WHO guideline on the use of glucagon-like peptide-1 (GLP-1) therapies for the treatment of obesity in adults

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Abbreviations and acronyms

BMI	body mass index
CINeMA	Confidence in Network Meta-Analysis
EtD	evidence to decision
GDG	Guideline Development Group
GIP	glucose-dependent insulinotropic polypeptides
GLP-1	glucagon-like peptide-1
GRADE	Grading of Recommendations Assessment, Development and Evaluation
CERQual	Confidence in the Evidence from Reviews of Qualitative Research
DOI	declaration of interests
HbA1C	haemoglobin A1C (glycated haemoglobin)
IBT	intensive behavioural therapy
MACE	major adverse cardiac events
MCID	minimal clinically important difference
NAION	non-arteritic anterior ischemic optic neuropathy
NCD	noncommunicable disease
NFS	Department of Nutrition and Food Safety
OECD	Organization for Economic Co-operation and Development
PICO	population, intervention, comparison and outcomes
RCT	randomized controlled trial
rQES	rapid qualitative evidence synthesis
UHC	universal health coverage
UN	United Nations
WHO	World Health Organization

Glossary

Access (to health services): the ability, or perceived ability, to reach health services or health facilities in terms of location, timeliness and ease of approach.

Adult: a person older than 19 years of age.

Body mass index (BMI): is a surrogate marker of adiposity calculated as weight (kg)/height2(m2).

Care pathway (or clinical pathway): a structured multidisciplinary management plan (in addition to clinical guideline) that maps the route of care through the health system for individuals with specific clinical problems.

Clinical guidelines: systematically developed, evidence-based recommendations that support health workers and patients to make decisions about care in specific clinical circumstances.

Continuum of care: the spectrum of personal and population health care needed throughout all stages of a condition, injury or event throughout a lifetime, including health promotion, disease prevention, diagnosis, treatment, rehabilitation and palliative care.

Equity in health: the absence of systematic or potentially remediable differences in health status, access to health care and health-enhancing environments and treatment in one or more aspects of health across populations or population groups defined socially, economically, demographically or geographically within and across countries.

GLP-1 therapy: in the context of this guideline, the term glucagon-like peptide-1 (GLP-1) therapy refers to any one in a class of medicines (also commonly called incretin mimetics or GLP-1 receptor agonists) that can be delivered orally or via subcutaneous injection to mimic the effects of the naturally occurring hormone glucagon-like peptide-1 that in turn plays a critical role in metabolism by stimulating insulin secretion, delaying gastric emptying, inhibiting glucagon release and reducing food intake via central appetite suppression. This class also includes combination therapies such as dual GLP-1 and glucose-dependent insulinotropic polypeptide (GIP) receptor agonists. Currently the guidelines include liraglutide, semaglutide and tirzepatide.

Health: a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity.

Health benefits package: the type and scope of health services that a purchaser buys from providers on behalf of its beneficiaries.

Health service: any service (not limited to medical or clinical services) aimed at contributing to improved health or to the diagnosis, treatment and rehabilitation of individuals and populations.

Long term therapy: the continued administration of a drug or biologic product, generally defined as six months or longer of continuous use, and often extending to years or lifelong administration for chronic conditions. In the regulatory language of the United States Food and Drug Administration, “long-term use” is specifically highlighted in product labelling when there are uncertainties regarding safety or effectiveness with extended duration of therapy, or when the risk–benefit profile differs between short-term and prolonged use *(1)(2)*.

Multimodal obesity chronic care model: is a comprehensive, structured, long-term approach to the care and treatment of obesity that integrates, in a tailored fashion, multiple complementary interventions, which can be combined according to clinical indications - including intensive behavioral therapy (IBT), pharmacological therapies such as GLP-1 therapy, surgical options when appropriate, and health system supports - within a coordinated, patient-centered chronic care framework. It recognizes obesity as a complex, relapsing, chronic disease and emphasizes continuity of care, multidisciplinary collaboration, shared decision-making, and integration across all levels of the health system.

Obesity (in adults): defined as a BMI greater than or equal to 30 kg/m2.

Overweight (in adults): defined as a BMI ranging from 25.00 to 29.99 kg/m2.

Pharmacological therapy: the use of medications to prevent, manage or treat health conditions.

People-centred care: an approach to care that consciously adopts the perspectives of individuals, carers, families and communities as participants in and beneficiaries of trusted health systems that respond to their needs and preferences in humane and holistic ways. People-centred care also requires that people have the education and support they need to make decisions and participate in their own care.

Primary care: a key process in the health system that supports first-contact, accessible, continued, comprehensive and coordinated patient-focused care.

Primary health care: a whole-of-society approach to health that aims to maximize the level and distribution of health and well-being through three components: (a) primary care and essential public health functions as the core of integrated health services; (b) multisectoral policy and action; and (c) empowered people and communities.

Primary health care-oriented health system: health system organized and operated to guarantee the right to the highest attainable level of health as the main goal, while maximizing equity and solidarity. A primary health care-oriented health system is composed of a core set of structural and functional elements that support achieving universal coverage and access to services that are acceptable to the population and equity enhancing.

Referral: the direction of an individual to the appropriate facility or specialist in a health system or network of service providers to address relevant health needs. Counter-referral may occur when an individual is referred back to primary care for follow up care following a procedure in secondary or tertiary care.

Sex: refers to the different biological and physiological characteristics of females, males and intersex persons, such as chromosomes, hormones and reproductive organs.

Short-term therapy: the administration of a drug or biologic product for a limited duration, generally less than six months of continuous use, and typically intended to address acute or self-limiting conditions. In the regulatory language of the United States Food and Drug Administration, “short-term use” reflects the treatment duration studied in pivotal clinical trials and usually does not require additional labelling unless restrictions on duration are essential to ensure safety or effectiveness *(1)(3)*.

Well-being: a multidimensional construct aiming at capturing a positive life experience, frequently equated to quality of life and life satisfaction. Measures of well-being typically focus on patient-reported outcomes covering a wide range of domains, such as happiness, positive emotions, engagement, meaning, purpose, vitality and calmness.

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Further details about the guideline contributors and participants are included in **Annex A.**

Executive Summary

Introduction

Obesity is one of the defining health challenges of our time, affecting more than 1 billion people globally and contributing to millions of preventable deaths each year. Yet despite its scale and impact, the global response remains fragmented, underfunded and is often shaped by outdated views that frame obesity as a lifestyle issue rather than what it truly is: a chronic, progressive and relapsing disease.

This guideline offers evidence-informed recommendations on the use of glucagon-like peptide-1 (GLP-1) receptor agonists and glucose-dependent insulinotropic polypeptides (GIP)/GLP-1 dual agonists – a new generation of pharmacotherapies for treatment of people living with obesity. This is WHO's first clinical guidance on the pharmacological treatment of obesity in adults. It represents a critical step toward establishing a global standard of care – an evolving foundation upon which countries can build evidence-based, equitable and sustainable obesity treatment programmes. The guideline will be continuously updated and expanded in response to the evolving evidence base and emerging real-world data on safety, feasibility, effectiveness and system-level requirements.

Scope and purpose

This guideline is global in scope and intended for use across a wide range of settings, income levels and health system capacities. It focuses on the treatment of adults (>19 years) with obesity, which is defined as body mass index (BMI) ≥30 kg/m2. A separate WHO guideline is under development on the management of obesity in children and adolescents. This guideline aims to support the safe, equitable and appropriate inclusion of pharmacological therapy for adults as part of comprehensive obesity chronic care programmes. These programmes must move beyond a narrow focus on weight loss to address the full spectrum of associated health risks, obesity-related diseases and disorders and the broader social and structural determinants of health.

While not a standalone solution, this guideline represents one of many tools to support countries in designing comprehensive chronic care systems that incorporate pharmacological treatment as one option, while also building health systems that recognize obesity as the complex, lifelong condition it is. A successful transition to chronic care models requires more than clinical guidance – it also demands careful attention to health system capacity and a strong commitment to equity. Without deliberate investment and inclusive implementation strategies, the introduction of new therapies may exacerbate existing disparities in access, affordability and quality of care. Equity considerations must, therefore, be integrated throughout programmes – from procurement and service delivery to financing, information systems and workforce capacity development.

The key stakeholders that comprise the target audience of this guideline are national policy-makers, public health authorities, national clinical guideline developers and regulatory bodies. Further stakeholders the recommendation may benefit are healthcare providers, system managers, researchers, professional societies and people living with obesity organizations.

Methods

This guideline development process followed the methods and standards in the WHO handbook for guideline development, second edition and Grading of Recommendations, Assessment, Development and Evaluations (GRADE) for formulating evidence-informed recommendations and good practice statements.

The process involved synthesis and GRADE assessments of efficacy, effectiveness and safety evidence around GLP-1 receptor agonists and GIP/GLP-1 dual agonists for obesity and possible co-interventions alongside GLP-1 receptor agonists and GIP/GLP-1 dual agonists. It also involved synthesis and GRADE-Confidence in the Evidence from Reviews of Qualitative Research (CERQual) assessments of qualitative findings related to values and preferences, acceptability and potential equity impacts around the use of GLP-1 receptor agonists and GIP/GLP-1 dual agonists for obesity.

A Guideline Development Group (GDG) of researchers, clinicians, ethicists and people living with obesity was involved in the decision-making for the guideline and the development of recommendations and good practice statements.

Recommendations and good practice statements

This guideline includes two conditional recommendations and two good practice statements. Importantly, all recommendations and good practice statements include corresponding remarks which are included in the guideline along with other key information for understanding and implementing the interventions.

Good practice statement

Obesity is a chronic complex disease that requires lifelong care beginning with clinical assessment and early diagnosis. Once diagnosed, individuals should have access to comprehensive chronic care programmes offering sustained behavioural and lifestyle interventions. When appropriate, pharmacological, surgical or other therapeutic options may be used to support

effective disease management. In parallel, care should address the prevention and treatment of obesity-related complications and comorbidities.

Remarks:

- Chronic care requires a capacitated health system to ensure adequate resources are in place, including supporting governance, training of health workers, monitoring and evaluation, referral systems, procurement and supply chain and financial coverage.
- In the context of obesity chronic care programmes, personalized periodic monitoring of treatment response and side effects/adverse events is essential to ensure sustained adherence and achieve optimal health outcomes.

Conditional recommendation for, Moderate certainty evidence

In adults living with obesity, GLP-1 receptor agonists or GIP/GLP-1 dual agonists may be used as long-term treatment for obesity.

Remarks:

- The evidence for two GLP-1 receptor agonists (liraglutide and semaglutide) and one GIP/GLP-1 dual agonist (tirzepatide) was evaluated for the purpose of this recommendation.
- This recommendation was derived from clinical trials in which treatment with a GLP-1 receptor agonist was administered from 26 weeks to 240 weeks (median 52 weeks).
- Obesity is a complex chronic disease characterized by excessive adiposity that can impair health and is defined by WHO as a BMI equal to or greater than 30 kg/m2.
- While the randomized controlled trials (RCTs) that informed this recommendation included populations without specific BMI thresholds for overweight and obesity, with overweight and obesity defined per study, this recommendation applies to people with obesity (BMI ≥ 30 kg/m2) but does not include people with BMI between 27 kg/m2 and 30 kg/m2 in association with one or two obesity-related diseases and disorders.
- The critical outcomes evaluated to inform this decision were weight, quality of life, adverse events, major adverse cardiovascular events and mortality.
- The trial follow-up times were i) 6 months to less than 24 months; and ii) 24 or more months, with higher certainty of evidence for those with less than 24 months of follow-up.
- Long-term treatment refers to the continued use of a medication for six months or longer, as per existing regulatory guidance (see the glossary for a more complete definition).
- Limited data are currently available to inform practice around decisions about, or the health impact of, discontinuation of GLP-1 receptor agonists and GIP/GLP-1 dual agonists.
- In the process of establishing obesity chronic care programmes, consideration may be given to prioritizing those at higher risk of morbidity and mortality, while ensuring health equity across populations and settings.

Good practice statement

People living with obesity should receive context-appropriate counselling on behavioural and lifestyle changes - including, but not limited to, physical activity and healthy dietary practices - as an initial step toward more structured behavioural interventions. For individuals who are prescribed GLP-1 receptor agonists or GIP/GLP-1 dual agonists, counselling on behavioural and lifestyle changes should be provided as a first step to intensive behavioural therapy to amplify and support optimal health outcomes.

Remarks:

- Recommendations and good practice statements for physical activity are included in the WHO guidelines on physical activity and sedentary behaviour, which highlight that all age groups should limit the amount of time being sedentary and should incrementally increase the frequency, intensity and duration of physical activity, including muscle strengthening.
- According to the Food and Agriculture Organization of the United Nations and the World Health Organization, the core principles of a healthy diet apply to all population groups. The four core principles of a healthy diet are: 1) that they need to be adequate and provide enough essential nutrients to prevent deficiencies and promote health, without excess; 2) be balanced in energy intake, and energy sources (fats, carbohydrates and proteins); 3) be moderate in consumption of foods, nutrients or other compounds associated with detrimental health effects; and 4) be diverse and include a wide variety of nutritious foods within and across food groups. In people living with obesity, additional considerations are necessary to support weight loss, including lowering daily energy intake. However, this should be prescribed and monitored in conjunction with a trained health care provider, whenever possible.

Conditional recommendation for, Low certainty evidence

In adults living with obesity who are prescribed GLP-1 receptor agonists or GIP/GLP-1 dual agonists, intensive behavioural therapy may be provided as a co-intervention within a comprehensive multimodal clinical algorithm.

Remarks:

- In the trials informing this recommendation, intensive behavioural therapy (IBT), alongside GLP-1 receptor agonists or GIP/GLP-1 dual agonists, entailed goal setting on physical activity and diet, restriction of energy intake, counselling (e.g. weekly, 30-45 minutes) and periodic assessment of goal attainment.
- The critical outcomes that informed this decision were weight, quality of life and adverse events. Limited data were available on major adverse cardiac events and there were no data on mortality for the effects of IBT alongside GLP-1 receptor agonists or GIP/GLP-1 dual agonists.
- The data from the RCTs were limited to follow-up durations between 6 months and less than 24 months. There was no direct evidence for outcomes at or beyond 24 months.
- The systematic review identified lifestyle counselling, IBT, meal replacement and a lead-in phase with lifestyle changes as possible co-interventions. The analysis did not include any other co-interventions outside what was included in the trials.

1. Introduction

The World Health Organization (WHO) recognizes obesity as a chronic, progressive and relapsing disease. As per the International Classification of Disease 11, it is *"a chronic complex disease defined by excessive adiposity that can impair health. It is in most cases a multifactorial disease due to obesogenic environments, psycho-social factors and genetic variants. In a subgroup of patients, single major etiological factors can be identified (medications, diseases, immobilization, iatrogenic procedures, monogenic disease/genetic syndrome). Body mass index (BMI) is a surrogate marker of adiposity calculated as weight (kg)/height2 (m2). For adults, obesity is defined by a BMI greater than or equal to 30 kg/m2" (4)*. Hence, obesity is not merely a risk factor or lifestyle condition, but a disease itself, shaped by a complex interplay of biological, social, commercial and environmental determinants. With far-reaching health, economic and social consequences, obesity is now one of the most pressing global health challenges of the 21st century.

As of 2022, over 1 billion people are living with obesity globally, and prevalence is rising in nearly every country *(5)*. In 2021 alone, obesity was estimated to contributed to 3.7 million deaths from linked noncommunicable diseases (NCDs) *(6)*. The economic toll is staggering – projected to reach US$ 3 trillion annually by 2030, with high-prevalence countries potentially spending up to 18% of total health expenditure on obesity-related care *(7)*.

Despite the growing burden, the global response to obesity remains fragmented and under-resourced. Most health systems are not yet equipped to treat obesity as a chronic disease. Clinical pathways are often absent or disconnected, while provider training is limited and access to effective interventions is constrained – especially in low-resource and marginalized settings. These challenges are compounded by widespread stigma, misinformation and a lack of demand for care, all of which prevent many people living with obesity from receiving the services they need and deserve *(8)(9)(10)*.

Moreover, obesity continues to be treated in many public health strategies as a behavioural or modifiable risk factor – leading to delayed diagnosis, inadequate treatment and missed opportunities for comprehensive care. Until recently, pharmacological options for obesity management showed limited and often unsustainable impact. However, recent therapeutic advances, particularly glucagon-like peptide-1 receptor agonists (GLP-1 receptor agonists) and glucose-dependent insulinotropic polypeptides (GIP)/GLP-1 dual agonists, have transformed the treatment landscape *(11)(12)(13)(14)(15)(16)(17)*.

Originally developed for treatment of type 2 diabetes, these agents have demonstrated clinically significant and lasting reductions in body weight (5-16%) in clinical trials, along with an array of health benefits *(18)(19)(20)*. As of early 2025, 10 GLP-1–based therapies had received regulatory approval for obesity and/or diabetes treatment, with more than 40 compounds in development, including novel multi-receptor agonists.

These innovative medical therapies are making it possible to incorporate effective pharmacotherapy as one component of an integrated intervention into chronic obesity care models. Yet the expansion of access must be guided by robust evidence, health system alignment, public health priorities and principles of equity. There is an urgent need for global guidance that ensures the appropriate, safe and inclusive use of these therapies across diverse health systems.

This WHO guideline is grounded in the recognition that obesity is a chronic disease requiring long-term care that goes far beyond weight reduction alone. Effective obesity care must address the full spectrum of health, social and economic impacts of the disease, across the life course. It must be embedded in multimodal clinical algorithms that integrate behaviour change and lifestyle support, pharmacotherapy, long-term follow-up, social protection and supportive environments. Critically, this care must also reflect the lived experiences of people living with obesity, who play an essential role in the design, delivery and evaluation of effective and stigma-free services and policies.

1.1 Purpose

This WHO living guideline provides evidence-informed recommendations on the use of GLP-1 receptor agonists and GIP/GLP-1 dual agonists (herafter also referred to as "GLP-1 therapy" where appropriate) as part of chronic care for adults living with obesity.

It is intended to support country-level decision-making to promote the safe, equitable and appropriate integration of these therapies into service delivery models, including primary health care, NCD programmes, essential medicines lists and health benefits packages.

Specifically, the guideline aims to:

- provide indication for the use of GLP-1–based pharmacotherapies in adults with obesity;
- support the integration of pharmacological treatment into chronic, person-centered care models that go beyond weight loss to address broader health outcomes that are linked to obesity;
- identify research and implementation gaps, including those related to long-term safety, effectiveness, cost, access and acceptability;
- emphasize equity, rights-based approaches and the risk of exacerbating disparities in access to treatment; and
- elevate the voice and agency of people living with obesity in the shaping of care models, public policy and implementation

strategies.

1.2 Scope and target audience

This guideline is global in scope and intended for use across a wide range of settings, income levels, and health system capacities. It addresses the treatment of adults (>19 years) with obesity, defined as BMI ≥30 kg/m2. A separate WHO guideline is under development for clinical management of obesity in children and adolescents.

Pharmacological agents covered:

1. Liraglutide – daily subcutaneous GLP-1 receptor agonist.
2. Semaglutide – weekly subcutaneous or daily oral GLP-1 receptor agonist.
3. Tirzepatide – weekly subcutaneous GIP/GLP-1 dual agonist.

Primary target audiences include:

- national policy-makers and health authorities (e.g., NCD programmes, universal health care (UHC) benefit packages, essential medicines committees);
- clinical guideline developers and regulatory agencies;
- public health officials responsible for service delivery, financing and procurement; and
- people living with obesity, as co-creators of health care models and health service delivery.

Secondary audiences include:

- health care providers and clinical teams;
- health system managers and professional societies;
- researchers, academic institutions and implementation partners; and
- communities and the public at large, whose engagement is essential to reducing stigma and ensuring equitable implementation.

By putting equity, lifelong chronic care and the perspectives of those most affected at its centre, this guideline supports coherent, inclusive and sustainable chronic care programmes.

2. Methods

The WHO Department of Nutrition and Food Safety (NFS) led the development of this guideline. The process aligned with the WHO handbook for guideline development, second edition *(21)* and was based on the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach to formulating recommendations informed by evidence *(22)(23)*.

This guideline will be regularly updated to incorporate the latest scientific evidence and provide recommendations for the use of GLP-1 receptor agonists and other incretin-based therapies in the treatment of obesity in adults.

The process involved agreement on two guideline questions and a supplementary question, prioritization of critical and important outcomes for the guideline questions, synthesis of evidence through systematic reviews with GRADE assessments to determine the certainty of evidence for these outcomes and a rapid qualitative evidence synthesis (rQES) with GRADE-Confidence in the Evidence from Reviews of Qualitative Research (CERQual) to assess the confidence of qualitative findings, decision-making based on the GRADE Evidence-to-Decision (EtD) framework to develop recommendations with corresponding strength and certainty, and formulation of good practice statements related to the guideline questions.

2.1 Guideline contributors

Technical team members

The technical team involved in this guideline includes:

- A responsible technical officer, who conceptualized and oversaw the entirety of the guideline development process.
- Three consultants with specific content expertise contributed throughout the process including to the planning proposal for this guideline, supporting the technical team and the Guideline Development Group (GDG) in developing the guideline questions, outlining possible outcomes to be scored and prioritized by the GDG, supporting systematic review teams, drafting this guideline and more.
- Two methodologists, one of whom was independent of WHO, were involved in this guideline to ensure that WHO and GRADE best practice methods and standards were followed, including for prioritization and development of guideline questions and outcomes, synthesis of the evidence, assessment of the certainty and confidence of the evidence, and to facilitate the GRADE EtD process and formulation of recommendations as well as good practice statements within GDG meetings.

WHO Steering Group

The WHO Steering Group, which included experts in various departments at WHO including NFS, the Department of Noncommunicable Diseases, the Science Division, the Essential Medicines List, Integrated Health Services, and regional advisers from the six WHO Regional Offices, were consulted at various stages of the guideline development to give input into the content and the process followed.

GDG members

The GDG is comprised of individuals with expertise related to this guideline, including ethics, research, epidemiology, pharmacology, health economics, large scale public health programmes and policy-making, clinical practice in managing obesity in adults and people living with obesity, across all WHO regions (see **Annex A**). After assessing expertise, geographical representation and declaration of interests (DOIs), a total of 17 GDG members were included for the initial GDG meetings. An additional GDG member with expertise in cost-effectiveness was invited in November 2024 after input from the GDG that indicated that cost-effectiveness would be a key element of discussion for the purpose of developing the recommendations. One member of the GDG withdrew in April 2025 due to a lack of time.

There were two GDG co-chairs who were nominated by the technical team and agreed upon by the GDG at the first GDG meeting. These chairs were involved in managing discussions during the GDG meetings and facilitating the process to formulate recommendations and good practice statements.

The GDG met four times – in September and October 2024 and April and June 2025.

Systematic review teams

There were two external systematic review teams for the guideline questions who synthesized and assessed the evidence on efficacy, effectiveness and safety of the use of GLP-1 receptor agonists and GIP/GLP-1 dual agonists for management of adults living with

obesity for the three guideline questions that were prioritized by the guideline. The systematic review teams and the technical team met regularly to ensure that the systematic reviews were fit for purpose for this guideline, with the technical team giving input into the protocols, conduct of the review and the synthesis of the evidence including GRADE assessments.

The technical team led a rQES that informed GRADE EtD domains including values and preferences, equity and acceptability, from the perspective of people living with obesity and healthcare providers.

Observers

Observers from three organizations in official relations with WHO attended and presented at GDG meetings in April and June 2025 (see Observers in **Annex A**). The observers had no role in the decision-making process for formulating recommendations and good practice statements.

External reviewers

External reviewers including technical experts, representatives from countries who have joined the WHO Acceleration Plan to Stop Obesity, civil society representatives and people living with obesity, were invited to closely examine this guideline and give input. Specifically, external reviewers were asked to identify any errors, including data gaps, and to comment on the clarity and implications of this guideline for implementation. External reviewers were not permitted to alter the text of the recommendations.

Further details about the guideline contributors and participants are included in **Annex A.**

2.2 Management of conflicts of interest

All proposed GDG members were asked to submit a WHO DOI form, a WHO Confidentiality Agreement and a Curriculum Vitae for review prior to participating in any GDG meetings. These documents were reviewed by the WHO technical team led by the responsible technical officer. The WHO technical team conducted additional web searches including documenting conflicts of interest declarations in recent publications by GDG members. The Ethics, Risk and Due Diligence and Non-State Actors Department was also consulted on the inclusion of one GDG member.

Those declaring involvement in the boards of pharmaceutical companies producing GLP-1 receptor agonists or GIP/GLP-1 dual agonists, or as shareholders of those companies, were automatically excluded. For those that were investigators on trials on GLP-1 receptor agonists or GIP/GLP-1 dual agonists, they could be included only if they were not the Principal Investigator and if the funds were received through their institution.

The proposed list of GDG members, affiliations, WHO region, gender and expertise was published on WHO's website in August 2024 with a deadline for public comments in September 2024. No public comments were received but one proposed GDG member from this list was excluded due to conflicts of interest identified by the WHO Regional Office for Europe.

GDG members were asked to share any new interests as they arose and were asked to state any conflicts of interest at the start of each of the GDG meetings including any changes to their DOIs.

Additional information about conflicts of interest of GDG members is included in **Annex B**.

Furthermore, members of all systematic review teams, consultants, methodologists and external reviewers were asked to complete the standard WHO DOI form for review by the responsible technical officer.

2.3 Agreement on guideline questions and prioritization of outcomes

At the first GDG meeting in September 2024, the GDG provided input on two proposed guideline questions, including feedback on the population, interventions, comparisons and outcomes (PICO) questions and study designs.

The two proposed questions focused on:

1. The use and indications of GLP-1 receptor agonists and GIP/GLP-1 dual agonists for the treatment of adults living with obesity.
2. The identification of potential co-interventions that could be included in multimodal clinical algorithms alongside GLP-1–based therapies.

During this meeting, the Secretariat also presented an initial list of potential outcomes relevant to the guideline questions on the basis of outcomes included in the existing trials. The GDG members reviewed and provided feedback on this list and were invited to suggest any additional outcomes they believed were missing.

Following the meeting, GDG members were asked to complete an online survey to score and prioritize the proposed outcomes. They were encouraged to consider which outcomes matter most to those affected by future recommendations. Outcomes were rated for importance using the GRADE-recommended Likert scale from 1 to 9, with the following categories:

- 1 to 3 - not important.
- 4 to 6 - important but not critical.
- 7 to 9 - critical importance.

All GDG members were invited to score the outcomes and the critical and important outcomes – identified based on their mean scores – were included to inform the development of the guideline questions. In line with WHO and GRADE methods, critical outcomes were prioritized for decision-making, including for determining the overall certainty of the recommendations.

Following the first meeting, the Secretariat incorporated input from the GDG and compiled a final list of outcomes based on survey responses. At the second GDG meeting in October 2024, the Secretariat presented the average scores for all outcomes, with the critical and important ones highlighted. The Secretariat proposed the inclusion of a supplementary question on the discontinuation of GLP-1 receptor agonists and GIP/GLP-1 dual agonists in adults living with obesity. The GDG endorsed this addition, recognizing its relevance to clinical decision-making and the importance of addressing it in the guideline. The supplementary question was assigned the same set of critical and important outcomes as the other questions but it was deemed that given the emerging evidence it was going to be addressed in an update.

By the end of the October 2024 meeting, the GDG had agreed on two final guideline questions and a supplementary question to guide the associated systematic reviews.

The guideline questions and outcomes, along with minimal clinically important differences (MCID), are included in **Annex C**.

2.4 Synthesis and assessment of the certainty and confidence of evidence

To inform the first guideline question on the use and indication of GLP-1 receptor agonists and GIP/GLP-1 dual agonists in the treatment of adults living with obesity, three systematic literature reviews were conducted by a single review team.

1. A systematic review on the efficacy and safety of liraglutide for the treatment of adults living with obesity *(18)*.
2. A systematic review on the efficacy and safety of semaglutide for the treatment of adults living with obesity *(19)*.
3. A systematic review on the efficacy and safety of tirzepatide for the treatment of adults living with obesity *(20)*.

The systematic review teams prepared GRADE Evidence Profiles for several comparisons across the three systematic reviews, including for each type of GLP-1 receptor agonist and GIP/GLP-1 dual agonist with various comparisons, including placebo, and at two follow-up times (6 months to less than 24 months as well as 24 or more months). Analysis comprised pairwise meta-analysis and assessment of evidence from randomized clinical trials (RCTs) specifically, with GRADE assessments done for each critical and important outcome based on a minimally contextualized approach. Evidence could be downgraded for risk of bias, indirectness, inconsistency, imprecision and publication bias.

To inform the second guideline question, a fourth additional evidence synthesis was conducted by the same systematic review team. This review focused on the use of co-interventions alongside GLP-1 therapy in the treatment of obesity *(24)*. This was a secondary analysis of the trial evidence that was identified within the above three systematic reviews on the efficacy and safety of GLP-1 therapy for management of adults living with obesity. The systematic review team performed an additive component network meta-analysis (full interaction model). This included any possible co-interventions alongside GLP-1 therapy, in comparison to a common control, that were identified in the RCTs within the first guideline question and could be synthesized within this component network meta-analysis. The component network meta-analysis, with corresponding Confidence in Network Meta-Analysis (CINeMA) assessments (adapted by the authors, with an average of the certainty of the ratings of the combinations that included that component for individual component effects), was done for critical outcomes for the purpose of decision-making by the GDG *(25)(26)*.

To inform the supplementary guideline question on the discontinuation of GLP-1 receptor agonists and GLP-1/GIP dual agonists, a fourth systematic review was conducted by another review team *(27)*. The study designs were broader for this particular question, with RCT evidence included as well as single-arm data from non-randomized studies of interventions and open-label extensions of RCTs, acknowledging that the certainty would likely be lower based on GRADE assessments. The systematic review team completed

pairwise meta-analysis of RCT data. They prepared GRADE Evidence Profiles for RCT evidence of discontinuation versus continuation of GLP-1 receptor agonists and GIP/GLP-1 dual agonists and for pooled means and incidence in single-arm studies which was considered as observational evidence, starting at low certainty based on GRADE.

Finally, a rQES was done to understand the values and preferences, acceptability and potential equity impacts around the use of GLP-1 receptor agonists and GIP/GLP-1 dual agonists, from the perspective of adults living with obesity and health professionals involved in the management of obesity *(28)*. This rQES included studies that used qualitative study designs, qualitative methods for data collection and qualitative methods of analysis, as well as mixed methods studies with qualitative data. The technical team completed GRADE-CERQual assessments to evaluate the confidence in qualitative findings based on four domains, including methodological limitations, coherence, adequacy of data and relevance *(29)*.

Of note, while the recommendations apply to adults older than 19 years of age, all systematic reviews for this guideline included studies involving people living with obesity who were age 18 and above in order to be more inclusive in terms of the evidence.

The systematic reviews were registered in PROSPERO, apart from the component network meta-analysis which was a secondary analysis of studies in the first guideline question.

The GRADE Evidence Profiles can be found in Web Annex A and the GRADE-CERQual Evidence Profile table can be found in Web Annex B.

2.5 Formulating recommendations and good practice statements

For the GDG meetings held in April and June 2025 to develop recommendations, a quorum of at least 70% was required. Accordingly, for decision-making purposes, this was defined as the presence of at least 13 of the 18 GDG members.

The decision-making process for developing recommendations followed the GRADE EtD framework where judgements are made by the GDG for each EtD domain. Formulation of strength and certainty was reached by consensus. According to the WHO handbook for guideline development, second edition, *"consensus decision-making is a process whereby the consent of all committee members is pursued" (21)*. The consensus process was facilitated by the guideline methodologists in collaboration with the GDG co-chairs.

Given the virtual format of the GDG meetings, Zoom polls were occasionally used to gauge preliminary positions and aid discussion. At the start of the April 2025 GDG meeting, and prior to reviewing any evidence, the GDG agreed a priori on a decision rule: if full consensus could not be reached, a supermajority of 60% agreement would be required to proceed.

The systematic review teams presented the evidence for the respective guideline questions at the GDG meetings. The methodologists prepared GRADE EtD frameworks for these questions to consolidate the evidence and facilitate judgements for the various GRADE domains *(30)*.

The GDG made judgements using the GRADE EtD framework for the use of GLP-1 receptor agonists and GIP/GLP-1 dual agonists in the treatment of obesity in adults, specifically focusing on the three agents: liraglutide, semaglutide and tirzepatide.

For the EtD domains of problem, values, resources required, certainty of evidence on resources, cost-effectiveness, equity, acceptability and feasibility, the GDG made a single judgement across all three pharmacological agents.

However, for the domains of desirable effects, undesirable effects, certainty of the evidence and balance of effects, the GDG made separate judgements for each agent. These deliberations took place during the April 2025 GDG meeting, which primarily addressed the first guideline question.

In the fourth GDG meeting in June 2025, which focused on the second guideline question, the GDG made judgements across a GRADE EtD framework for intensive behavioural therapy (IBT) as a co-intervention alongside GLP-1–based therapies for managing obesity in adults.

Following the completion of judgements for each EtD framework, the GDG then determined whether to formulate a recommendation. If a recommendation was to be made, the group also made a decision on the overall certainty of the evidence, guided by critical outcomes and the four categories defined in Table 1 *(23)(31)*:

Table 1. The four categories of certainty of evidence according to GRADE

Certainty	Definition
High	We are very confident that the true effect lies close to that of the estimate of the effect

Certainty	Definition
Moderate	We are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect
Very low	We have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect

The GDG also determined the direction and strength of the recommendations, which could be either strong or conditional, based on several factors. These included the balance of desirable and undesirable effects, the certainty of the evidence (as outlined above), variability in values and preferences and resource use *(23)*.

- A strong recommendation reflects high confidence by the GDG that the desirable effects of an intervention clearly outweigh the undesirable ones.
- A conditional recommendation is made when the GDG is less certain about the balance of effects or when there is likely to be greater variability in values, preferences or resource considerations *(21)(23)*.

In addition to formal recommendations, the GDG also formulated good practice statements related to the guideline questions. According to GRADE guidance, a good practice statement may be formulated when the following criteria are met *(32)*:

- the statement is clear, actionable and essential for healthcare practice;
- the net benefit of implementing the statement is large;
- the effort required to collect and summarize direct evidence would be disproportionate to the value it would add; and
- there is a clear and explicit rationale, supported by indirect evidence, for issuing the statement.

2.6 Limitations of the guideline development process

Three key limitations were encountered in the development of this guideline.

First, a formal synthesis of economic evidence was not conducted to inform the GRADE EtD domains related to resource use, certainty of evidence on required resources and cost-effectiveness. However, the GDG included an expert in health economics, and judgements for these domains were made based on expert consensus and contextual knowledge.

Second, the guideline question on the efficacy and safety of GLP-1 receptor agonists and GIP/GLP-1 dual agonists for the treatment of adults living with obesity was informed by a synthesis of evidence from RCTs. While RCTs are the gold standard for assessing efficacy, they may not fully capture the range and frequency of safety concerns, especially those emerging over the long term. Future evaluations of safety should incorporate data from other sources, such as observational studies, post-marketing surveillance and real-world evidence, to ensure a more comprehensive understanding of potential adverse effects.

Third, it was noted that most of the studies included in the systematic reviews that informed this guideline were funded by the drug manufacturers. This raised the need for independent research to avoide any real or perceived conflict of interest.

3. Guiding principles

This guideline will contribute to the right to the enjoyment of the highest attainable standard of health exercised through comprehensive laws, policies and practices.

This guideline will aim to ensure access to health services without discrimination on the basis of sex, gender, age, ethnicity or disability.

This guideline will support allocation of adequate resources and supplies across all levels of the health system.

This guideline will promote human rights through people-centered policies and protects people living with obesity and obesity-related diseases and disorders in a context free of weight-based stigma and discrimination.

This guideline has been developed with the participatory input of people living with, and communities affected by, obesity and other NCDs and will be implemented with their continuing engagement in the delivery of services and accountability framework.

This guideline has been developed through the lens of a public health approach to guide the scale-up, consolidation and sustainability of essential health services.

4. Recommendations and good practice statements

Practice Statement

Obesity is a chronic complex disease that requires lifelong care beginning with clinical assessment and early diagnosis. Once diagnosed, individuals should have access to comprehensive chronic care programmes offering sustained behavioural and lifestyle interventions. When appropriate, pharmacological, surgical or other therapeutic options may be used to support effective disease management. In parallel, care should address the prevention and treatment of obesity-related complications and comorbidities.

Remarks:

- *Chronic care requires a capacitated health system to ensure essential functions are in place, including supporting governance, training of health workers, monitoring and evaluation, referral systems, procurement and supply chain, and financial coverage.*
- *In the context of obesity chronic care programmes, personalized periodic monitoring of treatment response and side effects/adverse events is essential to ensure sustained adherence and achieve optimal health outcomes.*

Justification

The GDG recognized the importance of this good practice statement, emphasizing that obesity is a chronic complex disease requiring lifelong management, including the prevention and treatment of obesity-related diseases and disorders. As such, effective obesity care must go beyond weight management to include measures aimed at preventing disease progression and the development of obesity-related diseases and disorders. To achieve this, health systems must establish chronic-term care structures capable of supporting individuals throughout the life course, recognizing that treatment modalities may vary across populations, settings and over time.

This message was strongly supported by the GDG members, which included people living with obesity. Furthermore, the rQES study among people living with obesity, highlighted that management of obesity is a “lifelong journey” *(24)*.

Conditional recommendation for , Moderate certainty evidence

In adults living with obesity, GLP-1 receptor agonists or GIP/GLP-1 dual agonists may be used as long-term treatment for obesity.

Remarks:

- *The evidence for two GLP-1 receptor agonists (liraglutide and semaglutide) and one GIP/GLP-1 dual agonist (tirzepatide) was evaluated for the purpose of this recommendation.*
- *This recommendation was derived from clinical trials in which treatment with a GLP-1 receptor agonist was administered from 26 weeks to 240 weeks (median 52 weeks).*
- *Obesity is a complex chronic disease characterized by excessive adiposity that can impair health and is defined by WHO as a BMI equal to or greater than 30 kg/m2.*
- *While the RCTs that informed this recommendation included populations without specific BMI thresholds for overweight and obesity, with overweight and obesity defined per study, this recommendation applies to people with obesity (BMI ≥ 30 kg/m2) but does not include people with BMI between 27 kg/m2 and 30 kg/m2 in association with one or two obesity-related diseases and disorders.*
- *The critical outcomes evaluated to inform this decision were weight, quality of life, adverse events, major adverse cardiovascular events and mortality.*
- *The trial follow-up times were i) 6 months to less than 24 months; and ii) 24 or more months, with higher certainty of evidence for those with less than 24 months of follow-up.*
- *Long-term treatment refers to the continued use of a medication for six months or longer, as per existing regulatory guidance (see the glossary for a more complete definition).*
- *Limited data are currently available to inform practice around decisions about, or the health impact of, discontinuation of GLP-1 receptor agonists and GLP-1/GIP dual agonists.*
- *In the process of establishing obesity chronic care programmes, consideration may be given to prioritizing those at higher risk of morbidity and mortality, while ensuring health equity across populations and settings.*

Evidence to decision

Benefits and harms

Liraglutide

The GDG agreed that there are small desirable effects as well as small undesirable effects of liraglutide for obesity in adults, and that liraglutide is probably favoured in terms of the balance of effects.

This was predominantly based on the comparison of liraglutide versus placebo, which is included in the research evidence section within MAGICapp for the critical outcomes (with full GRADE Evidence Profiles in Web Annex A, for all comparisons and for critical and important outcomes). There were also data on liraglutide compared to orlistat (very low certainty evidence) and to structured programmes targeting lifestyle modification (very low to low certainty evidence), respectively, which are displayed in Web Annex A.

Semaglutide

The GDG agreed that there are moderate to large desirable effects from semaglutide and small undesirable effects from semaglutide in adults with obesity, and that, overall, the balance of effects favours semaglutide.

This was mainly based on evidence of semaglutide compared to placebo, as shown in the research evidence section in Web Annex A for the critical outcomes. The GDG also reviewed evidence of semaglutide compared to liraglutide, and noted semaglutide may result in greater reductions in weight than liraglutide, the results of which for the critical outcomes are in the research evidence section.

Tirzepatide

The GDG agreed that there are small desirable effects and small or uncertain undesirable effects from tirzepatide for obesity, and that overall tirzepatide is favoured or probably favoured.

This was based on evidence comparing tirzepatide to placebo which is included in the research evidence section in Web Annex A for critical outcomes.

The most common side effects of GLP-1 therapies are gastrointestinal, including nausea, vomiting, constipation, and diarrhea, affecting up to 50% of people with obesity and typically resolving after treatment stops. Less common gastrointestinal events—such as biliary disease, acute pancreatitis, bowel obstruction, and gastroparesis—are still under evaluation. Thyroid cancer is listed as a potential risk in regulatory labeling, but its association with GLP-1 therapies remains under investigation. Numerous observational studies have implicated the GLP-1 RAs as increasing the risk of non-arteritic anterior ischemic optic neuropathy (NAION), though not all large studies have found a conclusive relationship between GLP-1 RAs and NAION and the current evidence is discordant. In 2025, the European Medicines Agency Pharmacovigilance Risk Assessment Committee found that NAION was a very rare adverse event of semaglutide, defined by an estimated incidence of up to 1 in 10,000 people suing semiglutiders *(33)*. However, it is unclear if these effects are also produced by other medications withing the same group due to lack of data.

Certainty of the evidence

Moderate

The GDG came to consensus on the overall certainty of the evidence for the use of GLP-1 receptor agonists and GIP/GLP-1 dual agonists for obesity being moderate based on the critical outcomes as shown in the research evidence section with full GRADE Evidence Profiles displayed in Web Annex A.

Liraglutide

The GDG agreed that the certainty of evidence around liraglutide for obesity is moderate. The certainty of the evidence was as follows for the critical outcomes for the comparison of liraglutide versus placebo:

- Weight, very low to moderate (in favour of liraglutide).
- Adverse events, very low to low (in favour of placebo).
- Major adverse cardiovascular events, very low to moderate (with little to no effect).
- Quality of life, moderate (with little to no effect).
- Mortality, very low.
- The clinical experience related to a longer use of this medicine was reflected in the GDG's overall certainty judgement, which was reached through voting during the EtD framework process.

Semaglutide

As with liraglutide, the GDG agreed that the certainty of evidence for semaglutide for obesity is moderate. The certainty for the critical outcomes for semaglutide versus placebo was as follows:

- Weight, moderate to high (in favour of semaglutide).
- Adverse events, very low to low (in favour of placebo).
- Major adverse cardiovascular events, low (with little to no effect).
- Quality of life, low to moderate (with little to no effect).
- Mortality, low to moderate (with little to no effect).

Tirzepatide

The GDG agreed that the certainty of the evidence for tirzepatide for obesity is low to moderate. The certainty for the critical outcomes for tirzepatide versus placebo was as follows:

- Weight, moderate (in favour of tirzepatide).
- Adverse events, very low to moderate (in favour of placebo).
- Major adverse cardiovascular events, very low to low (in favour of tirzepatide).
- Quality of life, low to moderate (with little to no effect).
- Mortality, very low.

Values and preferences

The GDG agreed that there is possibly important variability in how much people value the main outcomes, which was supported by qualitative findings and their experience, including from the perspective of people living with obesity and healthcare providers.

The GDG agreed that people living with obesity, as well as those around them, may have highly variable expectations about weight loss and these expectations may differ greatly across cultures and contexts. The GDG discussed that this was a key consideration in terms of considering stigma related to obesity, which the GDG felt may be heightened for people who do not lose weight from the use of GLP-1 therapy for obesity.

Resources

The GDG agreed that there are likely to be large costs around the use of GLP-1 receptor agonists and GLP-1/GIP dual agonists for treatment of obesity, but the costs are uncertain or may vary across settings and contexts. They therefore made a split judgement for this GRADE EtD domain on resources.

The GDG agreed that cost-effectiveness probably favours GLP-1 receptor agonists and GLP-1/GIP dual agonists but some GDG members thought that cost-effectiveness probably may not favour GLP-1 receptor agonists and GLP-1/GIP dual agonists. Some GDG members again emphasized that the cost-effectiveness varies and can be uncertain in many cases. They also made a split judgement for the domain of cost-effectiveness.

Equity

The GDG made a split judgement about the potential equity impacts of the use of GLP-1 receptor agonists and GLP-1/GIP dual agonists for treatment of obesity in adults.

They felt that the implementation of this intervention in some situations will probably reduce equity and in others will probably increase equity, but that the impacts on equity are likely to vary greatly. This is due to regional variation in accessibility, availability and cost of the medicines.

This decision was informed by the rQES findings on costs and the implications for who may be offered GLP-1 therapy in different contexts, which the GDG felt reflected the reality and could lead to possible inequities.

Acceptability

The GDG felt that GLP-1 receptor agonists and GLP-1/GIP dual agonists for obesity are acceptable or are probably acceptable to key interest-holders including people living with obesity and healthcare providers, based on qualitative findings from the rQES and their own expert and lived experience.

Feasibility The GDG acknowledged that there are several factors to consider with regards to the feasibility of implementing this intervention, but agreed that the use of GLP-1 receptor agonists and GLP-1/GIP dual agonists for treatment of obesity is feasible or probably feasible to implement in many settings and contexts.

Justification

The GDG came to consensus on a conditional recommendation in favour of the possible use of GLP-1 receptor agonists or GLP-1/GIP dual agonists as a treatment for obesity based on moderate certainty evidence around the critical outcomes. The summary of judgements across the GRADE EtD domains is included in **Annex D** with additional description in the EtD section linked to this recommendation.

The GDG felt that there are small desirable effects for the use of liraglutide or tirzepatide and moderate-to-large desirable effects for the use of semaglutide for management of obesity. Overall, they felt that GLP-1 receptor agonists and GIP/GLP-1 dual agonists for management of obesity are favoured or probably favoured. However, there was evidence indicating that there could be small undesirable effects for each of the GLP-1 receptor agonists and GIP/GLP-1 dual agonists, with some of the undesirable effects currently unknown for tirzepatide specifically.

The GDG recognized differences across the three medicines with respect to efficacy, safety, and feasibility. When individual outcomes such as weight reduction are considered, the molecules show different absolute and relative effects. However, when the overall balance of benefits and harms across all critical outcomes was assessed, the GDG concluded that each molecule represents a therapeutic option for which the net benefit prevails. The GDG therefore placed greater weight on this integrated assessment than on differences in single outcomes and issued a recommendation applying to the group of GLP-1 receptor agonists and GIP/GLP-1 dual agonists evaluated.

In addition, the GDG noted that 1) liraglutide is already registered, accessible, and more affordable in many low- and middle-income countries compared with semaglutide and tirzepatide: 2) the WHO Essential Medicines included GLP-1 therapies as a class for people with diabetes with associated obesity and other co-morbidities; and 3) its inclusion (would promote market competition and price reduction) among originator products in this evolving therapeutic area.

The GDG discussed at length the implications of both treatment and follow-up duration for the recommendation itself. Several GDG members expressed that the chronicity of the use of GLP-1 receptor agonists and GIP/GLP-1 dual agonists should be emphasized, leading to the addition of “long-term” to the recommendation. The GDG discussion also emphasized a need for further evidence regarding the relative benefits and potential harms associated with the use of GLP-1 therapy over longer treatment durations. This was one of two key reasons for this recommendation being conditional.

The GDG also discussed the evidence around discontinuation or withdrawal of GLP-1 receptor agonists and GIP/GLP-1 dual agonists in people living with obesity and concluded that the available information is insufficient to inform a clear recommendation or clinical management approach. This includes limitations in understanding of when discontinuation is appropriate as well as approaches to discontinuation and maintenance doses. The GDG did not make a specific recommendation on discontinuation of GLP-1 receptor agonists and GIP/GLP-1 dual agonists due to lack of evidence and limited clarity and certainty of the evidence available *(27)*.

With regards to other GRADE EtD domains that led the GDG to agree on a conditional recommendation, the GDG members considered that there was variability in terms of how much people value the critical outcomes including weight loss and maintenance, which was illustrated in the qualitative findings. They also considered that the impacts of implementing the use of GLP-1 therapy for obesity on health equity could vary and would probably reduce equity in some contexts and would probably increase equity in others. They acknowledged the dynamic situation in terms of possible impacts on equity.

Furthermore, the GDG highlighted that the costs of GLP-1 receptor agonists and GIP/GLP-1 dual agonists for obesity could be large, but the total cost and resources required remain uncertain or may vary across settings. They also considered that cost-effectiveness could vary, with the possibility of GLP-1 therapy being cost-effective or not in different contexts, with uncertainty around more exact estimates of cost-effectiveness.

The above points indicate the main reason that the GDG came to consensus on a conditional recommendation. However, there were several GDG members who proposed a strong recommendation. After further discussion, final consensus and agreement was reached on the conditional strength based on currently limited long-term data, variability of expectations about weight loss across cultures and context, concern around costs and cost-effectiveness, and equity implications.

References for decision making

- *(18)* Meza N, Bracchiglione J, Escobar Liquitay CM, Madrid E, Varerla L, Guo Y, et al. Liraglutide for adults living with obesity. Cochrane Database of Systematic Reviews 2025. Journal
- *(19)* Bracchiglione J, Meza N, Franco J, Escobar Liquitay CM, Novik VA, Oscar Vargas M, et al. Semaglutide for adults living with obesity. Cochrane Database of Systematic Reviews 2025. Journal
- *(20)* Franco J, Guo Y, Varela L, Aqra Z, Alhalahla M, Medina Rodriguez M, et al. Tirzepatide for adults living with obesity. Cochrane Database of Systematic Reviews 2025. Journal

Primary studies:

- *(34)* Donnan J, Huang R, Twells L. Patient Preferences for Attributes of Health Canada Approved Weight Loss Medications Among Adults Living with Obesity in Canada: A Qualitative Study. Patient preference and adherence 2022;16:911-923. Pubmed Journal
- *(35)* Primary studyFarrell E, Nadglowski J, Hollmann E, le Roux CW, McGillicuddy D. "What would be left of me?" Patient perspectives on the risks of obesity treatment: An innovative health initiative stratification of obesity phenotypes to optimise future obesity therapy (IMI2 SOPHIA) qualitative study. Obesity pillars 2024;12:100129. Pubmed Journal
- *(36)* Almaqhawi A, Alabdulqader RA, Alkhteeb NA, Alomair FI, Alhassan SR, Alnajjar JS. Impact of Fasting on Physical Activity Motivation and Weight Reduction in Patients Administered Glucagon-Like Peptide-1 Agonists: A Qualitative Study. Patient preference and adherence 2025;19:19-28. Pubmed Journal
- *(37)* Carmichael C, Jouravskaya I, Collins E, Burns D, Poon JL, Kitchen H, et al. Patient Experience of Treatment with Tirzepatide for Weight Management: Exit Interviews from SURMOUNT-4. The patient 2025;18(3):225-236. Pubmed Journal
- *(38)* Barnard-Kelly K, Whicher CA, Price HC, Phiri P, Rathod S, Asher C, et al. Liraglutide and the management of overweight and obesity in people with severe mental illness: qualitative sub-study. BMC psychiatry 2022;22(1):21. Pubmed Journal
- *(39)* Pierret ACS, Benton M, Sen Gupta P, Ismail K. A qualitative study of the mental health outcomes in people being treated for obesity and type 2 diabetes with glucagon-like peptide-1 receptor agonists. Acta diabetologica 2025;62(5):731-742. Pubmed Journal
- *(40)* Despain D, Hoffman BL. Optimizing nutrition, diet, and lifestyle communication in GLP-1 medication therapy for weight management: A qualitative research study with registered dietitians. Obesity pillars 2024;12:100143. Pubmed Journal
- *(41)* Andreassen P, Jensen SD, Bruun JM, Sandbæk A. Managing the new wave of weight loss medication in general practice: A qualitative study. Clinical obesity 2024;14(3):e12666. Pubmed Journal

Practice Statement

People living with obesity should receive context-appropriate counselling on behavioural and lifestyle changes - including, but not limited to, physical activity and healthy dietary practices - as an initial step toward more structured behavioural interventions. For individuals who are prescribed GLP-1 receptor agonists or GIP/GLP-1 dual agonists, counselling on behavioural and lifestyle changes should be provided as a first step to intensive behavioural therapy to amplify and support optimal health outcomes.

Remarks:

- *Recommendations and good practice statements for physical activity are included in the WHO guidelines on physical activity and sedentary behaviour (42), which highlight that all age groups should limit the amount of time being sedentary and should incrementally increase the frequency, intensity, and duration of physical activity, including muscle strengthening.*
- *According to the Food and Agriculture Organization of the United Nations and the World Health Organization (43), the core principles of a healthy diet apply to all population groups. The four core principles of a healthy diet are: 1) that they need to be adequate and provide enough essential nutrients to prevent deficiencies and promote health, without excess; 2) be balanced in energy intake, and energy sources (fats, carbohydrates and proteins); 3) be moderate in consumption of foods, nutrients or other compounds associated with detrimental health effects; and 4) be diverse and include a wide variety of nutritious foods within and across food groups. In people living with obesity, additional considerations are necessary to support weight loss, including lowering daily energy intake. However, this should be prescribed and monitored in conjunction with a trained health care provider, whenever possible.*

Justification

Multisectoral efforts to educate, create enabling food environments, and influence behaviours related to healthy diet and physical activity are essential to prevent and manage obesity. In addition to general counselling and education on healthy lifestyle changes for the general population and for individuals at high risk of developing obesity, the GDG strongly emphasized, within the context of the guidelines on the use and indication of GLP-1 therapies, the importance of context-appropriate behavioural counselling alongside the use of GLP-1 receptor agonists or GIP/GLP-1 dual agonists. For people living with obesity who are prescribed GLP-1 therapy, such counselling represents a minimum standard of care and a first step into structured behavioural interventions.

While the systematic review on multimodal clinical algorithms for GLP-1 receptor agonists or GIP/GLP-1 dual agonists identified lifestyle counselling as a possible co-intervention *(24)*, the evidence did not demonstrate that counselling augmented the efficacy of GLP-1 therapy. However, the GDG underlined that the rationale for this good practice statement rests not on incremental efficacy but on the principle that behavioural and lifestyle counselling is an essential, foundational component of obesity care. It serves as the starting point for structured approaches, including intensive behavioural therapy (IBT), which is addressed in a separate recommendation.

The GDG therefore considered it unnecessary to undertake a detailed analysis of the evidence or a GRADE assessment for this good practice statement. Counselling on behavioural and lifestyle changes is already widely implemented across primary health care, integrated

care pathways, and essential health service packages, and its desirable consequences clearly outweigh any potential harms. It is a common, feasible, low-risk intervention that provides an important platform on which more structured obesity care approaches can be built.

This good practice statement is consistent with and builds on existing WHO recommendations and principles related to counselling for healthy behaviours, including guidance on physical activity *(42)*, healthy diet *(43)(44)*, reducing sedentary behaviours *(42)*, avoiding tobacco and harmful use of alcoho *(44)*, and maintaining a regular sleep schedule.

Conditional recommendation for , Low certainty evidence

In adults living with obesity who are prescribed GLP-1 receptor agonists or GIP/GLP-1 dual agonists, intensive behavioural therapy may be provided as a co-intervention within a comprehensive multimodal clinical algorithm.

Remarks:

- *In the trials informing this recommendation, intensive behavioural therapy (IBT), alongside GLP-1 receptor agonists or GIP/GLP-1 dual agonists, entailed goal-setting on physical activity and diet, restriction of energy intake, counselling (e.g. weekly, 30-45 minutes), and periodic assessment of goal attainment.*
- *The critical outcomes evaluated to inform this decision were weight, quality of life, and adverse events. Limited data were available on major adverse cardiovascular events and there were no data on mortality for the effects of IBT alongside GLP-1 receptor agonists or GIP/GLP-1 dual agonists.*
- *The data from the RCTs were limited to follow-up durations between 6 months and less than 24 months. There was no direct evidence for outcomes at or beyond 24 months.*
- *The systematic review identified lifestyle counselling, IBT, meal replacement and a lead-in phase with lifestyle changes as possible co-interventions. The analysis did not include any other co-interventions outside what was identified in the trials.*

Evidence to decision

Benefits and harms

The GDG agreed that there are small-to-moderate desirable effects of IBT in addition to GLP-1 receptor agonists and GIP/GLP-1 dual agonists for obesity. The GDG acknowledged that the undesirable effects are unknown.

Overall, the GDG agreed that IBT as a co-intervention alongside GLP-1 receptor agonists or GIP/GLP-1 dual agonists is probably favoured as compared to GLP-1 receptor agonists and GIP/GLP-1 dual agonists alone.This was mainly based on the individual component effects of IBT as well as consideration of the effects of GLP-1 receptor agonists (liraglutide and semaglutide, specifically) with IBT versus placebo, in contrast to GLP-1 receptor agonists alone versus placebo. For the latter, the GDG had to consider the potential impact of the co-intervention IBT based on the evidence for each of these comparisons.

The critical outcomes for which there were data included weight, quality of life and adverse events below 24 months follow-up, which are shown in the research evidence section in Web Annex A.

Certainty of the evidence

Low

The GDG came to consensus that the overall certainty was low in terms of the evidence for IBT as a co-intervention alongside GLP-1 receptor agonists or GIP/GLP-1 dual agonists.

The certainty for the individual component effects for the critical outcomes, displayed in the research evidence section in Web Annex A, was low, which the GDG based their overall certainty judgement on.

The certainty for the critical outcomes was as follows for each of the relevant comparisons:

Liraglutide and IBT compared to placebo

- Weight, low to high (in favour of liraglutide and IBT).
- Adverse events, moderate (in favour of placebo).
- Major adverse cardiovascular events, no data.
- Mortality, no data.

Liraglutide compared to placebo

- Weight, no data or very low certainty.
- Adverse events, no data or low certainty (in favour of placebo).
- Major adverse cardiovascular events, no data.
- Mortality, no data.

Semaglutide and IBT compared to placebo

- Weight, low to high (in favour of semaglutide and IBT).
- Adverse events, moderate to high (in favour of placebo).
- Major adverse cardiovascular events, high (for little-to-no effect).
- Mortality, no data.

Semaglutide compared to placebo

- Weight, no data or low (in favour of semaglutide).
- Adverse events, no data or low to moderate (in favour of semaglutide).
- Major adverse cardiovascular events, no data.
- Mortality, no data.

Values and preferences	The GDG agreed that there is possibly important variability in how much people value the main outcomes, which was supported by qualitative findings and their experience. For example, people living with obesity, as well as those around them, may have highly variable expectations about weight loss and this may be strongly influenced by cultural elements and beliefs.
Resources	The GDG felt that there are likely to be moderate costs to IBT as a co-intervention. There were no included studies for cost-effectiveness.
Equity	The GDG agreed that the impact of IBT as a co-intervention alongside GLP-1 receptor agonists and GIP/GLP-1 dual agonists for obesity on equity is likely to vary depending on the setting and context.
Acceptability	The GDG felt that IBT as a co-intervention is acceptable to key interest holders, including people living with obesity and healthcare providers.
Feasibility	The GDG agreed that the feasibility of providing IBT as a co-intervention for adults living with obesity who are prescribed GLP-1 receptor agonists and GIP/GLP-1 dual agonists probably varies.

Justification

The GDG came to consensus on a conditional recommendation outlining that IBT may be provided as a co-intervention for people living with obesity who are prescribed GLP-1 receptor agonists or GIP/GLP-1 dual agonists. This was based on the finding from the literature reviews that IBT augmented the on-treatment efficacy of the GLP-1 receptor agonists and GIP/GLP-1 dual agonists; this finding was present across both semaglutide and liraglutide. The overall certainty of evidence for this recommendation was low based on the certainty across critical outcomes

The summary of judgements for GLP-1 receptor agonists and GIP/GLP-1dual agonists with IBT as a co-intervention for management of obesity is included in **Annex D** and explained in the EtD section alongside this recommendation.

For this guideline, all potential co-interventions that were identified within this evidence synthesis *(24)* were eligible to be considered for a recommendation in people living with obesity alongside GLP-1 therapy if they were deemed feasible or relevant. The GDG considered IBT to be a relevant and, in some contexts, feasible intervention and thus it was considered for inclusion in the recommendation. Counselling was included in a good practice statement as standard of care and as an initial step toward more structured behavioural and lifestyle interventions.

Based on limited evidence showing little-to-no effect, the GDG chose not to consider the other two co-interventions that were identified in the evidence synthesis, including meal replacement therapy and lead-in with lifestyle counselling. Meal replacement therapy would not be applicable for a global recommendation and there was very limited evidence which showed little-to-no effect. In terms of lead-in with lifestyle changes, there was also very limited evidence indicating little-to-no effect of this approach prior to the introduction of GLP-1 therapy for obesity.

In terms of this recommendation, there was evidence in favour of IBT as a co-intervention alongside GLP-1 receptor agonists or GIP/GLP-1 dual agonists, but the evidence was of low certainty overall which was a key reason for it being conditional.

Furthermore, as with the other recommendation on the use of GLP-1 receptor agonists and GIP/GLP-1 dual agonists for obesity, there is variability in terms of how much people living with obesity value critical outcomes such as weight, with different expectations for weight loss and maintenance.

In addition to this, the GDG felt that the impacts of IBT as a co-intervention on health equity in people living with obesity and the feasibility of implementing IBT are likely to vary across settings and contexts. Finally, the consideration of this evidence led to clarity on the fact that there are few trials that truly assess multimodal clinical algorithms for obesity that are inclusive of GLP-1 therapy in any setting, and that only the interventions included in the trial design were analyzed.

Reference for decision making

- *(24)* Franco J, Meza N, Guo Y, Bracchiglione J, Escobar Liquitay CM, Veroniki A, et al. Multimodal clinical algorithms with GLP-1RA or GLP1/GIP dual agonists for obesity in adults: a component-network meta-analysis. 2025.

5. Implementation considerations

The treatment with GLP-1 receptor agonists and GIP/GLP-1 dual agonists should be delivered in the context of chronic care, which requires a capacitated health system to ensure adequate resources are in place, including supporting governance, comprehensive training of health workers, monitoring and evaluation, referral systems, procurement, supply chain and financial coverage.

Countries and decision-makers should also consider locally derived or relevant transferable evidence and contextual factors, including cost-effectiveness evidence, budget impact analysis and social and ethical implications, to guide expanded access to GLP-1 therapy in their own contexts.

When countries adopt GLP-1 therapy as part of a chronic care model, they should be included in UHC and primary care benefit packages.Increased access to effective treatment options – particularly more equitable and affordable access to GLP-1 receptor agonists and GIP/GLP-1 dual agonists – is of critical importance to prevent obesity progression and the development of obesity-related diseases and disorders. Currently, the accessibility, affordability and availability of GLP-1 receptor agonists and GIP/GLP-1 dual agonists remain highly inadequate to meet the population-level needs. Strategies to improve access may include negotiating more favorable access and pricing conditions, facilitating market competition, implementing pooled procurement, supporting local production, adopting tiered pricing and applying voluntary or compulsory licensing. Ensuring access to multi-disciplinary care is also vital, and in some contexts, this can be supported by telehealth and digital platforms *(45)(46)*.

Countries and decision-makers should consider locally generated or transferrable evidence - such as cost-effectiveness data, budget impact analyses and social and ethical implications - to guide the appropriate integration of GLP-1 therapy into their health systems.

The integration of IBT with GLP-1 therapy may be facilitated by the adoption of task-shifting/task sharing among the clinical care team members in order to optimize resource use and ensure comprehensive, patient-centred care *(47)(48)(49)*.

6. Research needs and limitations

Over the past few years, GLP-1 receptor agonists and GIP/GLP-1 dual agonists have emerged as promising therapeutic options for obesity and related comorbidities. However, critical gaps remain regarding long-term efficacy, real-world effectiveness and equitable implementation across diverse settings and populations.

Future research needs are summarized below.

- To determine priority populations for the use of GLP-1 therapy over a full range of BMI values, alternative anthropometric measures (e.g., waist and hip circumference) and obesity-related diseases and disorders, as well as across age, sex and ethnic sub-populations.
- To assess the efficacy of GLP-1 receptor agonists or GIP/GLP-1 dual agonists on a broader range of health conditions, such as kidney disease in obesity, cognitive decline, addiction, impulse control and obesity secondary to medication in the mental health and intellectual disability population, as well as the full range of clinical benefits, harms and quality of life outcomes of the use of this medicine class over the long term (> 6 months).
- To investigate the potential impact of GLP-1 receptor agonists or GIP/GLP-1 dual agonists on fertility in women living with obesity as well as the safety of these medicines in pregnancy.
- To evaluate programmatic and health service delivery strategies for GLP-1 therapy as part of multimodal clinical algorithms, across high-, low- and middle-income countries, including the cost-effectiveness and budget impact of large-scale programmatic use of GLP-1 therapy in people living with obesity across these settings.
- To investigate optimal strategies for safe and effective titration, maintenance and/or therapy replacement, and discontinuation of GLP-1 receptor agonist and GIP/GLP-1 dual agonists on body composition and full range of health outcomes. Additionally, predictors of success and patient preferences should also be better understood across age groups, ethnicities and comorbidity profiles.
- To understand the optimal dose (how much in time, what type(s) and intensity of physical activity and what frequency per week), duration (for how long – weeks/months – during and after GLP-1 therapy), context (supervised and or unsupervised; use of digital tools) of physical activity and impact on body composition and health among people taking GLP-1 therapy.
- Facilitators and barriers to long-term GLP-1 receptor agonists and GIP/GLP-1 dual agonist treatment adherence and persistence (including real world data) and possible interventions to improve these.

7. Publication, dissemination, implementation, monitoring and evaluation

7.1 Publication strategy

The multi-faceted publication strategy for the WHO guideline on the use of GLP-1 therapy for the treatment of obesity in adults is designed to ensure a high degree of visibility, scientific credibility and broad, cross-sectoral reach. This includes:

- Publication of papers in high-impact peer-reviewed journals - such as the Journal of the American Medical Association (JAMA), the Cochrane library and The Lancet journals - highlighting the clincial and public health signifcanace of teh recommnedations and reinforcing their relevance for evidence-based decision-making.
- A global launch event targeting clinicians, researchers, health programme managers and policy-makers across all regions. The event will mark the formal launch and facilitate immediate engagement with key global audiences.
- Publications of one or more op-eds in broad reach, influential lay publications (newspapers, magazines).
- Dissemination of papers, through academic journals, such as Lancet Global Health, on health system preparedness to address obesity, through both treatment and prevention.
- Derivative knowledge products: the WHO Steering Group will also develop derivative tools to facilitate understanding, adaptation and implementation of these recommendations in local contexts.

7.2 Dissemination strategy

The dissemination strategy prioritizes broad stakeholder reach, uptake at the country level and alignment with WHO's broader obesity response frameworks. The different elements are outlined below.

7.2.1 Member State briefings

Strategic briefings will be conducted with Ministries of Health, Permanent Missions and WHO regional and country offices to raise awareness of the guideline and facilitate inclusion of its recommendations in national chronic care strategies for obesity.

7.2.2 Engagement through high-impact editorial networks

A coordinated series of publications will be disseminated in journals such as the JAMA network and affiliated journals, the Cochrane library, The Lancet journals and others to:

- present the evidence underpinning the recommendations;
- highlight implementation case studies and emerging lessons; and
- foster a global learning community integrating science, clinical care and health system innovation.

7.2.3 Translation and language accessibility

The executive summary, including key recommendations, will be translated into all six official United Nations (UN) languages and disseminated through WHO regional and country networks.

7.2.4 Integration into WHO Programmes and news platforms

The recommendations will be promoted through the WHO NFS and NCD departmental websites and via WHO meetings, partner newsletters and scientific conferences.

7.2.5 Collaboration with key partners

WHO will work in close collaboration with relevant clusters, departments and partnerships to ensure that dissemination aligns with broader strategies to address chronic diseases and advance UHC.

7.3 Implementation strategy

As with all WHO guidelines, the recommendations and the good practice statements will have different implications for their operationalization depending on context. The recommendations in this guideline can be used by policy-makers and health authorities in all countries, from low- to high-income, and are intended to assist integration of obesity chronic care programmes, also including GLP-1 therapy, in national health sector planning and clinical guidance at countries' discretion. Furthermore, the recommendations can inform the practice of health service providers, health workers and professional societies, as well as the research agenda of research and academic institutions. Importantly, the guideline can also play a role in raising awareness among the public at large and supporting people living with obesity to shape healthcare systems.

To support implementation, the guideline will be integrated into WHO's support for Member States in building chronic care systems for obesity as outlined below.

7.3.1 Integration with WHO Health Service Delivery Framework for integration of obesity prevention, care and treatment services.

The guideline will complement existing WHO guidance on obesity care across the life course and align with WHO's primary health care and service delivery models for integrated chronic care *(50)*.

7.3.2 Inclusion in the WHO Acceleration Plan to Stop Obesity

The guideline will be added as a core technical product under the WHO Acceleration Plan to Stop Obesity *(51)*. Implementation support will be extended to all countries in the Plan and beyond, via technical webinars and peer-learning exchanges.

7.3.3 Early adoption by frontrunner countries

Selected countries actively engaged in obesity chronic care programmes scale-up will serve as frontrunners in implementing the guideline. These countries will generate real-world insights that can inform global learning and scale-up and future versions of the guidelines.

7.3.4 Technical support and country-level guidance

WHO will support Member States in adapting the recommendations to national contexts, including:

- integrating GLP-1 therapy into chronic care packages;
- developing service delivery protocols and referral pathways; and
- ensuring equitable access, including through inclusion in essential medicines lists.

7.3.5 Capacity building and implementation tools

A WHO course to capacitate introduction and scale up of obesity chronic care programmes through a PHC approach including clinical management of obesity has been developed. Modules cover:

- Chronic Care Program Principles – Team-based approaches to enroll, retain, and improve outcomes; integration of obesity care within primary health care.
- Clinical Assessment & Diagnosis – Assessing obesity across the life course using BMI and waist circumference.
- Patient Monitoring & Retention – Embedding obesity prevention, care, and treatment in PHC; supporting adherence.
- Patient Motivation & Engagement – Evaluating readiness for multimodal obesity care using motivational interviewing.
- Behavioral Therapy Delivery – Applying principles of behavior change from WHO Academy training.
- GLP-1 Receptor Agonist Therapy – Case-based guidance on initiation and integration in PHC.
- Screening & Management of Obesity-Related Complications – Identifying and managing cardiovascular disease, type 2 diabetes, sleep apnea, and other complications.
- Referral & Back-Referral Management – Managing complex or treatment-resistant patients through case-based learning.

7.4 Implementation considerations and contextualization

To support national adaptation and successful uptake, the following considerations are emphasized:

- national working groups should assess current obesity treatment guidelines and determine the need for updates based on WHO recommendations; and
- adaptation should be participatory, evidence-informed and aligned with existing national health strategies.

7.5 Monitoring, updating and the role of early implementation

This WHO publication is designed to be dynamic and responsive to the evolving scientific landscape, emerging clinical data and real-world programmatic experiences, reflecting WHO's commitment to iterative evidence assessment and timely updates, ensuring that recommendations remain aligned with the best available data and practice realities. In this context, early implementation by selected frontrunner countries – many of which are frontrunners of the WHO Acceleration Plan to Stop Obesity *(51)* – serves as both a catalyst for national policy translation and a source of invaluable real-world evidence. These implementation experiences will provide critical data on feasibility, acceptability, service delivery pathways, health system readiness and equity in access to GLP-1 therapy. Outcomes from routine practice – including clinical effectiveness, safety monitoring and patient-reported outcomes – will be captured through structured country reporting and WHO-supported monitoring frameworks. This evidence, triangulated with newly published clinical trial data and

global pharmacovigilance findings, will feed into a continuous evidence review cycle conducted by the WHO Secretariat. This cycle will inform future updates and possible expansion of the recommendations, including modifications to indications, eligible populations, treatment discontinuation and maintenance.

The integration of implementation-derived evidence into the guideline update process represents a critical innovation in WHO's approach to normative guidance – bridging the gap between controlled trial data and the complexity of health service delivery in diverse settings. It also underscores WHO's commitment to equity, by ensuring that the voices and experiences of countries and populations affected by obesity are systematically reflected in the global evidence base.

8. Updating the guideline

As noted previously, given that the evidence base on GLP-1 therapy for obesity continues to evolve rapidly, WHO has designated this as a living guideline. The guideline will be updated as new data become available to inform or revise existing recommendations.

For this, the WHO Secretariat will continue to monitor and assess emerging evidence on a six-monthly basis that may influence or necessitate revisions to the current recommendations on the use and indications of GLP-1 receptor agonists and GIP/GLP-1 dual agonists. Such evidence may pertain to the desirable or undesirable effects of already investigated GLP-1–based therapies and related interventions, or may be relevant to other GRADE EtD domains, including resource use, cost-effectiveness, equity, acceptability and feasibility. It may also include head-to-head comparative studies, longer-term clinical trials, evidence on treatment discontinuation, substitution or sequencing of pharmacotherapy, as well as strategies to sustain long-term health outcomes.

The results of the six-monthly searches will be summarized by the external evidence review team(s). This information will then initially be assessed and discussed by a group comprising the WHO Guideline responsible technical officer, the external methodologist and the GDG co-chairs. Should any new evidence be assessed as being potentially consequential, then the full GDG will be consulted for further review and discussion. New evidence (including evidence relating to EtD factors) would be considered “potentially consequential” if it would change the strength or direction of the current recommendation(s) and/or warrant consideration of a new recommendation. This guideline will be facilitated by the use of MAGICapp and will involve updated versions with descriptions of what has been updated and/or added into the guideline to ensure any changes are clear to readers.

In addition, during the GDG meeting held in June 2025, consensus was reached on the next priority area: the identification of high-risk populations who are most likely to benefit from GLP-1–based therapy. The GDG agreed that this prioritization represents an essential step forward in light of current constraints related to incremental production capacity and varying levels of health system preparedness. The group emphasized that it will support a phased and equity-oriented expansion of the target population as therapeutic availability increases and health systems strengthen. Accordingly, the GDG will reconvene from 18 November 2025 to formulate and agree on a new guideline question. This question will guide a systematic literature review aimed at defining the criteria and conditions for identifying high-risk groups most likely to benefit from GLP-1–based therapy.

Other areas of evidence that will be monitored, and which the GDG may review in future, also include: consideration of other GLP 1–based therapies beyond liraglutide, semaglutide (subcutaneous) and tirzepatide, as more than 10 are already approved and over 40 are in development; further consideration of the role of oral formulations, particularly in health systems where cold chain or injection delivery poses challenges; additional components of the multimodal obesity chronic care model and addressing potential drug–drug interactions with medications commonly used for comorbid conditions such as HIV and cardiovascular disease, to support safer and context appropriate prescribing, especially in low- and middle-income countries.

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Annex B. Declaration of interests for the Guideline Development Group

Name	Interests disclosed and identified	Action taken
Louella Patricia D. Carpio	No interests declared. No conflicts identified through independent internet and publication searches.	None; full participation allowed
Omar Yaxmehen Bello-Chavolla	No interests declared. No conflicts identified through independent internet and publication searches.	None; full participation allowed
Faraja Chiwanga	No interests declared. No conflicts identified through independent internet and publication searches.	None; full participation allowed
Laura E. Downey	No interests declared. No conflicts identified through independent internet and publication searches.	None; full participation allowed
Ezekiel J. Emanuel	Ezekiel Emanuel declared that he has 50,000 shares in Alto Pharmacy Holdings and is on the Board of Advisors for this company. Following internal due diligence and review, in consultation with the Department of Compliance, Risk and Ethics, it was determined that the interests in such company were not in conflict with the scope with this guideline.	None; full participation allowed
Jeanette Hunter	No interests declared. No conflicts identified through independent internet and publication searches.	None; full participation allowed
David D. Kim	No interests declared. No conflicts identified through independent internet and publication searches.	None; full participation allowed
Nicola Magrini	No interests declared. No conflicts identified through independent internet and publication searches. Former Secretary, Expert Committee on Selection and Use of Essential Medicines, WHO (2014–2020).	None; full participation allowed
Dariush Mozaffarian (until April 2025, at which point he withdrew due to a lack of time)	Dariush Mozaffarian did not declare any conflicts of interest in relation to this guideline. In a 2023 publication he disclosed financial and non-financial interests, but upon review, these interests were determined not to have a direct link, benefit, commercial relationship, or interest specifically related to GLP-1 receptor agonists or dual GIP/GLP-1 agonists for obesity treatment.	None; full participation allowed
Hala Khaled Nawaiseh	No interests declared. No conflicts identified through independent internet and publication searches.	None; full participation allowed
Stephen Ogweno	No interests declared. No conflicts identified through independent internet and publication searches.	None; full participation allowed
Donal O'Shea	No interests declared. No conflicts identified through independent internet and publication searches.	None; full participation allowed
Karen Sealey	No interests declared. No conflicts identified through independent internet and publication searches. Former Special Adviser, UN and Partnerships, Pan American Health Organization.	None; full participation allowed
Nikhil Tandon	Nikhil Tandon reported that declared that that he is currently an investigator of a trial on semaglutide funded by Novo Nordisk, with no personal income received. Following review, the Director of NFS determined no conflict of interest exists due to no direct personal benefit or undue influence on guideline development.	None; full participation allowed
Yot Teerawattananon	No interests declared. No conflicts identified through independent internet and publication searches.	None; full participation allowed

Name	Interests disclosed and identified	Action taken
Francois Venter	No interests declared. In a 2024 publication, he disclosed institutional grants, drug donations, participation in commercial drug studies, honoraria, and unpaid participation in regional/government guideline groups, none directly related to GLP-1 receptor agonists. Following comprehensive assessment and review, it was determined that none of the disclosed interests constitute a conflict of interest given their institutional nature and lack of direct link to GLP-1 receptor agonists or dual GIP/GLP-1 agonists.	None; full participation allowed, but unable to act as GDG chair
Jin-Yi Wan	No interests declared. No conflicts identified through independent internet and publication searches.	None; full participation allowed
Veronika J. Wirtz	No interests declared. No conflicts identified through independent internet and publication searches.	None; full participation allowed

Annex C. Guideline questions and outcomes

There were two guideline questions that were initially prioritized for this guideline with a supplementary question on the discontinuation of GLP-1 receptor agonists or GLP-1/GIP dual agonists for obesity added upon agreement with the GDG during a GDG meeting that took place in October 2024.

Guideline questions
In adults ≥18 years old with overweight or obesity as defined per study, what is the efficacy and safety of treatment with GLP-1 receptor agonists or GIP/GLP-1 dual agonists compared with (1) no treatment or placebo or (2) structured programmes targeting lifestyle modification or (3) any other pharmacological intervention for obesity or (4) any other GLP-1 receptor agonists or GIP/GLP-1 dual agonists for managing obesity?
In adults ≥18 years old with overweight or obesity as defined per study, what are the effects of co-interventions within multimodal clinical algorithms for GLP-1 receptor agonists or GIP/GLP-1 dual agonists for managing obesity?
In adults ≥18 years old with overweight or obesity as defined per study using GLP-1 receptor agonists or GIP/GLP-1 dual agonists, what are the effects of discontinuation of GLP-1 receptor agonists or GIP/GLP-1 dual agonists (1) with and without down-titration period, (2) with and without association of other anti-obesity medications, (3) with and without association of lifestyle interventions compared with continuation of the weight-lowering medications?

The critical and important outcomes for all three guideline questions along with their scores based on a survey completed by the GDG were as follows:

Outcomes	Importance	Mean ± SD
Weight	Critical	8.0 ± 1.4
Quality of life	Critical	7.6 ± 1.2
Adverse events	Critical	7.1 ± 1.8
Major adverse cardiovascular event (MACE)	Critical	6.9 ± 1.6
Mortality	Critical	6.8 ± 2.1
Waist circumference	Important	6.4 ± 2.1
HbA1C	Important	6.3 ± 1.7
Metabolic dysfunction-associated steatotic liver disease	Important	6.3 ± 1.7
Heart failure	Important	6.2 ±1.8
Obstructive sleep apnea	Important	6.1 ± 1.5
Metabolic dysfunction-associated steatohepatitis	Important	6.0 ± 1.8
Blood pressure	Important	5.9 ± 1.6
Need for glucose-lowering therapy	Important	5.9 ± 1.7
Lipids	Important	5.6 ± 1.7
Need for lipid-lowering treatment	Important	5.5 ± 1.6
Cirrhosis	Important	5.4 ± 2.1
Need for antihypertensives	Important	5.3 ± 1.7

The thresholds for minimal clinically important differences (MCID) for the outcomes that were applied to the systematic reviews for the guideline question on efficacy and safety of treatment with GLP-1 receptor agonists or GIP/GLP-1 dual agonists, prepared by the systematic review team, were as follows:

Outcome domain	Outcome measure	Criteria for a minimal clinically important difference (MCID)
Weight	% weight change from baseline	5% in weight change, which is considered a standard MCID for this outcome and was used in previous reviews *(52)*
	Change in kg	Based on a median weight in control groups of approximately 100 kg, a 5% reduction in weight would correspond to 5 kg
	Change in BMI	Considering a change in 5 kg, based on an average height between 1.6 to 1.7 m this corresponds to a change of 1.7 to 1.95 BMI units
	People achieving a 5% weight reduction	We identified no standard MCID so we considered the general rule of a 25% relative change *(53)*, which corresponds to a 6% absolute difference
	People achieving a 10% weight reduction	We identified no standard MCID so we considered the general rule of a 25% relative change *(53)*, which corresponds to a 3% absolute difference
Adverse events	Non-serious adverse events	We identified no standard MCID so we considered a 5% absolute risk difference as a threshold
	Moderate adverse events	
	Adverse events leading to withdrawal	
	Serious adverse events	We established a 1% absolute risk difference as a threshold *(54)*
Major adverse cardiovascular event (MACE)	Myocardial infarction, stroke or heart failure (among other definitions)	We established a 5% absolute risk difference as a threshold
Quality of life	SF-36 mental component	We considered a MCID of 4 points *(55)*
	SF-36 physical component	We considered a MCID of 4 points *(55)*
	SF-36 physical functioning	We considered a MCID of 7 points *(56)*
	IWQoL-Lite-CT total	We considered a MCID of 16.6 points *(57)*
	IWQoL-Lite-CT physical functioning	We considered a MCID of 14.6 points *(57)*
Mortality	All-cause mortality	We set a threshold of 1% changes as clinically significant *(54)*
Waist circumference	cm	A reduction of 5-10% or 3-8 cm has been regarded as clinically relevant changes in adults *(58)(59)(60)*
Heart failure	Incidence	We established a 5% absolute risk difference as a threshold
	6 minute walking test	We established a difference in 14 meters as a MCID *(61)*
	Kansas City Cardiomyopathy Questionnaire	We identified a MCID of 5 points, considering that higher score indicates better functioning *(62)*
Diabetes-related outcomes	Fasting blood glucose	Every 1mmol/L (18 mg/dL) increase in fasting blood glucose have been associated with higher risk of all-cause mortality and severe cardiovascular outcomes in adults with or without diabetes *(63)(64)(65)*
	haemoglobin A1c (HbA1c)	A change of 0.5% to 1% in HbA1c levels has been related with higher risk of complications and mortality *(66)(67)(68)(69)* As a dichotomous outcome (people achieving an improvement of HbA1c) we used a 25% relative change (approximately 7% absolute difference)
	Need for glucose-lowering therapy	We identified no standard MCID so we considered the general rule of a 25% relative change *(53)*
Blood pressure-	Need for antihypertensives	We identified no standard MCID so we considered the general rule of a 25% relative

Outcome domain	Outcome measure	Criteria for a minimal clinically important difference (MCID)
related outcomes		change *(53)*
	Systolic blood pressure	A reduction of 5 mmHg is considered as clinically relevant *(70)*
	Diastolic blood pressure	A reduction of 2 mmHg is considered as clinically relevant *(71)*
Liver disease-related outcomes	% liver fat	We identified no standard MCID so we considered the general rule of a 25% relative change *(53)*
	Liver enzymes	A reduction of approximately 10 IU/L in ALT and 5 IU/L in AST has been regarded as clinically significant in adults with non-alcoholic fatty liver disease *(72)*
	Metabolic dysfunction-associated steatotic liver disease	We identified no standard MCID so we considered the general rule of a 25% relative change *(53)*
	Metabolic dysfunction-associated steatotic steatohepatitis	We identified no standard MCID so we considered the general rule of a 25% relative change *(53)*
	Cirrhosis	We identified no standard MCID so we considered the general rule of a 25% relative change *(53)*
Obstructive sleep apnea	Incidence	We identified no standard MCID so we considered the general rule of a 25% relative change *(53)*
	Apnea hypopnea index	We identified a MCID of 5 events per hour in the apnea hypopnea index *(73)*
	Epworth Sleepiness Scale	We identified a MCID between 2 and 3 points of the Epworth Sleepiness Scale *(74)*
Lipid metabolism-related outcomes	Total cholesterol	We considered a 10% change in these values as clinically meaningful considering their impact on cardiovascular risk *(75)(76)(77)*
	HDL cholesterol	
	LDL cholesterol	
	Triglycerides	We considered a 25% change as clinically meaningful considering their impact on cardiovascular risk *(78)*
	Need for lipid-lowering treatment	We identified no standard MCID so we considered the general rule of a 25% relative change *(53)*

Annex D. Summary of judgements for recommendations

Conditional recommendation for, Moderate certainty evidence

In adults living with obesity, GLP-1 receptor agonists or GIP/GLP-1 dual agonists may be used as a long-term treatment for obesity.

GRADE EtD domain	Judgement		
	Liraglutide	Semaglutide	Tirzepatide
Problem	Yes		
Desirable effects	Small	Moderate/Large	Moderate
Undesirable effects	Small	Small	Small/Uncertain
Certainty of evidence	Moderate	Moderate	Low/Moderate
Values	Possibly important variability		
Balance of effects	Probably favours liraglutide	Favours semaglutide	Favours/Probably favours tirzepatide
Resources required	Large costs/Uncertain/Varies		
Certainty of evidence of resources required	No data presented		
Cost-effectiveness	Probably favours GLP-1 receptor agonists and GIP/GLP-1 dual agonists/Probably favours no GLP-1 receptor agonists and GIP/GLP-1 dual agonists/Varies/Uncertain		
Equity	Probably reduced/Probably increased/Varies		
Acceptability	Yes/Probably yes		
Feasibility	Yes/Probably yes		

Conditional recommendation for, Low certainty evidence

In adults living with obesity who are prescribed GLP-1 receptor agonists or GIP/GLP-1 dual agonists, intensive behavioural therapy may be provided as a co-intervention within a comprehensive multimodal clinical algorithm.

GRADE EtD domain	Judgement
Problem	Yes
Desirable effects	Small/Moderate
Undesirable effects	Don't know
Certainty of evidence	Low
Values	Possibly important variability
Balance of effects	Probably favours IBT
Resources required	Moderate costs
Certainty of evidence of resources required	No data presented
Cost-effectiveness	No included studies
Equity	Varies
Acceptability	Yes
Feasibility	Varies

References

1. US Food and Drug Administration. International Council for Harmonisation. E1A: The Extent of Population Exposure to Assess Clinical Safety for Drugs Intended for Long-Term Treatment of Non-Life-Threatening Conditions. Silver Spring 1995. Website

2. US Food and Drug Administration. Long Term Follow-Up After Administration of Human Gene Therapy Products: Guidance for Industry. Silver Spring 2020. Website

3. US Food and Drug Administration. Indications and Usage Section of Labeling for Human Prescription Drug and Biological Products — Content and Format: Guidance for Industry. Silver Spring 2018. Website

4. World Health Organization. International Classification of Disease 11 (ICD-11). 5B81 Obesity. 2025. Website

5. NCD Risk Factor Collaboration. Worldwide trends in underweight and obesity from 1990 to 2022: a pooled analysis of 3663 population-representative studies with 222 million children, adolescents, and adults. The Lancet 2024. Journal

6. GBD 2021 Risk Factor Collaborators. Global Burden of 88 Risk Factors in 204 Countries and Territories, 1990–2021: a systematic analysis for the Global Burden of Disease study 2021. Lancet 2024. Journal

7. Okunogbe A, Nugent R, Spencer G, Powis J, Ralston J, Wilding J. Economic impacts of overweight and obesity: current and future estimates for 161 countries. BMJ Glob Health 2022. Journal

8. Carrasco D, Thulesius H, Jakobsson U, Memarian E. Primary care physicians' knowledge and attitudes about obesity, adherence to treatment guidelines and association with confidence to treat obesity: a Swedish survey study. BMC Prim Care 2022. Journal

9. Tikkanen R, Mossialos E, Djordjevic A, Wharting G. International profiles of health care systems 2020. 2020. Website

10. Brown CF, Zvenyach T, Paul E, Golden L, Varney C, Bays HE. Obesity and advocacy: A joint clinical perspective and expert review from the obesity medicine association and the obesity action coalition. Journal

11. US Food and Drug Administration.. FDA approves Byetta to treat type 2 diabetes. News release. 2005. Website

12. US Food and Drug Administration. FDA approves Saxenda (liraglutide) injection for chronic weight management. News release. 2014. Website

13. Margulies KB, Hernandez AF, Redfield MM. Effect of semaglutide in patients with HFpEF and obesity. The New England Journal of Medicine 2023. Journal

14. Kosiborod M, Bain SC, Hansen LS. GLP-1 receptor agonists and atherosclerotic outcomes: a meta-analysis. Lancet Diabetes Endocrinol 2022. Journal

15. Newsome PN, Buchholtz K, Cusi K. A placebo-controlled trial of subcutaneous semaglutide in nonalcoholic steatohepatitis. Lancet 2021. Journal

16. Gejl M, Gjedde A, Egefjord L. In Alzheimer's disease, 6-month treatment with GLP-1 analog prevents decline of brain glucose metabolism: a randomized, placebo-controlled study. Frontiers 2016. Journal

17. Athauda D, Foltynie T. GLP-1 receptor agonists in Parkinson’s disease: mechanisms of action and clinical trials. Lancet Neurol 2018. Journal

18. Meza N, Bracchiglione J, Escobar Liquitay CM, Madrid E, Varerla L, Guo Y, et al. Liraglutide for adults living with obesity. Cochrane Database of Systematic Reviews 2025. Journal

19. Bracchiglione J, Meza N, Franco J, Escobar Liquitay CM, Novik VA, Oscar Vargas M, et al. Semaglutide for adults living with obesity. Cochrane Database of Systematic Reviews 2025. Journal

20. Franco J, Guo Y, Varela L, Aqra Z, Alhalahla M, Medina Rodriguez M, et al. Tirzepatide for adults living with obesity. Cochrane Database of Systematic Reviews 2025. Journal

21. World Health Organization. WHO handbook for guideline development, 2nd ed. World Health Organization 2014. Website

22. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ (Clinical research ed.) 2008;336(7650):924-6 Pubmed Journal

23. Andrews J, Guyatt G, Oxman AD, Alderson P, Dahm P, Falck-Ytter Y, et al. GRADE guidelines: 14. Going from evidence to recommendations: the significance and presentation of recommendations. Journal of clinical epidemiology 2013;66(7):719-25 Pubmed Journal

24. Franco J, Meza N, Guo Y, Bracchiglione J, Escobar Liquitay CM, Veroniki A, et al. Multimodal clinical algorithms with GLP-1RA or GLP1/GIP dual agonists for obesity in adults: a component-network meta-analysis. 2025.

25. Papakonstantinou T, Nikolakopoulou A, Higgins JPT, Egger M, Salanti G. CINeMA: Software for semiautomated assessment of the confidence in the results of network meta-analysis. Campbell systematic reviews 2020;16(1):e1080 Pubmed Journal

26. Nikolakopoulou A, Higgins JPT, Papakonstantinou T, Chaimani A, Del Giovane C, Egger M, et al. CINeMA: An approach for assessing confidence in the results of a network meta-analysis. PLoS medicine 2020;17(4):e1003082 Pubmed Journal

27. Luo X, Zou X, Agarwal A, Ma J, Zhang J, Ren S, et al. Effect of discontinuation of GLP-1 receptor agonists on weight trajectories and metabolic outcomes in adults with obesity: a systematic review and pairwise meta-analysis. 2025. Website

28. Daniel AI, Manne-Goehler J, Oliver J, Johnsen JT, Siegfried N. Glucagon-like peptide-1 receptor agonists for obesity: a rapid qualitative evidence synthesis. 2025. Website

29. Lewin S, Booth A, Glenton C, Munthe-Kaas H, Rashidian A, Wainwright M, et al. Applying GRADE-CERQual to qualitative evidence synthesis findings: introduction to the series. Implementation science : IS 2018;13(Suppl 1):2 Pubmed Journal

30. Alonso-Coello P, Schünemann HJ, Moberg J, Brignardello-Petersen R, Akl EA, Davoli M, et al. GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 1: Introduction. BMJ (Clinical research ed.) 2016;353:i2016 Pubmed Journal

31. Hultcrantz M, Rind D, Akl EA, Treweek S, Mustafa RA, Iorio A, et al. The GRADE Working Group clarifies the construct of certainty of evidence. Journal of clinical epidemiology 2017;87:4-13 Pubmed Journal

32. Dewidar O, Lotfi T, Langendam MW, Parmelli E, Saz Parkinson Z, Solo K, et al. Good or best practice statements: proposal for the operationalisation and implementation of GRADE guidance. BMJ evidence-based medicine 2023;28(3):189-196 Pubmed Journal

33. World Health Organization. The use of semaglutide medicines and risk of non-arteritic anterior ischemic optic neuropathy (NAION). 2025. Website

34. Donnan J, Huang R, Twells L. Patient Preferences for Attributes of Health Canada Approved Weight Loss Medications Among Adults Living with Obesity in Canada: A Qualitative Study. Patient preference and adherence 2022;16:911-923 Pubmed Journal

35. Farrell E, Nadglowski J, Hollmann E, le Roux CW, McGillicuddy D. "What would be left of me?" Patient perspectives on the risks of obesity treatment: An innovative health initiative stratification of obesity phenotypes to optimise future obesity therapy (IMI2 SOPHIA) qualitative study. Obesity pillars 2024;12:100129 Pubmed Journal

36. Almaqhawi A, Alabdulqader RA, Alkhteeb NA, Alomair FI, Alhassan SR, Alnajjar JS. Impact of Fasting on Physical Activity Motivation and Weight Reduction in Patients Administered Glucagon-Like Peptide-1 Agonists: A Qualitative Study. Patient preference and adherence 2025;19:19-28 Pubmed Journal

37. Carmichael C, Jouravskaya I, Collins E, Burns D, Poon JL, Kitchen H, et al. Patient Experience of Treatment with Tirzepatide for Weight Management: Exit Interviews from SURMOUNT-4. The patient 2025;18(3):225-236 Pubmed Journal

38. Barnard-Kelly K, Whicher CA, Price HC, Phiri P, Rathod S, Asher C, et al. Liraglutide and the management of overweight and obesity in people with severe mental illness: qualitative sub-study. BMC psychiatry 2022;22(1):21 Pubmed Journal

39. Pierret ACS, Benton M, Sen Gupta P, Ismail K. A qualitative study of the mental health outcomes in people being treated for obesity and type 2 diabetes with glucagon-like peptide-1 receptor agonists. Acta diabetologica 2025;62(5):731-742 Pubmed Journal

40. Despain D, Hoffman BL. Optimizing nutrition, diet, and lifestyle communication in GLP-1 medication therapy for weight management: A qualitative research study with registered dietitians. Obesity pillars 2024;12:100143 Pubmed Journal

41. Andreassen P, Jensen SD, Bruun JM, Sandbæk A. Managing the new wave of weight loss medication in general practice: A qualitative study. Clinical obesity 2024;14(3):e12666 Pubmed Journal

42. World Health Organization. WHO guidelines on physical activity and sedentary behaviour. World Health Organization 2020. Website

43. World Health Organization & Food and Agriculture Organization of the United Nations. What are healthy diets? Joint statement by the Food and Agriculture Organization of the United Nations and the World Health Organization. World Health Organization 2024. Website

44. World Health Organization. Tackling NCDs: best buys and other recommended interventions for the prevention and control of noncommunicable diseases, 2nd ed. 2024. Website

45. World Health Organization. WHO Guideline: Recommendations on digital interventions for health system strengthening. 2019. Website

46. World Health Organization. Framework for the implementation of a telemedicine service. 2017. Website

47. World Health Organization. US President's Emergency Plan for AIDS Relief, Joint United Nations Programme on HIV/AIDS and World Health Organization. Task shifting: national redistribution of tasks among health workforce teams : global recommendations and guidelines. 2008. Website

48. World Health Organization. WHO recommendations: optimizing health worker roles to improve access to key maternal and newborn health interventions through task shifting. 2012. Website

49. World Health Organization. Recommendations on the delivery of health services for the prevention and care of sexually transmitted infections (Chapter 3.4).. 2025. Website

50. World Health Organization. Health service delivery framework for prevention and management of obesity. 2023. Website

51. World Health Organization. WHO acceleration plan to stop obesity. 2023. Website

52. Shi Q, Wang Y, Hao Q, Vandvik PO, Guyatt G, Li J, et al. Pharmacotherapy for adults with overweight and obesity: a systematic review and network meta-analysis of randomised controlled trials. Lancet (London, England) 2024;403(10434):e21-e31 Pubmed Journal

53. Guyatt GH, Oxman AD, Kunz R, Brozek J, Alonso-Coello P, Rind D, et al. GRADE guidelines 6. Rating the quality of evidence--imprecision. Journal of clinical epidemiology 2011;64(12):1283-93 Pubmed Journal

54. Schünemann HJ, Neumann I, Hultcrantz M, Brignardello-Petersen R, Zeng L, Murad MH, et al. GRADE guidance 35: update on rating imprecision for assessing contextualized certainty of evidence and making decisions. Journal of clinical epidemiology 2022;150:225-242 Pubmed Journal

55. Akaberi A, Klok FA, Cohn DM, Hirsch A, Granton J, Kahn SR. Determining the minimal clinically important difference for the PEmbQoL questionnaire, a measure of pulmonary embolism-specific quality of life. Journal of thrombosis and haemostasis : JTH 2018;16(12):2454-2461 Pubmed Journal

56. Ward MM, Guthrie LC, Alba MI. Clinically important changes in short form 36 health survey scales for use in rheumatoid arthritis clinical trials: the impact of low responsiveness. Arthritis care & research 2014;66(12):1783-9 Pubmed Journal

57. Kolotkin RL, Williams VSL, von Huth Smith L, Meincke HH, Qin S, Williams N, et al. Confirmatory psychometric evaluations of the Impact of Weight on Quality of Life-Lite Clinical Trials Version (IWQOL-Lite-CT). Clinical obesity 2021;11(5):e12477 Pubmed Journal

58. Verweij LM, Terwee CB, Proper KI, Hulshof CTJ, van Mechelen W. Measurement error of waist circumference: gaps in knowledge. Public health nutrition 2013;16(2):281-8 Pubmed Journal

59. Ross R, Neeland IJ, Yamashita S, Shai I, Seidell J, Magni P, et al. Waist circumference as a vital sign in clinical practice: a Consensus Statement from the IAS and ICCR Working Group on Visceral Obesity. Nature reviews. Endocrinology 2020;16(3):177-189 Pubmed Journal

60. Yuan YU, Liu K, Zheng M, Chen S, Wang H, Jiang Q, et al. Analysis of Changes in Weight, Waist Circumference, or Both, and All-Cause Mortality in Chinese Adults. JAMA network open 2022;5(8):e2225876 Pubmed Journal

61. Khan MS, Anker SD, Friede T, Jankowska EA, Metra M, Piña IL, et al. Minimal Clinically Important Differences in 6-Minute Walk Test in Patients With HFrEF and Iron Deficiency. Journal of cardiac failure 2023;29(5):760-770 Pubmed Journal

62. Butler J, Khan MS, Mori C, Filippatos GS, Ponikowski P, Comin-Colet J, et al. Minimal clinically important difference in quality of life scores for patients with heart failure and reduced ejection fraction. European journal of heart failure 2020;22(6):999-1005 Pubmed Journal

63. Cai X, Zhang Y, Li M, Wu JH, Mai L, Li J, et al. Association between prediabetes and risk of all cause mortality and cardiovascular disease: updated meta-analysis. BMJ (Clinical research ed.) 2020;370:m2297 Pubmed Journal

64. Cheng N, Zhang Y, Yang J, Li J, Ye L, Zhou Z, et al. Association Between Fasting Blood Glucose and All-Cause Mortality in a Rural Chinese Population: 15-Year Follow-Up Cohort Study. Diabetes therapy : research, treatment and education of diabetes and related disorders 2020;11(11):2691-2701 Pubmed Journal

65. Liao H-W, Saver J, Yeh H-C, Chen C-HS, Wu Y-L, Lee M, et al. Low fasting glucose and future risks of major adverse outcomes in people without baseline diabetes or cardiovascular disease: a systematic review and meta-analysis. BMJ open 2019;9(7):e026010 Pubmed Journal

66. Zeng R, Zhang Y, Xu J, Kong Y, Tan J, Guo L, et al. Relationship of Glycated Hemoglobin A1c with All-Cause and Cardiovascular Mortality among Patients with Hypertension. Journal of clinical medicine 2023;12(7) Pubmed Journal

67. Arnold LW, Wang Z. The HbA1c and all-cause mortality relationship in patients with type 2 diabetes is J-shaped: a meta-analysis of observational studies. The review of diabetic studies : RDS 2014;11(2):138-52 Pubmed Journal

68. Song BM, Lee JH, Woo HD, Cho MJ, Kim SS. Association between haemoglobin A1c and all-cause and cause-specific mortality in middle-aged and older Koreans: a prospective cohort study. Nutrition & metabolism 2022;19(1):46 Pubmed Journal

69. Zhong G-C, Ye M-X, Cheng J-H, Zhao Y, Gong J-P. HbA1c and Risks of All-Cause and Cause-Specific Death in Subjects without Known Diabetes: A Dose-Response Meta-Analysis of Prospective Cohort Studies. Scientific reports 2016;6:24071 Pubmed Journal

70. . Pharmacological blood pressure lowering for primary and secondary prevention of cardiovascular disease across different levels of blood pressure: an individual participant-level data meta-analysis. Lancet (London, England) 2021;397(10285):1625-1636 Pubmed Journal

71. Cook NR, Cohen J, Hebert PR, Taylor JO, Hennekens CH. Implications of small reductions in diastolic blood pressure for primary prevention. Archives of internal medicine 1995;155(7):701-9 Pubmed

72. Koutoukidis DA, Astbury NM, Tudor KE, Morris E, Henry JA, Noreik M, et al. Association of Weight Loss Interventions With Changes in Biomarkers of Nonalcoholic Fatty Liver Disease: A Systematic Review and Meta-analysis. JAMA internal medicine 2019;179(9):1262-1271 Pubmed Journal

73. Kim J, Tran K, Seal K, Fernanda A, Glenda R, Messier R, et al. 2017. Pubmed

74. Patel S, Kon SSC, Nolan CM, Barker RE, Simonds AK, Morrell MJ, et al. The Epworth Sleepiness Scale: Minimum Clinically Important Difference in Obstructive Sleep Apnea. American journal of respiratory and critical care medicine 2018;197(7):961-963 Pubmed Journal

75. Fager G, Wiklund O. Cholesterol reduction and clinical benefit. Are there limits to our expectations?. Arteriosclerosis, thrombosis, and vascular biology 1997;17(12):3527-33 Pubmed

76. Santos-Gallego CG, Badimón JJ. High-density lipoprotein and cardiovascular risk reduction: promises and realities. Revista espanola de cardiologia (English ed.) 2012;65(4):305-8 Pubmed Journal

77. Gould AL, Davies GM, Alemao E, Yin DD, Cook JR. Cholesterol reduction yields clinical benefits: meta-analysis including recent trials. Clinical therapeutics 2007;29(5):778-794 Pubmed Journal

78. Yang XH, Tu QM, Li LI, Guo YP, Wang NS, Jin HM. Triglyceride-lowering therapy for the prevention of cardiovascular events, stroke, and mortality in patients with diabetes: A meta-analysis of randomized controlled trials. Atherosclerosis 2024;394:117187 Pubmed Journal