

# Assessing the cost-effectiveness of subcutaneous semaglutide 2.4mg in the management of individuals with obesity and pre-diabetes in England

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## Aim

- The aim of this study was to assess the cost-effectiveness of semaglutide plus diet and exercise (D&E) compared with D&E alone in individuals with obesity and pre-diabetes in the UK based on the STEP 10 trial.

## Introduction

- Prediabetes and type 2 diabetes (T2D) are more prevalent amongst people living with obesity (PwO)<sup>1</sup>.
- T2D and obesity increase the risk of cardiovascular disease<sup>2</sup>.
- In the STEP clinical development program, once-weekly subcutaneous semaglutide (2.4mg) reduced body weight by 10-15% and reversed prediabetes in about 80% of patients.
- In the STEP 10<sup>3</sup> study the reversal of prediabetes and change in body weight were assessed at 52 weeks.

## Methods

- The Core Obesity Model (COM), a well established and validated Markov cohort model was used to conduct the analyses<sup>4,5</sup>.
- The risk of developing weight-related complications depends on age, body mass index (BMI), glycaemic status (categorical), blood pressure and lipid profile, and is predicted by published risk equations (QDiabetes, QRisk3, Framingham, UKPDS82).
- The cycle length is 3 months in the first year, and annual after the first year.
- The time horizon was 40 years.
- The COM was populated with baseline characteristics and treatment efficacy from STEP-10<sup>1</sup>.
- Baseline age and BMI were 53 (SE:11) years and 40.1 (6.9) kg/m<sup>2</sup> (Table 1).
- At 52 weeks, semaglutide plus D&E and D&E alone reversed prediabetes in 80% and 12% of patients, and decreased body weight by 13.9% and 2.7%, respectively (Table 2).
- Treatment duration in the base case was 20 years for sc semaglutide 2.4 mg and for D&E alone.
- It is assumed that treatment effect on BMI is maintained over the treatment duration.
- Default COM UK costs and utilities were applied<sup>6</sup>.
- The perspective of the NHS was considered using annual discounting rates of 3.5% on costs and outcomes.
- Several scenario analyses were performed: subgroups with different baseline BMI, number of comorbidities, proportions of prediabetes; different treatment durations; individuals losing ≥5% of body weight after 20 weeks (responders); different cardiovascular disease (CVD) risk equations.
- OWSA and PSA were conducted.<sup>6</sup>

Table 1: Baseline characteristics in STEP 10

	Mean	SD
Age	53	11
BMI (kg/m <sup>2</sup> )	40.1	6.9
SBP (mmHg)	131	15
Total cholesterol (mg/dL)	183.1	20
HDL-cholesterol (mg/dL)	46.3	25
Triglycerides (mg/dL)	138.43	45.8
Proportion smokers (current smoker)	15.90%	
Proportion females	71.00%	
Proportion on lipid-lowering drug	34.30%	
Proportion on antihypertensive medication	85%	
Proportion with high blood pressure	53.60%	
Proportion w pre-T2D	85.02%	
Proportion w T2D	0.97%	
History of ACS/stroke	4.3%	
HbA1c- Baseline non T2D patients	5.9%	

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

Table 2: Treatment efficacy using treatment policy estimand

	sc semaglutide 2.4 mg		D&E	
	Mean	SE	Mean	SE
BMI (%)	-13.90	0.70	-2.70	0.60
SBP (mmHg)	-8.76	1.06	-0.96	1.43
TC (mg/dL)	-10.47	2.9	0.16	0.49
HDL (mg/dL)	0.84	0.78	-0.59	0.93
HbA1c	-0.38%	0.00%	-0.07%	0.0%
Prediabetes reversal (%)	80.17%	3.70%	11.67%	4.14%

Abbreviations: BMI: body mass index; D&E: diet and exercise; HDL: high density lipoprotein; SBP: systolic blood pressure; SE: standard error, TC: Total cholesterol

## Results

- Treating individuals with obesity and prediabetes with sc semaglutide 2.4 mg and D&E for 20 years extends life expectancy with 1.68 years compared to D&E alone (undiscounted).
- It reduces the number of CVD events, heart failure hospitalisations and total knee replacements (Table 3).
- The total cost with semaglutide 2.4 mg is almost double the total cost of D&E (42,849GBP vs 23,458GBP; difference:19,391) but also 1.105 QALY are gained compared to D&E alone. The resulting ICER is 17,547GBP/QALY gained, well under the willingness to pay (WTP) threshold of 20,000GBP/QALY applied by NICE

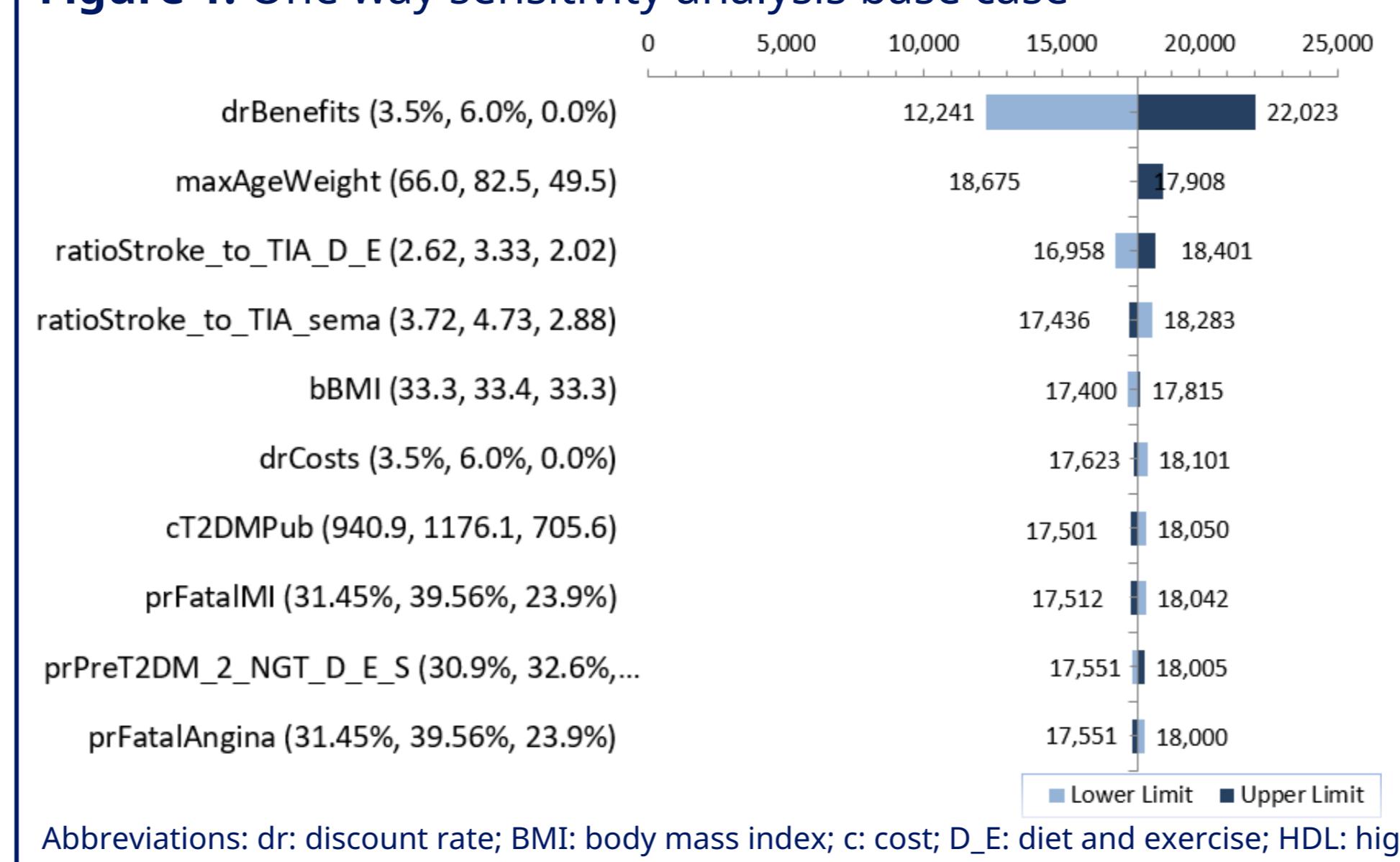
Table 3: Base case outcomes

	sc semaglutide 2.4 mg	D&E	Φ
CI - ACS-events	47.3%	52.5%	-5.2%
CI - Stroke or TIA events	20.0%	20.6%	-0.6%
CI- Knee replacement	24.5%	29.2%	-4.7%
CI- Heart Failure hospitalisation	2.1%	2.2%	-0.1%
<i>Cost-effectiveness</i>			
Total costs	42,849	23,458	19,391
Total QALY (undiscounted)	20.68	18.72	1.96
Total QALY (discounted)	13.62	12.52	1.105
Total LY (undiscounted)	25.33	23.65	1.68
Total LY (discounted)	16.50	15.68	0.827
ICER (Cost per QALY)	17,547		
Net Monetary Benefit (QALY)	2,711		
ICER (Cost per LY)	23,452		

Abbreviations: ACS: acute coronary syndrome; D&E: diet and exercise; ICER: incremental cost-effectiveness ratio; LY: life years; TIA: Transient Ischaemic Attack; QALY: quality adjusted life years; Φ: Difference; CI: Cumulative incidence

- The results of the different scenario analysis are reported in Table 4.
- The ICER improves with shorter treatment durations.
- Removing the development of weight-related cancer increases the ICER by 3,300GBP, slightly above the WTP.
- Replacing the proportion of individuals that reverse to NGT measured in STEP 10 (11.7%) by the value retrieved in STEP 1 (39.5%), increases the ICER by 2,000GBP, still under the WTP of 20,000GBP/QALY.
- The OWSA revealed that the discount rate on benefits is the most sensitive factor (Figure 1). Other parameters only have a small impact on the outcomes.
- All simulations fall in the north-east quadrant (higher cost, higher QALY) of the cost-effectiveness plane with 90% of the simulations with an ICER under the WTP threshold (Figure 2).

Figure 1: One way sensitivity analysis base case

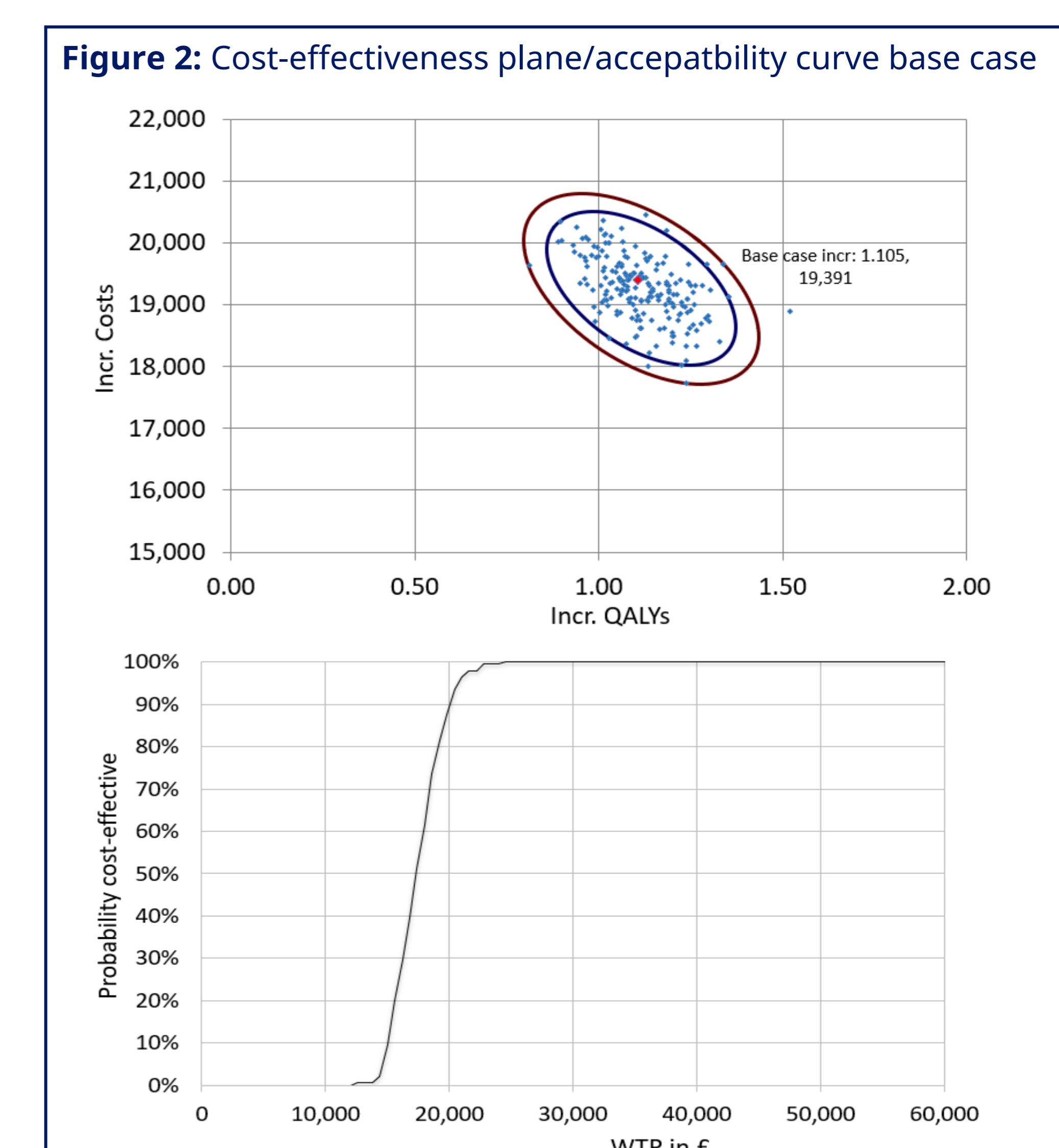


Abbreviations: dr: discount rate; BMI: body mass index; c: cost; D\_E: diet and exercise; HDL: high density lipoprotein; pr: probability; T2DM: type 2 diabetes; NGT: normal glucose tolerance; TIA: transient ischaemic attack  
Definitions: drBenefits: discount rate on health outcomes; maxAgeWeight: the maximum age to which BMI is increasing; ratioStroke\_to\_TIA\_D\_E: ratio between stroke and TIA in patients treated with D&E for recurrent events; ratioStroke\_to\_TIA\_sema: ratio between stroke and TIA in patients treated with semaglutide for recurrent events; bBMI: baseline BMI; drCosts: discount rate on costs; cT2DMPub: cost of microvascular complications of T2DM from the public payer's perspective; prFatalMI: probability fatal MI; type 2 diabetes; prPreT2DM\_2\_NGT\_D\_E: probability to move from type 2 diabetes to normal glucose tolerance; prFatalAngina: probability fatal angina

Table 4: Scenario analysis

	SC semaglutide 2.4 mg		D&E				
	Total costs	LY	QALY	Total costs	LY	QALY	ICER
Base case	20 years	42,849	16.5	13.62	23,458	15.68	12.52 17,547
<i>Other treatment durations</i>							
1 year	25,633	15.44	12.25	24,807	15.35	12.14	7,152
2 years	26,806	15.53	12.38	24,647	15.39	12.18	11,097
5 years	30,141	15.79	12.71	24,238	15.49	12.31	14,715
10 years	35,109	16.14	13.16	23,779	15.63	12.46	16,257
40 years	49,027	16.90	14.03	23,422	15.75	12.59	17,695
<i>Subpopulations</i>							
BMI ≥ 35kg/m <sup>2</sup>	44,685	16.2	13.08	25,587	15.24	11.9	16,105
BMI ≥ 30kg/m <sup>2</sup> +							
≥ 1 additional comorbidities	41,976	15.88	13.08	22,516	15.06	12.02	18,305
BMI ≥ 35kg/m <sup>2</sup> +							
≥ 2 additional comorbidities	43,733	15.12	12.70	25,443	14.06	10.91	14,432
BMI ≥ 35kg/m <sup>2</sup> at high risk of CVD	44,830	16.15	13.01	25,781	15.16	11.8	15,756
≥ 5% weight loss	43,926	16.46	13.59	23,458	15.68	12.52	19,091
<i>Framingham risk of first CVD</i>							
TxD=20 years	42,841	16.34	13.47	23,613	15.48	12.34	17,084
<i>Excluding cancers</i>							
TxD=20 years	41,282	16.57	13.69	21,500	15.94	12.75	20,989
<i>Applying prediabetes reversal from STEP 1 in D&amp;E (39.5%)</i>							
TxD=20 years	42,849	16.50	13.62	22,320	15.73	12.58	19,740

Abbreviations: BMI: body mass index; CVD: cardiovascular disease D&E: diet and exercise; ICER: incremental cost-effectiveness ratio; LY: life years; QALY: quality adjusted life years; Tx: treatment duration



## Discussion

- The study duration of the STEP 10 trial was 52 weeks. This is too short to observe differences in hard outcomes, such as the risk of complications and mortality.
- Surrogate study endpoints related to risk factors of complications and mortality and their progression over time need to be used in specific risk prediction equations
- However, weight loss and reversing prediabetes tend to delay the development of diabetes. Also, blood pressure and lipids are immediately affected by weight loss.
- The effects of weight loss on BMI, lipid levels, blood pressure and glycaemic status are the cornerstones of the current modeling exercise

## Conclusion

Semaglutide 2.4mg is a cost-effective treatment option for individuals with obesity and pre-diabetes in the UK based on the results of the STEP 10 trial.