Long-Term Cost-Effectiveness of Tirzepatide versus Placebo for Individuals with Type 2 Diabetes and Obesity

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INTRODUCTION

Diabetes and obesity are both highly prevalent and high-cost chronic conditions in the US:

- Diabetes is estimated to impact 38% of the adult population and 11.6% of the U.S. population[1].
- US obesity prevalence increased from 30.5% to 41.9% between 1999 and 2020[2].
- In 2022, diabetes cost the U.S. $412.9 billion, including $306.6 billion in direct medical costs and $106.3 billion in indirect costs[3].
- The estimated annual medical cost of obesity in the United States was nearly $173 billion in 2019[2].

FDA approved Tirzepatide (TZP) for:

- The treatment of type 2 diabetes in adults in May 2022[4];
- Weight management in adults with obesity or overweight in November 2023[5].
- TZP is a dual glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 receptor (GLP-1R) co-agonist medication[6].

Knowledge Gaps:

- To date, there are three published cost-effectiveness analyses of TZP that focused on only diabetes[7-9];
- There are no published cost-effectiveness studies of TZP on both diabetes and obesity;
- The American Diabetes Association recommends that people living with T2D focus on lowering blood sugar and weight management to address both hyperglycemia and its underlying pathophysiologic driver (obesity) [10];
- Given TZP's potential benefits in addressing obesity and hyperglycemia for T2D, it's urgent to determine the cost-effectiveness of TZP on both diabetes and obesity.

AIM

Evaluate the long-term cost-effectiveness of TZP (10 or 15mg once weekly) compared to the placebo group (reduced calorie diet and increased physical activity only) in individuals with type 2 diabetes and obesity.

METHODS

Data Source:

- The data comes from the SURMOUNT-2 study (NCT04657003), a 72-week, multicentered, double-blind, parallel-group phase 3 clinical trial, that was conducted in 77 sites across 7 countries and areas and focused on investigating the safety and efficacy of Tirzepatide in adults living with obesity and type 2 diabetes (T2DM)[6]. Participants in the trial were diagnosed with T2DM.

Main Inclusion Criteria[6]:

- Have a BMI ≥27 kg/m²;
- Have a diagnosis of T2DM with HbA1c ≥7% (≥53 mmol/mol) to ≤10% (86 mmol/mol);
- T2D treated with diet or exercise alone or any oral glycemic-lowering agent EXCEPT DPP-4 inhibitors or GLP-1R agonists;
- Have a history of at least 1 self-reported unsuccessful dietary effort to lose body weight;

METHOD (cont.)

Study Groups:

I. TZP 15mg	Once weekly From 2.5mg, increased by 2.5mg every 4 weeks, the 20th week achieve the target dosage
II. TZP 10mg	Once weekly From 2.5mg, increased by 2.5mg every 4 weeks, the 12nd week achieve the target dosage
III. Placebo	Once weekly

Lifestyle Considerations:

- All participants across the three groups received lifestyle management counseling during the whole 72 weeks.

Model Structure:

The Building, Relating, Assessing, and Validating Outcomes (BRAVO) of the Diabetes Model, was innovated and built based on the ACCORD trial data in 2018 with 17 risk equations, used for diabetes risk estimation and simulation[11].

Event Module	Risk Factors Module	Mortality Module
Predicts macrovascular events, microvascular events, and adverse events.	Predicts the progression of key risk factors based on their values from the previous cycle and other risk factors.	Predicts patient death and explores the cause of death, differentiating between cardiovascular disease (CVD) and other causes

Perspective: US healthcare perspective

Simulation duration: 40 years; (20 and 30 years as sensitivity analysis)

- The baseline age of the trial is 54 years old, and the life expectancy at birth in the U.S. has been 73, 79 for men and women respectively in 2021[12], thus, this study chose the three durations.

Assumptions:

1. The 72 weeks' treatment effect data was supposed to be steady during the first five years;
2. Mean height /smokers/education proportion is the same as ACCORD clinical trial, as well as the disutility and clinical history data at baseline[13];
3. The cost of basic medicines for diabetes across three arms is the same as the CDC data in BRAVO model[11,18];
4. The treatment effects of 72 weeks of SURMOUNT 2 were the same as 52 weeks;
5. The price of TZP was sourced from GoodRx in Dec 2023, and with the estimated 37% of GLP-1RA rebates[14-15];
6. Cost and QALY are discounted by 3% every year in the BRAVO model setting;
7. The threshold of willingness to pay is $100,000[16-17] per QALY.

Model Input:

Patient Demographics and Clinical Characteristics

Parameters	Tirzepatide 10mg	Tirzepatide 15mg	Placebo	Total	Data Source
Age	54.3 (10.7)	53.6 (10.6)	54.7 (10.5)	54.2 (10.6)	SURMOUNT-2
Gender (% of Females)	51	51	50	51	SURMOUNT-2
Duration of T2D	8.8 (6.9)	8.0 (6.4)	8.8 (6.2)	8.5 (6.5)	SURMOUNT-2
Height #(m)	--	--	--	1.70(.01)	ACCORD
Race-White(%)	73	75	79	76	SURMOUNT-2
-Black(%)	11	7	7	8	SURMOUNT-2
-Hispanic(%)	59	61	60	60	SURMOUNT-2
-Others* (%)	18	21	16	18	SURMOUNT-2
Smokers# (%)	--	--	--	14 (.34)	ACCORD
Education above High school# (%)	--	--	--	25.97(.0043)	ACCORD

Others in the trial including Asian, Native Hawaiian or other Pacific Islanders, Multiple and not reported;

Hypoglycemia (Adverse Events)[6]

Degree	T-10mg	T-15mg	Placebo	Total
Severe	0	0	0	0
Level 2 Hypoglycemia	11 (4%)	15 (5%)	4 (1%)	30 (3%)
Aggregated rate (events/patient/year)	0.04	0.06	0.09	0.06
Symptoms associated with level 2 hypoglycemia	6 (2%)	13 (4%)	4 (1%)	23(2%)

Regional Distribution[6]

Regions (0-1)	T-10mg	T-15mg	Placebo	Total
United States	0.365	0.367	0.362	0.365
Europe	0.042	0.042	0.054	0.046
Asia	0.131	0.125	0.121	0.126
Others	0.462	0.466	0.463	0.464

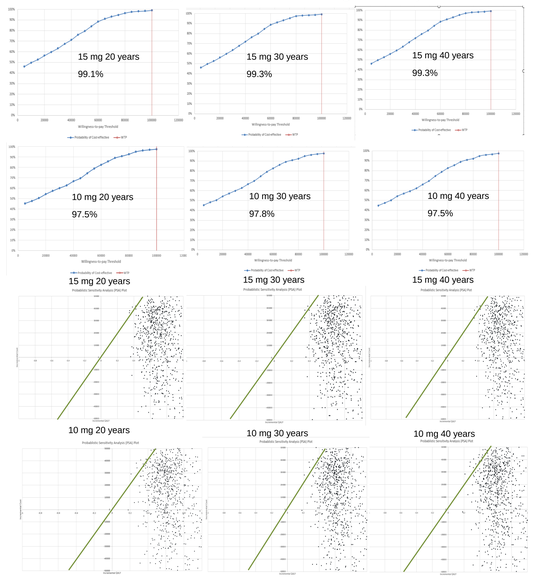
RESULTS

Treat Effects:

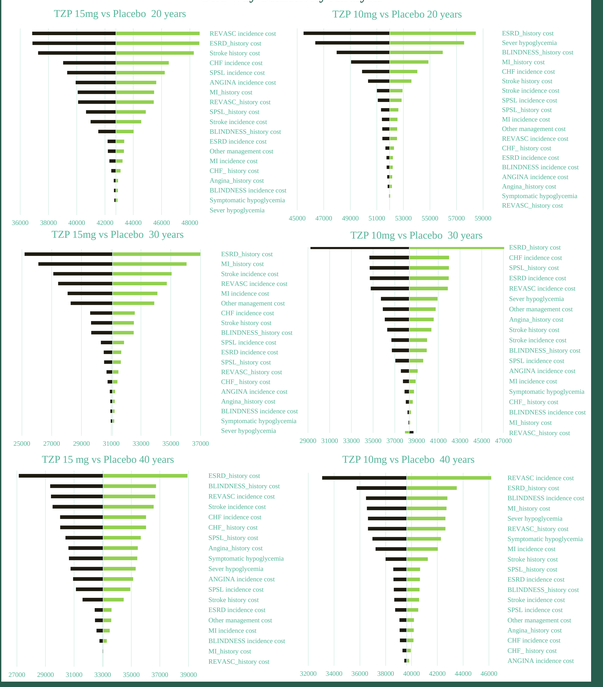
Treatment effects	Tirzepatide 10mg	Tirzepatide 15mg	Placebo
HbA1c (%)	-2.07 (0.06)	-2.08 (0.07)	-0.51 (0.07)
SBP (mmHg)	-5.9	-7.7	-1.2
Weight (kg)	-12.9 (0.6)	-14.8 (0.5)	-3.2 (0.5)
HDL (mg/dl)	6.9 (1.1)	9.6 (1.1)	1.1 (1.0)
LDL (mg/dl)	2.3 (1.8)	3.2 (1.8)	6.3 (1.9)

	15mg vs Placebo			10 mg vs Placebo		
Duration (Years)	20	30	40	20	30	40
Incremental Cost	19,544.46	18,550.80	21,433.54	20,992.96	19,979.86	22,432.27
Incremental QALY	0.4624	0.5968	0.6489	0.4040	0.5213	0.5661
Incremental Life-Years	0.1524	0.4562	0.7058	0.1300	0.3939	0.6075
Incremental ICER	42271.84	31085.10	33031.60	51968.62	38329.68	39627.61
Conclusion	Cost-effective					

Probability of Cost-effective & Willingness-to-Pay



One-way Sensitivity Analysis



RESULTS (cont.)

Risk Events	T 15- 40	HR-40	T15-30	HR-30	T15-20	HR-20
Stroke	**18.37%**	94.52%	**15.66%**	91.85%	**10.06%**	85.37%
Non-fatal	**13.98%**	93.68%	**13.09%**	91.97%	**9.21%**	85.44%
Fatal	**4.39%**	97.31%	**2.57%**	91.21%	**0.85%**	84.57%
MI	**27.06%**	97.91%	**23.73%**	96.31%	**16.23%**	92.63%
Non-fatal	**24.35%**	97.91%	**21.36%**	96.31%	**14.61%**	92.63%
Fatal	**2.71%**	97.91%	**2.37%**	96.31%	**1.62%**	92.63%
CHF	**13.99%**	83.34%	**11.57%**	80.98%	**6.85%**	77.27%
Non-fatal	**8.55%**	85.58%	**8.18%**	84.09%	**5.80%**	78.92%
Fatal	**5.44%**	80.04%	**3.39%**	74.32%	**1.05%**	69.28%
Angina	**14.56%**	87.45%	**12.99%**	85.80%	**9.17%**	81.72%
Revascularization	**42.60%**	91.13%	**39.78%**	89.91%	**30.94%**	86.69%
ESRD	**19.19%**	97.34%	**16.74%**	95.20%	**11.26%**	91.32%
Blind	**49.17%**	98.48%	**45.07%**	97.01%	**32.65%**	92.73%
SPSL	**53.95%**	97.09%	**49.86%**	95.61%	**36.29%**	90.49%
All cause Mortality	**90.88%**	98.34%	**61.86%**	94.85%	**28.75%**	92.98%
CVD Mortality	**60.01%**	92.48%	**39.67%**	87.84%	**16.56%**	82.72%
MACE Component	**93.42%**	93.94%	**70.41%**	90.87%	**38.37%**	86.71%

Risk Events	T 10- 40	HR-40	T10-30	HR-30	T10-20	HR-20
Stroke	**18.39%**	94.64%	**15.72%**	92.24%	**10.17%**	86.30%
Non-fatal	**14.02%**	93.93%	**13.14%**	92.35%	**9.31%**	86.33%
Fatal	**4.37%**	96.97%	**2.58%**	91.69%	**0.86%**	85.88%
MI	**26.92%**	97.41%	**23.62%**	95.87%	**16.19%**	92.37%
Non-fatal	**24.23%**	97.41%	**21.26%**	95.87%	**14.57%**	92.37%
Fatal	**2.69%**	97.41%	**2.36%**	95.87%	**1.62%**	92.37%
CHF	**14.45%**	86.03%	**12.00%**	83.95%	**7.12%**	80.31%
Non-fatal	**8.76%**	87.68%	**8.41%**	86.44%	**6.00%**	81.58%
Fatal	**5.68%**	83.60%	**3.59%**	78.64%	**1.13%**	74.12%
Angina	**14.71%**	88.37%	**13.14%**	86.82%	**9.31%**	82.99%
Revascularization	**43.30%**	92.62%	**40.51%**	91.57%	**31.64%**	88.67%
ESRD	**19.23%**	97.53%	**16.81%**	95.61%	**11.34%**	91.97%
Blind	**49.11%**	98.36%	**45.09%**	97.05%	**32.81%**	93.18%
SPSL	**53.85%**	96.89%	**49.81%**	95.52%	**36.38%**	90.71%
All cause Mortality	**91.10%**	98.58%	**62.34%**	95.58%	**29.04%**	93.91%
CVD Mortality	**60.66%**	93.48%	**40.39%**	89.45%	**16.95%**	84.63%
MACE Component	**93.96%**	94.48%	**71.05%**	91.70%	**38.78%**	87.64%

CONCLUSIONS and LIMITATIONS

Conclusion:

Both 15 mg and 10 mg of TZP once weekly are cost-effective compared to a placebo in the 20-, 30-, and 40-years simulations.

Limitations:

1. There is no long-term treatment effect data for TZP, and this study is based on the clinical trial's short-term results. The analysis will be updated when long-term used real-world data becomes available in the future;
2. Cost and utility data from ACCORD is from the pre-pandemic period and may be inaccurate after COVID-19 disrupted lifestyle habits and changed medical costs;
3. This study assumed patients would take routine medications for all 5 years which may not reflect actual practice;
4. The population used to build the BRAVO model might not accurately align with the SURMOUNT 2 population and the predicted aimed population, such as age and CVD-related characteristics;
5. Only 36.5% of SURMOUNT-2 clinical trial enrollees were based in the US, and the prediction based on this clinical trial may be different from the real U.S. population.

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