subcutaneous injections, thrice daily) Population: Adults with overweight/obesity with/without type 2 diabetes	Scopus, Cochrane Central Register, Google Scholar, ClinicalTrials.gov, Chinese Clinical Trial Register From inception to September 30, 2024 Countries: All studies conducted in China				MD = -3.25 kg (95%CI: -4.52 to -1.98), I^2 = 84%, P < 0.00001 <u>Percent body weight reduction</u> MD = -4.13% (95%CI: -4.87 to -3.39), I^2 = 54%, P < 0.00001 <u>BMI reduction</u> MD = -1.22 kg/m² (95%CI: -1.67 to -0.77), I^2 = 0%, P < 0.00001 <u>WC reduction</u> MD = -2.47 cm (95%CI: -3.74 to -1.19), I^2 = 46%, P = 0.0002 Odds of achieving 5% weight reduction: OR = 4.61 (95%CI: 3.07 to 6.93), I^2 = 0%, P < 0.00001 Odds of achieving 10% weight reduction: OR = 5.34 (95%CI: 2.78 to 10.25), I^2 = 0%, P < 0.00001	moderate (BMI reduction, WC reduction, weight reduction odds). Beinaglutide showed modest benefits in reducing body weight, BMI, and WC. No significant differences in glycemic or other metabolic endpoints compared to the control arm. Higher risks of adverse events (e.g., nausea, vomiting, dizziness) and treatment discontinuation due to adverse events. Longer-duration trials with multi-ethnic representation are needed for robust evidence.
Neves *et al.* 2025	N=7 RCTs, total of 2,559 participants	Drugs: GLP-1 receptor agonists (RAs) including semaglutide, exenatide, and albiglutide. Population: Patients with heart failure (HF) categorized into HFrEF and HFpEF phenotypes	PubMed, up to December 21, 2024.	RCTs. Varying definitions of HF phenotypes and inclusion criteria.	NR	HR	GLP-1 RAs were associated with a higher risk of worsening HF events in HFrEF patients (HR: 1.23 [95% CI: 1.00-1.51]); I^2 = 0% (P-heterogeneity = 0.476).	Quality NR. Key Points: GLP-1 RAs have heterogeneous effects across HF populations. They may increase the risk of worsening HF in patients with HFrEF, contrary to the benefits observed in HFpEF. Dedicated RCTs are needed to clarify the safety and efficacy of GLP-1 RAs in HFrEF patients. Mechanisms of adverse effects in HFrEF remain uncertain but may

							involve increased heart rate and intracellular cyclic adenosine monophosphate levels.
Otmani *et al.* 2025	N=5 RCTs, 6898 patients	Drug: Semaglutide (2.4 mg subcutaneous weekly). Population: Obese patients with heart failure (HF), irrespective of baseline ejection fraction (EF). Subgroups: Heart failure with preserved ejection fraction (HFpEF) and heart failure with reduced ejection fraction (HFrEF).	Cochrane Library, Web of Science, Embase, PubMed, and Scopus. From inception to August 2024.	BMI, WC	RR, MD	<u>Cardiovascular mortality (4 studies)</u> Event rate was 3.95% (104 of 2630 patients) in the semaglutide group while it was 5.5% (142 of 2583 patients) in the placebo group Risk ratio (RR): 0.74; 95% confidence interval (CI): 0.58–0.94; P = 0.02. Subgroup analysis: HFrEF: RR: 0.66; 95% CI: 0.47–0.92; P = 0.01. HFpEF: RR: 0.84; 95% CI: 0.59–1.22; P = 0.37. <u>Heart Failure Events</u> Event rate was 4.14% (109 of 2630 patients) in the semaglutide group, while in the placebo group, the event rate was 5.46% (141 of 2583 patients). Semaglutide did not result in a significant change in the risk of events in both HFpEF and HFrEF subgroups (RR, 0.54; 95% CI, 0.29–1.01; *P* = 0.05; I^2 = 62%) and (RR, 1.02; 95% CI, 0.73–1.43; *P* = 0.91; I^2 = 0%), respectively. The overall pooled analysis revealed no statistically significant difference between semaglutide and placebo (RR, 0.74; 95% CI, 0.50–1.08; *P* = 0.12; I^2 = 55%). <u>Serious Cardiovascular Events (3 studies)</u> Event rate was 17.92% (410 of 2288 patients) in the semaglutide group, while in the placebo	Cochrane risk-of-bias tool (ROB 2): 4 studies rated as low risk, 1 study rated as some concerns. Key points: Semaglutide reduced cardiovascular mortality and improved exercise capacity (6-MWD) and quality of life (KCCQ-CSS) Significant weight and waist circumference reduction. No major effect on serious gastrointestinal, hepatobiliary, or renal events. Increased risk of treatment discontinuation due to adverse events in HFrEF patients. Long-term studies recommended for further validation.

							group, the event rate was 23.23% (523 of 2248 patients). Semaglutide showed a statistically significant effect on the risk of events in both HFpEF and HFrEF subgroups (RR, 0.54; 95% CI, 0.29–0.99; *P* = 0.05; I^2 = 83%) and (RR, 0.82; 95% CI, 0.69–0.97; *P* = 0.02; I^2 = 0%), respectively. The overall pooled analysis was (RR, 0.67; 95% CI, 0.50–0.89; *P* = 0.007; I^2 = 70%) Kansas City Cardiomyopathy Questionnaire—Clinical Summary Score (KCCQ-CSS): Mean difference (MD): 7.72; 95% CI: 5.28–10.17; P < 0.001. 6-minute walk distance (6-MWD): MD: 14.83; 95% CI: 4.23–25.43; P = 0.006.	
Waqas *et al.* 2025	N=6 RCTs, 8788 patients	Drugs: GLP-1 receptor agonists (GLP-1RAs) including semaglutide, exenatide, and combination GLP-1RA/GIP agents like tirzepatide. Population: Patients with heart failure with mildly reduced or preserved ejection fraction (HFpEF), particularly those	PubMed, Scopus, and Cochrane Register of Clinical Trials. From inception to November 25, 2024. Countries: Trials conducted in multiple countries, including the United States, United Kingdom, and others.	RCTs	BMI	HR	GLP-1RAs significantly reduced worsening HF events and the composite outcome of CV death or worsening HF events. Composite Outcome (CV death or worsening HF events): HR: 0.68 [95% CI: 0.51–0.89], P = 0.006, I^2 = 47%. Worsening HF Events Alone: HR: 0.56 [95% CI: 0.38–0.82], P = 0.003, I^2 = 51%. No significant reduction was observed for CV death alone CV Death Alone: HR: 0.86 [95% CI: 0.67–1.12], P = 0.27, I^2 = 0%	All included trials were assessed as having a low risk of bias using the Cochrane Risk of Bias tool GLP-1RAs are promising therapies for HFpEF, particularly in patients with obesity or T2DM. No significant effect on CV death alone was observed. Challenges include high costs, limited access, and poor adherence.

		with obesity or type 2 diabetes mellitus (T2DM).						
Wen *et al.* 2025	N=41 RCTs, 15,126 patients	Drugs: 13 GLP-1 receptor agonists (GLP-1RAs) including Semaglutide, Liraglutide, Taspoglutide, Exenatide, Mazdutide, Dulaglutide, Survodutide, Cotadutide, Tirzepatide, Efinopegdutide, Bamadutide, Retatrutide, and Loxenatide. Population: Adults (≥18 years) with type 2 diabetes mellitus (T2DM) and overweight/obesity (BMI ≥ 24).	PubMed, Embase, Cochrane Library, Web of Science. From inception to December 20, 2024.	RCTs with intervention duration ≥ 12 weeks. Control groups received either placebo or another GLP-1RA	Body weight, BMI, percentage weight loss, waist circumference, hip circumference, waist-to-hip ratio	MD	<u>HbA1c:</u> Tirzepatide reduced HbA1c by -1.64 (-1.94, -1.35) compared to placebo - most significant reduction <u>Fasting Blood Glucose (FBG):</u> Tirzepatide reduced FBG by -2.10 (-2.95, -1.25) compared to placebo - most significant reduction <u>Body Weight:</u> Tirzepatide reduced weight by -9.89 (-11.29, -8.49) compared to placebo - most significant reduction <u>BMI:</u> Tirzepatide reduced BMI by -3.85 (-4.71, -2.99) compared to placebo - most significant reduction <u>SBP:</u> Semaglutide, Liraglutide, and Exenatide significantly reduced SBP compared to placebo. Semaglutide: Most significant reduction (-3.13; 95% CI: -5.30, -0.96) <u>DBP</u> None of the GLP-1RAs showed significant reductions in DBP compared to placebo. <u>Total Cholesterol (TC):</u> Loxentide significantly reduced TC compared to placebo (-0.40; 95% CI: -0.71, -0.09). Exenatide	High-quality studies assessed using the Cochrane Risk of Bias Tool and CINeMA. Consistency tests showed no significant inconsistency (P > 0.05). Funnel plots indicated low risk of publication bias. Key Points: Tirzepatide demonstrated superior efficacy in glycaemic control and weight reduction. GLP-1RAs were generally safe, with acceptable adverse event profiles. Blood Pressure: Semaglutide, Liraglutide, and Exenatide were effective in reducing SBP, but no significant effects were observed for DBP. Blood Lipids: Loxentide reduced TC, and Exenatide improved HDL-C, but no significant effects were observed for TG or LDL-C. These results suggest that while some GLP-1RAs may have modest benefits for blood pressure and lipid levels, their primary strengths lie in glycaemic control and weight reduction

							and Liraglutide also showed better performance than placebo. Triglycerides (TG): None of the GLP-1RAs showed significant reductions in TG levels compared to placebo. High-Density Lipoprotein Cholesterol (HDL-C): Exenatide significantly improved HDL-C compared to placebo (-1.10; 95% CI: -2.14, -0.07). Low-Density Lipoprotein Cholesterol (LDL-C): None of the GLP-1RAs showed significant reductions in LDL-C compared to placebo.	Subgroup analyses highlighted differences in efficacy based on intervention duration, dosage, and mechanisms of action. Limitations include missing evidence for some outcomes and potential publication bias.
Wong *et al.* 2025 (a)	N=47 RCTs with 23,244 participants	Drugs Studied: Liraglutide, Exenatide, Semaglutide, Dulaglutide, Danuglipron, Orforglipron, Efpeglenatide. Population: Adults with overweight or obesity (BMI ≥ 25 kg/m² for Asians, BMI ≥ 30 kg/m² for others), with or without diabetes.	PubMed, Embase, Cochrane Central Register of Controlled Trials (CENTRAL). From inception to October 4, 2024.	RCTs with follow up 4-104 weeks	Weight, BMI, WC	MD	Weight Reduction: Mean change of −4.57 kg (95% CI −5.35 to −3.78). I^2 = 97%. Diabetes subgroup: −2.69 kg (95% CI −3.21 to −2.17), I^2 = 92%. No diabetes subgroup: −9.19 kg (95% CI −11.52 to −6.85), I^2 = 97%. BMI Reduction: Mean change of −2.07 kg/m² (95% CI −2.53 to −1.62). I^2 = 97%. Diabetes subgroup: −1.22 kg/m² (95% CI −1.65 to −0.79), I^2 = 93%. No diabetes subgroup: −2.96 kg/m² (95% CI −3.70 to −2.23), I^2 = 96%. Waist Circumference Reduction:	Graded using GRADE system; most estimates downgraded by two levels due to severe statistical heterogeneity. Key Points: GLP-1 RAs demonstrated significant reductions in weight, BMI, and waist circumference. Greater efficacy observed in patients without diabetes compared to those with diabetes. Semaglutide showed the greatest treatment benefit across all measures. Oral GLP-1 RAs were comparable in efficacy to subcutaneous injections.

							Mean change of −4.55 cm (95% CI −5.72 to −3.38). I^2 = 94%. Diabetes subgroup: −2.45 cm (95% CI −3.43 to −1.47), I^2 = 79%. No diabetes subgroup: −6.23 cm (95% CI −8.16 to −4.30), I^2 = 95%.	Longer follow-up durations (>1 year) were associated with greater reductions in all measures.
Wong 2025 *et al.* (b)	N=30 RCTs, 37072 patients.	Drugs: Semaglutide, liraglutide, exenatide Population: Overweight or obese adult patients (BMI criteria: overweight: 25–30 kg/m², Asians: 23–30 kg/m²; obese: BMI ≥30 kg/m², Asians: BMI ≥25 kg/m²) with or without diabetes mellitus	PubMed, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL) From inception to February 13, 2024	RCT Follow-up duration ranged from 16 weeks to 34 months.	BMI BMI criteria: Overweight (25–30 kg/m², Asians: 23–30 kg/m²); Obese (BMI ≥30 kg/m², Asians: BMI ≥25 kg/m²)	MD	<u>Systolic Blood Pressure</u> -3.37 mmHg (95% CI -3.95 to -2.80) <u>Diastolic Blood Pressure</u> -1.05 mmHg (95% CI -1.46 to -0.65) For every 10 kg of weight loss, the extent of SBP and DBP reduction increased by a mean of 2.4 and 1.9 mmHg, respectively. Considerable statistical heterogeneity across both the overall and subgroup analyses of systolic and diastolic blood pressure.	Majority of studies had low risk of bias; 10 studies had moderate risk of bias (assessed using Cochrane Risk of Bias Tool) Key Points: GLP-1 RAs consistently reduced SBP and DBP across subgroups (diabetic status, drug type, administration route, treatment duration). Semaglutide showed the greatest BP reduction. Oral GLP-1 RAs were more effective than subcutaneous options. BP reduction increased with greater weight loss. No significant influence of baseline characteristics (age, BMI, HbA1c, hypertensive status) on BP reduction
Yin et al *et al.* 2025	N=29 RCTs, 37,348 eligible participants	Drugs: 9 GLP-1RA-based therapies, including orfroglipron,	PubMed, Embase, Cochrane, Web	RCTs	BMI	RR & MD	<u>Cardiovascular Events</u> Total cardiovascular events: RR 0.81 (95% CI: [0.76, 0.87])	Key Points: GLP-1RA-based therapies reduce cardiovascular events and all-cause mortality.

		tirzepatide, retatrutide, semaglutide, liraglutide, dulaglutide, efpeglenatide, exenatide, lixisenatide, and albiglutide. Population: Nondiabetic adults with overweight or obesity.	of Science, and ClinicalTrials.gov. From inception to June 18, 2024.				<u>Major adverse cardiovascular events (MACE):</u> RR 0.80 (95% CI: [0.72, 0.89]) <u>Myocardial infarction (MI):</u> RR: 0.72 (95% CI: [0.61, 0.85]) <u>All-cause mortality:</u> RR: 0.81 (95% CI: [0.71, 0.93]) <u>Cardiometabolic Parameters:</u> Systolic blood pressure: MD: −7.10 mmHg (95% CI: [−11.00, −2.70]) <u>BMI:</u> MD: −6.50 kg/m² (95% CI: [−7.90, −5.10]) <u>HbA1c:</u> MD: −0.39% (95% CI: [−0.52, −0.26]) <u>C-reactive protein:</u> MD −1.20 mg/dL (95% CI: [−1.80, −0.63]).	Distinct metabolic effects observed among different GLP-1RA-based drugs. Orforglipron, tirzepatide, and retatrutide showed specific efficacy in reducing SBP, BMI, and lipid profiles, respectively. GLP-1RA-based therapies significantly reduced cardiovascular events and improved cardiometabolic parameters. No significant differences were observed in cardiovascular death or stroke.
Cesaro *et al.* 2025	26 RCTs, 48,583 participants (25,879 treated with semaglutide)	Drug: Semaglutide (glucagon-like peptide-1 receptor agonist) Population: Adults aged 18 years or older, including those with Type 2 Diabetes Mellitus, obesity, or overweight. Studies included participants with and without pre-existing	PubMed, Embase, Web of Science, ClinicalTrials.gov Up to November 16, 2024	RCTs	BMI	OR	<u>Arterial Fibrillation</u> The pooled analysis demonstrated that semaglutide treatment was associated with a significant reduction in new-onset AF compared with the control arm, with an OR of 0.83 (95% CI, 0.70–0.98; P = 0.03) 17% reduction in new-onset AF incidence. Oral Formulation: OR = 0.48 (95% CI: 0.24–0.95, P = 0.04) Subcutaneous Formulation: OR = 0.93 (95% CI: 0.69–1.25, P = 0.62) Studies without SGLT2 inhibitors:	Treatment with semaglutide reduced the risk of new-onset atrial fibrillation by 17%, with the strongest effects observed in its oral formulation. The reduction in AF risk was independent of patient characteristics such as age, body mass index, or blood sugar levels and was particularly significant in studies without other concurrent therapies like SGLT2 inhibitors. Semaglutide significantly reduces new-onset AF, particularly with oral formulation.

		cardiovascular conditions.					OR = 0.79 (95% CI: 0.63–0.99, P = 0.04). Studies with SGLT2 inhibitors: OR = 0.86 (95% CI: 0.63–1.17, P = 0.33).	Effect independent of baseline characteristics like BMI and HbA1c. Mechanisms include weight reduction, glycaemic control, and anti-inflammatory effects. Results are robust but limited by low absolute AF event numbers and variability in detection methods. Future trials with systematic AF monitoring are recommended.
Liu L *et al.* 2025	N=154 studies with 112,515 participants.	Drugs Studied: Tirzepatide, Semaglutide, Liraglutide, Orlistat, Naltrexone/Bupropion, Phentermine/Topiramate, Naltrexone, Bupropion, Phentermine, Topiramate. Population: Individuals with overweight or obesity, including: Simple overweight/obesity. Weight-related complications and comorbidities.	PubMed, Web of Science, Cochrane Central Register of Controlled Trials. From inception to June 8, 2024.	RCTs	BMI, WC, Body weight, Body fat (%)	WMD and RRs	<u>Weight Loss:</u> Tirzepatide: WMD −11.69 kg (95% CI −19.22 to −4.15; I^2 = 100%; moderate certainty). Semaglutide: WMD −8.48 kg (95% CI −12.68 to −4.27; I^2 = 100%; moderate certainty). <u>Cardiometabolic Effects:</u> <u>T</u>irzepatide: Largest reductions in systolic BP (WMD −5.74 mmHg; 95% CI −9.00 to −2.48; I^2 = 99.8%) and triglycerides (WMD −0.77 mmol/L; 95% CI −0.85 to −0.69; I^2 = 3.2%; high certainty). Semaglutide and Liraglutide: Reduced risk of major adverse cardiovascular events (MACEs) (RR 0.83, 95% CI 0.74–0.92; I^2 = 0.0%; high certainty for Semaglutide). <u>Psychological Outcomes:</u> <u>Tirzepatide:</u> Greatest improvement in IWQOL-Lite total score (WMD 10.06; 95% CI 4.56–15.56; I^2 = 99.9%; moderate certainty).	Most outcomes supported by high to moderate certainty evidence. Lower certainty for some efficacy indicators due to heterogeneity and bias in certain studies. Key Points: Tirzepatide is the most effective for weight loss and cardiometabolic improvement. Semaglutide and Liraglutide offer cardiovascular protection by reducing MACEs risk. Naltrexone/Bupropion and Phentermine/Topiramate require caution due to adverse effects. Gastrointestinal side effects are common with GLP-1 receptor agonists.

		Psychiatric disorder-related overweight/obesity.					Topiramate: Increased risk of depression (RR 1.62; 95% CI 1.14–2.30; I^2 = 0.0%; high certainty). Adverse Events: Tirzepatide: Highest risk of discontinuation due to adverse events (RR 2.13; 95% CI 1.57–2.89; I^2 = 0.0%; high certainty).	Psychological risks (e.g., depression, anxiety) are notable for Topiramate and Phentermine/Topiramate
Liu S *et al.* 2025	N=24 RCTs, 9165 participants	Drugs: Retatrutide, Tirzepatide, Survodutide, Mazdutide, Efinopegdutide, AMG133 Population: Adults with overweight or obesity, with or without type 2 diabetes	PubMed, Cochrane, Web of Science, Embase, CNKI, WanFang Search Year/Range: Up to May 12, 2024	RCTs at least 12 weeks duration	Body weight, BMI, WC, Proportion of participants achieving weight loss >5%	MD and ORs	Weight Reduction: Tirzepatide: MD -12.78 kg (95% CI: -16.10 to -9.46) Retatrutide: MD -11.91 kg (95% CI: -19.00 to -4.82) Mazdutide: MD -5.31 kg (95% CI: -9.78 to -0.84) HbA1c Reduction: Tirzepatide: MD -1.87% (95% CI: -2.15 to -1.59) Mazdutide: MD -1.89% (95% CI: -2.43 to -1.35) Blood Pressure Reduction: Systolic BP: Tirzepatide MD -6.69 mmHg (95% CI: -7.62 to -5.75) Diastolic BP: Tirzepatide MD -3.73 mmHg (95% CI: -4.75 to -2.71)	Key Points: Multi-receptor drugs demonstrated substantial efficacy in weight management, glycaemic control, and blood pressure regulation. Non-diabetic populations showed more pronounced improvements in weight and blood pressure. Tirzepatide and Retatrutide were the most effective agents for weight loss. Safety profiles were generally favourable, with no significant increase in serious adverse events compared to placebo
Badve *et al.* 2025	11 trials involving 85,373 participants (29,386 female, 55,987 male)	Drugs: Semaglutide, Exenatide, Liraglutide, Dulaglutide, Albiglutide, Efpeglenatide, and Lixisenatide. Population: Participants with	MEDLINE, Embase, Cochrane Central Register of Controlled Trials. From database inception to March 26, 2024	Randomized controlled trials with at least 500 participants, comparing GLP-1 receptor agonists with placebo, with a minimum follow-up of 12 months.	BMI ≥27 kg/m² was used in the SELECT trial for participants without diabetes.	HR	Composite kidney outcome: Compared with placebo, treatment with GLP-1 receptor agonists resulted in an 18% reduction in the risk of the composite kidney outcome (HR 0·82, 95% CI 0·73–0·93; high-certainty evidence) in participants with type 2 diabetes The effect was similar when the SELECT trial was included (HR 0·81, 95% CI 0·72–0·92; high-certainty evidence;	High-certainty evidence for most outcomes (composite kidney outcome, MACE, all-cause death). Moderate-certainty evidence for kidney failure. Consistent benefits across subgroups regardless of diabetes status. No significant differences in serious adverse events, but higher treatment

type 2 diabetes (67,769) and participants without diabetes but with cardiovascular disease and elevated BMI (17,604).

Kidney failure:
Treatment with GLP-1 receptor agonists significantly reduced the risk of kidney failure by 16% (HR 0·84 [95% CI 0·72–0·99] for participants with type 2 diabetes; HR 0·84 [0·72–0·98] for participants with or without diabetes; moderate-certainty evidence) and the worsening of kidney function (HR 0·79 [95% CI 0·68–0·92] for participants with type 2 diabetes; HR 0·78 [0·68–0·91] for participants with or without diabetes; high-certainty evidence).

MACE:
Compared with placebo, treatment with GLP-1 receptor agonists resulted in a 13% reduction in the risk of MACE (HR 0·87, 95% CI 0·81–0·93; high-certainty evidence) in participants with type 2 diabetes (high-certainty evidence) and a 14% reduction when the SELECT trial was included in the analysis (HR 0·86, 95% CI 0·80–0·92; high-certainty evidence).

In participants with type 2 diabetes, GLP-1 receptor agonists significantly reduced the risk of individual components of MACE including cardiovascular death by 14% (HR 0·86, 95% CI 0·80–0·92), non-fatal myocardial infarction by 10% (HR 0·90, 0·82–0·99; and non-fatal stroke by 13% (HR 0·87, 0·79–0·96;; high-certainty evidence for all outcomes).

Hospitalization & All-cause death:
Treatment with GLP-1 receptor agonists significantly reduced the risk of hospitalisation for heart failure by 13%, and there was no significant heterogeneity in treatment effect by diabetes status. Compared with placebo, discontinuation due to adverse events in GLP-1 receptor agonist groups.

Results support GLP-1 receptor agonists as kidney-protective and heart-protective medications

							treatment with GLP-1 receptor agonists resulted in a 12% relative reduction in the risk of death due to any cause in participants with type 2 diabetes (HR 0·88, 95% CI 0·83–0·93; high-certainty evidence), and a 13% reduction (HR 0·87, 0·82–0·91; high-certainty evidence) when the SELECT trial was included	
Bari *et al.* 2025	Four RCTs, 79 participants	Drug: Dapagliflozin (SGLT2 inhibitor) Individuals with prediabetes and obesity	PubMed, EMBASE, Cochrane Library, Web of Science (Core Collection), Scopus Initial search conducted on January 6, 2024, updated in April 2025 Countries: Mexico (3 studies), China (1 study)	Eligible study designs included randomised controlled trials (RCTs), quasi-experimental studies, non-randomised studies, and controlled before–after studies	BMI, waist circumference, fat mass, WC	MD	<u>Dapagliflozin vs placebo</u> Body weight: Mean difference: –3.05 kg (95% CI: –8.18 to 2.09; 3 trials, n=78 I^2=0). BMI: Mean difference: –1.43 kg/m² (95% CI: –4.11 to 1.25; 3 trials, n=78, I^2 = 60%) Waist circumference: Mean difference: –1.85 cm (95% CI: –7.06 to 3.37; 2 trials n=48 I^2 =11%) Fasting plasma glucose: Mean difference: –0.47 mmol/L (95% CI: –0.90 to –0.05, 3 trials, n=78, I^2=58%) Total Cholesterol: Mean difference: 0.21 mmol/L (95% CI: –0.24 to 0.66; 2 trials, n=48, = I^2=0) Triglyceride: Mean difference: 0.08 mmol/L (95% CI: –0.20 to 0.35; 2 trials, n=48, = I^2=0) SBP: Mean difference: –2.12 mmHg (95 % CI: –7.39 to 3.16; 3 trials; 78 participants; I^2=0) DBP: Mean difference: –1.04mmHg (95 % CI: –5.07to 2.99; 3 trials; 78 participants; I^2=0)	Quality: Assessed using the Cochrane Risk of Bias tool. Two studies had unclear risks in random sequence generation and allocation concealment Key points: Dapagliflozin showed limited impact on body weight, BMI, and waist circumference. Statistically significant reduction in fasting plasma glucose. No serious adverse events reported, but some cases of urinary tract infections and cervicovaginal infections were noted. Small sample sizes and limited number of studies highlight the need for larger, well-powered trials
Adamou *et al.* 2024	N=11 randomised CV outcomes trials	82,140 individuals (34.6% women) with a cumulative follow-up of	Drugs: Dulaglutide, efpeglenatide, albiglutide, exenatide,	MEDLINE (via PubMed) and SCOPUS.	NR	RR	Stroke: RR: 0.85 (95% CI: 0.77–0.93); I^2 = 0% NNT=200 Non-Fatal Stroke: RR: 0.87 (95% CI: 0.79–0.95); I^2 = 0%. NNT=250	No significant bias detected using the Cochrane RoB 2.0 tool. Funnel plots showed no publication bias.

		247,596 person-years.	semaglutide, liraglutide, and lixisenatide Population: Individuals with diabetes mellitus (78.4%), obesity, or heart failure. Among the participants, 16.7% had experienced a previous stroke.	From the first available date until November 15, 2023.			Fatal Stroke: RR: 0.81 (95% CI: 0.62–1.06); I^2 = 0%.	Key Points: GLP-1 RAs significantly reduced stroke risk (16% relative reduction) and non-fatal stroke risk. No significant effect on fatal stroke due to low event numbers Subgroup analyses showed no interaction based on administration frequency, route, or diabetic status
de Oliveira Almeida *et al.* 2024	N=13 RCTs, 30512 participants	Drugs: Liraglutide, Semaglutide, Tirzepatide Population: Patients living with obesity or overweight without diabetes mellitus	PubMed, Cochrane Library, Embase From inception to November 5, 2023	RCTS	BMI	MD, RR	<u>Compared with placebo, GLP-1RA</u> Systolic Blood Pressure: MD −4.76 mmHg (95% CI −6.03, −3.50; p < 0.001; I^2 = 100%) Diastolic Blood Pressure: MD −1.41 mmHg (95% CI −2.64, −0.17; p = 0.03; I^2 = 100%) Myocardial Infarction: RR 0.72 (95% CI 0.61, 0.85; p < 0.001; I^2 = 0%) Unstable Angina: RR 0.84 (95% CI 0.65, 1.07; p = 0.16; I^2 = 0%) Stroke: RR 0.91 (95% CI 0.74, 1.12; p = 0.38; I^2 = 0%) Atrial Fibrillation: RR 0.49 (95% CI 0.17, 1.43; p = 0.19; I^2 = 22%) Deep Vein Thrombosis: RR 0.30 (95% CI 0.06, 1.40; p = 0.13; I^2 = 0%)	Quality: High-quality evidence for myocardial infarction. Moderate-quality evidence for unstable angina, atrial fibrillation, and deep vein thrombosis. Low-quality evidence for systolic blood pressure, diastolic blood pressure, and stroke Key points: In patients living with obesity or overweight and without diabetes: GLP-1 RA significantly reduced systolic blood pressure and diastolic blood pressure. GLP-1 RA was associated with a significant reduction in the occurrence of myocardial infarction. There were no significant differences between groups in the occurrence of

								unstable angina, stroke, atrial fibrillation, and deep vein thrombosis.
Serralde-Zuniga *et al.* 2022	N=19 trials with 2216 participants	Drug: Fluoxetine (Selective Serotonin Reuptake Inhibitor). Population: Adults (>18 years) with overweight (BMI 25–29.9 kg/m²) or obesity (BMI ≥30 kg/m²) based on WHO criteria.	Cochrane Library, MEDLINE, Embase, LILACS, Cochrane CENTRAL, ICTRP Search Portal, ClinicalTrials.gov. Search conducted up to January 2021.	RCTs	BMI, body weight (kg)	MD	Weight loss: −2.7 kg (95% CI −4 to −1.4; p < 0.001, 10 trials, n=956, low certainty of evidence in favour of fluoxetine). BMI reduction: −1.1 kg/m² (95% CI −3.7 to 1.4; 3 trials; 97 participants; very-low-certainty evidence). High heterogeneity observed due to variations in doses, durations, and participant characteristics.	Evidence Quality: Low-certainty evidence due to unclear risk of bias in randomization and blinding, and high attrition rates in some trials. Fluoxetine may lead to modest weight loss (−2.7 kg) and BMI reduction (−1.1 kg/m²) compared to placebo. Adverse events (e.g., dizziness, drowsiness, fatigue, insomnia, nausea) were approximately twice as common in fluoxetine groups than comparators.
Yu *et al* 2021	N=7 studies, 269 (132 in the acarbose group, 137 in the placebo group)	Drug: Acarbose Population: Patients with overweight and obesity but without diabetes patients (BMI ≥ 25 kg/m²)	PubMed, EMBASE, Cochrane, Science Citation Index Expanded From the establishment of each database to December 2019	RCTs	BMI	WMD	Triglycerides (TG): Weighted Mean Difference (WMD) = −0.21 mmol/L (95% CI −0.33, −0.09), P = 0.0006. I^2=53% BMI: WMD = −0.62 (95% CI −2.67, 1.44), P = 0.56. I^2=91% Systolic Blood Pressure: WMD = −7.87 (95% CI −15.53, −0.15), P = 0.05. I^2=88% Fasting Plasma Glucose: WMD = −0.02 (95% CI −0.29, 0.26), P = 0.9. I^2=80%	Quality: Studies were evaluated using the revised 7-point Jadad scale. Studies scoring 4–7 were classified as high quality. Median score = 3 (range 3-6) Key points: Study confirmed that acarbose can reduce triglyceride levels in obese or overweight people Although weight loss was not statistically significant, sensitivity analysis suggested the result was not stable; this might be related to the dose of the drug and the insufficient treatment duration

Acarbose was expected to improve metabolic markers such as triglyceride levels and may be used in the treatment of obese and overweight people

6.6 Systematic review and meta-analyses for the impact of bariatric surgery on weight loss, CV risk and CVD outcomes in people with or at risk of CVD

Table 6.6 Systematic review and meta-analyses for the impact of bariatric surgery on weight loss, CV risk and CVD outcomes in people with or at risk of CVD

MORTALITY / MACE								
Study	**n studies/ participants**	**Type of Surgery**	**Databases Searched & Year/Range/ Countries**	**Study Designs**	**Obesity Measure**	**Effect Estimate**	**Results ES (95%CI), heterogeneity**	**Quality & Key points**
Carsado *et al.* 2017	8 studies 23,647 participants.	Gastric plication, sleeve gastrectomy, vertical banded gastroplasty, (adjustable and nonadjustable gastric banding	MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials and the National Institutes of Health clinical trials database. From inception to July 4, 2016 Most studies conducted in Europe or USA.	Observational studies	BMI ≥ 35 kg/m^2	HR	<u>All-cause mortality (8 studies)</u> HR = 0.586 (95%CI = 0.515, 0.665), p < .001, I^2= 40%	Studies rated moderate-to-high quality, although most were retrospective studies. Key Points: Participants who underwent bariatric surgery had a significantly lower risk of all cause mortality compared to people who were unoperated.
Cui *et al.* 2023	40 studies 231,061 patients 395,440 controls	Roux-en-Y gastric bypass, sleeve gastrectomy, adjustable gastric band, vertical banded gastroplasty, biliopancreatic diversion, biliopancreatic diversion with duodenal switch, duodenal switch	PubMed and Embase From inception to June 4, 2022	Matched cohort studies	Not defined	HR	<u>MACE (5 studies)</u> HR = 0.58 (95%CI = 0.51, 0.66), p < .001, I^2= 50% <u>Cardiovascular mortality (8 studies)</u> HR = 0.38 (95%CI = 0.29, 0.50), p < .001, I^2= 36% <u>Atrial fibrillation (5 studies)</u> HR = 0.79 (95%CI = 0.68, 0.92), p = .003, I^2= 44% <u>Heart failure (10 studies)</u> HR = 0.52 (95%CI = 0.42, 0.65), p < .001, I^2= 57% <u>Myocardial infarction (10 studies)</u>	21 studies were ranked as 'good quality' and 19 studies were ranked as 'poor quality' Key points Bariatric surgery was related to a lower risk of cardiovascular outcomes including MACE, myocardial infarction and cardiovascular mortality. Bariatric surgery was also related to significantly lower risk of all-cause mortality.

							HR = 0.55 (95%CI = 0.41, 0.74), p < .001, I^2= 65% Stroke (10 studies) HR = 0.75 (95%CI = 0.63, 0.89), p < .001, I^2= 2% All-cause mortality (24 studies) HR = 0.52 (95%CI = 0.47, 0.58), p < .001, I^2= 69% Cancer mortality (5 studies) HR = 0.64 (95%CI = 0.37, 0.58), p < .001, I^2= 2% Diabetes mortality (2 studies) HR = 0.25 (95%CI = 0.11, 0.57), p < .001, I^2= 35%	
Pontiroli *et al.* 2020	14 studies 72,2667 patients 535,376 controls	LAGB gastric banding, RYGB gastric bypass, BPD biliopancreatic diversion, BIBP biliointestinal bypass, LSG sleeve gastrectomy	PubMed, Cochrane Library, MEDLINE, and Embase Search dates not reported	Controlled clinical studies	Not defined	OR	All patients All-cause mortality (9 studies) OR = 0.29 (95% CI = 0.17, 0.49), p = .001, I^2= 98% CVD mortality (4 or 5 studies) OR = 0.35 (95% CI = 0.15, 0.83), p = .017, I^2= 96% Cancer mortality (4 or 5 studies) OR = 0.31 (95% CI = 0.24, 0.40), p = .001, I^2= 41% Diabetes mortality (4 or 5 studies) OR = 0.25 (95% CI = 0.06, 0.97), p = .045, I^2= 90% Younger patients (below cohort median age) All-cause mortality OR = 0.78 (95% CI = 0.57, 1.06), p = .110, I^2= 67% CVD mortality (4 or 5 studies) OR = 0.62 (95% CI = 0.51, 0.74), p = .001, I^2= 98% Cancer mortality (4 or 5 studies)	All but 1 study rated as having no risk of bias or a low risk of bias. One study had a high risk of bias. Key points Bariatric surgery was related to a lower risk of all-cause, CVD, cancer, and diabetes mortality. Effect sizes were larger among older patients. Only the risk of CVD mortality was significantly decreased among younger patients.

								OR = 0.61 (95% CI = 0.30, 1.23), p = .166, I^2= 49% Diabetes mortality (4 or 5 studies) OR = 0.51 (95% CI = 0.16, 1.63), p = .259, I^2= 41% Older patients (above cohort median age) All-cause mortality OR = 0.23 (95% CI = 0.12, 0.44), p = .001, I^2= 98% CVD mortality (4 or 5 studies) OR = 0.32 (95% CI = 0.11, 0.90), p = .031, I^2= 96% Cancer mortality (4 or 5 studies) OR = 0.28 (95% CI = 0.17, 0.48), p = .001, I^2= 80% Diabetes mortality (4 or 5 studies) OR = 0.21 (95% CI = 0.05, 0.96), p = .044, I^2= 89%	
Sutanto *et al.* 2021	11 studies 74,042 patients 1,698,263 controls	Gastric Bypass, Gastric Banding, Vertical Banded Gastroplasty, Roux-en-Y Gastric Bypass, Sleeve Gastrectomy, Duodenal Switch, Biliopancreatic diversion with duodenal switch	PubMed/MEDLINE, ScienceDirect, Cochrane Library, Wiley Online Library and Springer databases From inception to July 2021	Randomized controlled trials and cohort studies	Not defined	OR	MACE (10 studies) OR = 0.49 (95%CI = 0.40, 0.60), p < .001, I^2= 93%	Studies rated moderate-to-high quality. Key points Bariatric surgery significantly reduced the risk of MACE in people with obesity and CVD.

Wiggins *et al.* 2020	18 studies 269,818 patients 1,270,086 controls	Gastric bypass, sleeve gastrectomy, adjustable gastric band, vertical banded gastroplasty, biliopancreatic diversion.	Medline (via PubMed), Embase, and Web of Science 1 January 2000 to 31 January 2020.	Cohort studies	Clinical diagnosis of obesity	OR	<u>All-cause mortality (11 studies)</u> OR = 0.62 (95%CI = 0.55, 0.69), p < .001, I^2= 72% <u>Cardiovascular mortality (3 studies)</u> OR = 0.50 (95%CI = 0.35, 0.71), p < .001, I^2= 29% <u>Type 2 diabetes (6 studies)</u> OR = 0.39 (95%CI = 0.18, 0.83), p = .010, I^2= 99% <u>Hypertension (5 studies)</u> OR = 0.36 (95%CI = 0.32, 0.40), p < .001, I^2= 32% <u>Dyslipidaemia (2 studies)</u> OR = 0.33 (95%CI = 0.29, 0.73), p = .001, I^2= 79% <u>Ischemic heart disease (5 studies)</u> OR = 0.46 (95%CI = 0.29, 0.73), p < .001, I^2= 79% <u>Cardiac failure (2 studies)</u> OR = 0.23 (95%CI = 0.05, 1.10), p = .066, I^2= 97%	Studies rated high quality. Key points Bariatric surgery significantly reduced the risk of all-cause mortality, CVD mortality, hypertension, and CAD.
Yang *et al.* 2023	15 studies 122,361 participants People with T2D	Metabolic and bariatric surgery	PubMed, Embase, Medline, and Web of Science January 2000 to February 20, 2023	Cohort studies	Not defined	OR	<u>MACE morbidity (13 studies)</u> OR = 0.65 (95%CI = 0.59, 0.72), I^2= 63% <u>MACE mortality (8 studies)</u> OR = 0.49 (95%CI = 0.36, 0.67), I^2= 69% <u>Cerebrovascular disease (4 studies)</u> OR = 0.65 (95%CI = 0.48, 0.87), I^2= 0% <u>Coronary artery disease (6 studies)</u> OR = 0.67 (95%CI = 0.50, 0.92), I^2= 83% <u>Atrial fibrillation (6 studies)</u> OR = 0.80 (95%CI = 0.71, 0.90), I^2= 0% <u>Stroke (5 studies)</u> OR = 0.62 (95%CI = 0.42, 0.93), I^2= 27% <u>Heart failure (8 studies)</u> OR = 0.46 (95%CI = 0.38, 0.56), I^2= 45% <u>Myocardial infarction (5 studies)</u> OR = 0.61 (95%CI = 0.47, 0.79), I^2= 0%	Key points Bariatric surgery was related to a lower risk of cardiovascular outcomes including MACE, myocardial infarction and stroke and heart failure.

Zhou *et al.* 2016	32 studies 302,188 participants	Roux-en-Y gastric bypass, laparoscopic adjustable gastric banding, sleeve gastrectomy, and biliopancreatic diversion with duodenal switch, vertical banded gastroplasty, duodenal-jejunal bypass liner, implantable gastric stimulation.	PubMed, EMBASE, and CENTRAL Inception to July 13, 2015.	Randomized controlled trial, non-randomized controlled trials, and cohort studies	BMI > 30 kg/m^2	OR	Randomized controlled trials All-cause mortality (7 studies) OR = 0.33 (95%CI = 0.01, 8.21) Heart failure (2 studies) OR = 0.33 (95%CI = 0.03, 3.19), I^2= 0% Ischemic heart disease (2 studies) OR = 0.96 (95%CI = 0.10, 9.55), I^2= 0% Any cancer (4 studies) OR = 0.77 (95%CI = 0.22, 2.71), I^2=0% Obesity-related cancer (3 studies) OR = 0.90 (95%CI = 0.14, 5.62), I^2= 0% Nonrandomized controlled trial/Cohort studies All-cause mortality (19 studies) OR = 0.38 (95%CI = 0.29, 0.50), I^2= 91% Myocardial infarction (5 studies) OR = 0.52 (95%CI = 0.26, 1.04), I^2= 82% Stroke (3 studies) OR = 0.48 (95%CI = 0.17, 1.38), I^2= 84% Angina (2 studies) OR = 0.33 (95%CI = 0.13, 0.83), I^2= 85% Heart failure (2 studies) OR = 0.12 (95%CI = 0.09, 0.17), I^2= 0% Any cancer (6 studies) OR = 0.65 (95%CI = 0.46, 0.91), I^2= 86% Obesity related cancer (4 studies) OR = 0.55 (95%CI = 0.35, 0.85), I^2= 89% Non-obesity related cancer (3 studies) OR = 0.66 (95%CI = 0.37, 1.19), I^2= 73%	Included studies were of modest quality Key points Bariatric surgery significantly reduced the risk of all-cause mortality, angina, heart failure, and cancer among non-randomized studies. Effects were not observed in RCTs.

CV Risk / CVD Outcomes

Study	n studies/ participants	Type of Surgery	Databases Searched & Year/Range/ Countries	Study Designs	Obesity Measure	Effect Estimate	Results ES (95%CI), heterogeneity	Quality & Key points
Chandrakumar *et al.* 2023	49 studies	Roux-en-Y gastric bypass, sleeve	PubMed, Embase, Cochrane Library,	Cohort studies	BMI > 30 kg/m^2	HR	Cardiovascular Mortality (13 studies)	All studies were rated as good quality

	Number of participants not reported.	gastrectomy, gastric banding	Google Scholar, and Web of Science From inception to January 3, 2022				HR = 0.48 (95%CI = 0.40, 0.57), p < .001, I^2= 71% <u>Coronary artery disease (6 studies)</u> HR = 0.68 (95%CI = 0.68, 0.91), p = .008, I^2= 62% <u>Myocardial infarction (16 studies)</u> HR = 0.53 (95%CI = 0.44, 0.64), p <.001, I^2= 79% <u>Heart failure (15 studies)</u> HR = 0.45 (95%CI =0.37, 0.55), p <.001, I^2= 87% <u>Atrial fibrillation (7 studies)</u> HR = 0.81 (95%CI =0.65, 1.01), p = .07, I^2= 87% <u>Cerebrovascular accident (21 studies)</u> HR = 0.68 (95%CI =0.59, 0.78), p < .001, I^2= 72%	Key Points: Participants who underwent bariatric surgery had a significantly lower risk of cardiovascular mortality, CAD, MI, HF, and cerebrovascular accident.
Goodarzi *et al.* 2025	13 studies 1396 participants	Laparoscopic adjustable gastric band, Roux-en-Y gastric bypass, sleeve gastrectomy	PubMed/MEDLINE, Embase, Scopus, and Web of Science. From inception to October 4, 2024	Randomized controlled trials and cohort studies	Not defined	Mean Difference	<u>Cardiovascular Disease Risk Score (3 studies)</u> MD = -1.94 (95%CI = -3.48, -0.40), p = .013, I^2= 93% <u>Waist circumference (7 studies)</u> MD = -0.59 (95%CI = -1.15, -0.03), p = .040, I^2= 76% <u>Total cholesterol (6 studies)</u> MD = -0.88 (95%CI = -1.57, -0.03), p = .011, I^2= 88% <u>High-density lipoprotein (7 studies)</u> MD = 0.63 (95%CI = 0.37, 0.90), p < .001, I^2= 78% <u>Low-density lipoprotein (7 studies)</u> MD = -0.45 (95%CI = -0.71, -0.19), p < .001, I^2= 78% <u>Triglycerides (8 studies)</u> MD = -0.66 (95%CI = -0.88, -0.44), p < .001, I^2= 70% <u>Diastolic blood pressure (5 studies)</u>	Studies rated moderate-to-high quality. Key Points: Bariatric surgery more effective than low energy diet at improve cardiometabolic risk profiles

							MD = -1.03 (95%CI = -1.83, -0.24), p = .011, I^2= 90% Systolic blood pressure (6 studies) MD = -0.70 (95%CI = -1.26, -0.15), p = .013, I^2= 83% Fasting blood sugar (6 studies) MD = -0.61 (95%CI = -1.03, -0.19), p < .001, I^2= 68% Hemoglobin A1c (8 studies) MD = -0.49 (95%CI = -0.83, -0.15), p < .001, I^2= 88% HOMA-IR (7 studies) MD = -0.65 (95%CI = -1.22, -0.08), p = .008, I^2= 82%	
Popov *et al.* 2017	40 studies 5668 participants	Intragastric Balloon	MEDLINE, EMBASE, and the Cochrane Register for Controlled Trials From inception to April 2016	Randomized controlled trials and observational studies	Not defined	Mean difference and OR	Randomized controlled trials HbA1C (3 studies) MD = -1.1 (95%CI = -1.6, -0.6), p < .001, I^2= 3% FBG (5 studies) MD = -12.7 (95%CI = -21.5, -4.0), p < .001, I^2= 94% TG (2 studies) MD = -19.0 (95%CI = -41.6, 3.5), p = .100, I^2= 88% SBP (2 studies) MD = -3.4 (95%CI = -8.5, 1.7), p = .200, I^2= 94% DBP (2 studies) MD = -2.9 (95%CI = -4.1, -1.8), p = .001, I^2= 0% EWL (3 studies) MD = 22.3 (95%CI = 8.9, 35.8), p < .001, I^2= 96% TBWL (8 studies) MD = 5.9 (95%CI = 3.7, 8.1), p < .001, I^2= 99% Waist circumference (8 studies) MD = -4.1 (95%CI = -6.9, -1.4), p = .003	Trials of low-to-moderate quality Key Points: Intragastric balloons effective at improving a range of CVD risk factors.

							, I^2= 91% Observational studies HbA1C (12 studies) MD = -0.6 (95%CI = -1.0, -0.3), p < .001, I^2= 95% FBG (18 studies) MD = -8.0 (95%CI = -11.0, -5.0), p < .001, I^2= 71% TG (12 studies) MD = -33.4 (95%CI = -42.0, 25.0), p < .0001, I^2= 59% SBP (10 studies) MD = -9.1 (95%CI = -12.0, -5.2), p < .001, I^2= 78% DBP (9 studies) MD = -4.6 (95%CI = -6.0, -3.0), p < .001, I^2= 67% EWL (11 studies) MD = 31.8 (95%CI = 27.3, 36.2), p < .001, I^2= 92% TBWL (11 studies) MD = 11.0 (95%CI = 9.5, 12.7), p < .001, I^2= 99% Waist circumference (11 studies) MD = -11.0 (95%CI = -13.0, -9.0), p < .001, I^2= 65% Hypertension resolved (8 studies) OR = 2.0 (95%CI = 1.8, 2.2). p < .001, I^2= 0%	
Tang *et al.* 2022	21 studies 250,232 patients 2,606,784 controls	Roux-en-Y gastric bypass, sleeve gastrectomy, adjustable gastric band, laparoscopic adjustable gastric band, gastric bypass, vertical banding gastroplasty, Duodenal switch	PubMed, EMBASE, and the Cochrane Central Register of Controlled Trials Inception to August 18, 2021	Cohort studies	Not defined	RR	MACE (11 studies) RR = 0.53 (95%CI = 0.45, 0.62), p < .001, I^2= 95% Myocardial infarction (10 studies) RR = 0.40 (95%CI = 0.30, 0.52), p < .001, I^2= 92% Stroke (8 studies) RR = 0.60 (95%CI = 0.46, 0.79), p < .001, I^2= 85% CV mortality (9 studies)	Key points Bariatric surgery was related to a lower risk of cardiovascular outcomes including CV mortality, MACE, myocardial infarction and stroke and heart failure.

							RR = 0.43 (95%CI = 0.35, 0.54), p < .001, I^2= 85% All-cause mortality (12 studies) RR = 0.44 (95%CI = 0.32, 0.59), p < .001, I^2= 94%	
van Veldhuisen *et al.* 2022	39 studies Number of participants not reported.	Roux-en-Y gastric bypass, sleeve gastrectomy, adjustable gastric band, duodenal switch, vertical banding gastroplasty, biliopancreatic diversion, biliointestinal bypass,	Pubmed and Embase Inception to 28 August 2021	Randomized controlled trials, cohort studies, case-control studies	Not defined	HR	All-cause mortality HR = 0.55 (95%CI = 0.49, 0.62), p < .001, I^2= 78% CV mortality HR = 0.59 (95%CI = 0.47, 0.73), p < .001, I^2= 71% Atrial fibrillation HR = 0.82 (95%CI = 0.64, 1.06), p = .120, I^2= 76% Heart failure HR = 0.50 (95%CI = 0.38, 0.66), p < .001, I^2= 71% Myocardial infarction HR = 0.58 (95%CI = 0.42, 0.76), p < .001, I^2= 82% Stroke HR = 0.64 (95%CI = 0.53, 0.77), p < .001, I^2= 80%	Key points Bariatric surgery was related to a lower risk of cardiovascular outcomes including CV mortality, heart failure, myocardial infarction and stroke.
Yan *et al.* 2019	10 studies 15,005 patients 34,911 controls	Roux-en-Y gastric bypass, sleeve gastrectomy, adjustable gastric band, biliopancreatic diversion, non-adjustable gastric banding, vertical banding gastroplasty	Cochrane library, Pubmed, and EMBASE Inception to January 31, 2019	Randomized controlled trials and cohort studies	BMI ≥ 35 kg/m^2	RR, HR and mean difference	Macrovascular events (9 studies) RR = 0.43 (95%CI = 0.27, 0.70), I^2= 94% Cardiovascular events (3 studies) HR = 0.52 (95%CI = 0.39, 0.71), I^2= 0% All-cause mortality (2 studies) HR = 0.65 (95%CI = 0.26, 1.64), I^2= 85% Myocardial infarction (7 studies) RR = 0.40 (95%CI = 0.26, 0.61), I^2= 62% Stroke (5 studies) RR = 0.53 (95%CI = 0.28, 1.01), I^2= 72% BMI (5 studies) MD = -8.49 (95%CI = -15.01, -1.98), I^2= 99% HbA1c% MD = -0.61 (95%CI = -0.92, -0.30), I^2= 100% HOMA-IR	Key points Bariatric surgery was related to a lower risk of macrovascular and cardiovascular events, and myocardial infarction. Results not significant for stroke or all-cause mortality.

							MD = -2.75 (95%CI = -3.48, -2.03), I^2= 31% Plasma glucose MD = -1.29 (95%CI = -2.62, 0.04), I^2= 94% SBP MD = -0.00 (95%CI = -0.11, 0.10), I^2= 0% DBP MD = 0.90 (95%CI = 0.82, 0.97), I^2= 0%	
Yan *et al.* 2016	6 studies 204 patients 206 controls	Roux-en-Y gastric bypass	PubMed, Embase, Cochrane Database, and Cochrane Clinical Trials Registry Inception to December 2015	Randomized controlled trial	BMI ≥ 30 kg/m^2	OR and mean difference	SBP (6 studies) MD = -2.83, (95%CI = -4.88, -0.78), p < .01 DBP (5 studies) MD = 0.28, (95%CI = -1.89, 2.45), p = .80 Triglyceride (5 studies) MD = -0.87, (95%CI = -1.17, -0.57), p < .001, I^2= 76% Total cholesterol (6 studies) MD = -0.40, (95%CI = -0.92, 0.12), p = .130, I^2= 89% HDLC (6 studies) MD = 0.24, (95%CI = 0.18, 0.30), p < .001, I^2= 19% LDLC (6 studies) MD = -0.32, (95%CI = -0.62, -0.02), p < .05, I^2= 75% Waist circumference (6 studies) MD = -15.60, (95%CI = -18.21, -13.00), p < .001, I^2= 0% BMI (6 studies) MD = -6.54, (95%CI = -9.28, -3.80), p < .001, I^2= 95% Fasting plasma glucose (4 studies) MD = -1.58, (95%CI = -3.58, 0.41), p = .120, I^2= 85% HbA1c (6 studies) MD = -1.25, (95%CI = -1.88, -0.63), p < .001, I^2= 89% T2D remission (5 studies) OR = 76.37 (95%CI = 20.70, 281.73), p <.001, I^2= 0%	Key points Bariatric surgery was related to a lower cardiovascular disease risk factors.

WEIGHT LOSS								
Study	**n studies/ participants**	**Type of Surgery**	**Databases Searched & Year/Range/ Countries**	**Study Designs**	**Obesity Measure**	**Effect Estimate**	**Results ES (95%CI), heterogeneity**	**Quality & Key points**
Cosentino *et al.* 2021	43 studies	Roux-en-Y Gastric By-Pass, Laparoscopic, Sleeve Gastrectomy, Biliopancreatic Diversion, duodenal switch, One Anastomosis Gastric Bypass		Randomized controlled trials	BMI ≥ 25 kg/m^2	Mean difference	<u>BMI (14 studies)</u> MD = -6.63, (95%CI = -8.29, -4.97), p < .001, I^2= 95%	Key points Bariatric surgery effective at causing weight loss.
De Luca *et al.* 2023	65 studies 6271 participants	Roux-en-Y Gastric By-Pass, Laparoscopic Adjustable Gastric Banding Laparoscopic Adjustable Gastric Banding, Vertical Banding Gastroplasty, Vertical Gastrogastrostomy, Sleeve Gastrectomy, Bilio-Pancreatic Diversion, Mini-Gastric By-Pass, Greater Curvature Plication Gastric, One-anastomosis gastric bypass, Duodenal switch, duodenojejunal bypass, Gastrostoplasty	MEDLINE and Embase Inception to December 1, 2022	Randomized controlled trials	Not defined	MD	<u>BMI (20 studies)</u> MD = -6.01, (95%CI = -6.93, -5.09), p < .001, I^2= 87% <u>Body weight (16 studies)</u> MD = -18.99, (95%CI = -22.73, -15.25), p < .001, I^2= 71% <u>Percent weight loss (13 studies)</u> MD = 17.70, (95%CI = 14.54, 20.87), p < .001, I^2= 90%	Key points Bariatric surgery effective at causing weight loss.
Kermansaravi *et al.* 2025	11 studies 318 patients 501 controls	Intragastric balloon	PubMed, Web of Science, Embase, and Scopus	Clinical trials and observational studies	Not defined	Mean difference	<u>Excessive weight loss (4 studies)</u> MD = 21.18 (95%CI = 15.51, 26.85), p < .001, I^2= 79% <u>BMI (6 studies)</u>	9 studies rated as low risk of bias, 2 studies rated as moderate risk of bias

			From inception to July 24, 2024				MD = -7.45 (95%CI = -10.57, -4.33), p < .001, I^2= 87%	Key Points: Intragastric balloon led to significant weight loss as a bridging procedure before bariatric surgery.
Pipek *et al.* 2024	6 studies 427 participants	Roux-en-Y gastric bypass, biliopancreatic diversion, laparoscopic sleeve gastrectomy, laparoscopic adjustable gastric banding	From inception to October 10, 2023	Randomized controlled trials	Not defined	Mean difference	Body weight (5 studies) MD = -22.05 (95%CI = -28.86, -15.23), I^2= 78% Waist circumference (4 studies) MD = -12.29 (95%CI = -15.00, -9.58), I^2= 0% BMI (4 studies) MD = -7.98 (95%CI = -10.48, -5.48), I^2= 86% Triglycerides (3 studies) MD = -0.71 (95%CI = -0.82, -0.59), I^2= 50% LDL (4 studies) MD = -0.51 (95%CI = -1.03, 0.01), I^2= 93% HDL (4 studies) MD = 0.13 (95%CI = 0.02, 0.23), I^2= 90% Cholesterol (3 studies) MD = -0.89 (95%CI = -1.59, -0.18), I^2= 95% Cardiovascular risk score (2 studies) MD = -0.08 (95%CI = -0.10, -0.06), I^2= 0% SBP (4 studies) MD = -4.49 (95%CI = -7.66, -1.33), I^2= 71% DPBP (4 studies) MD = -2.29 (95%CI = -4.26, -0.32), I^2= 60% HOMA (3 studies) MD = -2.94 (95%CI = -0.3.61, -2.27), I^2= 14% HbA1c (5 studies) MD = -0.97 (95%CI = -1.32, -0.62), I^2= 80%	Key Points: Bariatric surgery was more effective at weight loss and cardiovascular risk reduction compared to pharmacological treatments.

HYPERTENSION								
Study	**n studies/ participants**	**Type of Surgery**	**Databases Searched & Year/Range/ Countries**	**Study Designs**	**Obesity Measure**	**Effect Estimate**	**Results ES (95%CI), heterogeneity**	**Quality & Key points**

Dastjerdi *et al.* 2025	29 studies 1249 patients 1158 controls	Roux-en-Y Gastric Bypass, Bilio-Pancreatic Diversion, biliopancreatic diversion, gastric banding, laparoscopic adjustable gastric band,	PubMed, Scopus, Embase, and Cochrane From inception to May 2, 2024	Randomized controlled trials	Not defined	Mean difference	SBP (26 studies) MD = -4.51 (95%CI = -7.00, -2.01), p = .001, I^2= 67% DBP (25 studies) MD = -3.04 (95%CI = -4.77, -1.31), p = .001, I^2= 73% Fasting blood sugar (21 studies) MD = -30.44 (95%cI = -41.29, -19.60), p < .001, I^2= 81% HbA1c (24 studies) MD = -1.11 (95%cI = -1.41, -0.80), p < .001, I^2= 81%	Key Points: Bariatric surgery was more effective than non-surgical treatments at decreasing hypertension.
Sebastian *et al.* 2025	19 studies 1098 participants	Roux-en-Y Gastric Bypass, sleeve gastrectomy, laparoscopic adjustable gastric banding, gastric banding	MEDLINE (via PubMed), Google Scholar, ScienceDirect, and ClinicalTrials.gov 2002 to June 2024	Randomized controlled trials	Not defined	RR and mean differences	Hypertension remission (5 studies) RR = 2.77 (95%CI = 1.26, 6.10), p = .01, I^2= 81% SBP (16 studies) MD = -3.81 (95%CI = -5.55, -2.07), p < .001, I^2= 89%	Key Points: Bariatric surgery was effective at long term improvements in hypertension compared to non-surgical intervention
Wang *et al.* 2021	19 studies 1353 participants	Roux-en-Y Gastric Bypass, laparoscopic adjustable gastric banding, sleeve gastrectomy, Duodenal-Jejunal bypass liner	MEDLINE via PubMed, Embase, the Cochrane library, and Clinical Trials Registry From inception to May 1, 2021	Randomized controlled trials	BMI ≥ 28 kg/m^2	Mean difference	SBP (26 studies) MD = -3.94 (95%CI = -6.00, -1.88), p < .001, I^2= 0% DBP (25 studies) MD = -2.69 (95%CI = -3.99, -1.39), p < .001, I^2= 0%	Key Points: Bariatric surgery was effective at long term improvements in hypertension compared to non-surgical intervention
HEART FAILURE								
Study	**n studies/ participants**	**Type of Surgery**	**Databases Searched & Year/Range/ Countries**	**Study Designs**	**Obesity Measure**	**Effect Estimate**	**Results ES (95%CI), heterogeneity**	**Quality & Key points**
Berger *et al.* 2018	12 studies Number of participants not reported.	Roux-en-Y Gastric Bypass, Bilio-Pancreatic Diversion, biliopancreatic diversion, gastric banding, laparoscopic	PubMed, EMBASE and Cochrane Inception to September 30, 2017	Randomized controlled trials and observational studies	Not specified	RR	Heart failure (7 studies) RR = 0.28 (95%CI = 0.13, 0.59), p < .001, I^2= 95%	Key Points: Bariatric surgery significantly reduces the risk of heart failure.

		adjustable gastric band,						
Chokesuwattanaskul *et al.* 2020	7 cohort studies involving 7681 patients undergoing bariatric surgery.	Bariatric surgery (specific types of bariatric surgery are not specified).	MEDLINE, EMBASE, and Cochrane Database. From inception through March 2019.	Cohort Studies	NS	OR	<u>Atrial Fibrillation</u> Pooled Odds Ratio (OR): 0.42 (95% CI: 0.22–0.83) for atrial fibrillation risk reduction. Incidence of AF: 5.3% (95% CI: 1.9–13.8) at a median follow-up time of 7.9 years (IQR: 4.1–15.0 years).	The overall estimated incidence of AF following bariatric surgery was5.3%. Our study demonstrates a significant beneficial association between bariatric surgery and AF, with a 0.42-fold decreased risk of AF.
Pontiroli *et al.* 2023	10 studies 61,197 total participants (22,831 bariatric surgery patients and 38,366 control patients).	Restrictive surgeries: Vertical banded gastrotomy (VGB), Adjustable gastric banding (AGB). Metabolic surgeries: Laparoscopic sleeve gastrectomy (LSG), Roux-en-Y gastric bypass (RYGB). Mixed procedures: Gastrectomy (GA), Gastric resection (GR), Gastric intestinal bypass (GIB)	Databases: PubMed, Embase, Cochrane Library. Year/Range: From inception until October 30, 2022.	Cohort studies (prospective and retrospective). Controlled trials evaluating the appearance of atrial fibrillation in patients undergoing bariatric surgery compared to medical treatment.	BMI, WL %	OR	<u>Atrial Fibrillation</u> Bariatric surgery significantly reduced the appearance of incident atrial fibrillation Odds Ratio (OR): Overall OR = 0.665 (95% CI: 0.475–0.929), p = 0.017. Sensitivity analysis excluding one study: OR = 0.608 (95% CI: 0.454–0.814), p < 0.001.	NOS used- poor to good Bariatric surgery is associated with reduced incident atrial fibrillation, primarily through sustained weight loss. The effect was more significant for cohorts with higher weight loss percentages and lower diabetes prevalence. Age and BMI were important factors influencing the effect

6.7 Systematic review and meta-analyses for the impact of behavioural interventions on weight loss, CV risk and CVD outcomes in people with or at risk of CVD

Table 6.7 Systematic review and meta-analyses for the impact of behavioural interventions on weight loss, CV risk and CVD outcomes in people with or at risk of CVD

DIETARY INTERVENTION								
Study	**n studies/ participants**	**Diet interventions & Population**	**Databases Searched & Year/Range/ Countries**	**Study Designs**	**Obesity Measure**	**Effect Estimate**	**Results ES (95%CI), heterogeneity**	**Quality & Key points**
Khalafi *et al.* 2024	N= 24 studies, 2032 participants	Diet Interventions: Intermittent fasting (IF) compared to control diet (CON) and/or continuous caloric restriction (CR). Population: Adults with overweight and obesity. Intervention durations were ≥ 6 months.	PubMed, Web of Science, and Scopus. From inception to March 2024.	Randomised trials	Body weight, BMI, fat mass, fat-free mass, waist circumference, visceral fat.	WMD	<u>Body Composition</u> Compared with CON: IF decreased Body weight [WMD: 2.84 kg (95% CI: 4.37 to1.31), p = 0.001; 9 trials], BMI [WMD: 1.41 kg.m2 (95% CI: 2.04 to 0.77), p = 0.001; 4 trials] Fat mass [WMD: 3.06 kg (95% CI:4.21 to 1.91), p = 0.001; 4 trials], FFM [WMD: 0.81 kg (95%CI: 1.49 to 0.13), p = 0.01; 4 trials] WC [WMD: 3.85 cm (95%CI: 5.10 to 2.59), p = 0.001; 6 trials], visceral fat [SMD: 0.37(95% CI: 0.63 to 0.10), p = 0.006; 4 trials] Heterogeneity was not significant for BMI (I 2 = 0.00, p = 0.55), fat mass (I 2 = 0.00, p = 0.67), FFM(I2 = 0.00, p = 0.82), WC (I 2 = 0.00, p = 0.57), or visceral fat(I2 = 0.00, p = 0.87. There was significant heterogeneity for bodyweight (I2 = 5.69, p = 0.01)	Key Points: IF and CR are comparably effective for reducing body weight and adiposity. IF improves cardiometabolic health markers, including lipid profiles and blood pressure. Mode of IF and intervention duration are primary moderators of its effects. Poor compliance and adherence rates to dietary interventions remain a challenge.

Compared with CR:

IF did not decrease
Body weight [WMD: 0.53 kg (95% CI: 1.12 to0.05), p = 0.07; 22 trials]

BMI [WMD: 0.23 kg.m2 (95% CI: 0.55to 0.08), p = 0.14; 15 trials]

FFM [WMD: 0.04 kg (95% CI: 0.25 to 0.33), p = 0.78; 14 trials]

WC [WMD: 0.50 cm (95% CI: 1.36to 0.33), p = 0.25; 14 trials]

Visceral fat [SMD: -0.06 (95% CI:0.2 to 0.09), p = 0.45; 8 trials] significantly more than CR.

However, IF decreased fat mass [WMD: 0.70 kg (95% CI:1.32 to 0.07), p = 0.02; 14 trials] and body fat percentage [WMD: 0.59% (95% CI: 1.15 to 0.04), p = 0.03; 7 trials] significantly more than CR

Heterogeneity was not significant for body weight (I2 = 0.00, p = 0.90), BMI(I2 = 0.00, p = 0.83), fat mass (I 2 = 0.00, p = 0.99), body fat percent-age (I2 = 0.00, p = 0.73), FFM (I 2 = 0.00, p = 0.83), WC (I 2 = 0.00,p = 0.89), or visceral fat (I 2 = 0.00, p = 0.99)

Glycaemic Control
Compared to CON

IF resulted in significantly larger decreases in fasting glucose [WMD: 0.14 mmol/l (95% CI: 0.24 to 0.04), p = 0.003; 6 trials],
not fasting insulin [SMD: -0.28 (95% CI: 0.72 to 0.15), p = 0.006; 5 trials] or
HbA1c% [WMD: 0.07% (95% CI: 0.22 to 0.08), p = 0.36; 4 trials] compared to CON

Heterogeneity was not significant for glucose (I 2 = 0.00, p = 0.59), but there was significant heterogeneity for insulin (I 2 = 74.37, p = 0.004) andHbA1c% (I 2 = 61.02, p = 0.05

Compared to CR

IF did not decrease fasting glucose [WMD: 0.07 mmol/l (95% CI:0.15 to 0.01), p = 0.10; 15 trials], fasting insulin [SMD: -0.10 (95%CI: 0.30 to 0.10), p = 0.33; 9 trials], or HbA1c% [WMD: 0.004%(95% CI: 0.03 to 0.04), p = 0.84; 10 trials] significantly more than CR (Figures S45–S47 and Table 2). Heterogeneity was not significant for insulin (I 2 = 31.65, p = 0.16) or HbA1c% (I 2 = 0.00, p = 0.64), but was significant for fasting glucose (I 2 = 75.04, p = 0.001).

Lipids:
Compared to CON

IF did not decrease TC [WMD: 0.11 mmol/l (95% CI: 0.27 to 0.04),p = 0.15; 6 trials] or LDL [WMD: 0.08 mmol/l (95% CI: 0.20 to0.034), p = 0.15; 6 trials], but did increase HDL significantly more[WMD: 0.04 mmol/l (95% CI: 0.009 to 0.08), p = 0.01; 6 trials] and decrease TG significantly more [WMD: 0.12

mmol/l (95% CI: 0.21to 0.02), p = 0.01; 7 trials)

Compared to CR:

IF did not decrease TC [WMD: 0.01 mmol/l (95% CI: 0.10 to0.07), p = 0.75; 16 trials], LDL [WMD: 0.03 mmol/l (95% CI:0.11 to 0.04), p = 0.34; 16 trials], or TG [WMD: 0.04 mmol/l(95% CI: 0.11 to 0.01), p = 0.01; 16 trials], but did increase HDL[WMD: 0.03 mmol/l (95% CI: 0.009 to 0.08), p = 0.009; 16 trials]significantly more than CR

Heterogeneity was not significant for TC (I2 = 0.00, p = 0.60), LDL(I2 = 0.00, p = 0.75), HDL (I 2 = 0.00, p = 0.84), or TG (I 2 = 0.00,p = 0.47)

Blood Pressure

Compared to CON

IF decreased DBP significantly more [WMD: 2.24 mmHg (95% CI:4.17 to 0.32), p = 0.02; eight trials] and SBP that neared a significance [WMD: 2.53 mmHg (95% CI: 5.10 to 0.02), p = 0.05; eight trials] compared to CON

Heterogeneity was not significant for SBP (I2 = 8.37, p = 0.36) or DBP(I 2 = 27.26, p = 0.21).

Compared to CR

IF did not decrease SBP [WMD: 0.11 mmHg (95% CI: 1.24 to1.01), p = 0.84; 15 trials], but did decrease DBP [WMD: 0.91 mmHg(95% CI:

							1.72 to 0.09), p = 0.02; 15 trials] significantly more than CR Heterogeneity was not significant for SBP (I 2 = 0.00, p = 0.61) or DBP (I 2 = 0.00, p = 0.88).	
Wu *et al.* 2025	20 studies with 1393 participants (689 in treatment groups, 704 in control groups).	Diet Intervention: 5:2 diet (fasting for 2 days per week, consecutive or non-consecutive, with calorie restriction or low-calorie meal replacements). Population: Adult patients diagnosed with overweight and/or obesity, stable weight in the last 3 months, no major medical conditions, regardless of gender, disease duration, nationality, or other factors	PubMed, The Cochrane Library, Web of Science, Embase. From database establishment to April 2024.	RCTS	BMI, body weight, waist circumference, body fat percentage, hip circumference, visceral fat, fat mass, fat-free mass.	MD	Compared to control, 5:2: Body weight -0.85 (-1.52, -0.17) BMI: –2.77 (–3.48, –2.06) WC: -0.77 (–1.29, –0.26) LDL-C: -0.24 (–0.45, –0.03) SBP: -2.93 (–4.06, –1.81) HOMA-IR: -0.34 (–0.70, 0.0)- but heavily influenced by one study. No significant differences were observed in visceral fat, total cholesterol, triglycerides, high-density lipoprotein (HDL), diastolic blood pressure, insulin, fasting blood glucose, glycated haemoglobin A1c, and heart rate.	RoB/GRADE: All indicators were presented as moderate- or low-quality evidence Key points: The 5:2 diet is effective for weight reduction and improving cardiovascular disease risk factors in overweight/obese individuals. Mild physical and psychological side effects (e.g., dizziness, fatigue, mood swings, constipation) were reported during fasting but resolved spontaneously. The diet is safe and feasible but requires monitoring of physical conditions during fasting periods for timely adjustments.
Zare *et al.* 2025	22 studies, 3562 participants	Diet Interventions: DASH diet compared to usual diets.	PubMed, Web of Science, Scopus.	Controlled clinical trials (randomized,	BMI ≥25 kg/m² or waist circumference >102 cm for males	WMD	Total Cholesterol (TC): WMD: -5.05 mg/dl (95% CI: -8.78, -1.31; p = 0.008). (I^2 = 94.5%, p < 0.001	Quality: Most studies classified as high quality;

	(1790 in DASH group, 1772 in control group).	Population: Overweight/obese individuals (BMI ≥25 kg/m² or waist circumference >102 cm for males and >88 cm for females).	Search conducted until January 2024. Countries: Studies conducted in Iran (9), USA (7), Brazil (2), Australia (2), Egypt (1), Korea (1).	double-blinded, single-blinded, parallel, cross-over designs).	and >88 cm for females.		LDL-C: WMD: -5.33 mg/dl (95% CI: -8.54, -2.11; p = 0.001). (I^2 = 95.92%, p < 0.001). VLDL-C: WMD: -3.26 mg/dl (95% CI: -6.19, -0.34; p = 0.029). (I^2 = 39.95%, p = 0.172). Triglycerides (TG): WMD: -0.03 mg/dl (95% CI: -0.93, 0.87; p = 0.954). (I^2 = 88.2%, p < 0.001) HDL-C: WMD: -0.3 mg/dl (95% CI: -1.37, 0.78; p = 0.587). (I^2 = 92.59%, p < 0.001).	two studies classified as moderate quality. GRADE Assessment: High Certainty: LDL-C, VLDL-C. Moderate Certainty: TC, TG, HDL-C. Key Points: DASH diet significantly reduces TC, LDL-C, and VLDL-C levels. No significant effects on TG and HDL-C levels. Greater reductions observed in interventions ≤8 weeks. Mechanisms include reduced saturated fat intake, increased fiber, weight loss, and antioxidant effects. Results applicable globally but lack studies from Europe.
Zaman *et al.* 2023	Studies, 927 participants	Diet Interventions: Time-restricted eating (TRE) with eating windows ranging from 4 to 12 hours daily.	MEDLINE Complete, Web of Science, Scopus, Cochrane Library, Academic Search Complete, Food Science Source, Open.	Parallel-arm randomized controlled trials (RCTs) (13 studies).	BMI, body weight, waist circumference, fat mass, lean body mass.	MD	Body weight reduction: MD -2.26 kg (95%CI: -3.10 to -1.43; P < 0.00001; I^2 = 93%). Waist circumference reduction: MD -2.35 cm (95%CI: -4.43 to -0.27; P = 0.03; I^2 = 81%).	Quality: Risk of bias (RoB) assessed using Cochrane RoB-2 tool.

Population: Adults with excessive weight and obesity-related metabolic diseases, including prediabetes and Type 2 Diabetes Mellitus. Participants had a BMI above the normal cutoff (26.4–38.9 kg/m²) and ranged in age from 27 to 74 years.	Dissertations, Education Research Complete, Psychology and Behavioural Sciences Collection. Search conducted until May 2022. Countries: Studies were conducted in the United States (7), Brazil (3), China (3), Switzerland (1), and Germany (1).	Randomized crossover trial (RXT) (1 study). Non-randomized controlled trial (NRCT) (1 study) Duration: Interventions lasted between 3 weeks and 12 months.	Fat mass reduction: SMD -0.63 (95%CI: -1.10 to -0.17; P = 0.008; I^2 = 83%). Lean body mass reduction: MD -0.64 kg (95%CI: -1.11 to -0.16; P = 0.009; I^2 = 75%).	Seven studies had high RoB; eight studies had concerns regarding RoB. Key Points: TRE significantly reduced body weight, waist circumference, fat mass, lean body mass, blood glucose, insulin, and triglycerides. Subgroup analysis showed shorter eating windows (4–6 hours) had more pronounced effects compared to longer eating windows (10–12 hours). No significant changes in HbA1c, HOMA-IR, total cholesterol, LDL-C, HDL-C, systolic and diastolic blood pressure, or heart rate. Shorter eating windows (4–6 hours) yield better results but may pose adherence challenges. Larger, high-quality trials are needed to confirm findings and determine optimal eating duration for cardiovascular disease prevention.	

Melgar *et al.* 2023	9 RCTs, 1,628 adults (561 in vegetarian diet (VD) arm, 587 in omnivorous diet arm).	Diet Interventions: Vegetarian diets (VDs) classified as lacto-ovo-vegetarian (4 RCTs) and vegan diets (5 RCTs). Lacto-ovo-vegetarian diets exclude meat, fish, and poultry. Vegan diets exclude all animal products, including dairy. Population: Adults with overweight (BMI ≥25 to <30 kg/m²) or obesity (BMI ≥30 kg/m²).	PubMed, EMBASE, Scopus, Web of Science. From inception to February 2, 2022.	RCTs 3 to 24 months (6–24 months for lacto-ovo-vegetarian diets; 3–5.5 months for vegan diets).	Anthropometric measures: Weight, BMI, waist circumference (WC), hip circumference (HC), body fat percentage.	MD	Vegetarian diet: Weight: MD −3.60 kg (95% CI −4.75 to −2.46), I^2 = 61%. BMI: MD −0.87 kg/m² (95% CI −1.80 to 0.06), I^2 = 90%. WC: MD −3.00 cm (95% CI −6.20 to 0.20), I^2 = 91%. HC: MD −0.86 cm (95% CI −3.46 to 1.74), I^2 = 0%. Glucose: MD −10.64 mg/dL (95% CI −15.77 to −5.51), I^2 = 0%. HbA1c: MD −0.40% (95% CI −0.89 to 0.10), I^2 = 98%. Insulin: MD −3.83 mU/L (95% CI −8.06 to 0.40), I^2 = 41%. SBP: MD −0.25 mmHg (95% CI −2.58 to 2.07), I^2 = 74%. DBP: MD −1.57 mmHg (95% CI −3.93 to 0.78), I^2 = 94%.	Study quality: Very low for most outcomes due to high heterogeneity and imprecision. Low for HC and body fat percentage. Key Points: VDs may reduce weight and glucose but have no significant effects on other anthropometric, metabolic, or blood pressure outcomes. Larger RCTs with longer follow-up periods and better adherence are needed to confirm findings. Subgroup analyses showed similar results for vegan and lacto-ovo-vegetarian diets.
Senkus *et al.* 2024	31 RCTs Total of 5316 participants across studies.	Medical Nutrition Therapy (MNT) provided by dietitians, including: DASH diet. Sodium reduction. Potassium increase. Caloric restriction. Physical activity goals.	MEDLINE, CINAHL, Cochrane Central. Studies published between 1985–2022. Countries: Studies conducted globally, including the United States, Brazil, Norway,	RCTs Duration: Interventions ranged from 1 month to 5 years. Contacts: Minimum of 2 dietitian	BMI, body weight, WC	MD	SBP: MD: -3.63 mmHg (95% CI: -4.69, -2.56 mmHg); I^2 = 67.6%. DBP: MD: -1.99 mmHg (95% CI: -2.59, -1.39 mmHg); I^2 = 57.3%. Body Weight:	Quality: Certainty of evidence graded using GRADE methodology: Moderate certainty for SBP, DBP, body weight, and CVD risk score. Low certainty for waist circumference and arterial stiffness.

		Individualized dietary plans. Population: Adults aged ≥18 years with prehypertension or hypertension. Some studies included participants with comorbidities like obesity, dyslipidaemia, or elevated cardiovascular disease risk.	Korea, Canada, Australia, and others.	contacts over 4 weeks.			MD: -1.93 kg (95% CI: -2.64, -1.21 kg); I^2 = 74.1%. BMI: MD: -0.25 kg/m² (95% CI: -0.45, -0.04 kg/m²); I^2 = 3.6%. Waist Circumference: MD: -1.04 cm (95% CI: -2.04, -0.04 cm); I^2 = 24.2%. Stroke incidence: RR: 0.34 (95% CI: 0.14, 0.81); P = 0.02. HTN incidence: RR:0.46(0.22,0.97) MI: RR: 0.83 (95% CI: 0.48, 1.42); P = 0.49. CVD risk score: Standardized Mean Difference (SMD): -0.20 (95% CI: -0.31, -0.08); P < 0.001. MNT likely reduces CVD risk score.	Very low certainty for endothelial function and quality of life. Key Points: MNT provided by dietitians significantly improves blood pressure, body weight, and CVD risk factors. Dietitian-led interventions are effective both individually and as part of multidisciplinary teams. Interventions employing DASH diet, sodium reduction, and caloric restriction showed greater effectiveness. MNT reduces the need for antihypertensive medications and improves stroke risk but has unclear effects on myocardial infarction and mortality.
Lei *et al*. 2022	33 RCTS, 3,939 participants (1,978 on low-carbohydrate diets (LCD) and 1,961 on low-fat diets (LFD)).	LCD: Carbohydrate intake ≤40% of total energy or ≤50 g/day (very low carbohydrate diets). LFD: Fat intake <30% of total energy.	PubMed, EMBASE, and Cochrane Library. Studies published up to March 30, 2022. Countries: North America (19 studies),	RCTs from 6-24mth duration	BMI Overweight: BMI ≥25 kg/m² (≥23 kg/m² for Asian studies). Obesity: BMI ≥30 kg/m².	WMD	Triglycerides (TG): Greater reduction in LCD (WMD: –0.14 mmol/L; 95% CI: –0.18 to –0.10 mmol/L; low heterogeneity, I^2=21.3%). HDL-C: Greater increase in LCD (WMD: 0.07 mmol/L; 95% CI: 0.06–0.09 mmol/L; low heterogeneity, I^2=35%).	Risk of bias: 6 studies had high risk, 3 had low risk, and the rest had moderate risk. Evidence quality: Low to very low due to study

		Population: Overweight and obese adults (BMI ≥25 kg/m² or BMI ≥30 kg/m²; for Asian studies, BMI ≥23 kg/m² or BMI ≥30 kg/m²). Participants included those with or without basic diseases such as diabetes, hypertension, and hyperlipidaemia	Asia (3 studies), Oceania (4 studies), Europe (7 studies).				Total Cholesterol (TC): Greater reduction in LFD (WMD: 0.14 mmol/L; 95% CI: 0.07–0.20 mmol/L; low heterogeneity, I^2=29%). LDL-C: Greater reduction in LFD (WMD: 0.10 mmol/L; 95% CI: 0.06–0.14 mmol/L; low heterogeneity, I^2=35%). Diastolic Blood Pressure (DBP): Greater reduction in LCD (WMD: –0.87 mmHg; 95% CI: –1.41 to –0.32 mmHg; low heterogeneity, I^2=0%). Weight Loss: Greater reduction in LCD (WMD: –1.33 kg; 95% CI: –1.79 to –0.87 kg; low heterogeneity, I^2=20%). No significant difference: Systolic blood pressure (SBP) and fasting blood glucose.	limitations, inconsistency, and indirectness. Key Points: Both diets have specific benefits, and the choice of diet may depend on individual metabolic indicators and weight loss goals. LCD showed greater benefits for TG, HDL-C, DBP, and weight loss. LFD was more effective for reducing TC and LDL-C. No significant differences in long-term effects (24 months). Subgroup analyses revealed no differences in participants with diabetes, hypertension, or hyperlipidaemia. Long-term clinical efficacy and effects of carbohydrate/fat sources need further research.
Hernandez *et al.* 2025	26 RCTs, Total participants: 10,352	Intervention: Mediterranean Diet (MED)	PubMed, EMBASE, Web of Science, Scopus, Cochrane Library,	RCTs Median follow-up: 6 months (range: 1.5	BMI, body weight, WC, WHR	MD	BMI: MD −0.61 kg/m² (95% CI −1.14 to −0.09; 17 RCTs; very low QoE)	Quality of Evidence (QoE): Very low for most outcomes (GRADE methodology)

Population: Overweight or obese adults (≥18 years) without cardiovascular disease (CVD) Control groups: Various diets (e.g., low-fat, low-carbohydrate, vegan, vegetarian, conventional diets) or advice/no treatment	ClinicalTrials.gov, ClinicalTrialsRegister.eu Search range: Until October 24, 2023	months to 4.8 years)	Waist Circumference: MD −2.48 cm (95% CI −3.99 to −0.96; 17 RCTs; very low QoE) Triglycerides: MD −7.93 mg/dL (95% CI −13.48 to −2.39; 19 RCTs; very low QoE) Fatty Liver Index: MD −12.26 (95% CI −23.96 to −0.56; 3 RCTs; very low QoE) MED also non-significantly lowered SBP (MD, −1.7 mm Hg; 95% CI, −4.39 to 0.99; 14 RCTs; very low QoE) and DBP (MD, −1.24 mm Hg; 95% CI, −2.99 to 0.52; 14 RCTs; very low QoE) MED non-significantly lowered blood glucose (MD, −0.2 mg/dL; 95% CI, −0.61 to 0.21; 17 RCTs; very low QoE), insulin (MD, −0.95 mIU/L; 95% CI, −2.19 to 0.29; 15 RCTs; very low QoE), HOMA-IR (MD, −0.26; 95% CI, −0.63 to 0.11; 13 RCTs; very low QoE), and HbA1c (MD, −0.08%; 95% CI, −0.21 to 0.04; 6 RCTs; very low QoE) MED was also associated with significantly lower weight (MD, −1.36 kg; 95% CI, −2.23 to −0.19; 23 RCTs; very low QoE) and waist-to-hip ratio (MD, −0.01; 95% CI, −0.03 to −0.003; 4 RCTs; low QoE), non-significantly lower HC (MD, −0.15 cm; 95% CI −5.6 to 5.3; 3 RCTs; very low QoE), and non-significantly higher body fat percentage (MD, 0.07%; 95% CI, −0.62 to 0.77; 9 RCTs; very low QoE). Heterogeneity: High for several outcomes (I^2 > 60%)	Key Points: MED significantly reduced BMI, WC, triglycerides, and fatty liver index. No significant changes in other cardiovascular risk factors. Limited data on clinical outcomes; only one trial (2018 PREDIMED) reported a 35% lower risk of myocardial infarction, stroke, or CV death (HR 0.65; 95% CI 0.50–0.85). High risk of bias in 27% of trials; 58% had some concerns.

Silverii *et al.* 2022	25 RCTS: 1233 cases on low-carbohydrate (LC) diets and 1209 cases on balanced diets.	Diet Interventions: LC diets: Defined as mild LC (26%-45% of total calories from carbohydrates) and very LC (<26% of total calories or <130 g of carbohydrates daily). Control diets: Non-carbohydrate–restricted diets (45%-60% of total calories from carbohydrates). Population: Individuals with a body mass index (BMI) >30 kg/m² (obese individuals).	PubMed, Cochrane, clinicaltrials.gov, and Embase. Up to November 1, 2021. Countries: Trials conducted in various countries, including the United States, Italy, Spain, and the United Kingdom.	RCTS with a minimum duration of 12 weeks. Trials included dietary interventions combined with equivalent non-pharmacological interventions (e.g., physical activity, psychological support).	BMI, body weight	LC diets were associated with a significantly higher reduction of body weight at 3-4 (MD −2.59 [−3.93, −1.25] kg, P = .0001) and 6-8 months (MD −2.64 [−4.32, −0.95] kg, P = .002) with respect to balanced diets, with no heterogeneity (I2 = 0). The difference in reduction of body weight between the two arms was no longer significant at 10-14 months (−2.30 [−5.00, +0.41]) kg, I^2 = 19) and it totally disappeared at 18-30 months (MD +0.89 [−2.32, +4.10] kg, I^2 = 0). BMI Reduction: At 3-4 months: MD −1.66 kg/m² (95% CI: −2.70, −0.61), P = .002. No significant difference at other time points. Differences in fasting plasma glucose between LC diets and control arms were not statistically significant at any time point LC diets were associated with a significant increase of HDL cholesterol at 10-14 (MD 2.38 [0.29, 4.47] mg/dl) and 18-30 months (MD 4.94 [0.30, 9.57] mg/dl), but not at 3-4 and 6-8 months (Table S2), whereas no difference in total or LDL cholesterol was found at any time point (Table S2). A reduction in triglycerides was observed at 3-4, 10-14 and 18-30 months (MD −1.78-20.63 [−35.37, −5.89], −27.09 [−38.29, −15.90] and −23.26 [−45.53, −0.98] mg/dl, respectively), but not at 6 months. No difference was found in blood pressure at any time point, with the only exception of lower diastolic	Quality of Evidence: High for body weight at 3-4, 6-8, and 10-14 months; BMI at 3-4 months. Moderate for weight at 18-30 months; BMI at 6-8 and 10-14 months. Low for BMI at 18-30 months and renal function outcomes Key Points: LC diets are effective for short-term weight loss but show no clear advantage in the long term. Cardiovascular risk factors (e.g., triglycerides, HDL cholesterol) improved in the long term. Renal safety remains undetermined due to limited reporting. Psychological well-being improved with weight loss, but no significant differences between LC and control diets.

							blood pressure at 3-4 and 6-8 months in LC diets (MD −3.22 [−5.90, −0.53] and −1.78 [−3.10, −0.45] mmHg, respectively; Table S2).	
Ge *et al.* 2020	121 studies, 21,942 participants	Diet Interventions: 14 popular named diets (e.g., Atkins, DASH, Zone, Mediterranean, Weight Watchers, etc.) and three control diets (usual diet, dietary advice, low fat diet). Population: Adults aged ≥18 years who were overweight (BMI 25-29) or obese (BMI ≥30).	Medline, Embase, CINAHL, AMED, and CENTRAL. Year/Range: From database inception until September 2018.	RCTS Minimum follow-up of 3 months, with outcomes assessed at 6 and 12 months.	BMI	NMA	Weight loss at 6 months: Low carbohydrate diets (4.63 kg), low fat diets (4.37 kg), moderate macronutrient diets (slightly less). Blood pressure reduction at 6 months: Systolic (5.14 mm Hg for low carbohydrate, 5.05 mm Hg for low fat), diastolic (3.21 mm Hg for low carbohydrate, 2.85 mm Hg for low fat). LDL cholesterol reduction: Low fat diets (7.08 mg/dL), moderate macronutrient diets (5.22 mg/dL). HDL cholesterol increase: Low carbohydrate diets (2.31 mg/dL). C-reactive protein: No significant differences. Weight Loss: Low carbohydrate vs. usual diet: 4.63 kg (95% CI: 3.42 to 5.87). Low fat vs. usual diet: 4.37 kg (95% CI: 3.02 to 5.72). Blood Pressure: Systolic reduction for low carbohydrate: 5.14 mm Hg (95% CI: 3.01 to 7.32). Diastolic reduction for low carbohydrate: 3.21 mm Hg (95% CI: 1.89 to 4.53).	Quality: Moderate certainty evidence for most outcomes at 6 months; low certainty evidence at 12 months due to inconsistency and imprecision. Key Points: Most diets showed modest weight loss and cardiovascular risk factor improvements at 6 months. Effects diminished at 12 months, except for the Mediterranean diet (LDL cholesterol reduction). Differences between diets were small to trivial, allowing individuals to choose based on preference. Adherence to diets was not consistently reported, which may have influenced long-term results

Wang *et al.* 2020	22 RCTs, 1865 participants	Diet interventions included whole grain foods such as barley, oat, wheat, rye, and quinoa. Population: Obese/overweight adults (BMI ≥ 24 kg/m²).	PubMed, Embase, Cochrane Central Register of Controlled Trials. Year/Range: No time restriction mentioned.	RCTs >2 wks	BMI, WC	MD	Wholegrain v control- Body weight: Mean difference (MD) = -0.5, 95% CI [-0.74, -0.25], I^2 = 35%, p < 0.0001. CRP: MD = -0.36, 95% CI [-0.54, -0.18], I^2 = 69%, p < 0.0001. LDL-C: MD = -0.08, 95% CI [-0.16, 0.00], I^2 = 27%, p = 0.05. Waist circumference: MD = -0.12, 95% CI [-0.92, 0.68], I^2 = 44%, p = 0.76. Systolic blood pressure: MD = -0.11, 95% CI [-1.55, 1.33], I^2 = 3%, p = 0.88. Diastolic blood pressure: MD = -0.44, 95% CI [-1.44, 0.57], I^2 = 15%, p = 0.39. Fasting glucose: MD = -0.05, 95% CI [-0.12, 0.01], I^2 = 31%, p = 0.11.	Risk of bias assessed using the Cochrane Collaboration's tool. Some studies had high performance bias due to lack of blinding in dietary interventions. Key Points: Whole grain diet slightly reduces body weight and CRP in obese/overweight adults. No significant effects observed for LDL-C, waist circumference, blood pressure, or fasting glucose. Greater effects observed in patients with chronic metabolic disorders besides obesity. Discrepancies among studies attributed to differences in diet types and monitoring approaches.
Astbury *et al.* 2019	23 RCTs, 7884 adults (4411 in intervention groups and 3852 in	Diet Interventions: Meal replacements (MR) included discrete foods, food products,	MEDLINE, Embase, PsycINFO, CINAHL, Web of Science, Cochrane Controlled Register of Trials (CENTRAL).	RCTs Follow-up duration: 1 year minimum, with some studies reporting	Body weight, BMI, WC, body fat %		<u>Weight change at 1 year:</u> MR diet vs diet only: Mean difference −1.44 kg (95% CI −2.48, −0.39; I^2 = 38%).	Quality: Six studies judged at low risk of bias across all domains.

comparator groups)	or drinks replacing one or more meals daily. Comparators included diets without MR, diets with support, or minimal intervention. MR interventions were categorized as: MR diet. MR diet + support. MR diet + enhanced support. Population: Adults aged ≥18 years with BMI ≥25 kg/m². Excluded: pregnant women, individuals with eating disorders, bariatric surgery patients, or those using pharmacotherapies for weight loss. Majority were women (median 79% female), mean age 47.7 years, mean baseline BMI 34.5 kg/m²	From database inception to August 2018. Countries: Studies conducted in the USA (15), Germany (3), Australia (1), China (1), Malaysia (1), Singapore (1), Thailand (1).	outcomes at 2 and 4 years. Excluded: studies with diets providing <3347 kJ (800 kcal)/day or total diet replacement (TDR).	MR diet + support vs diet + support: Mean difference −2.22 kg (95% CI −3.99, −0.45; I^2 = 81%). MR diet + support vs diet only: Mean difference −3.87 kg (95% CI −7.34, −0.40; I^2 = 60%). MR diet + enhanced support vs diet + support: Mean difference −6.13 kg (95% CI −7.35, −4.91; I^2 = 19%). MR diet + support vs minimal intervention: Results varied significantly across studies. MR interventions consistently led to greater weight loss at 1 year compared to comparators. Odds of achieving ≥5% weight loss: Statistically significant across all comparisons. Odds of achieving ≥10% weight loss: Statistically significant in 4 out of 5 comparisons. HbA1c consistently improved in MR groups. Mixed results for glucose, insulin, lipids, and blood pressure.	Five studies judged at high risk of bias in at least one domain. Remaining studies had unclear risk of bias in at least one domain. Key Points: MR interventions are effective for weight loss at 1 year, especially when combined with support. Weight loss benefits are sustained up to 4 years in some studies. MR interventions may improve diet quality and adherence to energy deficits. Limited data on adverse events, but no evidence of harm reported. MR could be recommended for inclusion in weight management programs.

Dinu *et al.* 2018	13 meta-analyses of observational studies and 16 meta-analyses of randomized controlled trials (RCTs), covering a total population of over 12,800,000 subjects.	Intervention: Mediterranean diet. Population: Adults (>18 years) from observational studies and RCTs.	Databases: Medline (1950–February 2017), Embase (1980–February 2017), Scopus (through February 2017), Cochrane database of systematic reviews, and Google Scholar (up to February 2017).	Observational studies: Prospective cohort studies, cross-sectional studies, and case-control studies. RCTs.	BMI, body weight, WC	HR, OR, MD	Convincing evidence for reduced risk of overall mortality: RR 0.91 (0.89,0.93) cardiovascular diseases: RR 0.67 (0.58,0.77) coronary heart disease: RR 0.72 (0.60, 0.86) Myocardial infarction: RR 0.67 (0.54,0.83) CV mortality: RR 0.75 (0.68,0.83) Stroke: RR 0.76 (0.60, 0.96) Other: Overall cancer incidence, neurodegenerative diseases, and diabetes (P-value < 0.001, large sample size, and low heterogeneity). Suggestive or weak evidence for site-specific cancers, inflammatory parameters, and metabolic parameters. No evidence for bladder, endometrial, and ovarian cancers, or LDL-cholesterol levels.	Quality: Medium-to-high quality scores (mean ± SD: 16.36 ± 2.36) based on the AMSTARMedSD tool. Key Points: Robust evidence for overall mortality, cardiovascular diseases, and diabetes. Limited evidence for other outcomes due to heterogeneity in dietary assessment methods and study designs. Recommendations for future studies to adopt uniform methodologies and better designs.

EXERCISE INTERVENTION

Study	n studies/ participants	Diet interventions & Population	Databases Searched & Year/Range/ Countries	Study Designs	Obesity Measure	Effect Estimate	Results ES (95%CI), heterogeneity	Quality & Key points
Li P *et al.* 2023	26 RCTs, 1418 participants	Aerobic exercise Population: Overweight or obese	PubMed, Embase, and Cochrane Library.	RCTs	BMI	SMD	Flow Mediated Dilatation Compared to that of the control group, FMD was significantly improved at a small effect	No studies were rated as low risk of bias. 12 studies had some concerns due to

	(654 males and 764 females)	older adults (≥60 years) with or without comorbidities	January 1989 to October 30, 2022.		Overweight: BMI ≥25 kg/m² and <30 kg/m². Obese: BMI ≥30 kg/m².		level in the exercise group [SMD 0.46, 95% CI (0.16, 0.75), I2= 80.1%, P 0.002]. <u>Pulse Wave Velocity:</u> There was a significant difference in PWV between the two groups after exercise intervention [SMD 0.88, 95% CI (1.70, 0.06), I2 93.6%, P 0.036], suggesting that exercise intervention can significantly reduce PWV to a high degree. <u>Augmentation Index:</u> The results of Aix [SMD 1.61, 95% CI (3.79, 0.58), I2 ¼ 97.5%, P 0.150] between the exercise group and the control group were statistically significant.	incomplete information. 4 studies were rated as high risk of bias. Key points: Regular aerobic exercise for more than 24 weeks improved FMD by small effect sizes and for more than three times per week improved FMD by moderate effect sizes. PWV was reduced, but no significant effect was observed on Aix. Obesity may blunt the beneficial effects of aerobic exercise, and additional interventions may be required for obese older adults. Sex differences were observed, with females showing better improvement in PWV compared to males.
Portes *et al.* 2023	N=13 RCTs	Type of Exercise: Continuous aerobic exercise, including cycling, treadmill running, elliptical machine, swimming, walking, jogging, and rowing.	PubMed, Scopus, and Cochrane. January 2005 to December 2021.	RCTs or pre-post	BMI: Mean BMI ≥ 30 kg/m² was used to define obesity.	SMD	<u>Pulse Wave Velocity:</u> Pre- vs. Post-Intervention: SMD = 0.263 (95% CI: 0.101 to 0.426, p = 0.001). Pre- vs. Post-Intervention: Significant reduction in central arterial stiffness (PWV decreased by −0.20 to −1.40 m/s).	69.2% of studies were rated "Excellent," and 30.78% were rated "Good" based on Downs and Black criteria. Key Points:

		Population: Obese adults (BMI ≥ 30 kg/m²), aged 26–69.1 years. Some participants had associated comorbidities such as type 2 diabetes, hypertension, metabolic syndrome, or chronic kidney disease.					Control vs. Exercise SMD = 0.241 (95% CI: −0.116 to 0.599, p = 0.186).	Aerobic exercise reduces central arterial stiffness in obese adults. Reduction in arterial stiffness is clinically relevant, as a 1 m/s increase in PWV corresponds to a 15% higher risk of cardiovascular diseases and all-cause mortality. Effects were observed even in short interventions (e.g., 4 weeks). Mechanisms include increased nitric oxide production and improved vascular function. Limitations: Associated comorbidities and medication use may mask isolated effects of exercise.
Wang H *et al.* 2023	28 RCTs, 1620 participants Network MA	Exercise Types: Aerobic Exercise (AE), Resistance Training (RT), Combined Aerobic and Resistance Training (CT), High-Intensity Interval Training (HIIT)	PubMed, Cochrane, Embase, Web of Science 1990 to February 2023	RCTs 4-48 weeks (mostly 12 weeks) Mostly 3/7	BMI, Body weight, WB, %BF	WMD	<u>Anthropometric Outcomes:</u> Body Weight: AE showed the best reduction (−2.35 [−4.05, −0.64]). BMI: AE was most effective (−0.9 [−1.38, −0.42]). Waist Circumference:	Quality: Moderate; most studies had unclear risk of bias in randomisation and blinding of participants but low risk in outcome assessment and reporting. Key points:

		Population: Adults with overweight or obesity (BMI ≥ 25 kg/m²)					HIIT (−5.93 [−10.71, −1.15]) and CT (−5.94 [−8.33, −3.55]) were most effective. Percentage Body Fat: HIIT showed the greatest reduction (−3.93 [−5.73, −2.12]). <u>Glucose Metabolism:</u> Fasting Blood Glucose: HIIT (−14.31 [−22.47, −6.16]). Fasting Insulin: HIIT (−5.94 [−10.48, −1.40]). HOMA-IR: HIIT (−3.01 [−5.08, −0.94]). <u>Lipid Profile</u>: Triglycerides: HIIT (−20.55 [−37.20, −3.91]). HDL: HIIT (8.00 [2.18, 13.82]). LDL: HIIT (−8.67 [−14.82, −2.53]). <u>Cardiorespiratory Fitness:</u> VO2 max: HIIT (7.41 [4.37, 10.45]).	AE is optimal for reducing body weight and BMI. HIIT is most effective for improving body composition, glucose metabolism, lipid profile, and cardiorespiratory fitness. Long-term exercise (>9 weeks) yields better results for anthropometric and metabolic outcomes. HIIT is time-efficient but may not suit individuals without a training foundation.
Batrakoulis *et al.* 2022	81 RCTs 4,331 individuals (59% female; mean age: 38.7 ± 12.3 years)	Exercise Types: Continuous Endurance Training (CET) Interval Training (INT)	MEDLINE, Embase, Scopus, Web of Science From inception to September 2020	RCTs Mean intervention duration of 21 ± 18 weeks	Body weight, BMI, WC, WHR, %BFM FFM	MD	See NMA Table for league table comparisons <u>Body Mass:</u> Combined Training (CT): Effect size: −2.57 [95% CI: −3.78 to −1.36]	25 studies had low risk, 40 raised concerns, and 16 had high risk of bias. Key Points:

Network MA	Resistance Training (RT) Combined Aerobic and Resistance Training (CT) Hybrid-Type Training (HYB) Population: Overweight and obese adults (BMI ≥ 25 kg/m²), aged 18–64 years, with no diagnosed comorbidities or signs/symptoms of noncommunicable diseases.	Countries: North America (28%), Asia (26%), Europe (20%), Oceania (14%), South America (12%)	(range: 3–104 weeks)	Continuous Endurance Training (CET): Effect size: −2.39 [95% CI: −3.10 to −1.67] Interval Training (INT): Effect size: −2.27 [95% CI: −3.46 to −1.08] Hybrid-Type Training (HYB): Effect size: −2.23 [95% CI: −4.34 to −0.11] <u>Body Mass Index (BMI):</u> No meaningful reductions in BMI were observed in the network comparison. Hybrid-Type Training (HYB): Highest probability of being the most effective exercise mode in reducing BMI (33.9%). Hybrid-Type Training (HYB): Effect size: −8.30 [95% CI: −13.27 to −3.33] Combined Training (CT): Effect size: −3.98 [95% CI: −5.51 to −2.45] Interval Training (INT): Effect size: −3.58 [95% CI: −5.86 to −1.30] Resistance Training (RT): Effect size: −2.99 [95% CI: −4.26 to −1.72] Continuous Endurance Training (CET): Effect size: −3.73 [95% CI: −4.94 to −2.52] <u>Waist-to-Hip Ratio (WHR):</u> No statistically meaningful reductions were seen in WHR for any exercise type. <u>Body Fat (BF):</u> Continuous Endurance Training (CET): Effect size: −4.63 [95% CI: −7.31 to −1.96] Combined Training (CT): Effect size: −2.76 [95% CI: −5.42 to −0.09] Hybrid-Type Training (HYB): Effect size: −2.63 [95% CI: −5.12 to −0.14]	Combined Training : Best for improving body mass, body fat, fat-free mass, total cholesterol, low-density lipoprotein, fasting insulin, homeostatic model assessment for insulin resistance, systolic blood pressure, diastolic blood pressure, cardiorespiratory fitness , and muscular strength. Clinical Implications: Multicomponent exercise approaches (CT and HYB) are recommended for adults with overweight/obese adults to maximise cardiometabolic health benefits. HYB and INT are time-efficient and promote enjoyment, making them suitable for real-world applications.

Interval Training (INT): Effect size: −2.16 [95% CI: −3.69 to −0.62]

Fat-Free Mass (FFM):
All exercise types induced an increase in FFM (0.23–1.63 kg), but these improvements were not statistically meaningful

Glucose Metabolism Outcomes:
Fasting Glucose (FG):

Combined Training (CT): Effect size: −4.62 [95% CI: −8.46 to −0.78]
Continuous Endurance Training (CET): Effect size: −3.98 [95% CI: −6.69 to −1.27]
Interval Training (INT): Effect size: −3.55 [95% CI: −6.73 to −0.37]
Hybrid-Type Training (HYB): Highest probability of reducing FG (69%).

Fasting Insulin :
Resistance Training (RT): Effect size: −5.36 [95% CI: −8.71 to −2.01]
Combined Training (CT): Effect size: −4.86 [95% CI: −8.21 to −1.52]
Interval Training (INT): Effect size: −2.81 [95% CI: −5.11 to −0.52]
Combined Training (CT): Most effective exercise mode for lowering FI (86% probability).

Homeostatic Model Assessment for Insulin Resistance (HOMA-IR):
Combined Training (CT): Effect size: −1.05 [95% CI: −1.70 to −0.41]
Interval Training (INT): Effect size: −0.80 [95% CI: −1.27 to −0.32]

Continuous Endurance Training (CET): Effect size: −0.78 [95% CI: −1.21 to −0.34]
Combined Training (CT): Most effective exercise mode for reducing HOMA-IR (65.2% probability).

Glycated Haemoglobin (HbA1c):
Interval Training (INT): Effect size: −0.42 [95% CI: −0.77 to −0.07]
Interval Training (INT): Highest probability of being ranked best for reducing HbA1c (72.2%).

Resting Cardiovascular Function Outcomes:

Systolic Blood Pressure (SBP):
Combined Training (CT): Effect size: −5.58 [95% CI: −9.18 to −1.99]
Resistance Training (RT): Effect size: −3.82 [95% CI: −6.11 to −1.53]
Interval Training (INT): Effect size: −3.41 [95% CI: −6.81 to −0.02]
Continuous Endurance Training (CET): Effect size: −2.99 [95% CI: −5.10 to −0.88]
Combined Training (CT): Highest probability of reducing SBP (65.4%).

Diastolic Blood Pressure (DBP):
Combined Training (CT): Effect size: −4.70 [95% CI: −8.18 to −1.23]
Resistance Training (RT): Effect size: −2.96 [95% CI: −5.22 to −0.70]
Continuous Endurance Training (CET): Effect size: −2.53 [95% CI: −4.70 to −0.37]
Combined Training (CT): Most effective modality for improving DBP (65.1% probability).

							Mean Arterial Pressure (MAP): Resistance Training (RT): Effect size: −6.20 [95% CI: −10.77 to −1.63] Continuous Endurance Training (CET): Effect size: −5.68 [95% CI: −9.30 to −2.07] Resistance Training (RT): Highest likelihood of being ranked best for decreasing MAP (56%). Resting Heart Rate (RHR): Continuous Endurance Training (CET): Effect size: −2.98 [95% CI: −5.90 to −0.05] Hybrid-Type Training (HYB): Effect size: −5.63 [95% CI: −9.94 to −1.31] Hybrid-Type Training (HYB): Highest probability of being the most effective modality for lowering RHR (65.2%).	
Armstrong *et al.* 2022	N=25 RCTs, 686 adults (Aerobic exercise groups = 1019; Control groups = 699).	Type of Exercise: Aerobic exercise (AEx), including moderate intensity, vigorous intensity, and high-intensity interval training (HIIT). Population: Adults aged ≥18 years with overweight or obesity. Overweight: BMI 25–29.9 kg/m² (Caucasian) or BMI ≥23–24.9 kg/m² (Asian/South Asian). Obesity: BMI ≥30 kg/m² (Caucasian) or	Medline, Embase, Cochrane (via OvidSP), Scopus, SPORTDiscus. From earliest records to March 10, 2021. Countries: Studies included participants from various regions, including Asian ethnicities and Caucasian populations.	RCTs	WC or imaging-derived VAT	MD	WC: Mean Reduction in Waist Circumference: 3.2 cm (95% CI −3.87, −2.51, p ≤ 0.0001) compared to control. Vigorous intensity exercise produced superior WC reduction (−4.2 cm; 95% CI −4.99, −3.42, p < 0.0001) compared to moderate intensity (−2.50 cm; 95% CI −3.22, −1.79, p = 0.058). Association: Change in WC was significantly associated with change in VAT (β = 4.02; 95% CI 1.37, 6.66, p = 0.004) and bodyweight (β = 0.7 kg; 95% CI 0.38, 1.04, p = 0.0001). Heterogeneity: High heterogeneity observed (I^2 = 92.4%).	Evidence graded as "low certainty" due to risk of bias, inconsistency, and imprecision. Key Points: Regular aerobic exercise reduces WC modestly (~3.2 cm). Vigorous intensity exercise may offer superior benefits compared to moderate intensity. Reduction in WC is associated with reductions in VAT and bodyweight,

		BMI ≥25 kg/m² (Asian/South Asian). Participants included those with abdominal obesity, type 2 diabetes, metabolic syndrome, non-alcoholic fatty liver disease, and other comorbidities.						even with negligible weight loss. Exercise frequency (additional days per week) also contributed to greater WC reduction. No clear association between exercise volume and WC reduction.
Boppre *et al.* 2022	N=11 RCTs, 618 participants, 84% F	Type of Exercise: Aerobic exercise (5 studies): Treadmill walking, stationary cycling, outdoor cycling, or walking. Combined aerobic and resistance exercise (6 studies): Aerobic activities paired with resistance exercises like leg press, bench press, lateral pulldown, etc. No studies included resistance-only training. Population: Adults aged 18–65 years with severe obesity (BMI > 35 kg/m²) who	PubMed, Web of Science, Scopus, and EBSCO. Search conducted up to July 2021.	RCTs	BMI	MD	Overall Exercise Effects: SBP reduction: −5.33 mmHg (95% CI −8.99, −1.66; p < 0.01). Combined exercise effects: SBP reduction: −7.18 mmHg (95% CI −12.42, −1.94; p < 0.01). Triglycerides reduction: −17.56 mg/dL (95% CI −34.15, −0.96; p = 0.04). Exercise starting >6 months post-surgery: SBP reduction −7.71 mmHg (95% CI −13.12, −2.31; p < 0.01). Exercise duration >12 weeks: SBP reduction −5.78 mmHg (95% CI −9.91, −1.66; p < 0.01). Heterogeneity: Moderate to considerable heterogeneity (I^2 values varied across analyses).	Risk of Bias (RoB-2): 7 studies rated as low risk, 1 with some concerns, and 3 with high risk. Certainty of Evidence (GRADE): Moderate certainty for SBP findings Key Points: Exercise is effective in reducing SBP and triglycerides post-bariatric surgery compared to surgery alone. Limited additional benefits for lipid profile and glucose metabolism due to substantial effects of bariatric surgery alone.

		underwent bariatric surgery (e.g., Roux-en-Y gastric bypass, sleeve gastrectomy, adjustable gastric band, biliopancreatic diversion).						
Battista *et al.* 2021	N=54 Median total sample size was 38 (range: 10–404).RCTs,	Type of Exercise: Aerobic training (36 studies), resistance training (12 studies), combined aerobic and resistance training (8 studies), high-intensity interval training (HIIT) (11 studies). Population: Adults (≥18 years) with overweight (BMI ≥25 kg/m²) or obesity (BMI ≥30 kg/m²). Included participants with comorbidities such as type 2 diabetes, hypertension, dyslipidemia, metabolic syndrome, nonalcoholic fatty liver disease (NAFLD), and nonalcoholic steatohepatitis (NASH).	PubMed, Web of Science, Cochrane Library. Articles published up to April 2020.	RCTs	BMI	SMD or MD	<u>Insulin Resistance (HOMA-IR):</u> Overall Effect: SMD = −0.34 (95% CI: −0.49, −0.18), p < 0.0001, I^2 = 48%. Subgroup Analysis: Participants with Type 2 Diabetes: SMD = −0.50 (95% CI: −0.83, −0.17), p = 0.003, I^2 = 39%. Participants without Type 2 Diabetes: SMD = −0.31 (95% CI: −0.49, −0.13), p = 0.0007, I^2 = 45%. <u>Intrahepatic Fat:</u> Overall Effect: SMD = −0.59 (95% CI: −0.78, −0.41), p < 0.00001, I^2 = 0%. Subgroup Analysis by Exercise Type: High-Intensity Interval Training (HIIT): SMD = −0.89 (95% CI: −1.36, −0.41), p = 0.0002, I^2 = 0%. Aerobic Training: SMD = −0.56 (95% CI: −0.77, −0.35), p < 0.00001, I^2 = 0%. Resistance Training: SMD = −0.40 (95% CI: −1.06, 0.26), p = 0.24, I^2 = 0%. <u>Systolic Blood Pressure:</u>	11 studies rated as good, 20 as fair, and 23 as poor quality. Key Points: Exercise training improves cardiometabolic health in adults with overweight or obesity, including those with comorbidities. Aerobic training was the most frequently assessed type of exercise. HIIT demonstrated significant benefits for intrahepatic fat reduction. Individualised exercise prescriptions should be emphasised in obesity management. The reduction of systolic blood pressure, whatever the blood pressure status of participants, was about 3 mmHg.

							Overall Effect: MD = −2.95 mmHg (95% CI: −4.22, −1.68), p < 0.00001, I^2 = 63%. Hypertensive Participants: MD = −3.39 mmHg (95% CI: −5.31, −1.46), p = 0.0006, I^2 = 58%. Normotensive Participants: MD = −2.03 mmHg (95% CI: −5.32, 1.26), p = 0.23, I^2 = 31%. <u>Diastolic Blood Pressure:</u> Overall Effect: MD = −1.93 mmHg (95% CI: −2.73, −1.13), p < 0.00001, I^2 = 54%. Hypertensive Participants: MD = −2.06 mmHg (95% CI: −3.42, −0.70), p = 0.003, I^2 = 76%. Normotensive Participants: MD = −2.09 mmHg (95% CI: −3.45, −0.74), p = 0.002, I^2 = 0%.	
Su *et al.* 2019	N=22 studies, 620 participants (310 in the HIIT group, 310 in the MICT group)	Exercise: High-Intensity Interval Training (HIIT) and Moderate-Intensity Continuous Training (MICT) Population: Adults with overweight and/or obesity (BMI ≥ 25)	PubMed, Embase, Cochrane, CENTRAL, PEDro, CNKI From database inception to July 20, 2018	RCTs or CCTs	BMI, body weight, %body fat	SMD	<u>Body Composition:</u> Weight: HIIT (SMD = 0.305), MICT (SMD = 0.319) BMI: HIIT (SMD = 0.591), MICT (SMD = 0.727) Fat%: HIIT (SMD = 0.609), MICT (SMD = 0.647) VO2max: HIIT (SMD = -0.966), MICT (SMD = -0.690)	5 studies classified as low risk, 16 as moderate risk, 1 as high risk Key Points: HIIT and MICT provide similar benefits for body composition, VO2max, and TC. HIIT is superior in improving VO2max when intervals are ≥ 2 min or

							Subgroup: HIIT with intervals ≥ 2 min (SMD = 0.444, 95% CI: 0.037–0.851, P = 0.032) Lipid Metabolism: Total Cholesterol: HIIT (SMD = 0.467), MICT (SMD = 0.488) LDL: HIIT (SMD = 0.445), MICT (SMD = 0.287) Heterogeneity: High in some subgroups (I^2 not explicitly provided for all outcomes)	energy expenditure matches MICT. Publication bias significantly affects fat% results.
Ren *et al.* 2018	N=8 RCTs, 347 adults with obesity	Exercise Types: Aerobic exercise, resistance training, and combined aerobic-resistance exercise. Population: Adults (≥18 years) with obesity who underwent bariatric surgery (e.g., Roux-en-Y gastric bypass, gastric banding, sleeve gastrectomy, lap band).	PubMed, Embase, Cochrane Library, OVID, CINAHL. From inception of each database to May 2018. Countries: USA, England, Iran, Denmark.	RCTs	Body weight (kg), Body Mass Index (BMI, kg/m²), waist circumference (cm), fat mass (FM, kg), fat-free mass (FFM, kg), percentage of total body fat (BF%)	WMD	Weight Loss: Weighted Mean Difference (WMD) −1.94 kg (95% CI −3.18 to −0.69; p=0.002). (I2=51%). Physical Function: 6-minute walk distance (6MWD) WMD 29.67 m (95% CI 25.97 to 33.37; p<0.00001). Subgroup analysis showed greater weight loss for exercise starting ≥1 year after surgery (WMD −3.63 kg; 95% CI −5.35 to −1.91; p<0.0001) and combined aerobic-resistance exercise (WMD −3.12 kg; 95% CI −4.56 to −1.68; p<0.0001).	Quality: Moderate for body weight and BMI; low to very low for other outcomes due to performance bias, inconsistency, and imprecision. Key Points: Physical exercise after bariatric surgery provides additional weight loss and improved physical function. Limited sample size and heterogeneity of interventions are challenges.
Wewege *et al.* 2018	N=11 studies, 588 participants	Type of Exercise: Aerobic (12 interventions), Resistance (4 interventions),	Eight electronic bibliographic databases Earliest date to September 2017	RCTs minimum 4weeks duration	WC, Body weight, Body fat	MD	Aerobic Exercise: Waist circumference: −3.4 cm (95% CI: −4.8, −1.9) Fasting glucose: −0.15 mmol/L (95% CI: −0.30, −0.01)	Moderate quality (PEDRO) Key points: Aerobic exercise offers widespread benefits for MetS without T2D.

		Combined (0 interventions) Population: Adults with Metabolic Syndrome (MetS) without Type 2 Diabetes (T2D)					HDL-C: 0.05 mmol/L (95% CI: 0.01, 0.10) Triglycerides: −0.29 mmol/L (95% CI: −0.51, −0.10) Diastolic blood pressure: −1.6 mmHg (95% CI: −3.6, 0.4) Heterogeneity: Not significant (p > 0.10 for all analyses) Cardiorespiratory Fitness 4.30 ml/kg/min (2.91, 5.69)	Resistance exercise requires more studies to establish effects. Combined exercise data was unavailable. Longer duration (>12 weeks) and progression to higher intensity aerobic exercise may enhance benefits. Sex and age may influence exercise outcomes.
Liu Y *et al.* 2024	56 RCTs 3193 individuals diagnosed with overweight and obesity.	Types of Exercise: Aerobic exercise (32 studies). Resistance training (9 studies). Concurrent training (23 studies). Population: Overweight (BMI ≥ 25 kg/m²) or obese (BMI ≥ 30 kg/m²) individuals without other medical conditions.	PubMed, EMBASE, Cochrane Central Register of Controlled Trials, Web of Science, CNKI. January 2017 to March 2024. Countries: Studies conducted in 30 countries, including the USA, Brazil, China, Iran, Spain, South Africa, and others.	RCTs	BMI	SMDs and SURCA	Aerobic Exercise: Reduced insulin (SUCRA: 89.1%) and HbA1c (SUCRA: 95.3%). Resistance Training: Reduced total cholesterol (SUCRA: 99.9%), triglycerides (SUCRA: 100%), LDL (SUCRA: 100%), systolic blood pressure (SUCRA: 92.5%), and increased HDL (SUCRA: 100%). Concurrent Training: Reduced HOMA-IR (SUCRA: 93.8%), diastolic blood pressure (SUCRA: 71.2%), and glucose (SUCRA: 87.6%).	Quality Assessment: 47 studies classified as medium risk, 9 as high risk. Key Points: Resistance training is most effective for improving lipid profiles and systolic blood pressure. Aerobic exercise is optimal for reducing insulin and HbA1c levels. Concurrent training is effective for regulating diastolic blood pressure, glucose, and insulin resistance.

							Personalised exercise prescriptions are recommended based on individual health markers.
O'Donoghue *et al.* 2021	45 studies with a total of 3566 participants.	Exercise Types: Aerobic exercise; vigorous intensity (AE-V) Aerobic exercise; moderate intensity (AE-M) Resistance training; high load (R-HI) Resistance training; low-to-moderate load (R-LM) Population: Adults living with obesity (BMI > 30 kg/m² or body fat > 30% in women and >25% in men).	PubMed, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), CINAHL, Sport Discus. January 1998 to November 2019.	RCTs	BMI > 30 kg/m² or body fat > 30% in women and >25% in men.	<u>BMI</u> All four exercise interventions with an aerobic component(COM-HI: −2.79 [CI = −5.95, −0.36]; COM-LM: −1.56 [CI = −2.71,−0.41]; AE-V: −0.94 [CI = −1.72, −0.15] and AE-M: −1.76[CI = −2.58, −0.95]) were found to be significantly more effective in reducing BMI than control and were superior to resistance only interventions COM-HI was the best intervention in the network comparison for decreasing BM <u>WC</u> While all five exercise interventions reduced WC, COM-LM (−2.76 [CI = −4.52, −1.00]), AE-M (−2.31 [CI = −3.61, −1.02]) and AE-V (−2.03 [CI = −3.55, −0.52]) were superior to resistance interventions and achieved the best results compared with control. COM-LM (P score = 0.82) was the best exercise intervention in the network comparison for reducing WC The interventions that were found to significantly reduce bodyfat when compared with control were COM-HI (−2.82 [CI = −5.50,−0.14]), COM-LM (−2.15 [CI = −4.06, −0.25]) and AE-M (−1.70[CI = −3.16, −0.25]). The exercise intervention with the highest likelihood (P score = 0.80) of decreasing %BF was a combination of high-intensity aerobic and high-load resistance training	Key points While any type of exercise intervention is more effective than control, weight loss induced is modest. Combined high-intensity aerobic and high-load resistance training showed superior effects in decreasing abdominal adiposity, improving lean body mass, and increasing cardiorespiratory fitness High-intensity aerobic and high-load resistance training are the most effective exercise modalities for improving body composition and CRF in adults living with obesity. Weight loss induced by exercise interventions is modest, but improvements in CRF and metabolic health are significant