National Institute for Health and Care Excellence

Health Technology Evaluation

Semaglutide for preventing major cardiovascular events in people with cardiovascular disease and overweight or obesity [ID6441]

Response to stakeholder organisation comments on the draft remit and draft scope

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Comment 1: the draft remit and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	Novo Nordisk	Novo Nordisk agrees that this is an important topic for NICE to evaluate as a single technology appraisal (STA). Semaglutide for preventing major cardiovascular events in people with cardiovascular disease and living with overweight or obesity is a significant new therapeutic indication and so meets criteria to be eligible for appraisal. (NICE topic selection manual 4.1.4)	Thank you for your comment. No change to scope needed.
	British cardiovascular society	Sensible question/clinical scenario to investigate given a population who have both obesity and cardiovascular disease – large scale epidemiological population within the UK. Scope is vague about whether this is for diabetics or non diabetics or both and would benefit from clarification.	Thank you for your comment. The scope explains that semaglutide will be appraised within its now granted marketing authorisation. The marketing authorisation does not restrict

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			eligibility to diabetes status. Additional information has been added to the scope to clarify that semaglutide has been investigated in people with and without diabetes.
	The Association for the Study of Obesity	Single Technology Appraisal	Thank you for your comment. No change to scope needed.
	Pumping Marvellous	This is a highly appropriate evaluation of a technology that could be highly impactful as an addition to optimised therapies. It is multifactorial benefits across a patients domain.	Thank you for your comment. No change to scope needed.
	British Obesity Society	This evaluation is welcomed given the new evidence on cvd benefits and the proposed evaluation route is appropriate	Thank you for your comment. No change to scope needed.
	Kidney Research UK	We agree with the proposed evaluation route – single technology appraisal	Thank you for your comment. No change to scope needed.
Wording	Novo Nordisk	Novo Nordisk broadly agrees that the wording of the remit reflects the clinical and cost effectiveness of semaglutide as a treatment to reduce the risk of major cardiovascular events in people with cardiovascular disease and living with overweight or obesity (BMI ≥27kg/m2).	Thank you for your comment. The scope has been updated to refer to Wegovy specifically. This is because other Wegovy

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		The appraisal should consider specifying that this is semaglutide 2.4 mg. Other semaglutide doses are marketed but not licensed for this indication. Marketing authorisation for this indication was granted on 23rd July 2024.	Flextouch doses have a marketing authorisation for CVD.
	Diabetes UK	Wording should reflect person centred language and avoid use of “have obesity” “being overweight” etc, as recommended in the NICE draft guidance for overweight and obesity management (which endorses Obesity UK’s ‘Language Matters’)	Thank you for your comment. The scope has been updated to ensure alignment with the NICE style guide.
	British cardiovascular society	Yes the wording of the remit reflects the aim to assess both the clinical and cost effectiveness of this medication for preventing cardiovascular events.	Thank you for your comment. No change to scope needed.
	The Association for the Study of Obesity	Yes	Thank you for your comment. No change to scope needed.
	Pumping Marvellous	Wording is appropriate	Thank you for your comment. No change to scope needed.
	British Obesity Society	Yes	Thank you for your comment. No change to scope needed.
	Kidney Research UK	Semaglutide is associated with changes in multiple biomarkers of cardiovascular risk, including blood pressure, waist circumference, glycaemic control, nephropathy, and levels of lipids and C-reactive protein. These biomarkers are also closely associated with chronic kidney disease (CKD).	Thank you for your comment. The scope has been updated to identify CKD as a risk factor for CVD.

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		Cardiovascular events are more likely to occur with albuminuria present (and hence the presence of CKD) and less likely to occur if albuminuria is reduced [De Zeeuw D, et al. Circulation 2004;110:921–927. (Posthoc analysis of RENAAL trial)]	
	National Kidney Federation	Yes. Important to retain emphasis on co-morbidities and other risk factors, such as CKD.	Thank you for your comment. The scope has been updated to identify CKD and diabetes as a risk factor for CVD.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Novo Nordisk	Background Novo Nordisk broadly agrees with the information supplied; however, considers that some aspects of the background are inaccurate or incomplete. Proposed wording is suggested below to ensure accurate reflection of the appraisal. The first paragraph of the draft scope describes cardiovascular disease (CVD) prevention, reflecting the remit for this appraisal as risk reduction for patients with established CVD. Proposed amendments are suggested to describe the patient population and outstanding health need associated with this appraisal. Novo Nordisk agrees with the risk factors presented; however, two important points are missing, the independent impact of overweight and obesity on CVD	Thank you for your comment. The background section of the scope is meant to be a brief outline of the condition and its management.

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		and the residual risk associated with secondary cardiovascular (CV) events. We suggest the below amendments to incorporate these important points. Proposed amendments CVD refers to a range of conditions affecting the heart and circulatory systems. Individuals with established CVD, including survivors of prior CV events (e.g., myocardial infarction (MI), stroke, and diagnosis of peripheral arterial disease (PAD)) are at an increased risk of recurrent, including more severe, future events7,8. Risk factors for recurrent CV events include living with overweight or obesity, smoking, stress, diabetes, high blood pressure and high cholesterol. Additionally, people with a family history of CVD are at increased risk. Risk increases with age; men are more likely to develop CVD earlier and people from certain ethnic backgrounds are at increased risk9. Obesity, independent to other CV risk factors, increases the risk of development of CVD and the risk of death from CVD, with CVD-related mortality increased in individuals with increased BMI5,6. Deprivation and socioeconomic factors are associated with both CVD and living with overweight and obesity11-13. The epidemiological figures provided in the draft scope are not fully representative of the patient population with established CVD based on a history MI, stroke, or diagnosis of PAD, living with overweight or obesity. We suggest the information provided is revised to reflect the population under consideration. Proposed amendments There are more than 100,000 MIs requiring hospitalisation per year in the UK, with MI one of the UK's leading causes of death and most common cause of premature death1.Cerebrovascular disease, causing strokes, is also one of UK's biggest killers responsible for approximately 100,000 strokes and	

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		34,000 deaths each year1. Approximately two-thirds of people will survive a MI or stroke, with 1.4 million people alive in the UK who have survived a MI and 1.4 million alive in the UK who have survived a stroke or transient ischemic attack1. Of these survivors, it is estimated that 1 in 5 will go on to experience a recurrent (secondary) cardiac event14. People living with overweight and obesity are over-represented in these patient populations as overweight and obesity are independent risk factors for the development and progression of CVD, putting adults at increased risk of cardiovascular events10. More than a quarter of adults (26%) in the UK have obesity, and in addition, 38% have a BMI defined as overweight1. Several relevant guidelines related to secondary prevention of CVD have been omitted, with related NICE guideline CG238 referenced twice. Semaglutide 2.4 mg is used in addition to optimised standard of care and so referral is most appropriately focused on guidelines that focus on optimal CV risk management rather than identification of selected treatments (which do not encompass all relevant or appropriate treatments for secondary prevention of major adverse cardiovascular events). We suggest an overview of the relevant clinical guidelines. Proposed amendments NICE Clinical Guideline 238 makes recommendations for the risk assessment and reduction of CV events including lipid modification to lower levels of lipoproteins. Recommendations within CG238 associated with secondary prevention of CVD focus on lifestyle changes (behaviour change, cardioprotective diet, physical activity, weight management, alcohol consumption, smoking cessation, and avoidance of plant stanols/sterols). Lipid-lowering therapy is	

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		recommended for secondary prevention of CVD, aiming for a low-density lipoprotein (LDL) cholesterol target of 2.0 mmol per litre or less, or non-high-density lipoprotein (non-HDL) levels of 2.6 mmol per litre or less. Initial treatment is recommended as atorvastatin, escalated to additional lipid-lowering treatments (such as alirocumab, evolocumab, ezetimibe and inclisiran) if targets are not met. NICE Clinical Guideline NG185 provide recommendations for secondary prevention of acute coronary syndromes for people who have had a MI. This includes treatment with angiotensin-converting enzyme (ACE) inhibitors, dual antiplatelet therapy (aspirin plus a second antiplatelet) unless they have a separate indication for anticoagulation, beta-blockers, and statins. All people are recommended to be given advice about and offered a cardiac rehabilitation program with an exercise component, including health education and stress management components, psychological and social support, and advice on sexual activity. A changed diet is recommended to be advised as part of lifestyle changes after an MI (specifically a Mediterranean-style diet), advice on alcohol consumption, regular physical activity, smoking cessation, and weight management in line with CG43 [now updated as CG189]. NICE Clinical Guideline CG189 considers CVD to be a health risk associated with higher levels of central adiposity, also acknowledging the risk of developing CVD in people living with overweight or obesity. NICE Clinical Guideline NG136 considers the management of hypertension in adults recommending lifestyle interventions to people with suspected or diagnosed hypertension including recommendations on diet, alcohol consumption, caffeine consumption, dietary sodium intake, supplement use and smoking. Anti-hypertensive treatment is recommended in addition to lifestyle advice based on a person's blood pressure and clinical risk factors	

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		(e.g., established CVD). Targets are recommended as clinical blood pressure measurements less than 140/90 mmHg. The technology Novo Nordisk suggests amendment to the description of the technology, to reflect the marketing authorisation of semaglutide 2.4 mg in this indication, with description of the supporting trial evidence. Semaglutide 2.4 mg (brand name Wegovy, Novo Nordisk) was granted MHRA marketing authorisation in July 2024, indicated as an adjunct to a reduced-calorie diet and increased physical activity to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with established cardiovascular disease and either obesity or overweight (BMI ≥27 kg/m2). Semaglutide 2.4 mg in this indication is supported by the SELECT trial, a multi-centre, double-blind, randomised, placebo-controlled, event-driven superiority trial comparing semaglutide 2.4 mg with placebo in >17,000 adults aged 45 years or older who had pre-existing cardiovascular disease and a body-mass index of ≥27.	
	Diabetes UK	Hyperglycaemia has not been indicated as a risk factor for CVD or CVD events. Data shows us that every week, diabetes leads to more than 930 strokes, 660 heart attacks and 2,990 cases of heart failure (NDA Complications and Mortality Data. Based on data 2018-2020 data scaled up to UK diabetes population). Prediabetes, diabetes and metabolic syndrome are comorbidities that increase the risk of CVD.	Thank you for your comment. The scope has been updated to identify diabetes as a risk factor for CVD.
	British cardiovascular society	The background is brief but accurate. Some other NICE guidelines for secondary prevention of cardiovascular disease are referenced. There are	Thank you for your comment. The background section of the scope is meant to a

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		many other actions that could be considered and recommended in international guidance by the ESC or AHA. We presume that this review comes from the publication of the clinical trial SELECT which is not referenced. N Engl J Med 2023;389:2221-2232	brief outline of the condition and its management. The section would mainly focus on national guidelines as these are most relevant for practice in the NHS.
	The Association for the Study of Obesity	Yes, background information is accurate and complete.	Thank you for your comment. No change to scope needed.
	Pumping Marvellous	OK	Thank you for your comment. No change to scope needed.
	British Obesity Society	No issues	Thank you for your comment. No change to scope needed.
	Kidney Research UK	The background information mentions a number of risk factors which increase the risk of both developing CVD and experiencing a CV event. These include being overweight or obese, smoking, stress, alcohol use, high blood pressure and high cholesterol. Chronic kidney disease should be added to this list as it shares many risk factors and pathological processes as CVD and can lead to albuminuria. Albuminuria is an early marker of CVD [Versari D et al. Diabetes Care 2009;32:S314-S321.]	Thank you for your comment. The scope has been updated to identify CKD as a risk factor for CVD.

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Population	Novo Nordisk	Novo Nordisk suggests the below amendment to the population, to reflect the patient population studied with semaglutide 2.4 mg in this indication. Current wording Adults with a diagnosis of cardiovascular disease and a BMI of at least 27 kg/m2 Proposed wording Adults with established cardiovascular disease (defined as previous myocardial infarction, previous stroke, or symptomatic peripheral arterial disease) and a BMI of at least 27 kg/m2.	Thank you for your comment. The population has been updated to more closely reflect the marketing authorisation.
	Diabetes UK	Recent data published in Diabetes Care, indicates that semaglutide when used in people with preexisting cardiovascular disease and overweight or obesity but without diabetes, can reduce blood glucose levels and progression to type 2 diabetes (Kahn et al, 2024). Preventing type 2 diabetes or prolonging normoglycaemia (delaying type 2 diabetes) in turn would reduce the risk of CVD events. This population has not been accounted for within the current scope	Thank you for your comment. The population for the appraisal is bound by the marketing authorisation indication. The marketing authorisation does not exclude people with diabetes, as mentioned in the scope.
	British cardiovascular society	Yes UK population with obesity defined as BMI>27 and CVD. It would be useful to define whether this includes people with diabetes or not.	Thank you for your comment. The population for the appraisal is bound by

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			the marketing authorisation indication. The marketing authorisation does not exclude people with diabetes, as mentioned in the scope.
	The Association for the Study of Obesity	Yes	Thank you for your comment. No change to scope needed.
	Pumping Marvellous	Yes	Thank you for your comment. No change to scope needed.
	British Obesity Society	I agree that the defined population is appropriate	Thank you for your comment. No change to scope needed.
Subgroups	British cardiovascular society	Scope does not make reference to diabetes status – if this is based/driven by the results of the SELECT trial then this was in a non diabetic population. Evidence in those with and without type II diabetes should be considered separately. It would be useful to know whether there is a level of obesity that demonstrates more efficacy e.g BMI>35 etc. Is there more efficacy in people with particular combinations of cardiovascular risk factors?	Thank you for your comment. Additional information has been added to the scope to clarify that semaglutide has been investigated in people with and without diabetes.

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	The Association for the Study of Obesity	It may be more cost effective for people with higher BMI (BMI > 35) or more obesity-related complications, as it will also improve these complications due to the weight loss achieved. Also, semaglutide 2.4mg once weekly has proven benefits for people with heart failure with preserved ejection fraction (HFpFF) with and without diabetes. STEP-10 demonstrates also reduction in progression to T2D for people with prediabetes. Additionally, semaglutide 2.4mg will improve glycaemia in people with T2D.	Thank you for your comment. Additional information has been added to the scope to clarify that semaglutide has been investigated in people with and without diabetes.
	Pumping Marvellous	Heart failure	Thank you for your comment. The scope has been updated to include people with heart failure as a potential subgroup.
	National Kidney Federation	We know that being overweight increases the risk for diabetes and high blood pressure and in turn, diabetes and high blood pressure are the two main causes of kidney disease. Studies have been done showing the benefit of weight management in treating kidney diseaseii, and reducing the risk of cardiovascular disease- the major cause of morbidity and mortality in CKD patients. The early identification of at-risk patients is key, with the pro-active management of such patients having the potential to be both time and cost effective. Renal replacement therapies place a high burden on both the patient and the NHS, are hugely time consuming, highly invasive and put increasingly untenable pressure on dialysis unit bed space.	Thank you for your comment. Additional information has been added to the scope to clarify that semaglutide has been investigated in people with and without diabetes.

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Comparators	Novo Nordisk	Novo Nordisk agrees that semaglutide 2.4 mg be used in addition to established clinical management for the prevention of major adverse cardiovascular events in adults with established cardiovascular disease and either obesity or overweight (BMI ≥27 kg/m2). This aligns with both the marketing authorisation of semaglutide 2.4 mg [5.1 Pharmacodynamic properties], and the supporting clinical trial, SELECT. SELECT (NCT03574597) evaluated the effect of semaglutide 2.4 mg relative to placebo when added to current standard of care, which included management of cardiovascular risk factors and individualized healthy lifestyle counselling (including diet and physical activity). Concomitant cardiovascular therapies could be adjusted at the discretion of the investigator, to ensure participants were treated according to the current standard of care for patients with established cardiovascular disease. Adjunct healthy lifestyle counselling was consistent with existing local standards of care (related to diet, physical activity, smoking and alcohol consumption) for adults with established cardiovascular disease and either obesity or overweight (BMI ≥ 27 kg/m2). The comparator would therefore accurately be established clinical management without semaglutide.	Thank you for your comment. No change to scope needed.
	British cardiovascular society	SGLT2 inhibitors We would not suggest a comparison to rivaroxaban or ticagrelor as the mechanism of action and rationale are very different.	Thank you for your comment. SGLT2 inhibitors are not specifically indicated for the prevention of major cardiovascular events in people with cardiovascular disease and will be captured in

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			established clinical management if appropriate.
	The Association for the Study of Obesity	Yes, these are appropriate. Actually, there is no other obesity medication with cardiovascular outcome data currently (liraglutide 3mg does not have cardiovascular outcome data in people without diabetes).	Thank you for your comment. No change to scope needed.
	Pumping Marvellous	I don't believe there is a comparator	Thank you for your comment. No change to scope needed.
	British Obesity Society	Yes	Thank you for your comment. No change to scope needed.
Outcomes	Novo Nordisk	The outcome measures to be considered should align with outcomes studied in the SELECT trial: • Major cardiovascular events avoided (including cardiovascular death, non-fatal MI, and non-fatal stroke) • All-cause death • Heart failure events • Worsening kidney function • Development of diabetes • Changes to CV risk factors • Body weight • Health related quality of life • Adverse effects of treatment	Thank you for your comment. The scope has been updated to include development of diabetes as an outcome. All other outcomes are accounted for in outcomes already included.

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	British cardiovascular society	These outcome measures are appropriate. It would be useful to understand these alongside timescale, medication compliance in the longer term and also what happens to outcome measures upon cessation of medication.	Thank you for your comment. Treatment discontinuation has been added to the outcomes. Outcome measures after stopping treatment will be considered as part of the evaluation, if applicable.
	The Association for the Study of Obesity	Yes, but consider also adding progression to diabetes, improvement in HbA1c for people with type 2 diabetes and improvement in knee osteoarthritis and hypertension. We understand that heart failure (especially heart failure with preserved ejection fraction) is going to be taken into account, as listed to these outcomes.	Thank you for your comment. Development of diabetes has been added to the outcomes.
	Pumping Marvellous	Mental Health should be included as an additional outcome – not specified	Thank you for your comment. This outcome is captured by the health related quality of life outcome.
	British Obesity Society	Yes	Thank you for your comment. No change to scope needed.
	Kidney Care UK	We are interested in the potential benefits of Semaglutide for people with kidney disease, following the publication of the FLOW trial which found participants (those with CKD and diabetes type 2) who received semaglutide experienced a 24% risk reduction of the composite primary endpoint,	Thank you for your comment. The scope has been updated to

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		including kidney outcomes and death due to cardiovascular and kidney causes, compared to those who received a placebo. Delaying the progression of CKD not only means people can avoid the difficult symptoms of kidney disease (e.g. extreme fatigue, itchiness and pain, and the burden of kidney replacement therapy), but it reduces people's risk of cardiovascular morbidity and mortality – for which CKD is a risk factor. More patients with CKD die from cardiovascular complications than from end stage kidney disease. Conversely, cardiovascular disease is associated with increased risk of CKD progression. Due to the emerging evidence for potential benefits of semaglutide in CKD and the interdependence between CKD and cardiovascular complications, we suggest developing the kidney function outcome within this HTA to include death from kidney causes, initiation of chronic kidney replacement therapy, significant (≥ 50%) decline in kidney function, or onset of persistent macroalbuminuria. (Perkovic V, Tuttle K, Rossing P et al (2024) Effects of semaglutide on chronic kidney disease in patients with type 2 diabetes. N Engl J Med 391:109-21)	include kidney function as an outcome.
	Kidney Research UK	The outcome measures listed in the draft scope include 'kidney function'. We believe this should be amended to read 'progression of kidney disease'. Reducing the progression of kidney disease improves patient outcomes (including reducing the risk of a CV event) and has a positive impact on NHS costs and economic burden [Kidney Research UK: Kidney disease: A UK public health emergency, June 2023]	Thank you for your comment. The scope has been updated to include kidney function as an outcome, which encompasses progression to kidney disease.

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Equality	Novo Nordisk	There are several potential equality issues associated with the availability of effective secondary cardiovascular preventative therapies across the UK. There is a known and acknowledged elevated cardiovascular risk in people of South Asian or sub-Saharan African ethnic origin4. Socioeconomic status also has an influence on the incidence and impact of obesity, compounded by the understanding that people living in England's most deprived areas are almost four times more likely to die prematurely from cardiovascular disease than those in the least deprived15-17. Compared with the general population, people with severe mental illness are more likely to develop and die from preventable conditions such as cardiovascular disease15. Insofar as available data allow, the appraisal should consider the potential differential impacts of treatment in groups of patients with additional clinical need.	Thank you for your comment. No change to scope needed. Potential equalities issues will be discussed by the committee.
	British cardiovascular society	The scope does not appear to exclude any group. However the evidence available For review is likely to have less representation from some ethnicities and this should be considered.	Thank you for your comment. No change to scope needed. Potential equalities issues will be discussed by the committee.
	The Association for the Study of Obesity	To minimise inequalities in access, primary care long-term prescription is important (and probably initiation of treatment from primary care), as well as ensuring that ICBs will have the budget to support medication provision equivalently across the country. There needs to be tailored delivery and reasonable adjustments for neurodiversity	Thank you for your comment. No change to scope needed. Potential equalities issues will be discussed by the committee.

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	Pumping Marvellous	OK	Thank you for your comment. No change to scope needed.
	British Obesity Society	No changes suggested	Thank you for your comment. No change to scope needed.
Other considerations	Novo Nordisk	Every year in the UK approximately 200,000 people have a heart attack or stroke1. It is estimated that up to 20% of people who have a heart attack will be re-admitted to hospital due to a second event within five years14. A 20% reduction in major cardiovascular events will have an important impact on hospital admissions, reducing pressure on NHS resources at a time of extraordinary strain. Whilst this appraisal will evaluate the impact of reduced risk of major cardiovascular adverse events, the wider potential benefits associated with semaglutide mean this is likely to be an overall underestimate of the wider potential benefits to individuals, families, wider society, and health care organisations.	Thank you for your comment. No change to scope needed.
	Diabetes UK	Patchy access to specialist weight management services and demand for private prescriptions is creating inequalities in access to Wegovy for overweight and obesity in England and Wales and has had significant impact on prescribing for type 2 diabetes. It would be useful for NICE to consider how this appraisal decision fits within the current constraints in access for the broader eligible Wegovy population. Diabetes UK supports the need for risk stratification tools for people who would benefit the most from treatment. This appraisal offers the opportunity to support prioritisation of treatment with semaglutide.	Thank you for your comment. No change to scope needed.

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	British cardiovascular society	The current long term medication costs are not known and so a clear and transparent economic analysis will be very important.	Thank you for your comment. No change to scope needed.
Questions for consultation	Novo Nordisk	Where do you consider semaglutide will fit into the existing care pathway for preventing cardiovascular events in people with cardiovascular disease and living with overweight or obesity? People living with established cardiovascular disease who have overweight or obesity would be eligible for existing standard clinical care pathways associated with cardiac or stroke services, respectively. Any person who is being assessed for cardiovascular risk factor modification who meets the licensed indication should be eligible for consideration by their clinician. This would include (but would not necessarily be limited to) cardiac rehab clinics, lipid lowering clinics, cardiometabolic clinics and hypertension services. Would semaglutide be an add-on treatment to existing therapies? Which treatments for preventing cardiovascular events could semaglutide displace? The addition of semaglutide 2.4 mg would not displace other treatment options as semaglutide will be used as an add-on to existing therapy. In the SELECT trial patients were allocated to semaglutide or placebo. Investigators were encouraged to follow evidence-based recommendations in their choice of medical management of underlying cardiovascular	Thank you for your comment. No change to scope needed.

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		disease8.Treatments regimes were individualised and heterogenous, reflecting real-world clinical practice. Please select from the following, will semaglutide be: A. Prescribed in primary care with routine follow-up in primary care B. Prescribed in secondary care with routine follow-up in primary care C. Prescribed in secondary care with routine follow-up in secondary care D. Other (please give details): For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention. Semaglutide should be associated with A and B, reflecting that the population included in the appraisal is currently managed in both primary and secondary care. It is routine in the UK for this population to be managed initially in secondary care, with continuation predominantly in primary care. Novo Nordisk anticipates that semaglutide 2.4 mg will be for the most part initiated by (or on the recommendation of) a specialist, as part of secondary prevention, with continuation in primary care. There may be occasions where secondary prevention and cardiovascular risk reduction is being entirely managed in primary care and where it may be more appropriate, preferable to the patient, and more efficient for the wider health care system for the drug to be both initiated and continued in primary care. Access should therefore similarly enable initiation of therapy where facilities exist in primary care to support assessment and management of CVD (e.g., GPwSI).	

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		Would semaglutide be a candidate for managed access? Outcome benefits are shown so collection of additional data is not likely to provide significant additional value. Do you consider that the use of semaglutide can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits. Semaglutide has shown numerous wider clinical benefits and improvements on quality of life. Not all of the benefits associated with semaglutide were measured in the SELECT trial or are able to be included in a cost-effectiveness model; therefore, any analyses are conservative.	
	Diabetes UK	To increase access for the eligible population, the route for prescription of Wegovy under this appraisal would ideally be primary care.	Thank you for your comment. No change to scope needed.
	British cardiovascular society	Where do you consider semaglutide will fit into the existing care pathway for preventing cardiovascular events in people with cardiovascular disease and living with overweight or obesity? If approved, people identified in primary care with the eligibility criteria would have a consultation with the option for this medication to be added.	Thank you for your comment. No change to scope needed.

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		Would semaglutide be an add-on treatment to existing therapies? Yes it is most likely to be an add on to existing treatments for secondary prevention of cardiovascular disease. Which treatments for preventing cardiovascular events could semaglutide displace? Possibly SGLT 2 inhibitors unless there is a separate indication for these. Please select from the following, will semaglutide be: A. Prescribed in primary care with routine follow-up in primary care For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention. Would semaglutide be a candidate for managed access? Yes Do you consider that the use of semaglutide can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? It would be useful to look at the mental health related benefits in addition to the physical health benefits. Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits. Hopefully this will be available from the literature review.	

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	Kidney Research UK	In response to the question 'Do you consider that the use of semaglutide can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?', we would like to draw attention to the FLOW trial and the positive kidney outcomes associated with this study [Effects of Semaglutide on Chronic Kidney Disease in Patients with Type 2 Diabetes, Vlado Perkovic, M.B., B.S. et al, 24 May 2024]	Thank you for your comment. No change to scope needed.
Additional comments on the draft scope	Novo Nordisk	The intervention is currently: Semaglutide It is proposed to amend this to specify the brand name, dose, and formulation of semaglutide associated with this appraisal. Suggested: Semaglutide 2.4 mg (Brand name, Wegovy). A once-weekly subcutaneous injection that binds to and activates the glucagon-like peptide-1 (GLP-1) receptor.	Thank you for your comment. The scope has been updated to specify the brand Wegovy as the intervention.
	British cardiovascular society	It would be useful to understand from the pharmaceutical company whether they have data in terms of on treatment vs off treatment rather than intention to treat analysis.	Thank you for your comment. No change to scope needed.
	The Association for the Study of Obesity	Semaglutide 2.4mg once weekly needs to be prescribed long-term, without a 2 year-stopping rule (this is how it is currently prescribed for weight management in specialist weight management services). This was also the case in the SELECT trial, long term-prescription without lifestyle intervention, Addtionally, there is no point in having a 5% weight loss stopping rule as sub-analysis of SELECT trial did not demonstrare significant difference in cardiovascular events between people who achieved >5% weight loss and people who achieved <5% weight loss from baseline weight.	Thank you for your comment. No change to scope needed.

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	Kidney Research UK	Though not relevant for this evaluation, the potential benefits of semaglutide for chronic kidney disease patients are significant. Kidney Research UK calls on NICE to evaluate this treatment for CKD as early as possible. The close relationship between CVD and CKD can be explained by a manifestation of similar disease processes involved. CVD and kidney diseases have many types of markers in common, including clinical, pathophysiologic, histopathologic, biochemical, acute and chronic inflammation and subclinical signs of atherosclerosis. [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3043294/] Kidney Research UK's health economics report sets out the economic burden of kidney disease to the NHS and the economy. It found that kidney disease currently costs the economy £7bn a year, with direct costs to the NHS of £6.4bn. These are projected to grow to £13.9bn and £10.9bn by 2033 without urgent intervention to reduce progression to kidney failure. [Kidney Research UK: Kidney disease: A UK public health emergency, June 2023] It is important the health systems moves to treating patients holistically rather than in disease silos. This is particularly important for patients with CKD, CVD and diabetes where the diseases are closely linked. We would urge NICE to consider evaluating treatments with benefits across diseases in a more holistic way.	Thank you for your comment. NICE aims to publish guidance that is useful and usable for the NHS. The remit of this evaluation is to focus on the population specified in the marketing authorisation granted by the MHRA for this treatment.
	National Kidney Federation	Chronic kidney disease affects more than 10% of the UK population and is rapidly becoming more common as the population ages. The current economic burden of kidney disease in the UK is £7 billion per year, more than 3% of total NHS spending across the four nationsiii. This figure is only going to rise with people with diabetes, high-blood pressure, cardiovascular disease and obesity all at increased risk of developing kidney disease. Without direct	Thank you for your comment. The scope has been updated to include people with chronic kidney disease as a subgroup of interest, and kidney function as an outcome

Section	Consultee/ Commentator	Comments [sic]	Action
		intervention to increase rates of early diagnosis, prevent disease and increase treatment options, the cost to the NHS will continue to multiply. We know that being overweight increases the risk for diabetes and high blood pressure and in turn, diabetes and high blood pressure are the two main causes of kidney disease. Studies have been done showing the benefit of weight management in treating kidney diseaseiv, and reducing the risk of cardiovascular disease- the major cause of morbidity and mortality in CKD patients. The early identification of at-risk patients is key, with the pro-active management of such patients having the potential to be both time and cost effective. Renal replacement therapies place a high burden on both the patient and the NHS, are hugely time consuming, highly invasive and put increasingly untenable pressure on dialysis unit bed space. For some kidney disease is not preventable, but for others there is an opportunity to intervene at an early stage and reduce their disease progression or likelihood of developing kidney disease in the first place. Drugs such as Semaglutide, which can tackle one of the major risk factors of kidney disease have the potential to be a worthwhile investment both for the NHS, and for the patient and their loved ones. 1 Kidney disease: a UK health emergency, Kidney Research UK, 2023 1 https://www.ox.ac.uk/news/2020-11-04-new-research-confirms-obesity-cause-kidney-disease, Journal of the American Society of Nephrology, 2020.	of interest. The remit of this evaluation is to focus on the prevention of cardiovascular events.

The following stakeholders indicated that they had no comments on the draft remit and/or the draft scope

None