For committee, experts, company and EAG – no CON information

Tirzepatide for managing overweight and obesity

Technology appraisal committee A – 13 August 2024

Chair: James Fotheringham

Lead team: Ian Bernstein, Becky Pennington, Alan Thomas

External assessment group: Warwick Evidence

Technical team: Emma Bajela, Albany Chandler, Jacoline Bouvy

Company: Eli Lilly

Recap

NICE National Institute for Health and Care Excellence

Evaluation history

ACM1
Jan 2024

Committee unable to make recommendation without further information on weight management services

Information gathered from NHSE on potential composition of weight management services (company commented)

+

Analysis requested from company

+

Other stakeholders commented on committee's conclusions

ACM2
April 2024

Minded to make optimised recommendation (no cost effectiveness estimates reflecting preferred assumptions at meeting)

Company and EAG submitted analysis using committee's preferred assumptions + scenario analyses for weight management service composition for each arm

Optimised recommendation in draft guidance

ACM3
This meeting

Recommendation in draft guidance

Draft guidance recommendation:

1.1 Tirzepatide is recommended as an option for managing overweight and obesity, alongside a reduced-calorie diet and increased physical activity in adults, only if they have:

- an initial BMI of ≥ 35 kg/m^2 and
- at least one weight related comorbidity.

Lower BMI thresholds by 2.5 kg/m^2 for people from certain ethnic backgrounds

1.2 Consider stopping tirzepatide if less than 5% of the initial weight has been lost after 6 months of treatment.

Company's target population:

- People with a BMI ≥30 kg/m^2 with at least one weight-related comorbidity
    - Current recommendation excludes people with BMI **30–34.9 kg/m^2** with at least one weight-related comorbidity

Summary of committee conclusions at ACM2 (1)

Committee conclusions:

- Tirzepatide should be considered in primary and secondary care settings – primary comparator is diet and exercise support; semaglutide also appropriate comparator for people eligible for SWMS
- Likely to be challenges for implementation due to variability in existing diet and exercise support available in primary care - needed alongside tirzepatide. Decision making should be based on range of scenarios
- By excluding people with T2DM, SURMOUNT-1 did not cover the whole population who would potentially be offered tirzepatide in the NHS and who are covered by tirzepatide's marketing authorisation
- BMI distribution in SURMOUNT-1 different to population who would be eligible for tirzepatide - could limit generalisability; preferred to include adjustment for BMI distribution to reflect people who would have tirzepatide
- Appropriate to include people in baseline model population who have modelled complications and comorbidities
- Age-related natural increase in weight expected to some extent for people on tirzepatide – preferred to apply natural progressive increase in weight to both arms
- Uncertain how quickly benefits associated with tirzepatide lost after stopping – assumed weight regained in 2 years
- Prediabetes reversal loss likely to be driven by weight regain – prediabetes reversal loss in both arms should align with weight regain
- Appropriate to use data from SURMOUNT-1 at 48-weeks to inform proportion stopping tirzepatide at 6 months
- Not appropriate to include long-term stopping rule for tirzepatide

Summary of committee conclusions at ACM2 (2)

Key areas of uncertainty:

- Effectiveness data for tirzepatide is only available for 72-weeks
- If diet and exercise support included in SURMOUNT-1 reflects obesity weight management services that would be delivered in primary care
- Residual impact of having previously had a higher BMI - ICERs likely to be higher if considered

Further analysis committee asked to see:

- Different assumptions for obesity management service resource use for all arms
- Analysis of the long-term impact on outcomes from previously having had a higher BMI

Consultation responses

- Eli Lilly (company)
- NHS England
- Betsi Cadwaladr University Health Board
- Royal College of Physicians
- Royal college of General Practitioners
- Devon ICB
- Hertfordshire and west Essex ICB
- Web comments
- Expert comments

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Company Response

Company (Eli Lilly) response to consultation

- Seeking recommendation for BMI >30 + 1 weight-related comorbidity
- Primary care is equipped to deliver tirzepatide and associated D&E support
- Scenario that assumes no healthcare resource use in D&E arm inappropriate as benefits still included and assumes no costs associated with D&E
- BMI should have gamma distribution – better reflects BMI reported in community weight management services
- Strongly disagrees that natural increase in weight is appropriate while on tirzepatide
- UKPDS costs for T2DM have been inflated by EAG using PSSRU pay and prices index. Company claim standard practice is to use PSSRU Personal Social Services Index.
- Incorporating Haase data to account for residual impact of previous higher BMI has limitations - but shows there are uncaptured benefits associated with treating obesity before BMI progresses, so model may underestimate benefit for BMI 30 to 35
- Should consider wider societal benefit and potential for reduction in health inequalities when considering uncertainties

Themes from consultation comments

Theme	Stakeholder comments
Diet and exercise advice	• Agreement that D&E intervention needed, but need greater clarity on what the intervention is • Request to include guidance on dietary quality and not only calorie restriction (more deprived communities more likely to have malnutrition – equalities issue) • CG189 recommends MDT support alongside any weight management drug

Generalisability of SURMOUNT-1	• Population in SUMROUNT-1 not generalisable to real world population
	  • excluded people with severe psychological disorders, people waiting for surgery, diabetes, included large proportion of people with prediabetes
	  • ethnic profile of trial different to England and Wales population
	• Not considered safety and effectiveness for people with severe mental health disorders
	• Highest risk population less represented than lower risk population

Setting	• Support for primary care setting but specialist provision still needed • Disagreement with company that level of D&E in SURMOUNT-1 can be incorporated into ongoing care in primary care; others agree it could be with time • Scepticism over company's survey of GP's (presented at ACM2 indicating D&E support currently provided), suggest this is not reflective of ICBs across the country • 'GP with Extended Role in Lifestyle Medicine' could be highlighted as a suitable provider of weight management services • Definition of primary care would be useful – could be GPs or local authority services

Themes from consultation comments

Theme	Stakeholder comments
Recommended population	• ICB, HWE and RCP state that eligible cohort is too large and needs to be tightened
Diabetes treatment	• Widens eligibility for people with T2DM as per TA924, but no diabetes patients in trial
Long-term stopping rule	• Requests to include a 2-year stopping rule – no evidence for long-term effectiveness which is 1 of reasons stated for stopping rule in semaglutide TA875 • Others welcome no stopping rule • Other guidance needed on when to stop such as if weight is regained

Short-term stopping rule	• Rec to 'consider stopping tirzepatide after 6 months if less than 5% weight is lost' is too vague and open to interpretation – should be mandatory. *Note:*
	  • *wording in line with SPC*
	  • *mandatory short-term stopping rule consistent with economic modelling*

Safety	• No evidence of long-term safety; ongoing pharmacovigilance by MHRA and EMA • SURMOUNT-1 suggested increased severe hypoglycaemia and evidence that incretin-based weight loss drugs cause loss of lean mass leading to frailty • SPC includes precautions around acute pancreatitis, hypoglycaemia and pregnancy (should not be used in pregnancy)
BMI distribution in model	• Includes evidence from OHID 2021/22 local authority weight management services grant – this was delivered in community not primary care; subset of local authorities so not fully representative

Implementation – consultation comments

Theme	Stakeholder comments
Implementation issues	• Not implementable – recommendation too broad and unaffordable • Others agree that D&E intervention can be delivered in primary care, but most say not within 3 months • Will require significant additional training and long-term investment • Complications from rapid weight loss will add pressure to primary care • Deprived areas may find harder to implement, increasing health inequalities • Unclear how tirzepatide will fit into clinical pathway for obesity and comorbidities, including how other medicines may need to change
Implementation advice	• Targeted cohorts for phased implementation – highest clinical risk first -Use e.g. Edmonton criteria or King's criteria -Could prioritise people awaiting surgery, infertility/IVF or suffering severe complications -Many at highest risk currently referred to SWMS • Would welcome updated clinical guideline
Safe implementation	• NICE Medicines Optimisation Team note SpC states tirzepatide should not be used in pregnancy or women of childbearing potential not using contraception; non-oral or additional barrier contraception advised through titration • Prioritising tirzepatide implementation for people with fertility issues may not be appropriate • Due to potentially large number of people eligible, high number of people at risk from safety concerns

Implementation

Evaluation remit:

- Appraisal of clinical and cost effectiveness of tirzepatide within its marketing authorisation, for the management of obesity or overweight with at least one weight related comorbidity

Committee conclusions ACM1/2:

- Recognise challenges with implementation. Given remit for evaluating clinical and cost effectiveness of delivery of tirzepatide and uncertainty around how diet and exercise intervention will be delivered, appropriate to use range of scenarios for obesity management services in decision making

- **Funding variation:** NICE's methods allow for a funding variation to be requested by NHSE&I, which must be approved by NICE's guidance executive

Planned tools to be developed by NICE (subject to change):

- Recorded webinar: education and training/upskilling aimed at clinicians
- Decision support tool: aimed at patients and clinicians, choosing between treatment options
- Prescribing decision support: aimed at clinicians, will include information on tirzepatide and other obesity medicines
- Patient information support: summary of eligibility criteria for all medicines aimed at patients
- Formulary application template

- Are the Edmonton or King's criteria helpful for stratifying risk in people with obesity?

Are there any populations who could be considered for priority access to tirzepatide, if needed to aid implementation?

- Can safety concerns, for example around use in pregnancy, be addressed in guidance?

Remaining issues to be discussed

Issue	ICER impact
Currently recommended population includes people with T2DM but pivotal trial excludes those with T2DM	Unclear
Long-term treatment effect. No evidence to assume indefinite treatment effect	Moderate
SURMOUNT-1 population does not reflect probable BMI distribution in NHS practice	Moderate
Residual risk associated with long term obesity. Weight loss may not entirely reverse the effects of obesity	Moderate
Company considers EAG cost estimates for T2DM too low	Moderate

Key issues: Recommendation includes people with T2DM

Background

- Consultees raised that SURMOUNT-1 trial excluded people with TD2M so no cost effectiveness evidence for tirzepatide for managing obesity for people with T2DM was presented
- TA924 only recommends tirzepatide for people with T2DM with a BMI of 35 or above after triple therapy but the recommendation moves tirzepatide up to first line for this group

Company

- Model is not suited to modelling those with T2DM

EAG comments

- Agrees model is poorly suited to modelling people with T2DM; Key driver of ICER is avoidance or delay of T2DM - doesn't apply to people with T2DM
- If more people assumed to develop T2DM, ICER increases
- Assuming a proportion in the model have T2DM at baseline somewhat worsens the ICER
- Evidence that in population larger health gains for people with T2DM

Should the recommendation include T2DM given the model set up and evidence base?
Is tirzepatide weight loss benefit applicable to people with T2DM?

Abbreviations: T2DM, type 2 diabetes mellitus; ICER, incremental cost effectiveness ratio

Key issues: Long-term treatment effect

Background

- SH concerns around lack of long-term data on treatment effect
- Committee concluded long term treatment effect of tirzepatide beyond 72 weeks of SURMOUNT-1 data is uncertain and likely natural age-related weight gain tirzepatide would impact people taking tirzepatide
- EAG presented evidence from SCALE in liraglutide that suggests weight is regained over time while still on treatment

Company

- No evidence that treatment effect of tirzepatide wanes over time in people who continue to receive therapy and mechanism of action does not provide rationale for treatment effect waning
  - tirzepatide acts on 2 incretin hormone receptors regulating satiety and appetite and is disease modifying
- Evidence from SCALE was main driver of treatment effect waning but not robust as analysis may include people who discontinued liraglutide rather than waning effect (based on full analysis set who completed each visit + does not specify only from people remaining on treatment)
  - Liraglutide also less effective than tirzepatide which limits applicability of findings
- Extension phase data from semaglutide SELECT trial shows no loss of treatment effect over 221 weeks

What assumption for natural increase in BMI according to natural history weight gain while on tirzepatide is appropriate?

Key issues: Long-term treatment effect

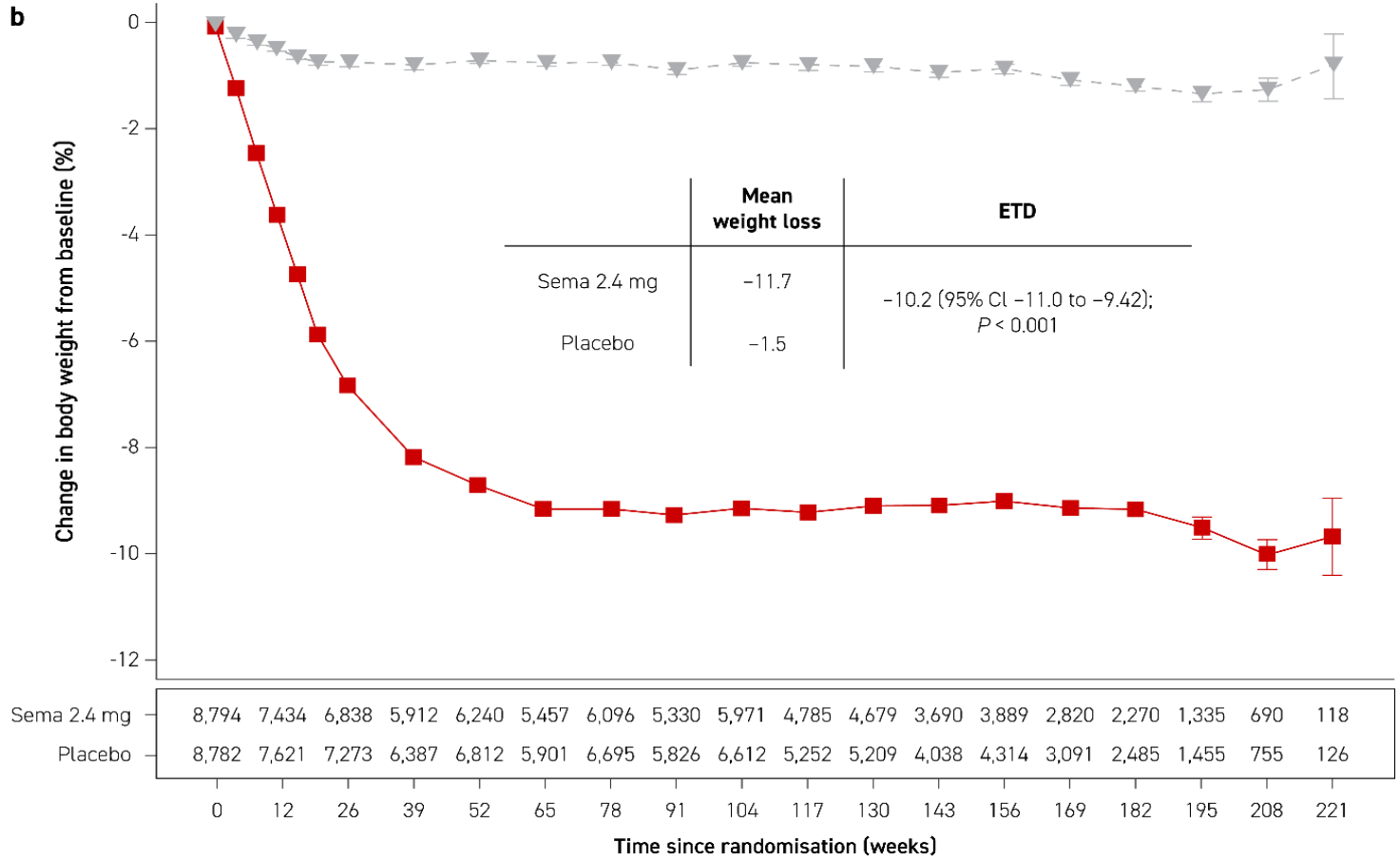
EAG comments

- Results sensitive to a treatment waning of an average annual loss of net BMI effect of 2% from year 5
- Assumes SCALE includes only people still on liraglutide as would be favourable to liraglutide and taken from TA664
- In SELECT trial follow up data drops off to around 1.5% by week 221 (n=118). But proportion of drop off similar to SCALE trial extension up to 160 weeks
- No evidence of either a decline in absolute effect or increase in net effect
- Base case retains natural weight gain in both arms from 72 weeks so there's constant net effect for tirzepatide
- Company used Ara et al. data to estimate natural increase in weight gain - included data for non-diabetic people only
- Suggests incorporating diabetic weight gain parameter from Ara into model
- Iyen et al. another appropriate source of natural weight gain data which pools people with and without diabetes

What assumption for natural increase in BMI according to natural history weight gain while on tirzepatide is appropriate?

Long-term treatment effect

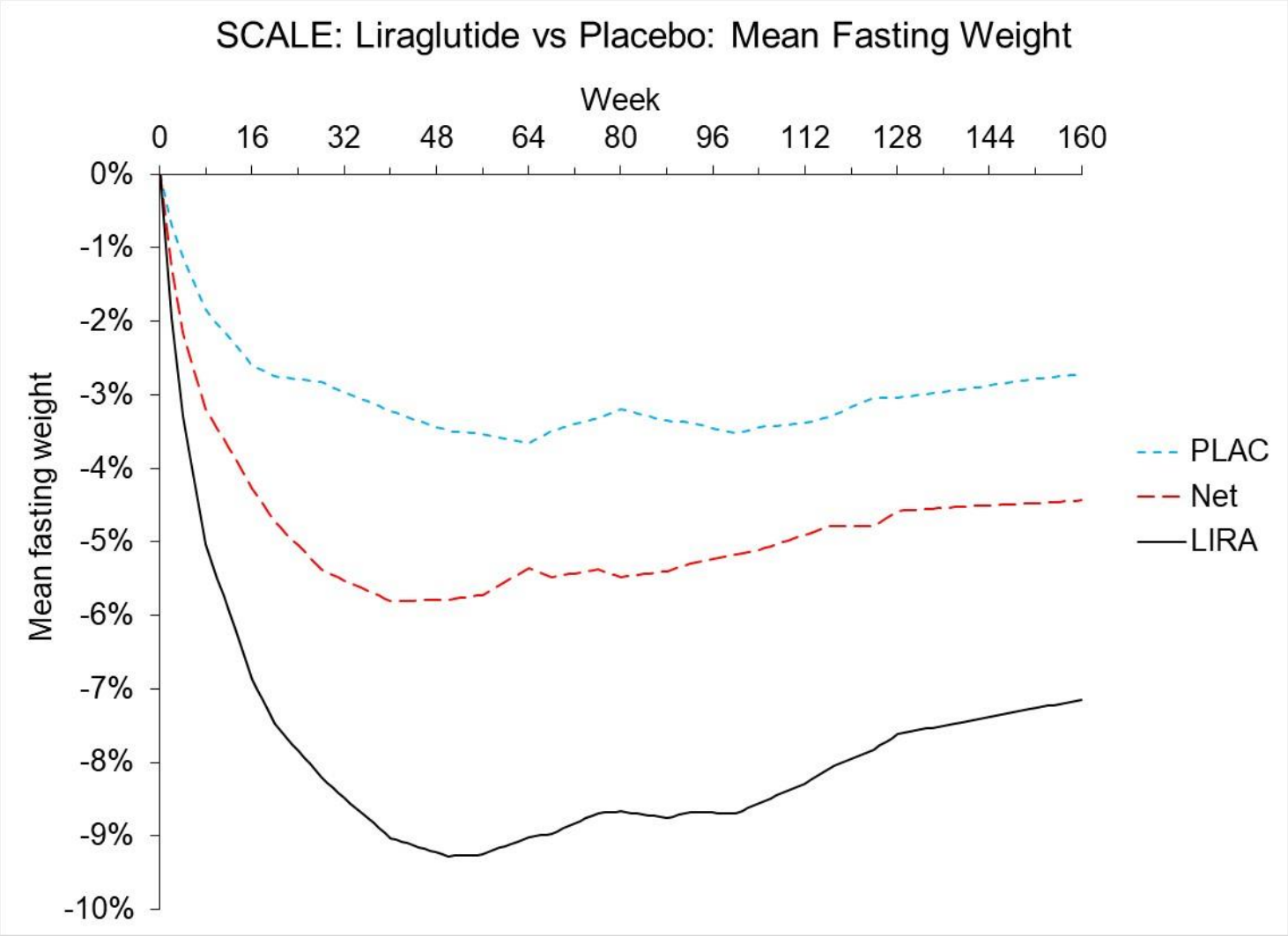
Percentage change in body weight over time in SELECT
(semaglutide in obesity; up to week 221 – on-treatment analysis)



EAG: Uncertain whether people in both arms still receiving diet and exercise support

Long term treatment effect

SCALE weight loss from baseline to 160 weeks: Prediabetes population



SCALE data suggests there may be a waning of both the absolute treatment effect and the net treatment effect for liraglutide over time

Key issues: The probable distribution of BMI

Background

- EAG did scenario analysis with HSE general population BMI distribution applied in model as better represented population eligible for tirzepatide
- Committee concluded it was appropriate to adjust for BMI in the model
- Committee requested to see detailed graduation for BMI distribution in SURMOUNT-1 (company has provided) to understand how well it matches distribution in clinical practice

Company

- Gamma distribution most appropriate as reflects BMI distribution in community weight management services and SURMOUNT-1 population – likely representative of people seeking treatment
- EAG's approach implies those with least severe disease and lowest risk of comorbidities *vastly* outnumbers those with most severe disease and does not reflect evidence for demographic of people with obesity who are seeking treatment in NHS; more likely that those with higher BMI will be driven to receive treatment
- IMPACT-O trial with data from UK primary care clinics shows BMI distribution lying between HSE and CWMS data. Company did scenario analysis with BMI sampling based on IMPACT-O data.

EAG comments

- Company assumed gamma distribution may not be a good fit at the lower end – supported by high proportion in SURMOUNT-1 with BMI 30 to 31
- EAG base case applies lognormal distribution based on HSE data in base case and presents scenarios applying normal distribution (on HSE), sampling from SURMOUNT-1 distribution and gamma distribution based on SURMOUNT-1

The probable distribution of BMI

BMI distributions in relevant sources

BMI (kg/m^2)	SURMOUNT-1 (ITT)	SURMOUNT-1 (target population)	Community Weight Management Services	Model (gamma distribution) – Company preference	General Population (HSE general population survey)	Model (normal distribution) – EAG preference	IMPACT-O*
30.0–34.9 (Class I)	37%	35%	40%	35%	66%	65%	55.6%
35.0–39.9 (Class II)	30%	29%	30%	32%	27%	29%	25.9%
40+ (Class III)	33%	35%	30%	33%	7%	7%	18.5%

IMPACT-O: data from the UK IQVIA Medical Research Database and The Health Improvement Network database (GP practice electronic medical records)
BMI data collected for 1,734,788 patients at primary care clinics throughout the UK between January 2018–September 2022

Patient expert view at ACM2: likely that people with BMI towards lower end of recommended range would seek treatment

Would proportion of people with BMI <35 who would receive tirzepatide in NHS practice be best reflected by proportion of people with BMI 30-34.9 seen in SURMOUNT-1, CWMS, general population or IMPACT-O?

Key issues: Weight loss may not reverse all effects of obesity

Evidence

- Hasse et al: assesses residual risk of obese who have lost weight vs those who have never been obese
- Khunti et al: assesses the risk of complications in varying BMIs (does not explore weight loss or residual risk)
- only incorporated in scenarios to show decision risk, not included in either of the company's or EAG's base cases

EAG comments

- EAG takes simple approach to incorporating findings due to limitations of the model and Hasse et al: reduces direct effects that complications with residual risks have on model outputs (e.g. if residual risks suggest model overestimates effect on T2DM by 100%, EAG halves T2DM direct effects in model, halving net effect of T2DM on model outputs)
- Company application of incorporation of residual effects incorrect: if residual effects suggest model overestimates effects of T2DM by 100%, direct effects of T2DM are doubled in each arm, doubling net impact of T2DM (improves ICER)
- Model estimates 24% average relative risk of T2DM over 10 years from 20% weight loss – lower than 0.5 hazard ratio suggested by Khunti data, so model may be overestimating risk reduction for T2DM from tirzepatide use
- Provides scenario reducing effect of T2DM on model outputs by 61% to adjust model risk of T2DM to that suggested by Khunti data - increases ICER
- Including similar adjustments for OSA, TKA, angina and MI further worsens ICERs, but not by much

How should uncertainty around residual effects of obesity be considered?

Cost of T2DM

Background

- Costs savings from avoidance of T2DM is model driver
- Committee concluded that EAG's approach – including UKPDS non-hospital costs and drug costs appropriate (which drug costs was not specified in draft guidance)

Company

- Costs from the UKPDS have been inflated by EAG incorrectly
- PSS index (reported in PSSRU) is standard practice and used in base case: costs in model for T2DM £803
- Also adds drug cost from Capehorn et al. £522 (average time since diagnosis 7 years)

EAG

- PSS index not appropriate – prefers NHS Cost Inflation Index which identifies appropriate measure for each item of spend across 4 categories to create overall inflation measure for the NHS
  - UKPDS non-inpatient T2DM cost, age 48, no complications inflated using NHSCII results in **gross** cost of £683 (vs company £803)
- Takes into account costs for obesity with no complications already in model (£233), removing these from costs associated with T2DM, resulting in **net** cost of T2DM management of £450
- Includes drug costs based on expected drugs intensification for newly diagnosed T2DM (£340 vs company £522)
- Scenarios also apply costs of microvascular complications from Capehorn

- Should costs for obesity with no complications already in the model be accounted for when determining costs associated with T2DM?
- Is the company's or EAGs inflation index and drug costs appropriate?

Summary of company and EAG and committee base case assumption differences (1)

Assumption	Company base case	EAG base case	Committee preferred assumptions
Cost of T2DM	• Gross cost T2DM without complications (UKPDS) inflated using P&P index (£803) • Drug costs from Capehorn et al (£522)	• Net costs T2DM without complications (UKPDS) inflated using NHS Cost Inflation Index (£450) • Drug costs modelled using UKPDS HbA1c evolution + NICE recommended drugs (£340)	• In line with EAG (Net costs T2DM without complications using NHS Cost Inflation Index (£450) with drug costs modelled with UKPDS HbA1c evolution + NICE recommended drugs • Note: DG not clear which drug costs to include
Long-term efficacy of tirzepatide	• Natural weight gain in only the diet and exercise arm from week 72	• Natural weight gain in both arms from week 72	• In line with EAG **plus** • Assuming tirzepatide stopping rates at 6 months • prediabetes reversal loss modelled to align with the approximate time in the model that baseline weight is regained in all arms

Summary of company, EAG and committee base case assumption differences (2)

Assumption	Company base case	EAG base case	Committee preferred assumptions
Distribution of BMI	Gamma distribution	Log- normal distribution	• Adjustment for BMI distribution in the model to reflect eligible population
Obesity management service	• Annual resource based on BMI from Ara et al. 2012: 4 GP visits, 8 nurse visits, 1 blood test • Applied to both arms for full time horizon	• NHSE proposed resource use while on tirzepatide • NHSE proposed resource use minus titration appointments for D&E for 2 years	• Range of scenarios to be used for decision making
Percentage needing psychological support	• Not included – *states no evidence that people on tirzepatide need more psychological support, so removes from both arms*	• In line with NHSE proposal (33%) – *results in higher costs for tirzepatide arm as D&E costs applied for 2 years*	• In line with EAG
Model cohort size	• 1000	• 20,000	• Not discussed

Cost-effectiveness results

vs diet and exercise

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Decision making framework

Committee decision making
What are committee preferred assumptions on the key issues? (see next slide)
What is the committee's preferred ICER threshold?
What is the committee's preferred ICER? (if this is a range, please state whether the committee want the lower, upper, or midpoint of range to be below threshold)
Is the ICER below preferred ICER threshold?
If yes, recommend for routine commissioning? (considering uncertainty, inequalities, innovation etc that might impact decision if close to threshold)

Decision making framework: key issues

Issues for decision making:
Inclusion of T2DM in recommendation (slide 14)
Assumption of indefinite treatment effect (slide 15-16)
Generalisability of SURMOUNT-1 population to probable BMI distribution in NHS practice (slide 19-20)
Impact of weight loss on reversing effects of long-term obesity (slide 21-22)
Cost estimates for T2DM (slide 23)

Company base case results: tirzepatide 15mg vs diet and exercise BMI ≥30 with at least one weight-related comorbidity (target population)

Treatment	Total Costs	Total QALYs	Incremental Costs	Incremental QALYs	ICER (Cost/QALY)
Company base case					
Diet and Exercise	£20,976	15.582			
Tirzepatide (15.0 mg)	£40,967	16.939	£19,991	1.357	14,735

Company subgroup results: tirzepatide 15mg vs diet and exercise BMI 30-34.9 with at least one weight-related comorbidity

Treatment	Total Costs	Total QALYs	Incremental Costs	Incremental QALYs	ICER (Cost/QALY)
Company base case					
Diet and Exercise	£17,816	16.196			
Tirzepatide (15.0 mg)	£38,242	17.068	£20,426	0.872	£23,425

Company scenario results: tirzepatide 15mg vs diet and exercise BMI ≥30 with at least one weight-related comorbidity

Company scenarios	ICER (Cost/QALY)
Company base case	**£14,735**
Obesity management services	
No costs in the diet and exercise arm but efficacy from SURMOUNT-1; NHSE-proposed resource use applied to tirzepatide arm only	£18,381
No costs and no efficacy in the diet and exercise arm; NHSE-proposed resource use in the tirzepatide arm	£14,289
NHSE-proposed resource use in diet and exercise arm without appointments specific to tirzepatide with SURMOUNT-1 efficacy; NHSE-proposed resource use in the tirzepatide arm	£14,943
Light-touch SURMOUNT-1 HCRU	£15,144
BMI distribution	
BMI sampling in line with IMPACT-O data	£19,717
Natural increase in BMI	
Constant annual increase after 10 years	£15,691
Constant annual increase after 20 years	£15,001
Residual risk	
Correction of EAG method for Haase scenario	£21,504

EAG base case analyses by subgroup: without Ara weight gain parameter

Tirzepatide 15mg vs diet and exercise support (includes EAG preferred assumptions)

No.	Population with EAG preferred assumptions	ICER (£/QALY)
1	Target group	£28,697
2	BMI 30-35	£37,151
3	BMI ≥ 35	£21,372
4	BMI ≥ 35, prediabetic	£19,504
5	BMI ≥ 35, prediabetic, high CVD risk	£20,689

EAG base case analyses by subgroup: with Ara weight gain parameter

Justification: Natural weight gain differs if you are diabetic or non-diabetic in Ara et al

No.	Population with EAG preferred assumptions	ICER (£/QALY)
1	Target group	£29,810
2	BMI 30-35	£38,601
3	BMI ≥ 35	£22,076
4	BMI ≥ 35, prediabetic	£20,398
5	BMI ≥ 35, prediabetic, high CVD risk	£21,553

Tirzepatide 15mg vs diet and exercise support (includes EAG preferred assumptions)

Scenarios on EAG base case: target population without Ara weight gain parameter (1)

Tirzepatide 15mg vs diet and exercise support

Scenario	ICER (£/QALY)
EAG base case	**£28,697**
BMI distributions from 2021 HSE with normal distribution	£29,243
BMI distributions from SURMOUNT-1 with gamma distribution	£25,512
BMI distributions sampling from SUMOUNT-1	£26,013
Waning of BMI effect of 2% annually from year 5 onwards	£34,231
Waning of the BMI effect of 2% annually from year 5 onwards with 15 year stopping rule	£32,489
Waning of the BMI effect of 2% annually from year 5 onwards with 25 year stopping rule	£33,178
Khunti with 61% adjustment for T2DM	£31,181
Khunti et al adjustment plus 79% OSA and 38% TKR adjustment	£31,904
Khunti et al adjustment plus OSA and TKR adjustment plus 33% adjustment for angina/MI	£31,963
No MDT (obesity management service) costs both arms	£23,173
No MDT (obesity management service) costs for diet and exercise and no clinical effects	£24,789
No annual weight gain on tirzepatide	£25,011

Scenarios on EAG base case: target population with Ara et al diabetic weight gain parameter (1)

Tirzepatide 15mg vs diet and exercise support

Scenario	ICER (£/QALY)
EAG base case	**£29,810**
BMI distributions from 2021 HSE with normal distribution	£30,529
BMI distributions from SURMOUNT-1 with gamma distribution	£26,233
BMI distributions sampling from SUMOUNT-1	£26,723
Waning of BMI effect of 2% annually from year 5 onwards	£36,228
Waning of the BMI effect of 2% annually from year 5 onwards with 15 year stopping rule	£34,013
Waning of the BMI effect of 2% annually from year 5 onwards with 25 year stopping rule	£34,715
Khunti with 61% adjustment for T2DM	£32,486
Khunti et al adjustment plus 79% OSA and 38% TKR adjustment	£33,220
Khunti et al adjustment plus OSA and TKR adjustment plus 33% adjustment for angina/MI	£33,283
No MDT costs both arms	£24,068
No MDT costs for diet and exercise and no clinical effects	£25,972
No annual weight gain on tirzepatide	£26,113

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Thank you.

Tirzepatide for managing overweight and obesity [ID6179]

Supplementary appendix

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Abbreviations and units

ASCVD: atherosclerotic cardiovascular disease

BMI: body mass index

CfB: change from baseline

CV(D): cardiovascular (disease)

GI: gastrointestinal

HDL: high-density lipoprotein

HRQoL: health-related quality of life

ICER: incremental cost effectiveness ratio

MDT: multi-disciplinary team

MI: myocardial infarction

NAFLD: non-alcoholic fatty liver disease

NMA: network meta-analysis

OAD: oral antidiabetic drug

OSA: obstructive sleep apnoea

QoL: quality of life

QW: once weekly

RCT: randomised controlled trial

SBP: systolic blood pressure

SD: standard deviation

SE: standard error

SmPC: summary of product characteristics

SWMS: specialist weight management service

T2DM: type 2 diabetes mellitus

TEAE: treatment emergent adverse events

UKPDS: UK Prospective Diabetes Study

All BMI measures are in mg/kg^2

 = model driver

 = impact on model not quantified

Tirzepatide (Mounjaro, Eli Lilly)

Technology details

Marketing authorisation (November 2023)	For weight management, including weight loss and weight maintenance, as an adjunct to a reduced-calorie diet and increased physical activity in adults with an initial BMI of: • ≥30 (obesity), or • ≥27 to <30 (overweight) in presence of at least 1 weight-related comorbid condition (e.g., hypertension, dyslipidaemia, OSA, CVD, prediabetes, or T2DM)
Related indication (NICE TA924)	Treatment of adults with insufficiently controlled T2DM only if: • Triple therapy is not effective or tolerated • BMI ≥ 35 and specific psychological or other medical problems associated with obesity or • BMI ≤ 35 and insulin therapy would have significant occupational limitations or weight loss would benefit other significant obesity related complications
Administration	Subcutaneous injection once weekly, using a pre-filled pen device Initiation: 2.5 mg once weekly; maintenance (after 4 weeks): 5mg once weekly; if needed, dose can be increased in 2.5 mg increments every 4 weeks up to 15 mg
Price	List price for 4-week supply: • 5 mg: £92.00 • 10 mg: £107.00 • 15 mg: £122.00

Equality considerations

- People with mental health disorders (especially those receiving atypical antipsychotics) may have increased risk of developing obesity but ability to access tirzepatide may be hindered by their mental health condition; people with mental health disorders were excluded from SURMOUNT-1
- People with disabilities are disproportionately affected by obesity but ability to access treatment may be adversely impacted by their disability
- Tirzepatide may be suitable for people with disabilities who are unable to provide consent or be eligible for bariatric surgery
- Cardiometabolic risk occurs at a lower BMI for people from South Asian, Chinese, other Asian, Middle Eastern, Black African or
  African-Caribbean family backgrounds, so lower BMI thresholds are a practical measure of overweight and obesity in these populations (thresholds are usually reduced by 2.5 to identify obesity status; NICE Clinical Guideline 189)
- Health inequalities lead to and exacerbate overweight and obesity, disproportionately affecting lower socio-economic communities

Inequity in treatment access

- Access to SWMS is inequitable across the country
- Office for Health Improvement and Disparities data (2022) suggests that tier 2 services are also not equitably distributed across the country or according to local need

King's obesity staging criteria

King's criteria is a scoring system which can capture health problems related to obesity and health benefits after weight loss

	Stage 0	Stage 1	Stage 2	Stage 3
Airway	Normal	Snoring	Sleep apnea require CPAP	Cor pulmonale
BMI	<30	30–35	35–50	>50
Cardiovascular	<25% risk	>25% risk	Heart disease	Heart failure
Diabetes	Normal	Impaired fasting glycemia	Type 2 diabetes	Uncontrolled type 2 diabetes
Economic	Normal	Suffered discrimination	Unemployed due to obesity	Requires financial support
Functional	Can manage 3 flights of stairs	Manage 1 or 2 flights of stairs	Manage <1 flight of stairs or requires walking aids	House bound
Gonadal	Normal	Irregular periods	PCOS/impotence	Infertility
Health status	Normal	Low mood or QoL	Moderate depression or poor QoL	Severe depression
Image	Normal	Does not like looking in mirror	Avoids mirrors/body image dysphoria	Severe eating disorder
Junction gastroesophagus	Normal	Heart burn	Esophagitis	Barrett esophagus
Kidney	Normal	Proteinuria	GFR < 60 mL/min	GFR < 30 mL/min
Liver	Normal	Raised LFT/NAFLD	NASH	Liver failure

Abbreviations: CPAP, continuous positive airway pressure; BMI, body mass index; PCOS, polycystic ovary syndrome; QoL, quality of life; GFR, glomerular filtration rate; LFT, liver function test; NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis.

Reproduced from Papamargaritis et al 2010

- Reproducible scoring system comprising 9 health domains : Airway, BMI, Cardiovascular. Diabetes, economic. fucntiional, gonodal, health status, image, junction gastroesophagus, kidney and liver
- King's criteria may shift focus of intervention from BMI to potential health gains in comorbidities and other aspects

The edmonton obesity staging criteria

Edmonton criteria is a staging system which may provide clinically relevant insight into health-related risk for those with obesity

- Proposed as an adjunct to BMI
- Classifies people with obesity into distinct groups based on their medical, psychological and functional health status.
- Stage 0 – no signs of obesity related risks
- Stage 1 - subclinical risk factors
- stages 2–4 are given in the presence of established obesity-related comorbidities.

Scenarios on EAG base case: target population without Ara weight gain parameter (2)

Tirzepatide 15mg vs diet and exercise support

Scenario	ICER (£/QALY)
EAG base case	**£28,697**
25% of microvascular complication costs (Capehorn et al.)	£28,118
50% of microvascular complication costs (Capehorn et al.)	£27,539
75% of microvascular complication costs (Capehorn et al.)	£26,960
100% of microvascular complication costs (Capehorn et al.)	£26,381
20% receive psychological support	£28,519
60% receive psychological support	£29,052
0% in BMI 30-35 group require SGLT2	--
Iyen weight gain parameter in both arms	£30,320

Scenarios on EAG base case: target population with Ara et al diabetic weight gain parameter (2)

Tirzepatide 15mg vs diet and exercise support

Scenario	ICER (£/QALY)
EAG base case	**£29,810**
25% of microvascular complication costs (Capehorn et al.)	£29,201
50% of microvascular complication costs (Capehorn et al.)	£28,593
75% of microvascular complication costs (Capehorn et al.)	£27,985
100% of microvascular complication costs (Capehorn et al.)	£27,377
20% receive psychological support	£29,625
60% receive psychological support	£30,179
Iyen weight gain parameter in both arms	£30,320
Tirz weight gain from week 221	£28,627