Cost-effectiveness of tirzepatide as an adjunct to reduced-calorie diet and increased physical activity versus diet and exercise alone for patients with obesity or overweight from the UK perspective

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Matthew Capehorn[1], Marc Evans[2], Erin Johansson[3], Jean-Baptiste Briere[3], Alun Davies[3], Jerome Evans[3], Fiona Godbeer[3], Naomi van Hest[4], Georgina Cotterill[5], Keith Tolley[6]

[1]Rotherham Institute for Obesity, Rotherham, UK; [2]University Hospital Llandough, Penarth, Cardiff, UK; [3]Eli Lilly and Company, Indianapolis, USA; [4]Costello Medical, Bristol, United Kingdom; [5]Costello Medical, London, United Kingdom; [6]Tolley Health Economics Ltd, Derbyshire, UK.

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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 D&E alone in 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) from a UK healthcare and Personal Social Services perspective.

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 D&E alone in patients with a BMI ≥30 kg/m^2, or with a BMI ≥27 kg/m^2 to <30 kg/m^2 with ≥1 obesity-related complication, driven by lower incidences of all obesity-related complications modelled.
- Sensitivity and scenario analyses reinforce the stability of the results across a range of tested variables and scenarios.

BACKGROUND

- Obesity is a multifaceted, long-term health challenge that is expected to affect 7 in 10 people in the UK by 2040.[1]
- Patients with obesity face an increased risk of multiple comorbidities including CV, respiratory, musculoskeletal, and metabolic conditions.[2, 3]
- The economic burden of obesity in the UK is substantial: the NHS spent an estimated £19.2 billion on overweight and obesity in 2021 with wider society costs estimated at £97.9 billion.[4]
- Obesity treatment is therefore crucial, not only for the morbidity and mortality of patients but for alleviating the considerable economic impact associated with obesity in the UK.
- Tirzepatide is indicated as an adjunct to a reduced-calorie diet and increased physical activity (hereafter referred to as D&E) in patients with a BMI of ≥30 kg/m², or ≥27 to <30 kg/m² and ≥1 weight-related comorbid condition by the MHRA and recommended for reimbursement by the Scottish Medicines Consortium for weight management in a subset of these patients.[5, 6]

KEY RESULTS

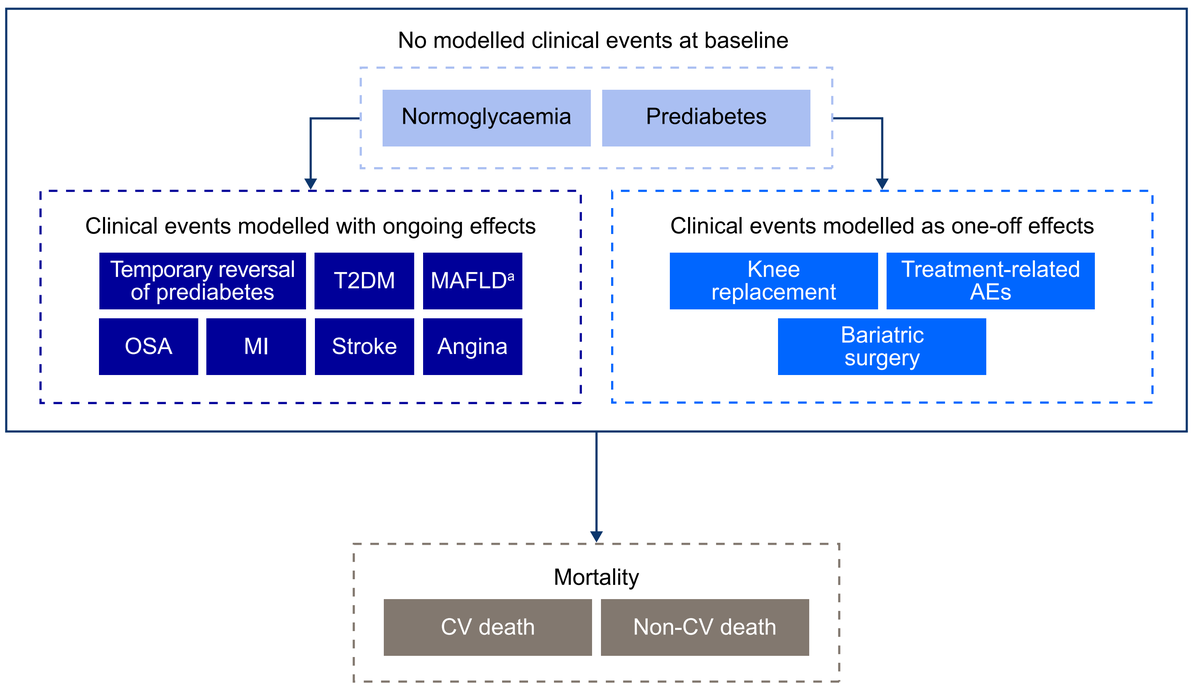
- All doses of tirzepatide were estimated to be cost-effective at the UK WTP threshold of £20,000/QALY gained (**Table 1**), with greater total costs and improved QALYs.
- The ICER stayed below the £20,000/QALY gained WTP threshold in all scenarios except one, which used an alternative risk equation for T2DM development. This particular equation, along with REGARDS (**Table 2**), were based on data from a smaller, US population, making them less representative of the UK perspective in this model compared to the base case (QDiabetes). Other key scenarios are detailed in **Table 2**.
- All obesity-related complications modelled were estimated to decrease for patients receiving tirzepatide (**Figure 2**).
- The probabilistic sensitivity analysis estimated that at the UK WTP threshold, all doses of tirzepatide were cost-effective versus D&E alone in 100% of simulations based on 1,000 patients.
- In the deterministic sensitivity analysis, tirzepatide remained below the £20,000/QALY gained WTP threshold for all pairwise comparisons versus D&E alone.

Methods

Model Approach

- As shown in **Figure 1**, an individual patient simulation was developed to evaluate the costs and long-term clinical outcomes of once-weekly tirzepatide treatment adjunct to D&E versus D&E alone over a lifetime horizon and from a UK healthcare and Personal Social Services perspective to capture the long-term impact of obesity on clinical events and complications.
- 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 obesity-related complications, healthcare resource use, health-related quality of life, and mortality.
- Patients could discontinue tirzepatide due to adverse events or lack of response.
- Assumptions were made regarding treatment efficacy beyond the end of the 72-week SURMOUNT-1 trial follow-up, with surrogate endpoints for patients on treatment held constant (except for weight in the D&E arm which increased in line with natural trajectories), while patients who discontinued treatment reverted to the corresponding levels of the D&E arm at a linear rate over the three years following discontinuation.

Figure 1: Model structure



[a]Previously termed NAFLD.

Model Inputs

- Clinical and economic systematic literature reviews were conducted prior to model build to identify inputs for the model, where relevant.
- Treatment efficacy of all tirzepatide doses and D&E were sourced from the SURMOUNT-1 efficacy estimand.[7]
- 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.[8–14]
- Aligned to the model perspective, costs included in the model were healthcare system costs, including treatment acquisition and administration, obesity monitoring and MDT resource use, clinical events, and adverse event management costs.
- Utility values captured the impact on quality of life of BMI, long-term obesity-related complications, adverse events and other acute clinical events.[15–18]

Model Outputs

- Primary model outputs were ICERs (cost/QALY gained), costs and QALYs (**Table 1**). Secondary model outputs were key health outcomes such as the incidence of T2DM and CV complications (**Figure 2**).
- Uncertainty was assessed through scenario analyses (e.g. with alternative risk equations and assumptions; **Table 2**) and sensitivity analyses to explore the robustness of the results.
- The probabilistic sensitivity analysis assessed the stability of the model results to combined uncertainty in parameter values, whilst the deterministic sensitivity analysis determined the key inputs influencing the results by adjusting their values by their upper and lower 95% CI, or by applying a 20% base variation from the mean value if CIs or SE were not reported.

Table 1: Discounted deterministic cost-effectiveness results

	Treatment comparison (versus D&E alone)		
	TZP 5 mg	**TZP 10 mg**	**TZP 15 mg**
Model outcome			
Inc costs	£14,238	£16,844	£20,115
Inc QALYs	1.000	1.221	1.272
ICER (cost/QALY gained)	**£14,233**	**£13,792**	**£15,819**

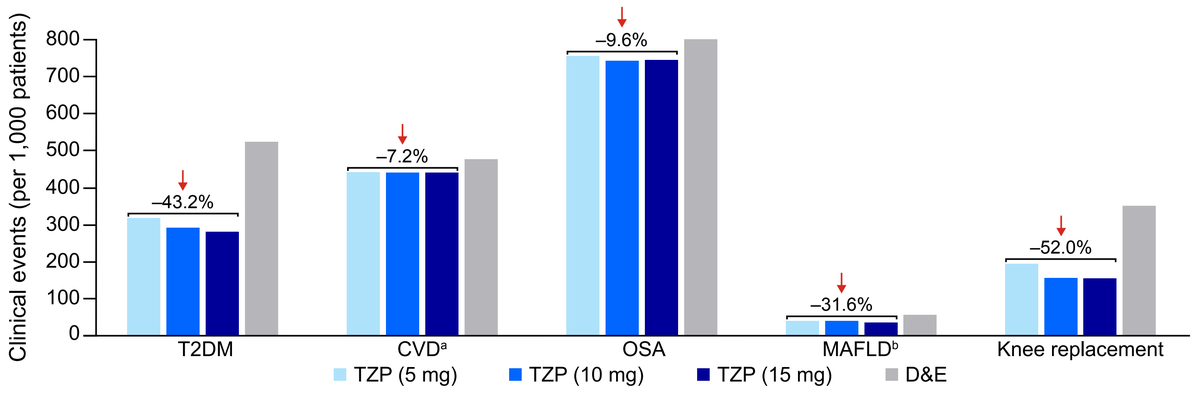
All doses of tirzepatide adjunct to D&E.

Table 2: Scenario analysis results (ICER)

			Treatment comparison (versus D&E alone)		
Variable	**Base case**	**Scenario**	**TZP 5 mg**	**TZP 10 mg**	**TZP 15 mg**
Base case			£14,233	£13,792	£15,819
Time of prediabetes reversal for D&E	4 Weeks	24 Weeks	£14,215	£13,776	£15,806
Apply discontinuation due to adverse events	3 Years only	Indefinitely	£14,717	£13,591	£15,868
Efficacy waning period post-discontinuation	3 Years	2 Years	£14,279	£13,838	£15,863
Risk equation for development of T2DM	QDiabetes[8]	REGARDS[19]	£18,607	£17,458	£19,805
Risk equation for development of T2DM	QDiabetes[8]	Framingham Offspring Study[20]	£20,263	£18,969	£21,109
Risk equation for initial CVD event	QRisk3[9]	Framingham Heart Study[21]	£14,071	£13,917	£16,043

All doses of tirzepatide are adjunct to D&E. All values represent the ICER (cost/QALY) compared to D&E alone.

Figure 2: Incidence of clinical events predicted by the cost-effectiveness model



All doses of tirzepatide are adjunct to D&E. The percentages displayed on the graph represent the average reduction in the incidence of events across tirzepatide doses versus D&E alone. [a]CVD refers to a combination of angina, stroke and MI. [b]Previously termed NAFLD.

Abbreviations: AE: adverse event; **BMI:** body mass index; **CI:** confidence interval; **CV:** cardiovascular; **CVD:** cardiovascular disease; **D&E:** diet and exercise; **ICER:** incremental cost-effectiveness ratio; **Inc:** incremental; **MAFLD:** metabolic dysfunction-associated fatty liver disease; **MDT:** multidisciplinary team; **MHRA:** Medicines and Healthcare products Regulatory Agency; **MI**: myocardial infarction; **NAFLD:** non-alcoholic fatty liver disease; **NHS:** National Health Service; **OSA:** obstructive sleep apnoea; Personal Social Services; **QALY:** quality-adjusted life year; **SE:** standard error; **TZP:** tirzepatide; **T2DM:** type 2 diabetes mellitus; **UK:** United Kingdom; **US:** United States; **USA:** United States of America; **WTP:** willingness-to-pay.

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