Cost-effectiveness of tirzepatide versus liraglutide (both adjunct to a reduced-calorie diet and increased physical activity) in patients with obesity or overweight from a UK perspective

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OBJECTIVE

- To determine the cost-effectiveness of tirzepatide (5 mg, 10 mg, 15 mg) as an adjunct to diet and exercise (D&E) compared to liraglutide (3 mg) as an adjunct to D&E in the following populations:
  - SURMOUNT-1 trial population (patients with a BMI ≥30 kg/m^2 [obesity], or with a BMI ≥27 kg/m^2 to <30 kg/m^2 with ≥1 obesity-related complication [overweight]).
  - Liraglutide's NICE recommended population (patients with a BMI of ≥35 kg/m^2 with non-diabetic hyperglycaemia and a high risk of CVD).

CONCLUSION

- At the UK WTP threshold of £20,000/QALY gained, the model estimated that tirzepatide as an adjunct to D&E is a cost-effective use of healthcare resources compared to liraglutide as an adjunct to D&E in both the SURMOUNT-1 trial population and liraglutide's NICE recommended population.
- All doses of tirzepatide were dominant (less costly, more effective) over liraglutide in the SURMOUNT-1 trial population.

BACKGROUND

- In the UK, the NHS spent £19.2 billion on overweight and obesity in 2021 alone, with wider total costs to the UK economy estimated at £97.9 billion, increasing to £109.4 billion per year by 2040.[1]
- Patients with obesity or overweight are at an increased risk of multiple comorbidities including CV and respiratory conditions among others.[2, 3] Effective obesity treatment is therefore essential for reducing patient morbidity and mortality, as well as to mitigate the significant economic impact of obesity.
- Tirzepatide as an adjunct to reduced-calorie diet and increased physical activity (referred to as D&E) has been approved by the MHRA in 2023 for weight management in adults with an initial BMI of ≥30 kg/m^2 (obesity), or ≥27 to <30 kg/m^2 with ≥1 weight-related comorbid condition (overweight).[4] This was the target population in this economic evaluation, hereafter referred to as the SURMOUNT-1 trial population.
- The comparator in this evaluation is liraglutide (3 mg), a GLP-1 receptor agonist licensed as an adjunct to D&E in the same approved population as tirzepatide.[5] However, liraglutide is recommended by NICE in a more restricted population (patients with a BMI of ≥35 kg/m^2 with non-diabetic hyperglycaemia and a high risk of CVD) and for use within SWMS (alongside D&E).[6] A subgroup analysis was therefore explored in liraglutide's NICE recommended population.

KEY RESULTS

- All doses of tirzepatide were estimated to be cost-effective versus liraglutide:
  - In the SURMOUNT-1 trial population, tirzepatide was dominant over liraglutide 3 mg with per patient cost savings of £8,151, £5,597, and £2,456 for tirzepatide 5, 10 and 15 mg, respectively (**Table 1**).
  - In the liraglutide's NICE recommended population, tirzepatide was associated with increased costs and increased QALYs versus liraglutide, corresponding to positive INHBs for all tirzepatide doses.
- The PSA estimated that under the UK WTP threshold (£20,000/QALY gained), tirzepatide was cost-effective in 96–100% of simulations compared to liraglutide in the SURMOUNT-1 trial population.
- All five obesity-related complications modelled were estimated to have lower incidence for patients taking tirzepatide compared to liraglutide (**Figure 1**). The estimated reductions in incidence were particularly high for knee replacements and T2DM, with decreases of up to 44% and 32%, respectively, depending on the tirzepatide dose.
- The cost-effectiveness results were driven by the observed comparative clinical outcomes for key risk factors including prediabetes reversal and weight loss (**Figure 2**). Weight-loss followed a linear rate of change from baseline to the latest data point in the NMA trials, remaining constant thereafter.

Methods

Model Approach

- An individual patient simulation evaluated the costs and long-term clinical outcomes of once-weekly tirzepatide treatment versus liraglutide (both adjunct to D&E) over a lifetime horizon to capture the long-term impact of obesity on clinical events and complications.
- The model adopted a UK healthcare and Personal Social Services perspective.
- The pivotal Phase 3 SURMOUNT-1 trial was used as the base case target population.[7] A 3.5% discount rate was applied for costs and effects.
- Impact of the intervention was measured by tracking risk factors including patient weight, systolic blood pressure, high-density lipoprotein and total cholesterol over time and assessing their effect on various health outcomes.
- Key model assumptions:
  - Tirzepatide was administered indefinitely, except when a patient discontinued due to AEs or lack of response. The same was true for liraglutide, however, an additional two-year stopping rule for liraglutide was applied when analysing liraglutide's NICE recommended population to reflect the maximum treatment duration for SWMS.
  - Surrogate endpoints were modelled by assuming a linear rate of change from baseline to the most recent point of data availability from the trials in the NMA (72 weeks for tirzepatide; 52 weeks for liraglutide in the trial population, 56 weeks for liraglutide in the subgroup population), remaining constant after this timepoint.[7–10]
  - In both treatment arms, surrogate endpoints reverted to the corresponding levels of a hypothetical D&E arm at a linear rate over three years following discontinuation.

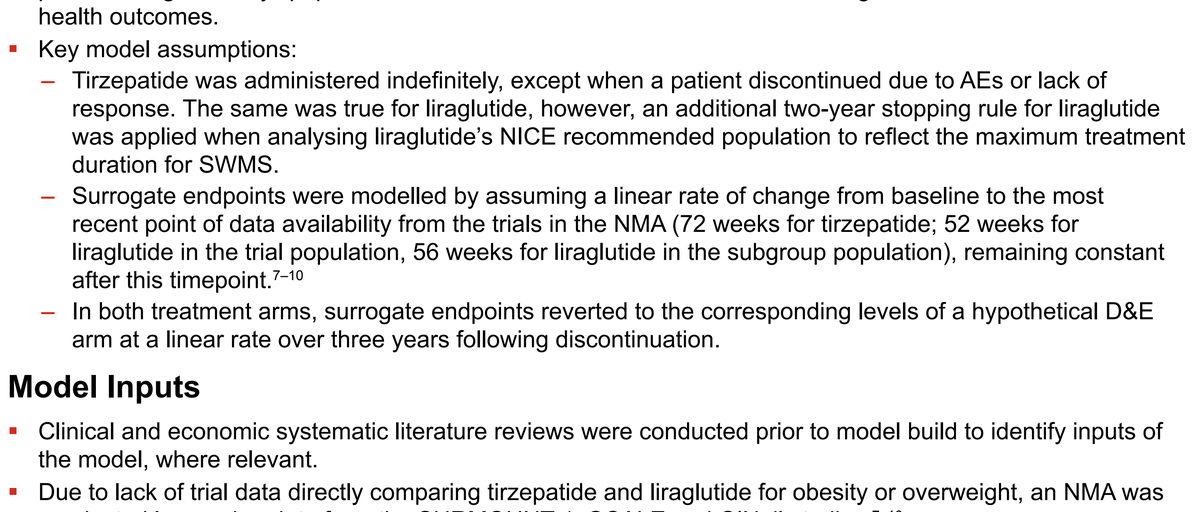
Model Inputs

- Clinical and economic systematic literature reviews were conducted prior to model build to identify inputs of the model, where relevant.
- Due to lack of trial data directly comparing tirzepatide and liraglutide for obesity or overweight, an NMA was conducted leveraging data from the SURMOUNT-1, SCALE and O'Neil studies.[7–10]
- Based on data availability, the NMA was conducted using the efficacy estimand in the SURMOUNT-1 trial population and the treatment-regimen estimand in liraglutide's NICE recommended population.
- Published risk equations—selected based on their external validity, sample size, use in previous economic models, and data recency—were used to determine the incidence of clinical events and complications.[11–17]
- Utility values captured the impact on quality of life of BMI, long-term obesity-related complications, adverse events and other acute clinical events.[18–21]
- Aligned to the model perspective, costs included in the model were healthcare system costs, including treatment acquisition and administration, obesity monitoring and multidisciplinary team resource use, clinical events, and adverse event management costs.
  - An additional SWMS cost (£1,796 per patient per year) was applied to liraglutide when analysing liraglutide's NICE recommended population to reflect its reimbursement criteria.[22]

Model Outputs

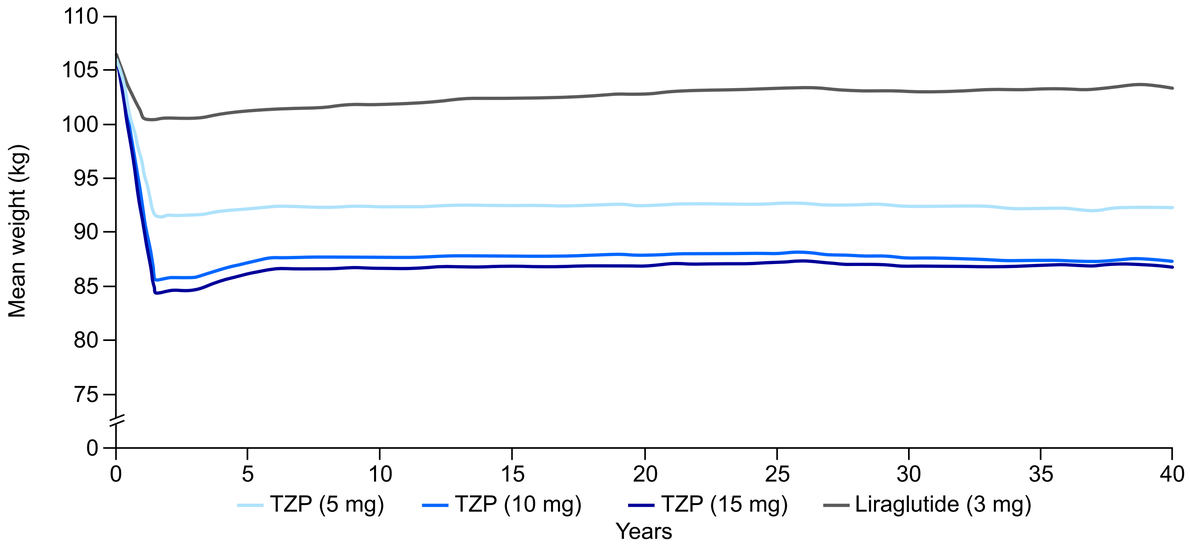
- Primary model outputs were QALYs, costs, INHB and ICERs (cost/QALY gained) (**Table 1**).
- Sensitivity analyses were performed to evaluate the robustness of the results, with a PSA conducted to assess the stability of the model outcomes under combined uncertainty in parameter values.
- Secondary model outputs were key health outcomes such as the incidence of T2DM and CV complications (**Figure 1**).

Figure 1: Incidence of clinical events predicted by the cost-effectiveness model



All interventions are adjunct to D&E. Results presented are from the SURMOUNT-1 trial population (patients with a BMI ≥30 kg/m^2, or BMI ≥27 kg/m^2 to <30 kg/m^2 + ≥1 obesity-related complication). The percentages displayed on the graph represent the average reduction in the incidence of events across tirzepatide doses vs. liraglutide. In this figure, [a]CVD refers to a combination of angina, stroke and MI.
[b]Previously termed NAFLD.

Figure 2: Mean weight trajectory over time



Results presented are from the SURMOUNT-1 trial population analysis (patients with a BMI ≥30 kg/m^2, or BMI ≥27 kg/m^2 to <30 kg/m^2 + ≥1 obesity-related complication). All interventions are adjunct to D&E.

Table 1: Discounted deterministic cost-effectiveness results

	Treatment comparison (versus liraglutide 3 mg)					
	SURMOUNT-1 trial population[a]			Liraglutide's NICE recommended population[b]		
	TZP 5 mg	TZP 10 mg	TZP 15 mg	TZP 5 mg	TZP 10 mg	TZP 15 mg
Model outcome						
Inc costs	-£8,151	-£5,597	-£2,456	£4,500	£6,359	£9,144
Inc QALYs	0.624	0.849	0.880	0.833	1.015	1.163
ICER (cost/QALY gained)	**TZP dominant[c]**	**TZP dominant[c]**	**TZP dominant[c]**	**£5,401**	**£6,265**	**£7,864**
INHB[d]	**1.031**	**1.129**	**1.003**	**0.608**	**0.697**	**0.706**

All interventions are adjunct to D&E. [a]Patients with BMI ≥30 kg/m^2 or BMI ≥27 kg/m^2 to <30 kg/m^2 + ≥1 obesity-related complication; [b]Patients with a BMI of ≥35 kg/m^2 with non-diabetic hyperglycaemia and a high risk of CVD; [c]Less costly and more effective; [d]A positive INHB implies that the health benefits gained outweigh the additional costs incurred by the intervention, at a WTP threshold of £20,000/QALY gained.

Abbreviations: BMI: body mass index; **CV:** cardiovascular; **CVD:** cardiovascular disease; **D&E:** diet & exercise; **GLP-1:** glucagon-like peptide-1; **ICER:** incremental cost-effectiveness ratio; **Inc:** incremental; **INHB:** incremental net health benefit; **MAFLD:** metabolic dysfunction-associated fatty liver disease; **MHRA:** Medicines and Healthcare products Regulatroy Agency; **MI:** myocardial infarction; **NAFLD:** non-alcoholic fatty liver disease; **NHS:** National Health Service; **NICE:** National Institute for Health and Care Excellence; **NMA:** network meta-analysis; **OSA:** obstructive sleep apnoea; **QALY:** quality-adjusted life year; **PSA:** probabilistic sensitivity analysis; **SWMS:** specialist weight management service; **T2DM:** type 2 diabetes mellitus; **TZP:** tirzepatide; **UK:** United Kingdom; **USA:** United States of America; **WTP:** willingness-to-pay.

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References: 1. Institute for Global Change. Unhealthy Numbers: The Rising Cost of Obesity in the UK. Last accessed: June 2024. **2.** Fruh SM. J Am Assoc Nurse Pract 2017;29:S3-s14. **3.** NICE. Clinical Knowledge Summary Obesity. Volume 2024. **4.** MHRA. Mounjaro 15 mg solution for injection in pre-filled pen. 2023. **5.** MHRA. Saxenda 6mg/ml solution for injection in pre-filled pen. 2021 **6.** NICE. TA664. **7.** Jastreboff et al. N Engl J Med. 2022. **8.** Pi-Sunyer X et al. N Eng J Med 2015;373:11–22. **9.** O'Neil PM et al. Lancet. 2018; 392(10148):637–49. **10.** Ciudin et al. Efficacy and safety of tirzepatide, liraglutide and semaglutide in patients with obesity: A Bayesian network meta-analysis of RCTs. Presented at ISPOR EU 2024. Poster #CO113. **11.** Hippisley-Cox J et al. BMJ 2017;359. **12.** Hippisley-Cox J et al. BMJ 2017;357. **13.** D'Agostino RB et al. Am Heart J 2000;139:272–281. **14.** Hayes AJ et al. Diabetologia 2013;56:1925–1933. **15.** Wendelboe AM et al. Am J Prev Med. 2003;25:290–295. **16.** Erridge S et al. Obes Surg. 2021;31:1986–1993. **17.** Loomis AK et al. J Clin Endocrinol Metab. 2016;101:945–952. **18.** Sæltoft F et al. Qual Life Res 2009;18:1293–1299. **19.** Sullivan PW et al. MDM 2011;31:800–804. **20.** Campbell J et al. Am J Manag Care 2010;16:e174–87. **21.** Kim N et al. J Manag Care Spec 2022; 28:740–752. **22.** NICE. Early Value Assessment GID-HTE10007.