



# Cost-Effectiveness Analysis of Oral Semaglutide as the Second-Line and Third-Line Treatment for Type 2 Diabetes Patient

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## Background

Most incident diabetes cases were type 2 diabetes (T2D), and diabetes persists over a patient’s lifetime and is associated with significant morbidity and mortality. Prolonged suboptimal glycemia control is associated with an increased risk of macrovascular and microvascular complications, resulting in a substantial economic impact.

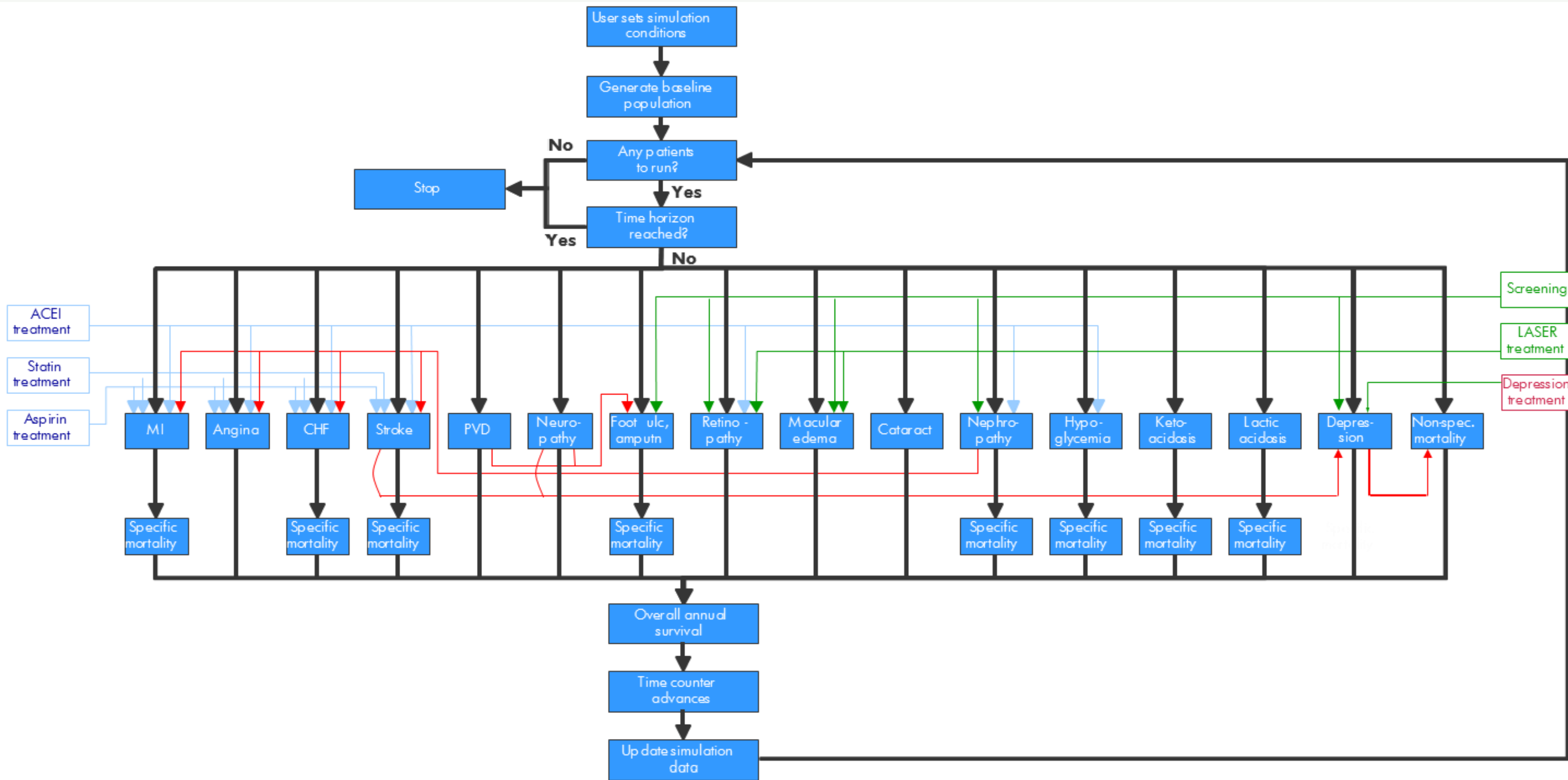
These diabetes-related complications are among the leading causes of death in patients with T2D; CVD accounts for 52% of deaths, malignant neoplasms account for 14%, renal disease (including diabetic nephropathy) for 11%, and diabetes for 3%. Diabetes-related complications also have a considerable negative impact on patient health-related quality of life (HRQoL).

The clinical goal in the treatment of T2D is to achieve reasonable glycemia control with minimal hypoglycemia and other side effects to avoid micro- and macrovascular complications. The study aimed to assess the long-term cost-effectiveness of oral semaglutide for the treatment of patients with T2D with inadequate glycaemic control on metformin.

## Model Overview

Alternatives	2L treatment after metformin or sulfonylurea monotherapy for patients with high CV risk	3L treatment
Patient	T2D patients with major CV events with inadequate glycemia control on metformin or sulfonylurea	T2D patient received metformin or sulfonylurea and combined with DDP4 or SGLT2 or GLP-1 for six months, but still inadequate glycemia control (HbA1c >7.5%)
Intervention	Oral semaglutide 14 mg + Metformin 500mg, QD	Oral semaglutide 14 mg + Metformin 500mg + Glimepiride 2mg, QD
Comparators	<ul style="list-style-type: none"><li>• Liraglutide 18mg (1.35mg/per day) + Metformin 500mg, QD</li><li>• Dulaglutide 0.75mg + Metformin 500mg, QD</li></ul>	<ul style="list-style-type: none"><li>• Liraglutide 18mg (1.35mg/per day) + Metformin 500mg + Glimepiride 2mg, QD</li><li>• Dulaglutide 0.75mg + Metformin 500mg + Glimepiride 2mg, QD</li></ul>
Outcomes	Life expectancy, Quality-adjusted Life-years (QALYs), complication-free years, Direct medical costs, Incremental cost-effectiveness ratio (ICER)	

- **Analytic perspective:** National Health Insurance Administration (NHIA) (payer perspective)
- **Time horizon:** Lifetime with 1-year cycle length
- **Price year and discount rate:** The price year is 2023 and all costs are reported in European dollars (€). The discount rate is 3%.
- **Model Structure:** A microsimulation model (IQVIA Core Diabetes Model [CDM] version 9.5)



## Results

- The ICER for each QALY gained with oral semaglutide was €19,525 when compared to liraglutide and €33,664 in comparison with dulaglutide for the secondary treatment of T2D patients.
- For the third-line treatment of T2D patients, the ICER per QALY gained of oral semaglutide was €21,818 when compared to liraglutide and was €17,826 while compared to dulaglutide.
- When using 3 time GDP per capita as the ICER threshold, the probability of oral semaglutide as the 2L treatment being cost-effectiveness was 69.3% (vs liraglutide) and 52.9% (vs dulaglutide). The probability of oral semaglutide in 3L treatment being cost-effectiveness was 64.0% and 53.5% compared to liraglutide and dulaglutide, respectively.

Table 4. Long-term cost-effectiveness outcomes of Alternative I (2L treatment for T2D patients with major CV history)

PIONEER 4 - Asia				
Discounted costs and health outcomes				
	Oral semaglutide 14 mg	Liraglutide 18mg	Difference	
Life expectancy (years)	12.01	11.91	0.1	
Quality-adjusted life year (years)	8.8	8.67	0.13	
Direct costs	39,977.39	37,443.06	2,534.34	
ICER per LE gained		25,703		
ICER per QALY gained		19,525		
PIONEER 10				
Discounted costs and health outcomes				
	Oral semaglutide 14 mg	Dulaglutide 0.75mg	Difference	
Life expectancy (years)	11.91	11.85	0.06	
Quality-adjusted life year (years)	8.66	8.64	0.02	
Direct costs	40,443.29	39,840.70	602.59	
ICER per LE gained		10,425		
ICER per QALY gained		33,664		

Table 5. Long-term cost-effectiveness outcomes of Alternative II (3L treatment for T2D patients)

PIONEER 4 - Asia				
Discounted costs and health outcomes				
	Oral semaglutide 14 mg	Liraglutide 18mg	Difference	
Life expectancy (years)	12.01	11.91	0.1	
Quality-adjusted life year (years)	8.8	8.67	0.13	
Direct costs	39,274.23	36,621.15	2,653.07	
ICER per LE gained		50,439		
ICER per QALY gained		21,818		
PIONEER 10				
Discounted costs and health outcomes				
	Oral semaglutide 14 mg	Dulaglutide 0.75mg	Difference	
Life expectancy (years)	11.91	11.85	0.06	
Quality-adjusted life year (years)	8.66	8.64	0.02	
Direct costs	40,155.54	39,561.94	593.60	
ICER per LE gained		9,049		
ICER per QALY gained		17,826		

## Model Inputs

### Baseline characteristics

Summary statistics for T2D patients in different alternatives were derived from the Taiwan Diabetes Registry data. Two different cohorts of T2D patients received 2L treatment and 3L treatment were identified.

### Healthcare resource use and cost inputs

Adult patients with T2D were identified from the National Health Insurance Research Database (NHIRD) and cost of each adverse events were defined using the diagnoses.

Table 1. Baseline characteristics of different alternative cohorts.

	Had CV History (n=600)		With OADs >=2 (n=1053)	
	Cohort 1		Cohort 2	
	mean	SD	mean	SD
<b>Demographics and risk factors</b>				
Age (years)	66.13	12.70	60.48	14.17
Duration of diabetes (years)	10.21	10.40	12.00	9.52
Proportion of Male (%)	38.50		38.50	
HbA1c (%)	7.75	1.77	8.28	2.86
Systolic blood pressure (mmHg)	132.56	17.66	133.06	16.63
Diastolic blood pressure (mmHg)	74.72	11.60	76.87	11.15
Total cholesterol (mg/dL)	166.12	37.94	168.60	42.02
HDL cholesterol (mg/dL)	45.82	14.61	46.92	14.80
LDL cholesterol (mg/dL)	93.40	32.04	93.59	31.56
Triglycerides (mg/dL)	153.41	118.64	156.43	144.27
BMI (kg/m²)	26.99	4.38	26.92	4.80
eGFR (ml/min/1.73m²)	74.89	33.18	85.01	33.91
Heart rate (bpm)	80.13	11.98	83.02	11.98
Waist: hip ratio	0.70	0.12	0.71	0.11
Serum creatinine (mg/dl)	1.28	1.37	1.05	0.81
uACR (mg/mmol)	0.24	1.10	0.49	6.25
Hemoglobin (gr/dl) <sup>a</sup>	13.83	1.39	13.83	1.39
WBC (10 <sup>6</sup> /ml) <sup>a</sup>	6.99	1.88	6.99	1.88
Serum Albumin (mg/dl) <sup>a</sup>	4.32	0.27	4.32	0.27
Percentage smokers (%)	37.50		31.91	
Cigarettes per day	19.37	14.00	19.48	14.70
Alcohol consumption (oz/week) <sup>b</sup>	5.00		5.00	
<b>Baseline cardiovascular complications, %</b>				
Myocardial infarction	9.50		1.71	
Angina	10.50		0.85	
Peripheral vascular disease	24.83		3.80	
Stroke	8.67		1.71	
Congestive heart failure	2.33		0.57	
Atrial fibrillation <sup>a</sup>	2.44		2.44	
Left ventricular hypertrophy <sup>a</sup>	1.22		1.22	
<b>Baseline renal complications, %</b>				
Microalbuminuria	3.00		3.13	
Gross proteinuria	3.00		3.13	
End-stage renal disease	0.83		0.09	
<b>Baseline retinopathy complications, %</b>				
Background diabetic retinopathy	11.50		11.68	
Proliferative diabetic retinopathy	5.67		4.94	
Severe vision loss	0.33		0.38	
Macular edema	3.50		1.61	
Cataract <sup>b</sup>	7.80		7.80	
<b>Baseline neuropathy, ulcer and amputation, %</b>				
Neuropathy	11.17		7.69	
Uninfected ulcer	0.83		0.47	
Infected ulcer <sup>c</sup>	0.00		0.00	
Healed ulcer <sup>c</sup>	0.00		0.00	
Amputation	0.50		0.95	
<b>Baseline depression, %</b>				
	11.67		6.65	

Table 2. The annual cost of complication and adverse events

Cost (€)	Annual cost of event year		Annual cost of follow-up	
	mean	SE	mean	SE
<b>CVD complication</b>				
MI	6,863.74	159.40	909.82	69.81
Angina	1,015.77	51.24	477.34	77.27
CHF	4,590.06	161.54	2,563.94	188.41
Stroke	5,085.36	107.17	1,161.91	52.72
Stroke death within 30 days	3,002.87	135.55		
PVD	5,706.81	425.82	2,727.82	989.31
<b>Renal complication</b>				
Hemo Dialysis	16,240.77	215.13	16,364.03	200.85
Peritoneal Dialysis	11,140.56	317.09	11,300.15	390.75
Renal Transplant	12,032.40	1,163.48	5,652.45	1,192.18
<b>Acute adverse event (per event)</b>				
Non-severe hypoglycemia	139.73	1.75		
Severe hypoglycemia	1,673.26	32.96		
Keto event	1,545.56	57.87		
Lactic acid event	1,835.64	480.58		
Edema onset	129.39	7.11		
Edema follow-up	190.57	31.83		
<b>Eye disease</b>				
Laser treatment (per event)	155.84	4.08		
Cataract operation (per event)	598.00	1.17		
Post cataract surgery care	132.89	19.68		
Blindness	730.46	138.89	85.59	19.80
<b>Neuropathy complication</b>				
Neuropathy	393.33	8.56	361.75	9.80
Gangrene treatment	988.20	58.03		
Infected ulcer	173.51	3.71		
Amputation (per event)	5,996.64	742.91		

### Treatment effects and adverse event

- The treatment effects and adverse events data underlying the simulations were obtained from the Asian population in the PIONEER trials.
- Analyses using the treatment policy estimated data at 52 weeks from the oral semaglutide clinical trials were used in the base case analyses.

### Health Utility Inputs

- The baseline utility of type 2 diabetes patients in Taiwan were sourced from Taiwan Diabetes Registry data (0.92±0.09 for cohort 1 and 0.93±0.08 for cohort 2)

Table 3. Treatment effect and biomarker evolution over time

	PIONEER 4 - Asia		PIONEER 10	
	Oral semaglutide 14 mg	Liraglutide 18mg	Oral semaglutide 14 mg	Dulaglutide 0.75mg
<b>Treatment effect (change from baseline), mean±SE</b>				
HbA1c (%)	-1.82±0.13	-1.27±0.13	-1.69±0.08	-1.37±0.11
BMI (kg/m²)	-1.67±0.25	-0.63±0.25	-0.61±0.10	0.34±0.14
SPB (mmHg)	-1.95±2.07	-1.69±2.16	-1.40±1.00	-1.60±1.43
DBP (mmHg)	-1.45±1.22	-0.15±1.27	-	-
Total cholesterol (mg/dL)	-11.35±3.47	-11.66±3.82	-0.30±0.06	-0.37±0.08
LDL-cholesterol (mg/dL)	-10.54±3.18	-7.29±3.49	-	-
HDL-cholesterol (mg/dL)	1.23±1.20	-1.80±1.28	0.01±0.02	0.00±0.02
Triglycerides (mg/dL)	-11.42±9.52	-9.32±10.65	-	-
eGFR (mL/min/1.73m²)	-1.08±0.73	-3.00±0.81	-	-
<b>Hypoglycemia event rates applied while patients received treatment</b>				
Non-severe hypoglycemia event rate (per 100 patient years)	52.90	19.44	38.28	27.98
Severe hypoglycemia event rate (require medical assistant (per 100 patients years)	3.11	6.48	3.00	0.00
Proportion of non-severe hypoglycemia event that are nocturnal	22.58	17.24	20.77	20.00
Proportion of severe hypoglycemia events that are nocturnal	3.23	3.45	3.08	0.00

Fig 1. CEAC of 2L treatment for T2D patients with major CV history

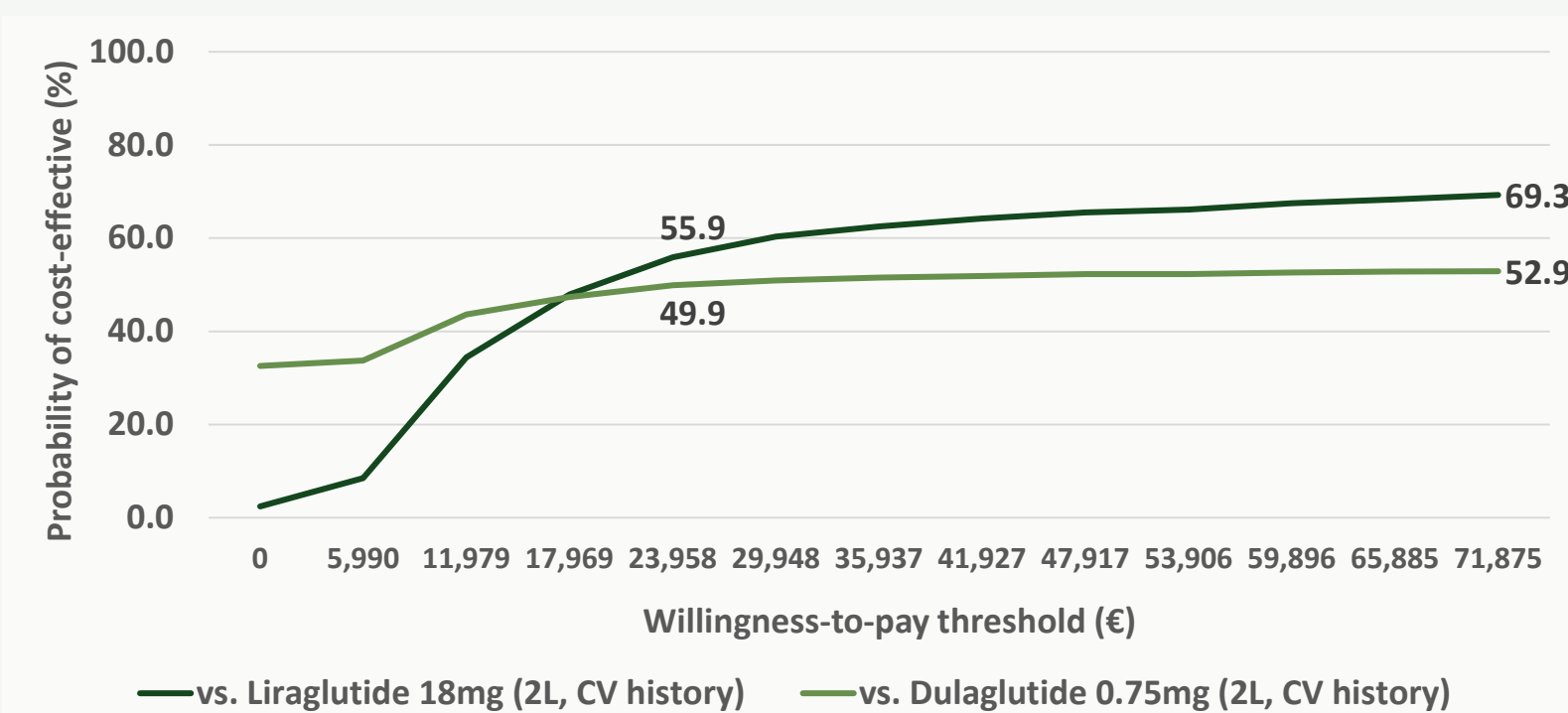


Fig 2. CEAC of 3L treatment for T2D patients

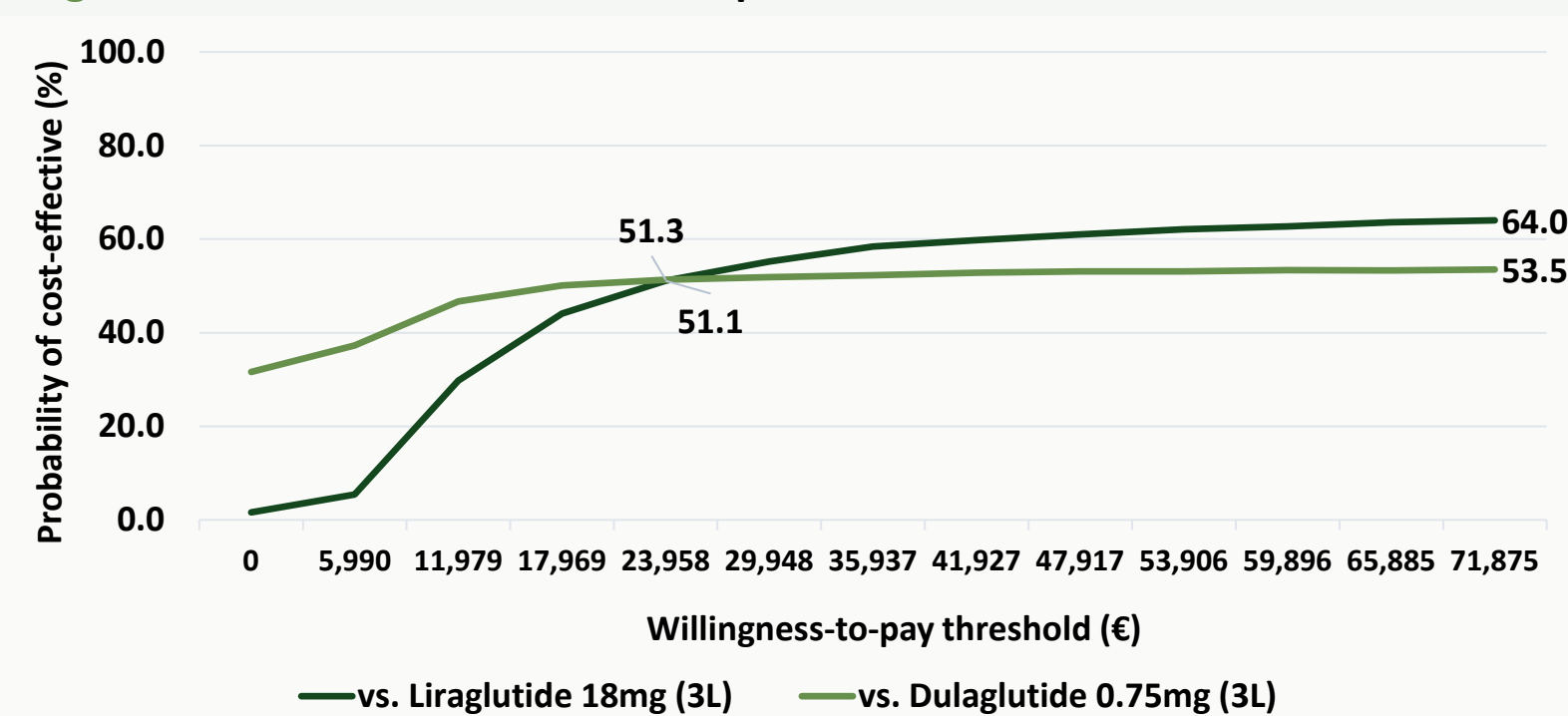


Fig 3. Scatterplot for T2D patients with major CV history

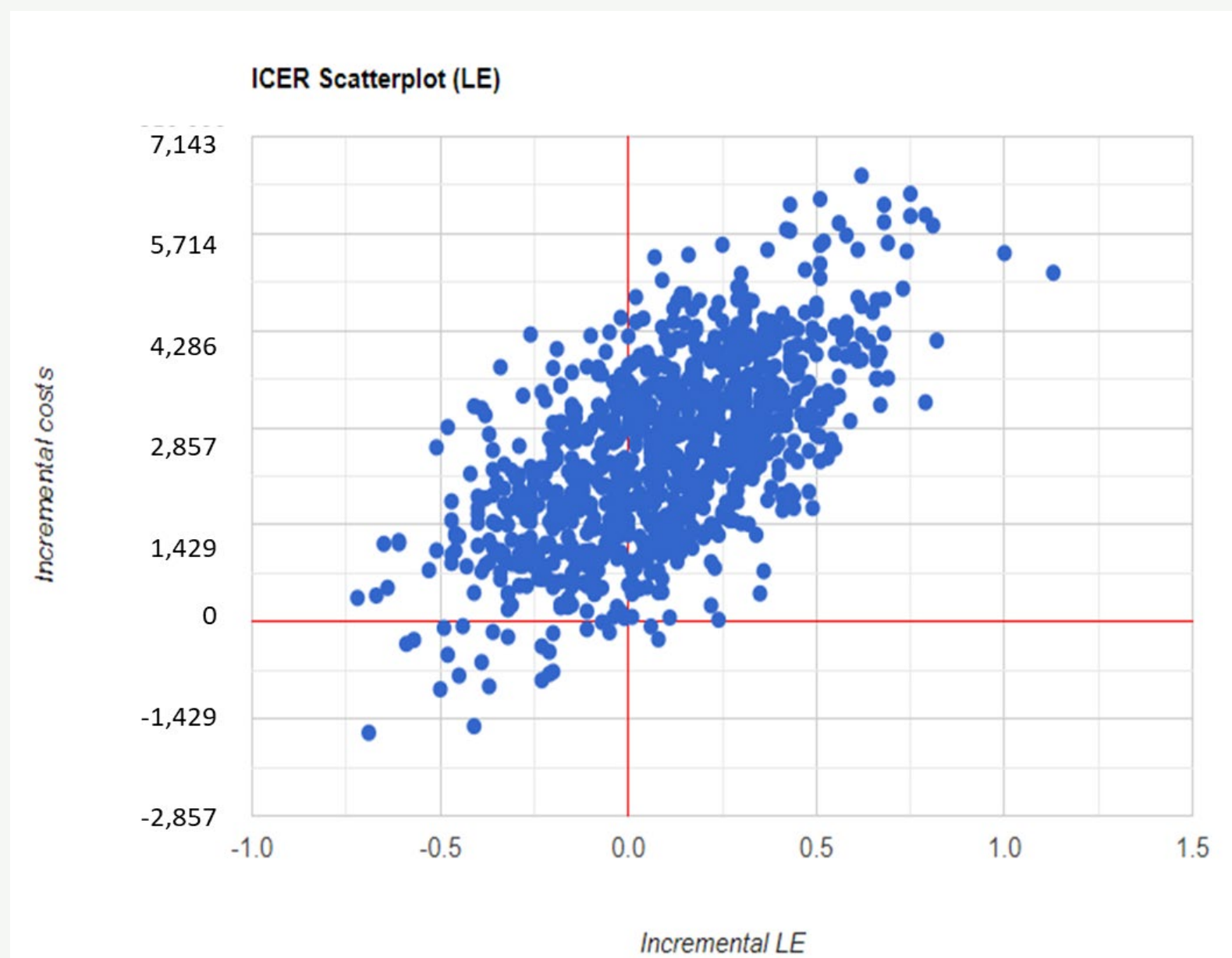
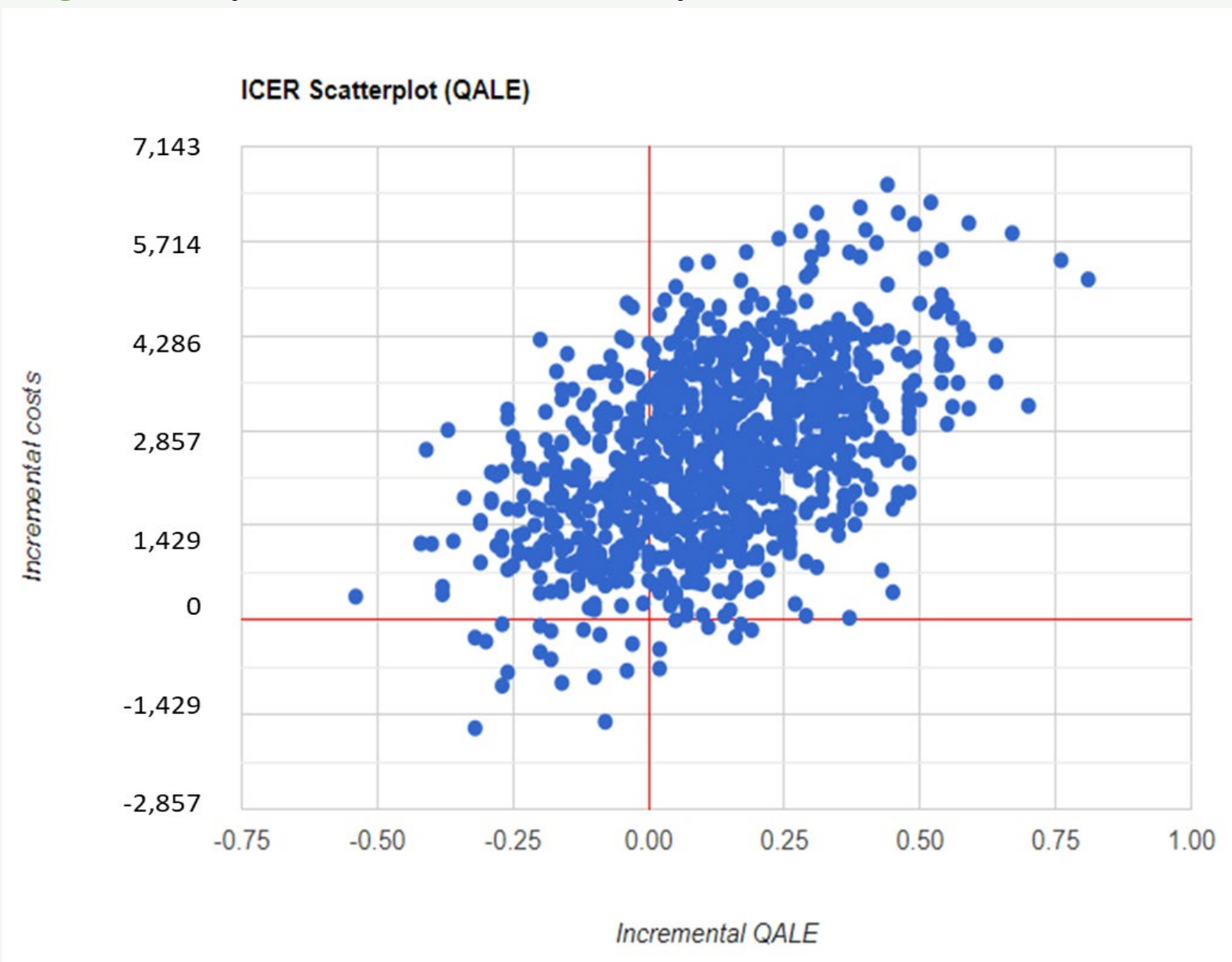


Fig 4. Scatterplot for 3L treatment for T2D patients



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