

Assessing the cost-effectiveness of semaglutide 2.4 mg in the management of people with obesity and knee osteoarthritis in the UK

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Mafalda Ramos¹; Inger Smith²; Karthik Ramakrishnan³; Mark Lamotte¹

Aim

This study assessed the cost-effectiveness of subcutaneous (SC) semaglutide 2.4 mg with diet and exercise (D&E) versus D&E alone in the management of individuals with obesity and knee osteoarthritis in the UK using data from the STEP 9 study.

Introduction

- Knee osteoarthritis (KneeOA) is the most prevalent form of osteoarthritis and is a well-known complication of obesity.¹
- Guidelines recommend weight loss to alleviate KneeOA symptoms and prevent disease worsening.²
- Semaglutide, a GLP-1 receptor agonist approved for obesity, was evaluated in patients with obesity + KneeOA in the STEP 9 study and showed a significant benefit in reducing KneeOA pain symptoms and weight loss.³

Methods

- The Core Obesity Model (COM), a well established and validated Markov cohort model was used to conduct the analyses^{4,5}. The model estimates the cost-effectiveness of interventions on the basis of increased weight loss and reduction of obesity related complications.
- The COM was adapted, sourcing utilities dependent on the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores specific to people with KneeOA from the published Osteoarthritis Policy model (OAPoL)⁶. In a scenario analysis, the OAPoL utilities were re-estimated using STEP 9 trial data using an SF-36 to EQ-5D-3L utility mapping algorithm.⁷
- Several equations to predict the risk of total knee replacement (TKR) were added to the COM: 1) Pharmetrics Plus derived (BMI driven)⁸; 2) Australian real-world data (BMI driven)⁹; 3) WOMAC score change driven¹⁰. In the base case the Wendelboe et al 2003 equation (BMI driven) was used¹¹.
- The time horizon was 40 years.
- The COM was populated with baseline characteristics and treatment efficacy from STEP 9³. Starting age and BMI in the model were 56 years and 40.3 kg/m², respectively (Table 1).
- At 68 weeks, semaglutide plus D&E and D&E alone decreased WOMAC score with 8.3 and 5.5 points, and decreased BMI by 13.7% and 3.2%, respectively (Table 2).
- Treatment duration in the base case was 20 years for SC semaglutide 2.4 mg and 2 years for D&E. The latter to allow for natural progression.
- It was assumed the treatment effect on BMI was maintained over the treatment duration. After stopping treatment, a catch-up weight gain is assumed based on the STEP-1 extension trial.¹² Further, a natural annual progression of BMI of 0.1 kg/m² was assumed until the age of 66 years after which BMI decreases with 0.1 kg/m² per year.
- UK costs were applied from a published source¹³.
- The NHS perspective was considered, with a willingness-to-pay (WTP) threshold of £20,000/QALY to establish cost-effectiveness.

Table 1: Baseline characteristics in STEP 9

	Mean	SD
Age	56	10
BMI (kg/m ²)	40.3	7.3
SBP (mmHg)	132	15
Total cholesterol (mg/dL)	183.1	20
HDL-cholesterol (mg/dL)	46.3	25
Triglycerides (mg/dL)	138.43	45.8
Prop. smokers (current smoker)	8.40%	
Prop. Females	81.60%	
Prop. on lipid-lowering drug	20.90%	
Prop. on antihypertensive medication	48.40%	
Prop. with high blood pressure	51.80%	
History of ACS/stroke	1.8%	
WOMAC pain score	14.18	3.2

Abbreviations: ACS: acute coronary syndrome; BMI: body mass index; D&E: diet and exercise; HDL: high density lipoprotein; SBP: systolic blood pressure; SD: standard deviation; SE: standard error; T2D: type 2 diabetes; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index; prop: proportion

- Discount rates of 3.5% were applied annually to both costs and outcomes.
- Sensitivity analyses (SA) were conducted, along with several scenario analyses.

Table 2: Treatment efficacy (treatment policy estimand)

	SC semaglutide 2.4 mg		D&E	
	Mean	SE	Mean	SE
BMI (%)	-13.71	0.49	-3.22	0.70
SBP (mmHg)	-6.88	0	-1.22	1.43
WOMAC pain score	-8.3	0.33%	-5.5	0.49

Abbreviations: BMI: body mass index; D&E: diet and exercise; SBP: systolic blood pressure; SE: standard error; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index

Results

- In the D&E arm, approximately 30% of patients underwent knee replacement. Semaglutide reduced this cumulative incidence by 6%.
- The incremental cost per QALY was 11,910GBP/QALY, gained.

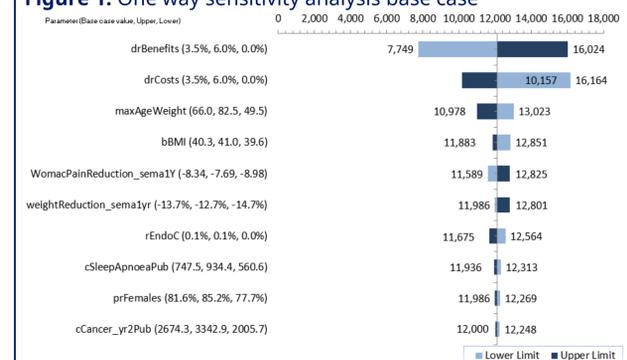
Table 3: Base case outcomes

	SC semaglutide 2.4 mg	D&E	Difference
<i>Cumulative incidence</i>			
Knee replacement (%)	24.37	30.57	-6.20
<i>Cost-effectiveness</i>			
Total costs (£)	44,306	21,198	23,108
Cost of knee replacement (£)	1,266	1,723	457
Total QALYs	11.81	9.86	1.96
Total LYs	15.84	14.85	0.99
ICER (cost/QALY)	11,873		
Net monetary benefit (£)	15,817		
ICER (cost/LY)	23,459		

Abbreviations: D&E: diet and exercise; GBP: Great Britain Pound; ICER: incremental cost-effectiveness ratio; LY: life years; QALY: quality adjusted life years

- Results from different scenario analyses are presented in Table 4.
- Three scenarios (Scenario 3-5) resulted in a similar or improved incremental cost-utility ratio (ICER) versus the base case:
 - Scenario 4: Note that this scenario yields a quite high number of knee replacement.
 - Scenario 5: This scenario is producing the best ICER, due to a higher incremental QALY from higher utility difference between patients on semaglutide and D&E, respectively.
- The highest ICERs was obtained in scenario 1. Here, treatment duration was 2 years in both treatment arms. This scenario yielded a higher ICER value due to reduced effect of semaglutide in the prevention of TKR and other obesity-related complications.

Figure 1: One way sensitivity analysis base case



Abbreviations: dr: discount rate; BMI: body mass index; c: cost; D_E: diet and exercise; HDL: high density lipoprotein; pr: probability; T2DM: type 2 diabetes; NGT: normal glucose tolerance; TIA: transient ischaemic attack

Definitions: drBenefits: discount rate on health outcomes; drBenefits: discount rate on costs; maxAgeWeight: the maximum age to which BMI is increasing; bBMI: baseline BMI; WomacPainReduction_sema: decrease in WOMAC pain score versus baseline in semaglutide arm; weightReduction_sema1yr: weight reduction with semaglutide at 1 year; rEndoC: risk of endometrial cancer; c SleepApnoeaPub: cost of sleep apnoea from the NHS perspective; prFemales: the proportion of females starting the analysis; cCancer_yr2Pub: subsequent year cost of cancer from the NHS perspective

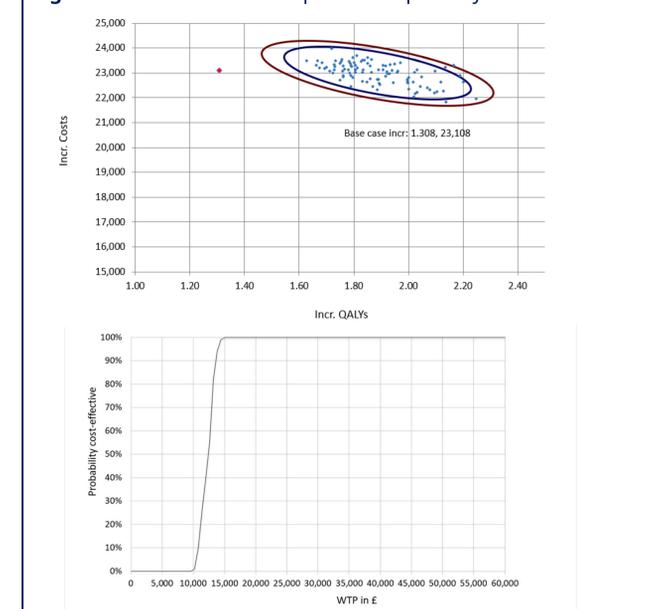
Table 4: Scenario analysis

	SC semaglutide 2.4 mg			D&E			ICER
	Total costs (£)	QALY	TKR (%)	Total costs (£)	QALY	TKR (%)	
<i>Base case</i>	44,306	11.81	24.37	21,198	9.86	30.57	11,873
Scenario 1: 2-year treatment duration in semaglutide arm	24,366	9.97	30.32	21,198	9.86	30.57	22,664
Scenario 2: using Chen risk of TKR	44,750	11.73	31.41	21,534	9.80	35.48	12,021
Scenario 3: using WOMAC driven risk of TKR	43,822	11.79	13.73	20,513	9.83	17.20	11,880
Scenario 4: using Pharmetrics®-Plus risk of TKR	44,960	11.71	35.45	21,789	9.77	40.37	11,976
Scenario 5: using OAPoL utilities based on STEP-9	44,306	11.69	24.37	21,198	8.91	30.57	8,285
Scenario 6: no impact on ORC other than TKR	38,053	12.74	27.71	12,049	10.99	35.07	14,813

Abbreviations: BMI: body mass index; CVD: cardiovascular disease D&E: diet and exercise; ICER: incremental cost-effectiveness ratio; ORC: obesity-related complications (cancer, CVD, prediabetes reversal, lipid levels, development of type 2 diabetes, sleep apnoea); QALY: quality adjusted life years TKR: Total Knee Replacement

- Scenario 6 shows that ignoring the treatment effect on important co-morbidities (such as CVD, cancers, prediabetes, hyperlipidaemia or sleep apnoea) has a negative impact on the ICER, while remaining cost-effective.
- The SA revealed that the discount rate on benefits and costs are the most sensitive factor (Figure 1). This due to delaying obesity-related complications such as TKR. Other parameters only have a small impact on the outcomes.
- The PSA shows that all simulations fell in the north-east quadrant (i.e. higher cost, higher QALY) of the cost-effectiveness plane with 100% of the simulations with an ICER under the WTP threshold (Figure 2).

Figure 2: Cost-effectiveness plane/acceptability curve base



Abbreviations: Incr: incremental; QALY: quality adjusted life year, WTP: willingness to pay

Discussion

- The study duration of the STEP 9 trial was 68 weeks. This is too short to observe differences in hard outcomes such as the risk of TKR
 - As such, changes in BMI were applied using different risk equations to predict long-term risk of TKR
 - The Pharmetric Plus derived risk equation resulted in the highest risk of TKR events
- KneeOA based EQ-5D utilities was not available in STEP-9.
 - As such, published evidence on utilities based on changes in WOMAC pain scores was used. These were further updated using STEP 9 data.
- The COM is a cohort model, not a patient level model, hence making it difficult to model patient heterogeneity, complex interaction between patient characteristics and outcomes.

Conclusion

Treatment with semaglutide and D&E can be considered cost-effective versus D&E alone in people with obesity and KneeOA in the UK for a WTP threshold of 20,000GBP/QALY gained.

References

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