National Institute for Health and Care Excellence

Health Technology Evaluation

Tirzepatide for managing overweight and obesity ID6179

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

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment 1: the draft remit and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	Eli Lilly and Company Limited	Yes, this is an appropriate topic to refer to NICE for Single Technology Appraisal.	Comment noted.
	Association for the Study of Obesity	Single Technology Appraisal.	Comment noted.
	British Obesity and Metabolic Surgery Society (BOMSS)	Single technology appraisal is appropriate.	Comment noted.
	Department for Health and Social Care (Office for	Strongly support this evaluation.	Comment noted.

Section	Stakeholder	Comments [sic]	Action
	Health Improvement)		
	Royal College of Physicians (RCP)	This is entirely appropriate.	Comment noted.
Wording	Eli Lilly and Company Limited	Yes, the remit broadly reflects the clinical and cost effectiveness of tirzepatide for the treatment of adults with a body mass index (BMI) of: • ≥30 kg/m^2 (obese) or ≥27 kg/m^2 to <30 kg/m^2 (overweight) and at least one weight-related comorbidity	Thank you for your comment. No change to the scope required.
	British Obesity and Metabolic Surgery Society (BOMSS)	Wording is appropriate.	Thank you for your comment. No change to the scope required.
	Royal College of Physicians (RCP)	Suggest changing the opening sentence to use people first language. People with obesity or people with overweight with adiposity-related comorbidities.	Thank you for your comment. The scope has been updated in light of the comment.
Additional comments on the draft remit	Eli Lilly and Company Limited	Timing issues: Initial results from the SURMOUNT-1 trial have demonstrated substantial and sustained reductions in body weight for patients receiving 5 mg, 10 mg or 15 mg tirzepatide once weekly vs placebo over 72 weeks. Additionally, tirzepatide is the first pharmacological intervention for obesity	Thank you for your comment. No change to the scope required.

Section	Stakeholder	Comments [sic]	Action
		which has shown an average reduction in body weight of >20% in a Phase 3 trial, with 50% and 57% of patients receiving 10 mg and 15 mg, respectively, achieving a ≥20% reduction in body weight, compared to 1.3% of patients receiving placebo.[1] There remains a high unmet need for new clinically effective treatments for managing overweight and obesity.	Comment noted. Thank you for your comment. NICE aims, where possible, to provide timely guidance in line with marketing authorisation. No action needed.
	British Obesity and Metabolic Surgery Society (BOMSS)	Timing issues: Treatment for people living with severe obesity is a serious and urgent problem for those affected and the NHS.	Comment noted. Thank you for your comment. NICE aims, where possible, to provide timely guidance in line with marketing authorisation. No action needed.
	Department for Health and Social Care (Office for Health Improvement)	Timing issues: Semaglutide is launching in the UK soon and Tirzepatide likely offers more clinically effective weight loss. It is important that the most clinically and cost-effective treatments are made available on the NHS as quickly as possible, therefore the appraisal of Tirzepatide is important.	Comment noted. Thank you for your comment. NICE aims, where possible, to provide timely guidance in line

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			with marketing authorisation. No action needed.
	Royal College of Physicians (RCP)	Timing issues: Urgent	Comment noted. Thank you for your comment. NICE aims, where possible, to provide timely guidance in line with marketing authorisation. No action needed.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Eli Lilly and Company Limited	This section broadly captures the background information of obesity.	Comment noted.
	Novo Nordisk Ltd	As WHO states, obesity is associated with many and varied weight related consequences that exceed the list provided in the draft scope background section. Additional weight related consequences include cancer, gallbladder disease, mental health issues etc. For clarity we propose amending the relevant sentence as follows: Other conditions associated with obesity ***include but are not limited to*** non-alcoholic fatty liver disease, non-diabetic hyperglycaemia, subfertility,	Thank you for your comment. The background section has been updated.

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		osteoarthritis, dyslipidaemia, obstructive sleep apnoea and idiopathic intracranial hypertension.	
	Association for the Study of Obesity	It may be preferable to use as first phrase the following: Obesity is a prevalent, complex, progressive and relapsing chronic disease, characterized by abnormal or excessive body fat (adiposity), that impairs health.	Thank You for your comment. The background section is intended to be brief and the prevalence has been captured at a later stage within the scope. Impairments to health have been captured in the scope. Changes have been made to the scope to reflect obesity is a complex condition.
	British Obesity and Metabolic Surgery Society (BOMSS)	Ethnic groups could be clearly specified as including those with a South Asian, Chinese, other Asian, Middle Eastern, Black African or African-Caribbean family background. The above groups are at greater health risks at lower BMI threshold. Overweight for these is BMI 23 kg/m^2 to 27.4 kg/m^2 and obesity: BMI > 27.5 kg/m^2 There should be a link to the NICE TA for semaglutide 2.4 mg for managing people with overweight or obesity here too.	Comment noted. The wording of the scope has been updated to reference Clinical guideline 189. Comment noted. Semaglutide final guidance has been included.

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	Department for Health and Social Care (Office feisty or Health Improvement)	The background on Liraglutide does not make it clear that it must be prescribed in a secondary care tier 3 specialist weight management service. The background could include information on the structure of weight management services.	Thank you for your comment. The background section is intended to be brief and would not include which care setting the drug can be accessed or the structure of the service provided to patients. No change to scope required.
		The background could include that Semaglutide has been recommended but has not yet launched.	Comment noted. Semaglutide final guidance has been included which links to the guidance page on the NICE website. This has a statement that the technology is not commercially available.
		It is not clear from the background that Tirzepatide, Liraglutide and Semaglutide are administered via subcutaneous injection.	Thank you for your comment. The background section is intended to be brief. No

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			change to scope required.
	Royal College of Physicians (RCP)	In the Background suggest change to 'complex, chronic progressive medical condition'	Comment noted. The scope has been updated.
		This section should align with the NICE guidance regarding overweight and obesity, which was published in Sept 2022 or at least link to this. People with a South Asian, Chinese, other Asian, Middle Eastern, Black African or African-Caribbean family background are prone to central adiposity and their cardiometabolic risk occurs at lower BMI, so use lower BMI thresholds as a practical measure of overweight and obesity: overweight: BMI 23 kg/m^2 to 27.4 kg/m^2 obesity: BMI 27.5 kg/m^2 or above.	Comment noted. The wording of the scope has been updated to reference clinical guideline 189.
		There should be a link to the NICE TA for semaglutide 2.4 mg for managing people with overweight or obesity here too.	Comment noted. Semaglutide final guidance has been included.

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Population	Eli Lilly and Company Limited	The population in the draft scope has been defined appropriately.	Thank you for your comment. No change to the scope required.
	Association for the Study of Obesity	Yes, we agree that the medication should be approved in accordance with the population studied in clinical trials.	Comment noted. No change to the scope required.
	British Obesity and Metabolic Surgery Society (BOMSS)	Yes.	Comment noted.
	Department for Health and Social Care (Office for Health Improvement)	It is unclear from the definition if BMI thresholds are reduced by 2.5kg/m^2 for people from ethnic minority backgrounds. Weight-related co-morbidities could be defined for clarity.	Comment noted. Where appropriate and relevant, the committee may consider this during the appraisal. Comment noted. The background section is intended to be brief, not designed to capture all details. Where relevant, companies and stakeholders are welcome to submit evidence in detail for the committee's

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			consideration in the appraisal process..
	Royal College of Physicians (RCP)	Yes.	Comment noted.
Subgroups	Eli Lilly and Company Limited	None.	Comment noted.
	Association for the Study of Obesity	1. For people of ethnic minorities, we will need to use lower BMI thresholds (usually reduced by 2.5 kg/m^2). 2. The use of tirzepatide is expected to be particularly cost-effective in people with BMI≥35 kg/m^2 and obesity-related complications (such as prediabetes, obstructive sleep apnoea, hypertension, non alcoholic steatohepatitis). 3. It is also important to establish the long-term use of the medication – we do not agree with discontinuation of treatment as this will lead to inevitable weight regain and loss of the majority of the clinical benefits (similar to what has been demonstrated at the STEP-1 trial extension for semaglutide 2.4mg, Wilding et al, DOM, 2022, PMID 35441470).	Comment noted. Where relevant and appropriate, and if evidence allows, the committee may consider this during the appraisal. Comment noted. No change to the scope required. Comment noted. The committee can only appraise the technology

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		4. Moreover, people living with obesity and awaiting important interventions/operations (such as renal transplant, orthopaedic operations or IVF) and required to reach specific weight loss cut offs before being eligible for treatment may also benefit from access to the medication (even at BMI<35 kg/m^2).	based on the evidence submitted. Comment noted. If evidence allows, results for relevant subgroups may be considered by the committee during the appraisal.
		5. The same doses of tirzepatide have been approved for use in people with type 2 diabetes – the NICE guideline for use of tirzepatide in people with type 2 diabetes needs also to be taken into account, so the same criteria are used in both guidelines for this population.	Comment noted. No change to the scope required.
	British Obesity and Metabolic Surgery Society (BOMSS)	The BMI criteria will need to be lowered in line with recent NICE guidance for different ethnic groups.	Comment noted. Where relevant and appropriate, and if evidence allows, the committee may

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		People with a BMI of 35 (with the caveat of reducing this in different ethnic groups) are most likely to benefit the most. People who need to reduce their weight in order to have other procedures for example: • Abdominal, gynaecological or urological surgery. • BMI > 50 before bariatric surgery • Orthopaedic surgery • IVF • Organ transplantation	consider this during the appraisal.. Comment noted. If evidence allows, results for relevant subgroups may be considered by the committee during the appraisal.
	Department for Health and Social Care (Office for Health Improvement)	Given that some comparators (Liraglutide and Semaglutide) are licensed for a license for BMI >30 kg/m^2, but NICE recommend them for a BMI>35kg/m2, are there specific groups with a BMI between 30-35kg/m2 (other than people with a weight related comorbidity) for whom the drug should be considered or prioritised?	Comment noted. Where relevant and appropriate, and If evidence allows, results for relevant subgroups may be considered by the committee during the appraisal.
	Royal College of Physicians (RCP)	The BMI criteria will need to be lowered in line with recent NICE guidance for different ethnic groups.	Comment noted. Where relevant and appropriate, and if evidence allows, the

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		People with a BMI of 35 (with the caveat of reducing this in different ethnic groups) are most likely to benefit the most. People who need to reduce their weight in order to have other procedures for example: • Abdominal, gynaecological or urological procedure. • In people with BMI of 50 or more prior to bariatric surgery • Prior to orthopaedic surgery • Prior to IVF • Prior to solid organ transplantation	committee may consider this during the appraisal. Comment noted. Where relevant and appropriate, and If evidence allows, results for relevant subgroups may be considered by the committee during the appraisal.
Comparators	Eli Lilly and Company Limited	Consistent with the conclusions of the Committee across three previous appraisals in obesity and overweight management [ID3850, TA664, TA494],[2-4] orlistat is not widely used in clinical practice due to poor efficacy and undesirable side effects which lead to poor adherence and treatment outcomes.[2-4] This is highlighted by data published by the National Health Service (NHS), which demonstrate a consistent decline in the prescription of orlistat over the last decade [5] Based on these data demonstrating the limited role of orlistat within current UK clinical practice, and the clear Committee determinations made in prior appraisals in this indication, orlistat should not be considered a relevant comparator for tirzepatide for the management of overweight and obesity.	Comment noted. At the scoping stage, the list of comparators is inclusive. Although clinical expert comments in TA494, TA664 and ID3850 indicated that orlistat is not widely used, it is listed as an available treatment option in CG189. For completeness, it has

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			been kept in the scope as a comparator.
	All about obesity	Yes – I hope that all the suggested comparators are included, especially Semaglutide.	Thank you for your comment. No change to the scope required.
	Association for the Study of Obesity	Yes, but ideally liraglutide and semaglutide should have the approved dose for treatment of obesity – liraglutide 3mg once daily and semaglutide 2.4 mg once weekly.	Thank you for your comment. The scope is intended to be a brief overview and would not include drug dosage. No change to scope required.
	British Obesity and Metabolic Surgery Society (BOMSS)	Add the approved weight management doses e.g. liraglutide 3mg and semaglutide 2.4 mg.	Thank you for your comment. The scope is intended to be a brief overview and would not include drug dosage. No change to scope required.
	Department for Health and Social Care (Office for	Other relevant comparators could include Total Diet Replacement and bariatric surgery.	Thank you for your comment. Bariatric surgery is only available to a minority of people

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	Health Improvement)		therefore it is not considered a comparator.
	Royal College of Physicians (RCP)	Add the approved weight management doses e.g. liraglutide 3mg and semaglutide 2.4 mg.	Thank you for your comment. The scope is intended to be a brief overview and would not include drug dosage. No change to scope required.
Outcomes	Eli Lilly and Company Limited	The outcome measures presented broadly capture the most important health-related benefits of tirzepatide.	Thank you for your comment. No change to the scope required.
	Association for the Study of Obesity	Yes.	Comment noted.
	British Obesity and Metabolic Surgery Society (BOMSS)	Yes, outcomes are appropriate.	Comment noted.

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	Department for Health and Social Care (Office for Health Improvement)	Does mortality refer to all-cause mortality? Implications of stopping the drug treatment (on weight and other outcomes)	Comment noted. Yes, it refers to all-cause mortality.
	Royal College of Physicians (RCP)	Yes, the outcomes listed are appropriate.	Comment noted.
Equality	Eli Lilly and Company Limited	BMI variations between different ethnicities: Some ethnicities have comorbidity risk factors that are of concern at lower BMIs. NICE therefore recommends that lower BMI thresholds should be used for people with a South Asian, Chinese, other Asian, Middle Eastern, Black African or African-Caribbean family background to prompt earlier intervention in these populations.[6] Access inequalities for treatment for other disabilities: There are often barriers associated with accessing other disabilities among people with overweight and obesity. According to a report by the Royal College of Surgeons, around 31% of NHS Clinical Commissioning Groups include measures to restrict elective surgery, such as hip and knee replacements, for patients who are obese.[7] This means that patients above a certain BMI may have to wait for prolonged periods while losing weight prior to being considered eligible for elective surgery.[8]	Thank you for your comment. These equalities considerations are formally addressed in the Equalities Impact Assessment form.

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		Socioeconomic inequalities: People in deprived areas often face significant barriers to accessing affordable, healthy food and to regularly exercising, translating into a higher prevalence of overweight and obesity in people of lower socioeconomic status.[9] This is highlighted by the data published by Office for Health Improvement and Disparities for 2020/21 which demonstrate that the prevalence of excess weight is 9% higher than the least deprived areas.[10]	Although socioeconomic status is not a protected characteristic under the Equality Act 2010, where appropriate, the committee may consider the impact on population groups experiencing health inequalities arising from socioeconomic factors during the appraisal.
	Association for the Study of Obesity	We should use lower BMI thresholds (as described before) for people of ethnic minorities.	Comment noted. Where relevant and appropriate, the committee may

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			consider this during the appraisal.
		Access to medication: Currently, there is significant variability in access to specialist weight management services (Tier 3 and Tier 4 weight management services) at different areas of the UK. Moreover, some specialist weight management services do not always have access to pharmacotherapies for treatment of obesity (lack of medical support for medication prescription). We suggest that the medication should be offered both i) by specialist weight management teams (Tier 3 and Tier 4 services) that are based either in primary or secondary care, and ii) by primary care, considering how prevalent the disease of obesity is. For the second scenario (when medication is prescribed by primary care), we need to ensure that patients have access to dietitian, physical activity advice and/or psychological support where needed. Ideally, prescription of tirzepatide could be done by GPs with an interest in obesity and they could be supported by a secondary care centre in weight management. Overall, we can use as example the prescription of GLP-1 receptor analogues for type 2 diabetes - the medication is initiated at the primary care and only complex cases are sent to secondary care (e.g patients who are already on insulin).	Comment noted. Issues related to implementation regarding access to services cannot be addressed in a technology appraisal. Access to treatment is outside the remit of NICE technology appraisal guidance.
	British Obesity and Metabolic	People living with obesity frequently experience difficulty in accessing treatment because of weight stigma and geographic disparity in provision of and access to NHS weight management services. In addition many weight	Comment noted. Issues related to implementation regarding access to

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	Surgery Society (BOMSS)	management services do not have experience or expertise in the prescription of these medicines. To ensure equity of access to effective medical treatment the NHS will need to enable prescription from primary care or other health care providers with an appropriate level of knowledge and expertise. Those administering medication should also provide lifestyle support including nutritional advice, physical activity advice and psychological support. The comments above also apply to other weight management drugs including Liraglutide and semaglutide prescribed at management dose. In addition to the outcome measures described, data should be collected that will permit analysis of equity of access to and use of this drug geographically and also with indications of social and economic deprivation to determine whether those with the greatest health care need are accessing treatment.	services cannot be addressed in a technology appraisal. Access to treatment is outside the remit of NICE technology appraisal guidance.
	Department for Health and Social Care (Office for Health Improvement)	People from ethnic minority groups may need to access these drugs at a lower BMI than people from White ethnic groups. This is not reflected in the population. Outcomes in people with complex needs should be considered compared to people without.	Comment noted. Where relevant and appropriate, the committee may consider subgroups during the appraisal. These equality considerations will be formally addressed in

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			the Equalities Impact Assessment form.
	Royal College of Physicians (RCP)	Access to specialist weight management services is a postcode lottery, with a third of England have no services. Limiting the prescribing of these to specialist hospital based weight management services will mean that many people are unable to access these. This means we need a mechanism by which, primary care physicians can be supported to offer anti-obesity medications. However, anti-obesity medications are an adjunct to a lifestyle intervention (reduced energy diet and increased physical activity). People living with overweight/ obesity who are prescribed these medications need to have access to nutritional support, physical activity advice and psychological support. Access to appropriate scales etc is also important. A way forward would be to link community based weight management services/ primary care with secondary care centres to provide a hub and spoke mechanism. This will allow complex patients to be identified and seen in secondary care and also ensure that people who would benefit from bariatric/metabolic surgery are referred. Currently, the number of people able to access liraglutide 3mg as per the NICE TA is woeful as Integrated Care Systems have not commissioned these leaving most people unable to access this. There need to be mechanisms in place to ensure that this is not repeated.	Thank you for your comment. Access to treatment is outside the remit of NICE technology appraisal guidance.

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		As commented above it is key that the correct BMI criteria (as per recent NICE update) for people with a South Asian, Chinese, other Asian, Middle Eastern, Black African or African-Caribbean family background are used to ensure that people from these family backgrounds have access to treatment at an appropriate BMI for their ethnicity (and are not declined access on the basis of criteria for people from a White family background).	Comment noted. Where relevant and appropriate, the committee may consider this during the appraisal.
Other considerations	Eli Lilly and Company Limited	The following inequality should be considered relevant for this appraisal: **Provision and access to Tier 3 services:** The NICE recommendations for which patients should be able to access Tier 3 services mean that there are patients with lower BMIs (<35.0 kg/m^2) and obesity-related complications who may gain a significant clinical benefit from weight loss but are not able to access the pharmacological treatments that are available.[11] In addition, although the tiered system and NICE guidance provides a broad guide, NHS provision for the management of obesity varies across the UK, which means the treatments that are available to patients are not consistent throughout the country.[11]	Thank you for your comment. Issues related to implementation regarding access to services cannot be addressed in a technology appraisal.
	All about obesity	Length of treatment – Obesity is a chronic condition, we need to look at treatments as if they are for a chronic condition too.	Thank you for your comment. No change to the scope required.
	Association for the Study of Obesity	The use of a stopping rule for tirzepatide may allow the targeted use of the medication from people who will receive more benefit from its use. We suggest a stopping rule of 5% weight loss at 6 months.	Comment noted. Recommendations are based on the marketing authorisation and

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		The NICE guideline for tirzepatide use for people with type 2 diabetes needs also to be taken into account	evidence provided. No change to scope required.
	British Obesity and Metabolic Surgery Society (BOMSS)	Less than 5% total weight loss or more after 3 months of maximum dose indicates that the treatment is not effective, and people should be offered referral into specialised weight management services and consideration given to stopping treatment	Comment noted. No change to the scope required.
	Royal College of Physicians (RCP)	A stopping rule for people who do not achieve 5% total weight loss or more after 3 months of maximum tolerated dose could be considered.	Comment noted. Recommendations are based on the marketing authorisation and evidence provided. No change to scope required.
Questions for consultation	Eli Lilly and Company Limited	**Q1) Which treatments are considered to be established clinical practice in the NHS for overweight and obesity?** Despite the increasing prevalence of obesity in the UK and the benefits of treating obesity with pharmacotherapy, effective and tolerable treatments for overweight and obesity remain very limited for the population of relevance to this appraisal. As described above, orlistat is available for is available to patients with a BMI ≥30 kg/m^2 or ≥28 kg/m^2 with other weight-related comorbidities. However, orlistat is associated with undesirable side effects, insufficient weight loss and poor adherence, which means it is now rarely used in UK clinical practice.[5] In December 2020, liraglutide was approved for use within secondary care by a specialist multidisciplinary Tier 3 weight management service for patients with a BMI ≥35 mg/kg^2 with non-diabetic hyperglycaemia and high	Thank you for your comment.

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		cardiovascular risk.[3] However, these strict eligibility criteria mean that some patients accessing Tier 3, such as those with a BMI 30–35 kg/m^2 for whom Tier 2 interventions have been unsuccessful,[6] do not meet the criteria to receive this treatment despite the potential benefits it could offer. Semaglutide has also recently been recommended by NICE for use in adults with a BMI of ≥30 kg/m^2, or ≥27 kg/m^2 to <30 mg/kg^2 in the presence of at least one weight-related comorbidity, under the condition it is used for a maximum of 2 years within a specialist weight management service (SWMS) providing multidisciplinary management of overweight and obesity.[2] However, this product is yet to launch within the UK, meaning patients are at present not able to benefit from this treatment. Given the limited population of patients currently able to benefit from available recommended pharmacotherapies, many patients with overweight and obesity rely on lifestyle intervention alone to manage their condition. However, evidence suggests that lifestyle interventions alone are not enough to help patients lose weight and maintain weight loss.[12] As such, there remains a substantial unmet need for novel treatment options that allow a broader population of people with overweight and obesity to benefit from pharmacotherapy. **Q2) Is bariatric surgery a relevant comparator for adults with a BMI of ≥30 kg/m² or ≥27 kg/m² to <30 kg/m2 and at least one weight-related comorbidity?** In England, bariatric surgery is available for patients with a BMI ≥40 kg/m^2, or between 35–40 kg/m^2 and other significant disease accessing SWMS. However, previous appraisals in this indication (TA494, TA664) have highlighted that bariatric surgery is rarely used in clinical practice, with only around 0.1% of eligible patients actually receiving this treatment.[3, 4] More recent data (2020) suggests that this figure is even lower, at around 0.002%.[11] As such, it is not realistic that bariatric surgery would be considered	Thank you for your comment. Bariatric surgery is only available to a minority of people therefore it is not considered a comparator.

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		part of established clinical management for the population of relevance to this appraisal, and subsequently, it is not a relevant comparator for tirzepatide. Nevertheless, to account for the fact that bariatric surgery is available for some patients in England as part of SWMS,[6] it is anticipated that bariatric surgery will be included in the economic model as a downstream event; the incidence of bariatric surgery in the base case will likely be informed by NHS data, and this will likely be modifiable in sensitivity analyses. **Q3) Where do you consider tirzepatide will fit into the existing care pathway for managing overweight and obesity?** As highlighted in Question 1, there remains an unmet need for patients with overweight and obesity, given the limited population of patients currently able to benefit from effective pharmacotherapies. Novel treatment options may particularly benefit patients with a BMI of 27–30 kg/m² with one weight-related comorbidity, as although these patients can benefit greatly from weight loss of 10–15%,[2] the only pharmacological treatment available for these patients is orlistat, which is currently rarely used in clinical practice due to efficacy and tolerability issues.[5] Given this unmet need and provided the economic evidence allows, tirzepatide would be best positioned for patients with a BMI ≥27 kg/m² with one weight-related comorbidity and for patients with a BMI ≥30 kg/m^2 as an adjunct to diet and exercise. **Q4) Are there any other subgroups of people in whom tirzepatide is expected to be more clinically effective and cost effective or other groups that should be examined separately?** No.	Thank you for your comment. Thank you for your comment. Thank you for your comment.

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		Q5) Would tirzepatide be a candidate for managed access? Commercial plans for access are still to be determined, but it is anticipated that tirzepatide would not be considered a candidate for managed access. **Q6) Do you consider that the use of tirzepatide can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?** No.	Thank you for your comment.
	Novo Nordisk Ltd	**Which treatments are considered to be established clinical practice in the NHS for overweight and obesity?** Currently established clinical practice includes lifestyle interventions (such as diet and exercise) and pharmacotherapy and bariatric surgery. Lifestyle intervention in the form of diet and exercise counselling is essential in treating obesity and forms the basis of all treatment programmes. Pharmacotherapy treatments are typically available within specialist weight management services providing multidisciplinary management of overweight or obesity. Liraglutide 3mg is recommended by NICE to adults with a BMI ≥ 35 mg/kg^2 with non-diabetic hyperglycaemia and high CV risk and it is prescribed in secondary care by a specialist multidisciplinary Tier 3 weight management service (TA664). Semaglutide 2.4mg was recently recommended by NICE but a technology appraisal guidance has not been issued yet (GID-TA10765). Both treatments are prescribed alongside diet and exercise.	Thank you for your comment. Bariatric surgery is only available to a minority of people therefore it is not considered a comparator.

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		Is bariatric surgery a relevant comparator for adults with a BMI of ≥30 kg/m² or ≥27 kg/m² to <30 kg/m2 and at least one weight-related comorbidity? Bariatric surgery is only available to a small number of patients with obesity with a high BMI (a BMI of 40 kg/m2 or more, or between 35 kg/m2 and 40 kg/m2 and other significant disease) and is considered a last resort option.	Thank you for your comment.
	Association for the Study of Obesity	1. Which treatments are considered to be established clinical practice in the NHS for overweight and obesity? Answer: As described above at section comparators and at Appendix B i) Orlistat for managing obesity in adults with a BMI of 30 kg/m^2 or more, and in people with a BMI of 28 kg/m^2 or more with associated risk factors. ii) Liraglutide 3mg once daily as an option for managing overweight and obesity alongside a reduced-calorie diet and increased activity in adults with a BMI of at least 35 kg/m^2 (or at least 32.5 kg/m^2 for members of minority ethnic groups), non-diabetic hyperglycaemia and a high risk of cardiovascular disease. iii) Bariatric surgery for people with: a BMI of ≥40 kg/m^2; a BMI of between 35 kg/m^2 and 40 kg/m^2 and other significant disease, a BMI between 30 kg/m^2 and <35 kg/m^2 and with recent-onset of type 2 diabetes 1. Is bariatric surgery a relevant comparator for adults with a BMI of ≥30 kg/m² or ≥27 kg/m² to <30 kg/m^2 and at least one weight-related comorbidity?	Thank you for your comment.

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		Answer: Bariatric surgery is not a relevant comparator for people with BMI≥27 kg/m^2 and less than 30 (with at least one weight-related comorbidity) as in the UK this group very rarely undergo surgery. For people with BMI 30 to 34.9, again this group rarely can access surgery (usually people with recent onset type 2 diabetes). However bariatric surgery may be a relevant comparator for people with BMI≥35 kg/m^2 and obesity related complications or people with BMI≥40 kg/m^2. 2. Where do you consider tirzepatide will fit into the existing care pathway for managing overweight and obesity? Answer: Depending on person's BMI and complications, it could be first line treatment together with the lifestyle interventions, or otherwise second line treatment if target weight loss has not been achieved and/or maintained with lifestyle interventions. Finally, it could be considered for use after bariatric surgery, if there is significant weight regain or inadequate weight loss leading to recurrence of obesity-related complications. 1. Are there any other subgroups of people in whom tirzepatide is expected to be more clinically effective and cost effective or other groups that should be examined separately? **Answer:** Please see section above on subgroups 2. Would tirzepatide be a candidate for managed access? **Answer:** Yes	Thank you for your comment. Bariatric surgery is only available to a minority of people therefore it is not considered a comparator. Thank you for your comment. Thank you for your comment. Thank you for your comment.

Section	Consultee/ Commentator	Comments [sic]	Action
		3. Do you consider that the use of tirzepatide can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? **Answer:** No 4. Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits. **Answer:** The data from SURMOUNT-1 study (PMID: 35658024) which is a phase 3, double-blind, randomized clinical trial demonstrates the safety and efficacy of tirzepatide 5mg, 10mg and 15mg compared to placebo after 72 weeks of use in people with overweight and obesity. It should be noted that discontinuation of treatment will lead to inevitable weight regain and loss of the majority of the clinical benefits (similar to what has been demonstrated at the STEP-1 trial extension for semaglutide 2.4mg, Wilding et al, DOM, 2022, PMID 35441470).	Thank you for your comment. Thank you for your comment. The committee can only appraise the technology based on the evidence submitted.
	British Obesity and Metabolic Surgery Society (BOMSS)	**Which treatments are considered to be established clinical practice in the NHS for overweight and obesity?** Lifestyle modification Lifestyle modification and weight loss drug	Thank you for your comment.

Section	Consultee/ Commentator	Comments [sic]	Action
		Lifestyle modification + bariatric surgery **Is bariatric surgery a relevant comparator for adults with a BMI of ≥30 kg/m² or ≥27 kg/m² to <30 kg/m² and at least one weight-related comorbidity?** Bariatric surgery is only offered to people with a BMI of 35 or more with an obesity related co-morbidity (cut offs lowered in different ethnic groups) and rarely to people with a BMI of 30 or more with metabolic comorbidities. It is not a comparator for people with a BMI 27.0 to 29.9. **Where do you consider tirzepatide will fit into the existing care pathway for managing overweight and obesity?** Given the magnitude of weight loss seen in the clinical trials, tirzepatide would be most appropriate for people with a BMI of 35 or more or people with a BMI of 30 or more with adiposity related co-morbidities. **Are there any other subgroups of people in whom tirzepatide is expected to be more clinically effective and cost effective or other groups that should be examined separately?** Response detailed above. **Would tirzepatide be a candidate for managed access?**	Thank you for your comment. Bariatric surgery is only available to a minority of people therefore it is not considered a comparator. Thank you for your comment Thank you for your comment.

Section	Consultee/ Commentator	Comments [sic]	Action
		Yes. This would permit rapid collection of meaningful real life data that would describe the impact of an effective drug, together with lifestyle support in the NHS. **Do you consider that the use of tirzepatide can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?** No	Thank you for your comment. Thank you for your comment.
	Department for Health and Social Care (Office for Health Improvement)	Other questions to be answered include: What is the appropriate care setting to deliver Tirzepatide equitably to eligible patients across the country? Could it be delivered in primary care? Would specialist weight management services be an appropriate and equitable route for the delivery of Tirzepatide when they are not commissioned equally across England and the UK? Would digital weight management services as well as face to face services be an appropriate route for the delivery of Tirzepatide? What wraparound support (i.e., diet and physical activity) is required to support delivery of Tirzepatide in primary and/or secondary care? Can a distinction be drawn between what is essential to support cost effectiveness and what is dersirable?	Thank you for your comment. Access to care is outside of NICE technology appraisal remit. Where appropriate, the committee may consider issues relating to the primary and/or secondary care that may be relevant to the cost-effectiveness of the technology during the appraisal.

Section	Consultee/ Commentator	Comments [sic]	Action
	Royal College of Physicians (RCP)	**Which treatments are considered to be established clinical practice in the NHS for overweight and obesity?** Behavioural interventions alone Behavioural interventions + anti-obesity medications Behavioural interventions + bariatric/metabolic surgery	Thank you for your comment.
		Is bariatric surgery a relevant comparator for adults with a BMI of ≥30 kg/m² or ≥27 kg/m² to <30 kg/m² and at least one weight-related comorbidity? Bariatric surgery is only offered to people with a BMI of 35 or more with an obesity related co-morbidity (cut offs lowered in different ethnic groups) and rarely to people with a BMI of 30 or more with metabolic comorbidities. It is not a comparator for people with a BMI 27.0 to 29.9.	Thank you for your comment. Bariatric surgery is only available to a minority of people therefore it is not considered a comparator.
		Where do you consider tirzepatide will fit into the existing care pathway for managing overweight and obesity? Given the magnitude of weight loss seen in the clinical trials, tirzepatide would be most appropriate for people with a BMI of 35 or more or people with a BMI of 30 or more with adiposity related co-morbidities.	Thank you for your comment.
		Are there any other subgroups of people in whom tirzepatide is expected to be more clinically effective and cost effective or other groups that should be examined separately? Response detailed above.	Thank you for your comment.

Section	Consultee/ Commentator	Comments [sic]	Action
		Would tirzepatide be a candidate for managed access? Yes. Given, the poor uptake of liraglutide 3.0mg by CCGs/ICSs this would be a good initiative. Historically weight management treatments have very poor uptake. This would also allow collection of real world data using the National Obesity Audit **Do you consider that the use of tirzepatide can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?** No	Thank you for your comment. Thank you for your comment.
Additional comments on the draft scope	Eli Lilly and Company Limited	None.	Comment noted.
	Novo Nordisk Ltd	Liraglutide and semaglutide are also available in lower doses for the treatment of type 2 diabetes doses. To avoid any confusion, we propose amending here and in all relevant communications to liraglutide 3mg and semaglutide 2.4mg.	Thank you for your comment.
	Royal College of Physicians (RCP)	The availability of semaglutide for people with type 2 diabetes markedly in advance of this being available for weight management has generated problems with people being prescribed the diabetes dose off license. It would be good to afford the same issue with tirzepatide by expediting approval for weight management so that this is available at the same time for	Thank you for your comment.

Section	Consultee/ Commentator	Comments [sic]	Action
		both people with type 2 diabetes with overweight and obesity and for people with overweight and obesity without type 2 diabetes.	

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

Society for Endocrinology: No comments