Semaglutide and Tirzepatide for Obesity: Effectiveness and Value

Public Meeting — November 13, 2025

Meeting materials available at: https://icer.org/assessment/obesity-2025/

ICER
INSTITUTE FOR CLINICAL AND ECONOMIC REVIEW

NEW ENGLAND CEPAC
COMPARATIVE EFFECTIVENESS PUBLIC ADVISORY COUNCIL

Participating Members of the New England CEPAC

Jason H. Wasfy, MD, MPhil, New England CEPAC Chair,
Associate Professor at Harvard Medical School, Director of Outcomes Research, Massachusetts, General Hospital Cardiology Division, Mass General Brigham

- **Rob Aseltine, PhD,** Professor and Chair, Division of Behavioral Sciences and Community Health Director, Center for Population Health, UCONN Health
- **Austin Frakt, PhD,** Vice President and Chief Research Officer, Joint Commission
- **Rebecca Kirch, JD,** EVP, Policy and Programs for the National Patient Advocate Foundation (NPAF)
- **Stephen Kogut, PhD, MBA, RPh,** Professor of Pharmacy Practice, University of Rhode Island College of Pharmacy
- **Donald Kreis, JD,** Consumer Advocate, New Hampshire Office of the Consumer Advocate
- **Julie Kueppers, PhD, FNP,** Vice President of Clinical Analytics and Advocacy, Alera Group
- **Tara Lavelle, PhD,** Assistant Professor, Center for the Evaluation of Value and Risk in Health at Tufts Medical Center
- **Kimberly Lenz, PharmD, MBA, FAMCP,** Chief Pharmacy Officer, MassHealth; Office of Clinical Affairs, UMass Chan Medical School
- **Aaron Mitchell, MD, MPH**, Assistant Attending, Memorial Sloan Kettering Cancer Center
- **Josephine Porter, MPH**, Chief Strategy Officer, NH Center for Justice and Equity; Consultant, Institute for Health Policy and Practice; Co-Chair, All-Payer Claims Database Council; Board of Director Chair, NH Fiscal Policy Institute and Leadership Team for the NH Food Alliance
- **Jim Rebitzer, PhD,** Emeritus Peter and Deborah Wexler Professor of Management, Boston University, Questrom School of Business
- **Joseph Ross, MD, MHS,** Professor of Medicine (General Medicine) and Professor of Public Health (Health Policy and Management), Yale School of Medicine; Associate Physician of the Center for Outcomes Research and Evaluation, Yale-New Haven Health System; Co-Director, National Clinician Scholars Program, Yale University; Co-Director, Yale-Mayo Clinic Center for Excellence in Regulatory Science and Innovation (CERSI)
- **Jason L. Schwartz, PhD**, Associate Professor, Department of Health Policy and Management, Yale School of Public Health; Affiliated with Yale's Institution for Social and Policy Studies and the Section of the History of Medicine, Yale School of Medicine
- **Stephanie Vail, PharmD, MPH, BCPP, BCPS, FCCP,** Professor of Pharmacy Practice, University of New England College of Pharmacy

Patient Experts

Joe Nadglowski, President/CEO, Obesity Action Coalition

- *Joe Nadglowski has no personal relationships with industry. The Obesity Action Coalition receives 25% of financial support from health care companies including, Boehringer Ingelheim, Eli Lilly, Novo Nordisk, Amgen, Pfizer, AstraZeneca, Boston Scientific, Currax, Genentech, Intuitive, Kailera Therapeutics, Madrigal Pharmaceuticals, Medtronic, Regeneron, Rhythm Pharmaceuticals, Structure Therapeutics, Wave Life Sciences and Zealand Pharma.*

Michele Tedder, Director of Chronic Disease, Black Women's Health Imperative

- *Michele Tedder is an Obesity Action Coalition board member.*

Clinical Experts

Melanie Jay, MD, MS, Professor, Departments of Medicine and Population Health, NYU Grossman School of Medicine

- *No Conflicts of Interest to disclose.*

Alexa Triot, MD, Clinical Director of HCA Embedded Primary Care Weight Management Programs, Section of Primary Care, Division of General Medicine, Beth Israel Deaconess Medical Center

- *Dr. Alexa Triot's spouse works for Verve Therapeutics, a wholly owned subsidiary of Eli Lilly and Company.*

ICER Speakers

Sarah K. Emond, MPP
President & CEO

Grace Lin, MD
Evidence Author
Medical Director for HTA, ICER

David Rind, MD, MSc
Chief Medical Officer

Woojung Lee, PharmD, PhD
Lead Economic Modeler, Associate Director of Health Economics and Decision Modeling

Why are we here today?

“I’ve struggled with my weight pretty much my entire life. I was always the cute little chubby kid, and, you know, grew into the overweight adult eventually…through my life I tried many, many things to lose weight. If you put a checklist of different diets that have been out over the years. I could check all the boxes….over the years I developed a lot of internalized bias…and the noise externally around diet culture that it’s our fault…it wasn’t until I got to a really caring health provider who saw me and understood that obesity was a disease, and then helped me to understand that that’s what it is”.

Patient Living With Obesity

Why Are We Here Today?

- What happens the day these treatments receive FDA approval?
- Questions about:
  - What are the risks and benefits?
  - How do new treatments fit into the evolving landscape?
  - What are reasonable prices and costs to patients, the health system, and the government?
  - What lessons are being learned to guide our actions in the future?

The Impact on Rising Health Care Costs for Everyone

GALLUP®

APRIL 1, 2025

In U.S., Inability to Pay for Care, Medicine Hits New High

Rates among Hispanic, Black adults and those with lower incomes worsen markedly since 2021

Peterson-KFF
Health System Tracker

Health Spending

How much and why ACA Marketplace premiums are going up in 2026

Business Group on Health Survey: 9% Health Care Cost Increase for 2026

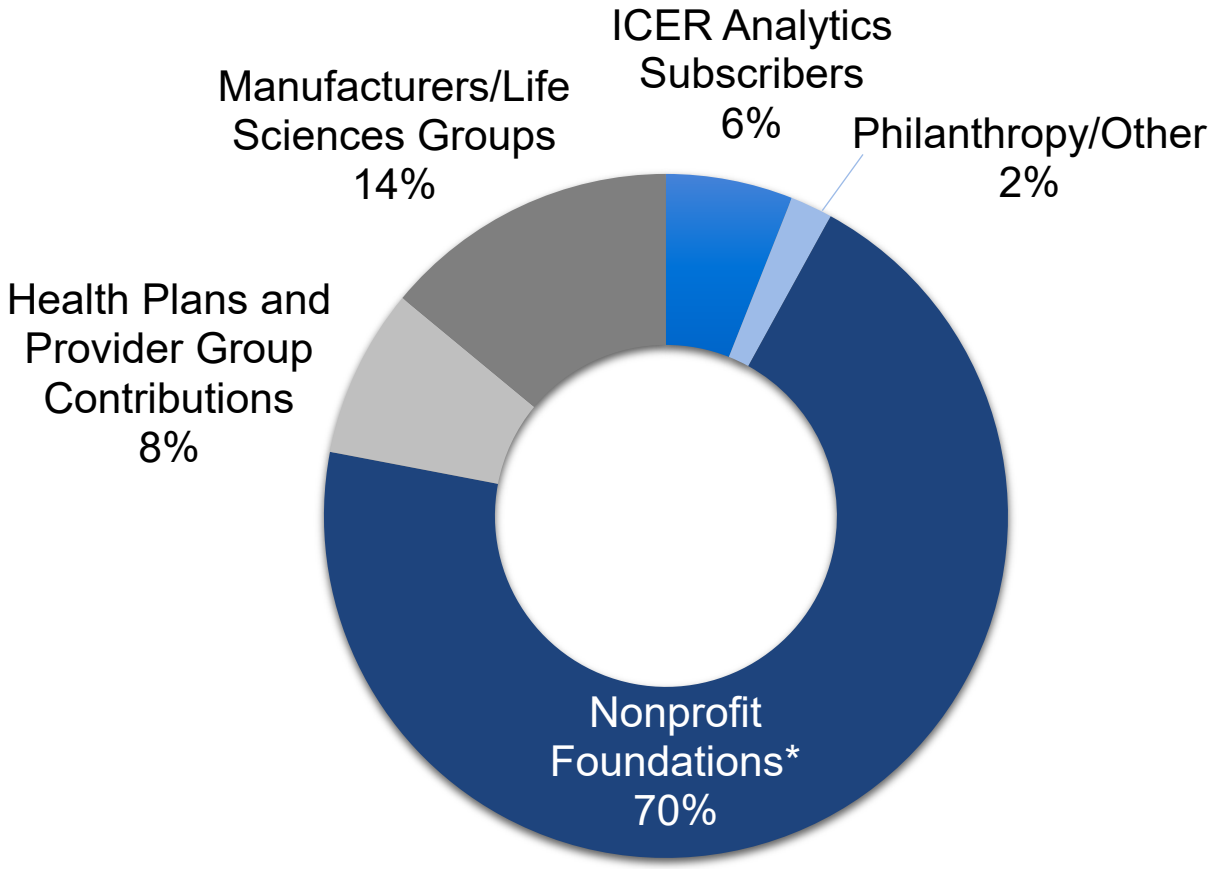
https://www.businessgrouphealth.org/newsroom/news-and-press-releases/press-releases/2026-employer-health-care-strategy-survey
https://www.healthsystemtracker.org/brief/how-much-and-why-aca-marketplace-premiums-are-going-up-in-2026/
https://news.gallup.com/poll/658148/inability-pay-care-medicine-hits-new-high.aspx

Organizational Overview

ICER
INSTITUTE FOR CLINICAL AND ECONOMIC REVIEW

NEW ENGLAND CEPAC
COMPARATIVE EFFECTIVENESS PUBLIC ADVISORY COUNCIL

2025 Funding and Managing COIs



Read our policies to manage potential conflicts of interest: https://icer.org/our-approach/policies/policies-to-manage-conflicts-of-interest/

ICER Policy Summit and non-report activities only

*ICER received significant funding from Arnold Ventures, The Patrick and Catherine Weldon Donaghue Medical Research Foundation, and the Peterson Center on Healthcare, LLC. Source: https://icer.org/who-we-are/independent-funding/sources-of-funding/

How Was the ICER Report Developed?

Guidance from patients, clinical experts, manufacturers, and other stakeholders

Evidence analysis in collaboration with the University of California San Francisco and cost-effectiveness modeling from ICER.

- **David Kim, PhD,** Assistant Professor of Medicine and Public Health Sciences University of Chicago
- **Joe Nadglowski,** Jr. President and CEO Obesity Action Coalition
- **Gitanjali Srivastava, MD, FACP, FAAP**, Professor of Medicine Department of Medicine, Division of Diabetes, Endocrinology & Metabolism Vanderbilt University School of Medicine
- **Michele Tedder, MSN, RN,** Director of Chronic Disease Black Women's Health Imperative
- **Dan Touchette, PharmD, MA**, Professor University of Illinois, Chicago
- **Alexa Triot, MD,** Clinical Director of HCA Embedded Primary Care Weight Management Programs, Section of Primary Care, Division of General Medicine Beth Israel Deaconess Medical Center

Structured to support **New England CEPAC** voting and policy discussion

Value Assessment Framework: Long-Term Value for Money

Agenda (ET)

10:00 AM	Meeting Convened and Opening Remarks
10:20 AM	Presentation of the Clinical Evidence
11:00 AM	Presentation of the Economic Model
11:40 AM	Public Comments and Discussion
11:55 AM	Lunch Break
12:45 PM	NE CEPAC Deliberation and Vote
2:00 PM	Break
2:15 PM	Policy Roundtable Discussion
3:45 PM	Reflections from NE CEPAC
4:00 PM	Meeting Adjourned

Presentation of the Clinical Evidence

Grace Lin, MD, MAS

Medical Director for Health Technology Assessment, Institute for Clinical and Economic Review

Professor of Medicine and Health Policy, University of California, San Francisco

ICER
INSTITUTE FOR CLINICAL AND ECONOMIC REVIEW

Key Team Members

Name	Title
Grace Lin, MD, MAS	Evidence Author
Shahariar Mohammed Fahim, PhD, MSc	Senior Research Lead
Finn Raymond, BS	Research Assistant

Disclosures

Financial support provided to Grace Lin from the Institute for Clinical and Economic Review (ICER). Dr. Lin also reports receiving research grant funding from the National Human Genome Research Institute, National Institute on Aging, Mt. Zion Health Fund, GRAIL, Inc., and the California Health Benefits Research Program.

Shahariar Mohammed Fahim and Finn Raymond have no conflicts.

Obesity

Disease Background

- Chronic disease that affects more than 40% of Americans
  - Mediated by genetic and environmental factors
- Higher rates of obesity in Black and Hispanic Americans; Asians may have effects at lower body mass index
- Impact on health is large
  - More than half have comorbidity – e.g., diabetes, hypertension, heart disease
  - Severe obesity can shorten life by 14 years
- Costly to healthcare system, estimated $172 billion in medical costs annually

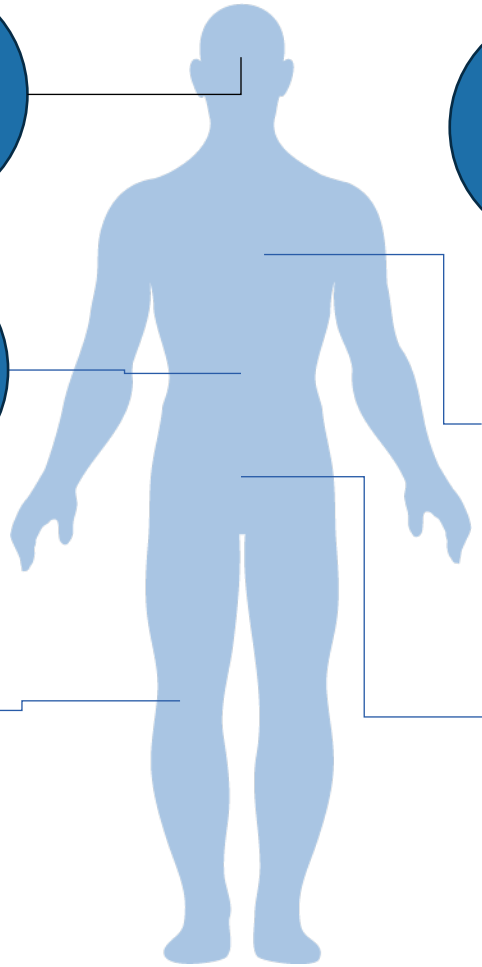
Consequences of Obesity

Depression
Anxiety

Type 2 diabetes

Metabolic-associated steatohepatitis (MASH)

Osteoarthritis



Obstructive sleep apnea

High blood pressure
High cholesterol

Chronic kidney disease

Insights from Discussions with Patients

- "Food noise" – intrusive thoughts about food, obsessing about food restrictions – is common
- Weight stigma associated with:
  - Low self-esteem, high rates of depression and anxiety
  - Delayed diagnoses, delays in preventive care
- Healthcare system unprepared to manage obesity as chronic disease
  - Failure to broach treatment until complications occur
  - Lack of comprehensive care: obesity medicine specialists, primary care providers with expertise, dietary education, psychological support, etc.
- Many treatments tried throughout their lifetime and lose/gain weight several times

Standard of Care and Management

- Obesity typically defined by body mass index (BMI):
  - Overweight: BMI ≥ 25 kg/m^2
  - Obesity: BMI ≥ 30 kg/m^2
  - Severe obesity: BMI ≥ 40 kg/m^2
- Treatment:
  - Lifestyle modifications
    - Typically result in 5-10% loss of body weight, but difficult to maintain
  - Obesity medications
    - Existing options include stimulants, combination oral medications (e.g., Qsymia, Contrave), GLP-1 RA, GLP-1/GIP RA
  - Bariatric surgery

BMI: Body mass index, GLP-1: glucagon-like peptide-1; GIP: glucose-dependent insulinotropic polypeptide

Interventions and Comparators

Intervention	Mechanism of Action	Delivery Route	Prescribing Information
Semaglutide (Wegovy®)	GLP-1 receptor agonist	Subcutaneous	0.25 mg - 2.4 mg weekly
Semaglutide (Oral)	GLP-1 receptor agonist	Oral	25 mg daily
Tirzepatide (Zepbound®)	GLP-1/GIP receptor agonist	Subcutaneous	2.5 mg -15 mg weekly

- Interventions were compared with lifestyle modifications and with each other

GLP-1: glucagon-like peptide-1; GIP: glucose-dependent insulinotropic polypeptide; mg: milligrams

Clinical Evidence

Objective

To evaluate the efficacy of **semaglutide (subcutaneous and oral) and tirzepatide added on to lifestyle modification** compared to lifestyle modification alone among adults without type 2 diabetes who are seeking medical management for weight loss and who are overweight with at least one obesity-related comorbidity or living with obesity.

Key Clinical Trials

Intervention	Key Clinical Trials (Weight)	Key Clinical Trials (CV Outcomes)
Injectable Semaglutide	STEP 1, 3, 5, 8, 10	SELECT
Oral Semaglutide	OASIS 4	SOUL, PIONEER 6
Tirzepatide	SURMOUNT 1, 3	SURPASS-CVOT
Tirzepatide vs. Injectable Semaglutide	SURMOUNT 5	---

- Meta-analysis was conducted using data from:
  - STEP 1, 3, 5, 8 for weight loss for injectable semaglutide
  - SOUL & PIONEER-6 for cardiovascular outcomes for oral semaglutide

Key Outcomes

- Patient-important outcomes
  - Weight loss from baseline
  - Health-related quality of life
  - Metabolic parameters (e.g., blood pressure, blood sugar, lipids)
- Cardiovascular risk reduction
- Other organ dysfunction (e.g., MASH, OSA, OA, diabetes, etc.)
- Harms

MASH: Metabolic Dysfunction-Associated Steatohepatitis, OA: Osteoarthritis, OSA: Obstructive Sleep Apnea

Results: Weight Loss

Drug	Source	% Weight Loss from Baseline, Mean Difference from Placebo (95% CI)	Participants with ≥20% Weight Loss, %
Injectable Semaglutide 2.4 mg	ICER Meta-Analysis (week 68)*	-13.1 (-15.0, -11.3)	32%†
Oral Semaglutide 25 mg	OASIS 4 (week 64)	-11.4 (-13.9, -9.0)	30%
Tirzepatide 15 mg	SURMOUNT 1 (week 72)	-17.8 (-19.3, -16.3)	57%

*ICER Meta-Analysis of STEP 1, STEP 3, STEP 5, and STEP 8 trials
†Data from STEP 1 trial

95% CI: 95% Confidence interval,
mg: milligram

Results: Tirzepatide versus Semaglutide (SURMOUNT-5)

Drug	% Weight Loss from Baseline, Unadjusted	Participants with ≥10% Weight Loss	Participants with ≥20% Weight Loss	Participants with ≥25% Weight Loss
Semaglutide	-15.4	61%	27%	16%
Tirzepatide	-21.8	82%	48%	32%

Results: Health-related Quality of life

- Improved SF-36 physical component score for injectable semaglutide, tirzepatide (not collected for oral semaglutide)
- Lower scores on SF-36 mental component score for injectable semaglutide, tirzepatide (not collected for oral semaglutide), but still improved over placebo
- Improved IWQOL-Lite-CT score for all three medications
  - More participants taking semaglutide (injectable/oral) achieved HRQoL improvements exceeding minimum clinically important difference vs placebo

HRQoL: Health-related quality of life, IWQOL-Lite-CT: Impact of Weight on Quality of Life-Lite Clinical Trial version, SF-36: Short-form-36

Results: Cardiovascular Outcomes

Drug	Source	Population	Risk of MACE, HR/RR (95% CI)	Risk of All-Cause Mortality, HR (95% CI)
Injectable Semaglutide	SELECT	Obesity with known CV disease	HR 0.80 (0.72, 0.90)	0.81 (0.71, 0.93)
Oral Semaglutide	ICER meta—analysis (SOUL, PIONEER-6)	T2D with CV disease, ***14 mg dose***	RR 0.86 (0.78 to 0.95)	---
Tirzepatide	SURPASS-CVOT	T2D with CV disease, ***vs. dulaglutide***	HR 0.92 (0.83, 1.01)	0.84 (0.75, 0.94)

95% CI: 95% confidence interval, CV: Cardiovascular HR: hazard ratio; RR: relative risk
T2D: Type 2 diabetes

Other Outcomes from Clinical Trials

- Treatment with semaglutide or tirzepatide
  - Improved systolic blood pressure, hemoglobin A1c, lipids, waist circumference
  - Decreased risk of developing diabetes
- Treatment with injectable semaglutide:
  - Decreased risk of developing severe kidney disease
  - Improved knee pain in osteoarthritis
  - Improved steatohepatitis and liver fibrosis and steatohepatitis
- Treatment with tirzepatide:
  - Improved obstructive sleep apnea

Harms

Key Points

- Majority of participants in all trials (78-96%) had adverse event; most commonly gastrointestinal side effects
- Serious adverse events were much less common (~10% for semaglutide, ~5% for tirzepatide)
- Discontinuation was less than 10% in all trials
- Gallbladder and pancreatic adverse events were rare
- Death was very rare (<1%)

Harms – Tirzepatide vs Semaglutide (SURMOUNT-5)

Adverse Event (AE)	Tirzepatide, %	Semaglutide, %
Any AE	76.7	79
Serious AE	4.8	3.5
Serious GI AE	4.5	3.7
Discontinuation Due to AE	6.1	8
Death	0	0

AE: Adverse event, GI: Gastrointestinal

Controversies and Uncertainties

Key Points

- Uncertainty of cardiovascular benefits, particularly oral semaglutide and tirzepatide
- Long-term weight loss maintenance and discontinuation have not been fully evaluated, including whether re-treatment is as efficacious as initial therapy
- Long-term harms (e.g., sarcopenia, risk of thyroid and pancreatic disorders) are not yet known
- Need additional data on subgroups, particularly in lower BMI groups

Benefits Beyond Health and Special Ethical Priorities

Key Points

- Access to obesity medications is challenging, new options and more effective therapies may be beneficial in closing treatment gap
- Black and Hispanic Americans have a higher prevalence of obesity.
  - Health Improvement Distribution Index: non-Hispanic Black adults =1.2 and Hispanic adults =1.1
- Improvement in health may impact caregiver burden, especially long-term
- Oral formulation of semaglutide offers an additional option for those not wanting injectable medication

Insights from Discussions with Patients

- Treatment with GLP-1 RAs has been “life-changing”
  - Helps manage “food noise” and relationship with food
- Barriers to treatment include:
  - Insurance coverage
    - Less than 20% of employers covered weight loss drugs in 2025; Medicare barred from coverage for weight loss only
  - Race/ethnicity – e.g., Black women less likely to be offered treatment
  - Financial barriers, including lack of patient assistance programs

Public Comments Received

- Consider conducting a network meta-analysis (NMA) including all three interventions
  - Relative effects of each drug known from the clinical trials, NMA would not change conclusions
- Consider using adjusted weight loss data, rather than unadjusted data, in the report
  - No evidence of subgroup effect by baseline BMI, therefore unadjusted data most appropriate

Summary

- Semaglutide and tirzepatide in addition to lifestyle modifications are effective for weight loss compared with lifestyle modifications alone.
- Cardiovascular benefit of oral semaglutide and tirzepatide is an area of uncertainty, difficulty comparing three drugs without more definitive data.
- All drugs appear to improve quality of life; injectable semaglutide and tirzepatide also have additional benefits outside of weight loss (e.g., MASH, OSA).
- Harms appear to be mainly GI side effects and are mostly tolerable.

GI: Gastrointestinal, MASH: Metabolic Dysfunction-Associated Steatohepatitis, OA: Osteoarthritis, OSA: Obstructive Sleep Apnea

ICER Evidence Ratings for Obesity Medications

Treatment	Comparator	Population	Evidence Rating
Injectable Semaglutide	Lifestyle modifications	Adults with obesity (BMI ≥ 30) or overweight (BMI ≥27) with comorbidity	A
Oral Semaglutide			A
Tirzepatide			A

BMI: Body Mass Index

ICER Evidence Ratings for Obesity Medications (2)

Treatment	Comparator	Population	Evidence Rating
Tirzepatide	Injectable semaglutide	Adults with obesity (BMI ≥ 30) or overweight (BMI ≥27) with comorbidity	P/I
Tirzepatide	Oral semaglutide		P/I
Oral Semaglutide	Injectable semaglutide		C-

BMI: Body Mass Index

Questions?

Semaglutide and Tirzepatide for Obesity: Effectiveness and Value

Woojung Lee, PharmD, PhD

Associate Director, Health Economics and Decision Modeling

Institute for Clinical and Economic Review

ICER
INSTITUTE FOR CLINICAL AND ECONOMIC REVIEW

Key Team Members

Name	Title
Woojung Lee, PharmD, PhD	Internal Health Economist
Marina Richardson, PhD, MSc	Internal Health Economist
Marie Phillips	Research Assistant

Disclosures

WL, MR, and MP are employees of the Institute for Clinical and Economic Review (ICER) and have no conflicts.

ICER's full policy for managing and disclosing potential conflicts of interest can be found here [link].

ICER's full policy for managing and disclosing potential conflicts of interest can be found here.

Objective

To evaluate the lifetime cost-effectiveness of **semaglutide (subcutaneous and oral) and tirzepatide added on to lifestyle modification** compared to lifestyle modification alone among adults without type 2 diabetes who are seeking medical management for weight loss and who are overweight with at least one obesity-related comorbidity or who are living with obesity.

Unmet Need

Condition	Absolute evLY Shortfall	Proportional evLY Shortfall
Obesity	6.2	20.4%
Other Example Conditions		
Osteoporosis	2.6	18.7%
High Cholesterol	1.7	10.9%
Multiple Sclerosis	18.9	52%

evLY: equal value of life years gained

Methods in Brief

Methods Overview

Domain	Approach
Model	Markov Model
Setting	United States
Perspective	Health Care Sector Perspective (base-case) Modified Societal Perspective (scenario)*
Time Horizon	Lifetime
Discount Rate	3% per year (costs and outcomes)
Cycle Length	1 year
Primary Outcome	Cost per quality-adjusted life year (QALY) gained; equal value of life year gained (evLY); life-years gained; the number of strokes and MIs averted.

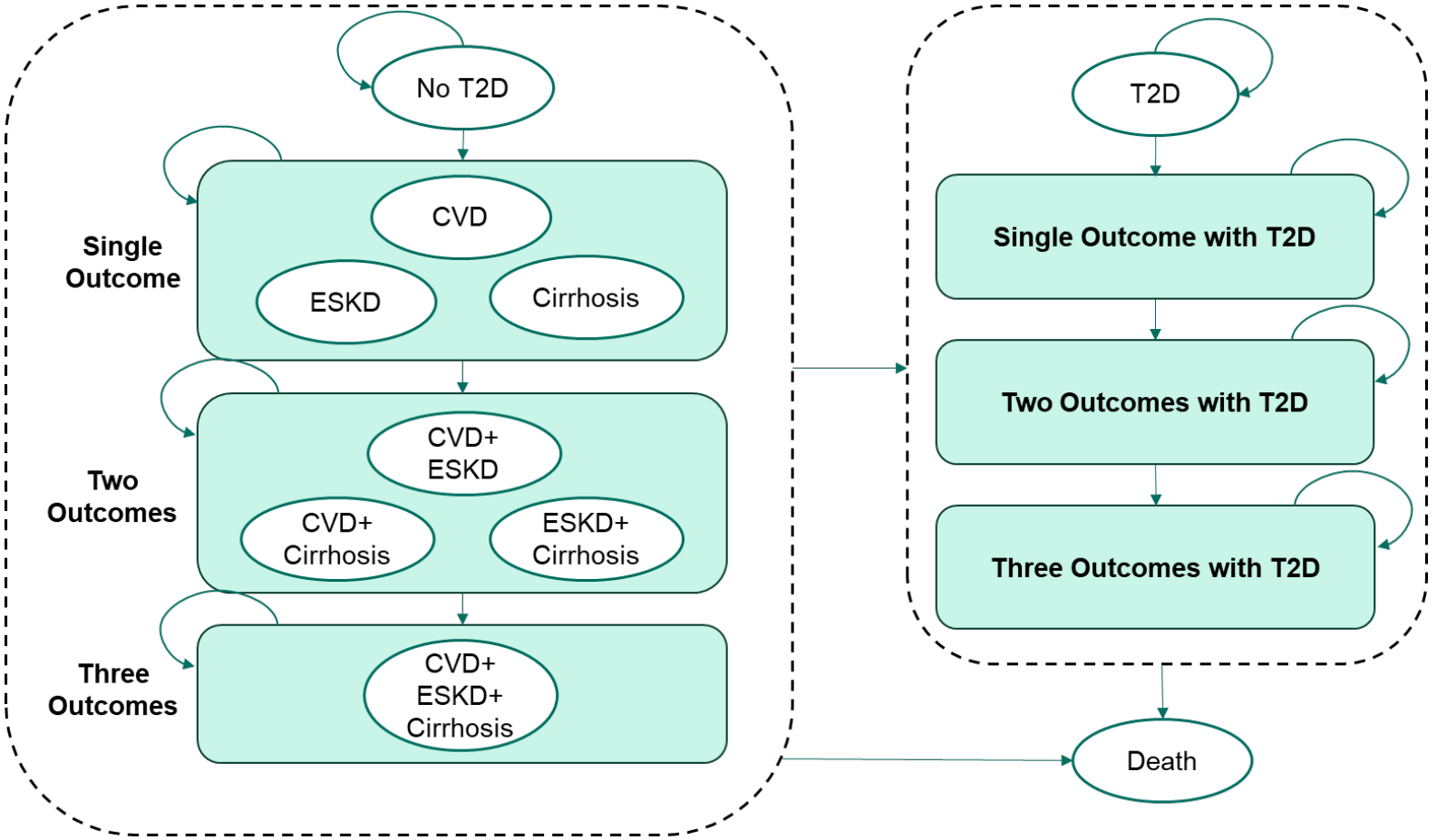
***Note:** The criteria for considering the modified societal perspective analysis as a co–base case are described in ICER's Reference Case

Model Cohort Characteristics

Baseline Characteristic	Value	Source
Mean Age	46 years	Gleason 2024; Ruseva 2025
Percent Female	79%	Rodriguez 2025
Mean BMI	37.6 kg/m^2	Rodriguez 2025
Percent Smoking	14.6%	CDC 2022
Percent CVD	6.5%	Ruseva 2025
Percent OSA	40.3%	Rodriguez 2025; Esmaeili 2025

BMI: Body Mass Index, CVD: Cardiovascular Disease, OSA: Obstructive Sleep Apnea

Model Schematic



- Proportions of patients who have **OSA** and those undergoing **knee/hip replacement** were tracked
- Within the CVD state, patient proportions in **CVD subtypes** were tracked:
  - Post MI
  - Post Stroke
  - Post MI and post stroke
  - HF post MI
  - Post stroke and HF post MI
  - Other CVD

CVD: Cardiovascular Disease, ESKD: End Stage Kidney Disease, HF: Heart Failure, MI: Myocardial Infarction, OSA: Obstructive Sleep Apnea, T2D: Type-2 Diabetes

Key Assumptions

- The included obesity-related outcomes and the direct impact of BMI on QoL are expected to reasonably capture the clinical benefits of weight-lowering medications.
- Direct cardiovascular effects of weight-lowering medications demonstrated in patients with diabetes can be extrapolated to estimate effects in obesity populations.
- Treatment discontinuation rates are based on the trial's intention-to-treat (ITT) population. Patients remaining on treatment during the trial period remain on therapy for the duration of the model and the weight loss achieved in the trial is maintained.
- Weight loss with a treatment is based on the weight loss observed in trials with the highest dose of that treatment.

Key Model Inputs

Treatment Effects on Body Weight

Parameter	Input	Source
LSM		
Change in Weight from Baseline by Year 1 (%)	-3.41%	ICER Pooled data*
Change in Weight from Baseline by Year 2 (%)	-2.60%	Garvey 2022 (STEP 5)
Injectable Semaglutide vs. LSM		
Absolute Difference in % Weight Change by Year 1	-13.14%	ICER MA
Absolute Difference in % Weight Change by Year 2	-14.00%	Garvey 2022 (STEP 5)
Oral Semaglutide vs. LSM		
Absolute Difference in % Weight Change by Year 1	-11.40%	Wharton 2025 (OASIS 4)
Absolute Difference in % Weight Change by Year 2	-12.46%	Garvey 2022 (STEP 5); Wharton 2025 (OASIS 4); Assumption
Tirzepatide vs. LSM		
Absolute Difference in % Weight Change by Year 1	-18.97%	Jastreboff 2025 (SURMOUNT-1)
Absolute Difference in % Weight Change by Year 2	-19.60%	Number provided by the manufacturer, digitized from Jastreboff 2025 (SURMOUNT-1)

*Pooled from STEP 1, STEP 3, STEP 5, STEP 8, OASIS 4, and SURMOUNT 1

Treatment Effects on Obesity-Related Outcomes
Type 2 Diabetes

Input	Value	Source
Annual Probability of Developing T2D, LSM	2.3%	Kahn 2024; Jastreboff 2025; Torgerson 2004; Le Roux 2017
HR of T2D, Injectable Semaglutide vs. LSM	0.27	Kahn, 2024 (SELECT)*
HR of T2D, Oral Semaglutide vs. LSM	0.27	Assumption
HR of T2D, Tirzepatide vs. LSM	0.07	Jastreboff, 2025 (SURMOUNT-1)*

*Prespecified secondary analysis

HR: Hazard Ratio, LSM: Lifestyle modification, T2D: Type-2 Diabetes

Treatment Effects on Obesity-Related Outcomes
Cardiovascular Disease

Input	Value	Source
Annual Probability of CVD for LSM	Estimated using the Framingham risk prediction model	D'Agostino 2008
HR of CVD, Injectable Semaglutide vs. LSM	0.80	Lincoff 2023 (SELECT)
HR of CVD, Oral Semaglutide vs. LSM	0.86	McGuire 2025 (SOUL); Husain 2019 (PIONEER 6)
HR of CVD, Tirzepatide vs. LSM	0.80	Assumed to be the same as SC Semaglutide

CVD: Cardiovascular Disease, HR: Hazard ratio, LSM: Lifestyle Modification

Treatment Effects on Obesity-Related Outcomes
Other Outcomes

Input	Value	Source
RR of ESKD Incidence	BMI 25-29.9 vs. <25: 1.08 BMI 30-34.9 vs. <25: 1.29 BMI 35-39.9 vs. <25: 1.50 BMI 40 or higher vs. <25: 1.71	Panwar 2015
RR of Cirrhosis Incidence	BMI 25-27.49 vs. <25: 1.05 BMI 27.5-29.9 vs. <25: 1.11 BMI 30-34.9 vs. <25: 1.49 BMI 35 or higher vs. <25: 1.77	Liu 2010
OR for Knee Replacement	Varies by sex and BMI categories	Wendelboe 2003
OR for Hip Replacement	Varies by sex and BMI categories	Wendelboe 2003
OR for OSA Prevalence	1.16 per 1 unit of BMI increase	Esmaeili 2025; authors' calculation

BMI: Body Mass Index, ESKD: End-stage kidney disease, OR: Odds ratio, OSA: Obstructive Sleep Apnea, RR: Risk ratio

Mortality

- Excess mortality attributable to obesity-related outcomes
- Probability of immediate death following an acute cardiovascular event

Input	Value	Source
Probability of Death from Acute MI	6.43%	OECD 2023
Mortality HR: Post MI	1.58	Majed 2015; Steven J Atlas, 2022
Probability of Death from Acute Stroke	6.69%	OECD 2023
Mortality HR: Post Stroke	3.13	Majed 2015; Steven J Atlas, 2022
Mortality HR: Other CVD	1.59	Pande 2011; Steven J Atlas, 2022
Mortality HR: HF Post MI	2.55	Gerber 2016
Mortality HR: T2D	1.16	Raghavan 2019
Mortality HR: ESKD	5.21	Lee 2023
Mortality HR: Cirrhosis	3.79	Simon 2021

ESKD: End-stage kidney disease, HR: Hazard ratio, MI: Myocardial Infarction

Utility

- Ongoing or short-term quality of life decrement due to obesity-related outcomes or events
- Additional quality-of-life impact of BMI, independent of obesity-related outcomes (-0.006 per one unit of BMI increase)
- Short-term quality of life decrement associated with severe GI side effects

Input	Value	Source
Multiplier: Post MI	0.95	Atlas 2022; Sullivan 2006
Multiplier: Post Stroke	0.94	Atlas 2022; Sullivan 2006
Multiplier: Other CVD	0.96	Atlas 2022; Sullivan 2006
Multiplier: HF post MI	0.93	Atlas 2022; Sullivan 2006
Multiplier: T2D	0.96	Atlas 2022; Sullivan 2006
Multiplier: ESKD	0.80	Yang 2015
Multiplier: Cirrhosis	0.73	ICER 2023; Flamm 2024
Multiplier: OSA	0.92 (with EDS); 0.97 (without EDS)	Cambron-Mellott 2022; Malhotra 2024
Acute Stroke*	0.19	Atlas, 2022; Matza 2015
Acute MI*	0.15	Atlas, 2022; Matza 2015
Knee Replacement*	0.17 (male); 0.20 (female)	NICE 2023; NICE 2021
Hip Replacement*	0.17 (male); 0.20 (female)	NICE 2023; NICE 2021
Severe GI AEs*	0.05	NICE 2019

*Short-term absolute utility decrement

AE: Adverse Event, BMI: Body Mass Index, CVD: Cardiovascular Disease, ESKD: End-stage kidney disease, GI: Gastrointestinal, HF: Heart failure, OSA: Obstructive Sleep Apnea, MI: Myocardial Infarction, T2D: Type-2 Diabetes

Drug Costs

Drug	Annual net price	Source
Injectable Semaglutide (Wegovy®)	$6,829†	SSR Health
Oral Semaglutide	$6,829*	Assumption
Tirzepatide (Zepbound®)	$7,973†	SSR Health

*Given the lack of available data, the net price of oral semaglutide was assumed to equal that of injectable semaglutide
†The annual net price already accounts for the use of direct-to-patient option available through NovoCare and LillyDirect.

Non-drug Costs

- Ongoing annual healthcare costs attributable to obesity-related outcomes
- One-time costs for acute cardiovascular events and surgeries
- One-time costs for severe GI side effects

Input	Value	Source
Post MI*	$9,248	Bishu 2020
Post Stroke*	$5,642	Girotra 2020
HF Post MI*	$19,294	Kazi 2024
Other CVD*	$8,253	Kazi 2024
T2D*	$7,825	Kazi 2024
ESKD*	$96,283	NIH NIDDK USRDS 2022
Cirrhosis*	$38,708	Younossi 2024
OSA*	$2,786	American Academy of Sleep Medicine 2016
Acute MI†	$34,151	Tajeu 2024
Acute Stroke†	$25,816	Tajeu 2024
Knee Replacement†	$31,341	Palsis 2018
Hip Replacement†	$23,630	Palsis 2018
Severe GI AE†	$9,148	McGregor 2023

*Ongoing annual costs
†One-off costs

AE: Adverse Event, CVD: Cardiovascular Disease, ESKD: End-stage kidney disease, GI: Gastrointestinal, MI: Myocardial Infarction, OSA: Obstructive Sleep Apnea, T2D: Type-2 Diabetes

Results

Base-Case Results

Treatment	Intervention Acquisition Costs	Total Costs	QALYs	evLYs	Life Years
Injectable Semaglutide*	$132,229	$447,925	16.79	16.81	20.39
Oral Semaglutide*†	$132,475	$449,980	16.68	16.70	20.35
Tirzepatide*	$158,493	$459,232	17.19	17.21	20.49
Lifestyle Modification	$9,036	$370,644	15.63	15.63	20.01

*Each treatment is added to lifestyle modification; therefore, intervention acquisition costs also include the costs of lifestyle modification.
†Based on an assumed price

Base-Case Incremental Results

Intervention vs. Comparator	Costs	QALYs	evLYs	Life Years
Injectable Semaglutide vs. LSM*	$77,281	1.16	1.18	0.38
Oral Semaglutide vs. LSM*†	$79,337	1.05	1.07	0.34
Tirzepatide vs. LSM*	$88,588	1.56	1.58	0.48

*Each treatment is added to lifestyle modification; therefore, intervention acquisition costs also include the costs of lifestyle modification.
†Based on an assumed price

Base-Case Incremental Results

Intervention vs. Comparator	Costs	QALYs	evLYs	Life Years
Injectable Semaglutide vs. LSM*	$77,281	1.16	1.18	0.38
Oral Semaglutide vs. LSM*†	$79,337	1.05	1.07	0.34
Tirzepatide vs. LSM*	$88,588	1.56	1.58	0.48

*Each treatment is added to lifestyle modification; therefore, intervention acquisition costs also include the costs of lifestyle modification.
†Based on an assumed price

Results at the New Medicare Price ($245 per month)

Intervention vs. Comparator	Costs	QALYs	evLYs	Life Years
Injectable Semaglutide vs. LSM*	$8,998	1.16	1.18	0.38
Oral Semaglutide vs. LSM*†	$10,899	1.05	1.07	0.34
Tirzepatide vs. LSM*	-$3,643	1.56	1.58	0.48

*Each treatment is added to lifestyle modification; therefore, intervention acquisition costs also include the costs of lifestyle modification.
†Based on an assumed price

Base-case Incremental Cost-effectiveness Ratio

Intervention vs. Comparator	Incremental Cost per QALY gained	Incremental Cost per evLY gained
Injectable Semaglutide vs. LSM*	$66,355	$65,280
Oral Semaglutide vs. LSM*†	$75,456	$74,143
Tirzepatide vs. LSM*	$56,622	$56,076

*Each treatment is added to lifestyle modification; therefore, intervention acquisition costs also include the costs of lifestyle modification.
†Based on an assumed price

Base-case Incremental Cost-effectiveness Ratio

Intervention vs. Comparator	Incremental Cost per QALY gained	Incremental Cost per evLY gained
Injectable Semaglutide vs. LSM*	$66,355	$65,280
Oral Semaglutide vs. LSM*†	$75,456	$74,143
Tirzepatide vs. LSM*	$56,622	$56,076

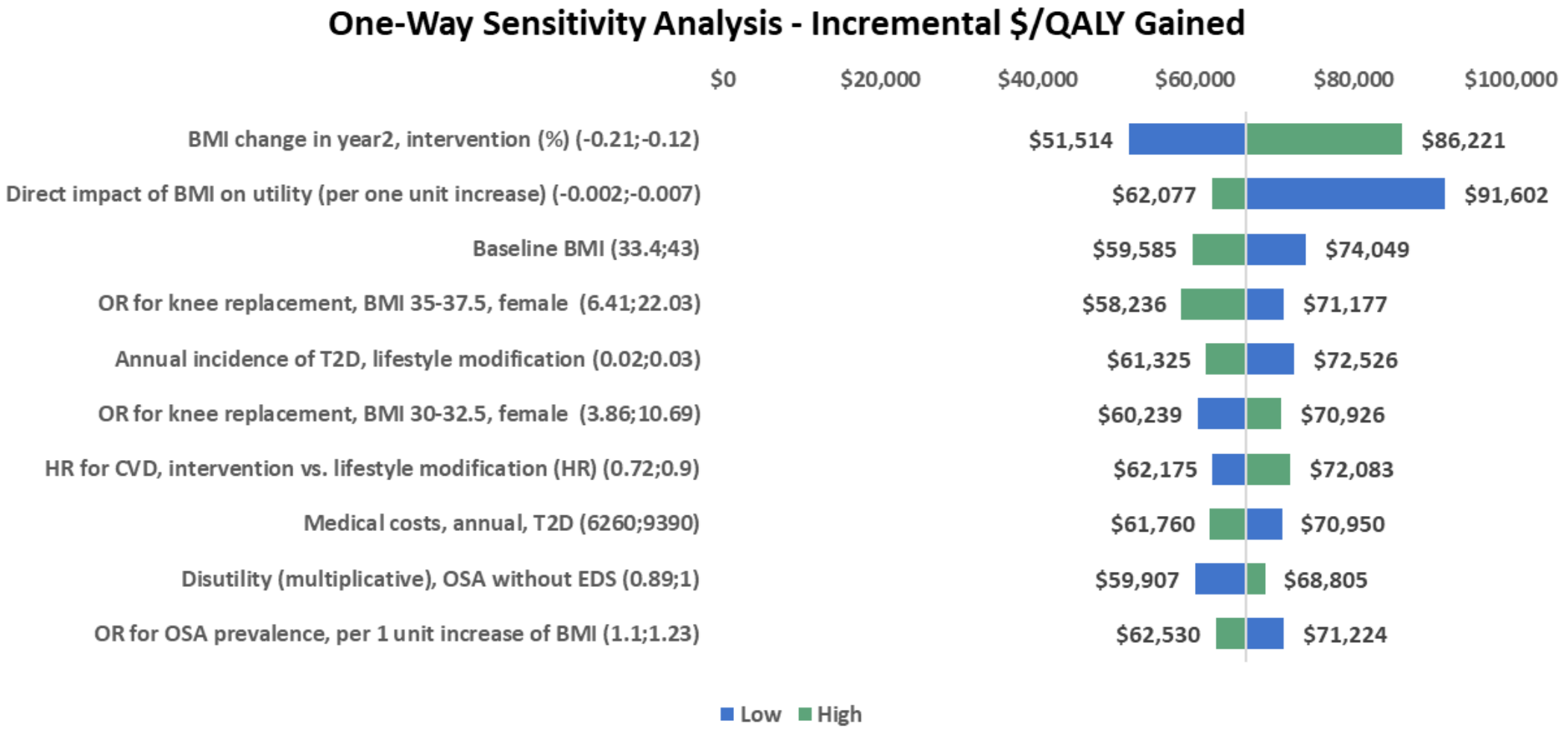
*Each treatment is added to lifestyle modification; therefore, intervention acquisition costs also include the costs of lifestyle modification.
†Based on an assumed price

Results at the New Medicare Price ($245 per month)

Intervention vs. Comparator	Incremental Cost per QALY gained	Incremental Cost per evLY gained
Injectable Semaglutide vs. LSM*	$7,726	$7,601
Oral Semaglutide vs. LSM*†	$10,366	$10,186
Tirzepatide vs. LSM*	More effective, less costly	More effective, less costly

*Each treatment is added to lifestyle modification; therefore, intervention acquisition costs also include the costs of lifestyle modification.
†Based on an assumed price

One Way Sensitivity Analyses



BMI: Body Mass Index, CVD: Cardiovascular Disease, EDS: Excessive Daytime Sleepiness, HR: Hazard ratio, OSA: Obstructive Sleep Apnea, OR: Odds Ratio, T2D: Type-2 Diabetes

Probabilistic Sensitivity Analysis

Drug	Cost-Effective at $50,000 per evLY gained	Cost-Effective at $100,000 per evLY gained	Cost-Effective at $150,000 per evLY gained	Cost-Effective at $200,000 per evLY gained
Injectable Semaglutide	16.9%	99.9%	100.0%	100.0%
Oral Semaglutide*	5.4%	96.4%	100.0%	100.0%
Tirzepatide	37.5%	99.9%	100.0%	100.0%

Note: Results are similar using cost per QALY gained
*Based on an assumed price

Scenario and Subgroup Analyses

	Injectible Semaglutide	Oral Semaglutide*	Tirzepatide
	Cost per evLY Gained		
Base-Case	$65,280	$74,143	$56,076
Modified Societal Perspective	$52,960	$61,406	$44,016
Subgroup Analysis			
BMI <30	$81,409	$86,875	$74,618
BMI ≥30	$65,329	$73,089	$55,989
BMI ≥35	$56,588	$69,703	$50,507
BMI ≥40	$64,554	$70,259	$52,008

Note: Results are similar using cost per QALY gained
*Based on an assumed price

Limitations

- **Uncertainty around long-term treatment effects beyond the trial period:** We assumed that weight loss as well as direct cardiovascular and diabetic effects observed in the trials are maintained throughout the treatment duration.

- **Uncertainty in measuring treatment effects on obesity-related outcomes:** Our model may underestimate benefits by excluding some obesity-related conditions but may overestimate benefits if model inputs were not fully adjusted (double counting).

- **Uncertainty in direct CVD effects:** There are varying degrees of uncertainty regarding the direct cardiovascular effects of the interventions as discussed in the clinical section.

- **Uncertainty around the real-world treatment patterns and associated outcomes:** Treatment discontinuation mirrored those observed in the ITT population of the trials, and alternative discontinuation scenarios were not modeled. Treatment persistence in this model may be higher than in the real-world settings.

- **Uncertainty around expected intervention prices:** There are uncertainties around the impact of the newly established lower prices for Medicare on prices for other payer types, and who will be able to access the treatments at the new prices.

Potential Budget Impact

Objective

- To estimate the potential total budgetary impact of the interventions of interest (injectable semaglutide, oral semaglutide, and tirzepatide), assuming all eligible patients initiate treatment over 5 years.

Methods

- The number of potential eligible population was estimated based on publicly available literature
  - US adults with obesity or overweight with comorbidities who do not have type 2 diabetes and are not currently using any anti-obesity medications (~92 million).
- Drug and non-drug costs for the first 5 years were derived from the cost-effectiveness analysis

Results

- At the net prices of each intervention of interest, the cumulative annual budget impact per patient was $6,908 in the first year and $17,422 by year 5.
- Fewer than 1% of eligible patients could receive treatment over 5 years before the ICER's potential budget impact threshold (2024-2025: $880 million) is met.

Results

- At the net prices of each intervention of interest, the cumulative annual budget impact per patient was $6,908 in the first year and $17,422 by year 5.
- Fewer than 1% of eligible patients could receive treatment over 5 years before the ICER's potential budget impact threshold (2024-2025: $880 million) is met.
  - Even assuming the new Medicare price ($245 per month) applies to all eligible patients in the US, the proportion of eligible patients who could be treated before reaching the ICER's budget impact threshold remains less than 1%.

Comments Received

- Earlier stages of liver fibrosis were not considered. Semaglutide recently received an indication based on the ESSECE trial for treatment of noncirrhotic MASH with moderate to advanced liver fibrosis and thus has potential to drive economic value by reducing healthcare costs and improving health outcomes.
    - While earlier stages of liver fibrosis may warrant treatment, F2 and F3 fibrosis primarily serve as risk factors for progression to clinically apparent disease, cirrhosis, and are generally not clinically apparent themselves.

Comments Received (cont'd)

- By applying a fixed annual budget impact threshold (i.e., $880 million in 2025) and relying on non-empirical uptake assumptions (i.e., 100% of the eligible population at the end of 5 years), ICER is limiting the utility and practical relevance of the budget impact analysis.
  - ICER's analyses of potential budget impact are intended to provide an alert if the anticipated cost to the overall health care system has the potential to exceed specific growth targets.
  - Expert opinion about desired use contributes to the decision about whether to issue an alert. That decision will be made for the Final Report after the Public Meeting.

Conclusions

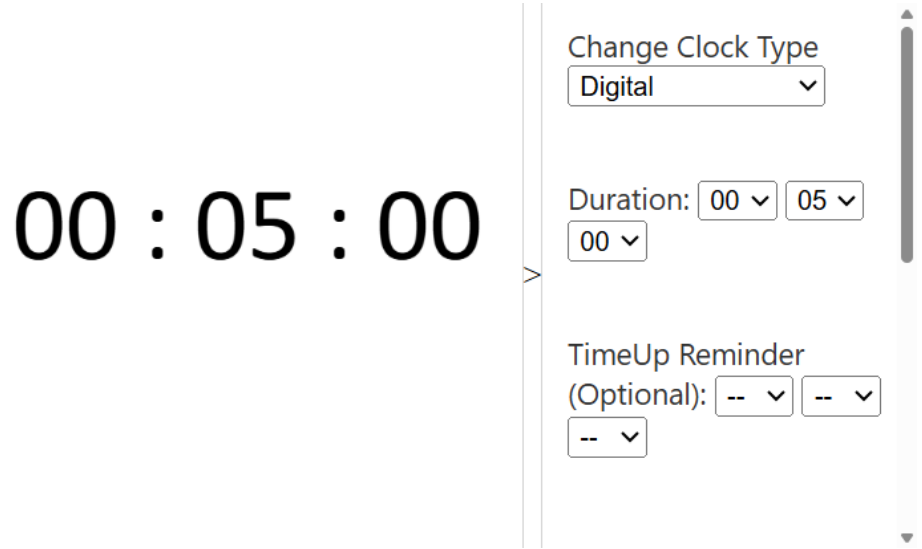
- At the current net price – or the assumed net price in the case of oral semaglutide – injectable semaglutide, oral semaglutide, and tirzepatide are cost-effective at commonly used cost-effectiveness thresholds.
- At current pricing and projected continued uptake, short-term potential budget impact exceeds ICER's potential budget impact threshold, raising concerns about affordability.
- At the new Medicare price, the drugs are even more cost-effective, with tirzepatide potentially being cost-saving, although concerns about affordability remain.

Questions?

Manufacturer Public Comment and Discussion

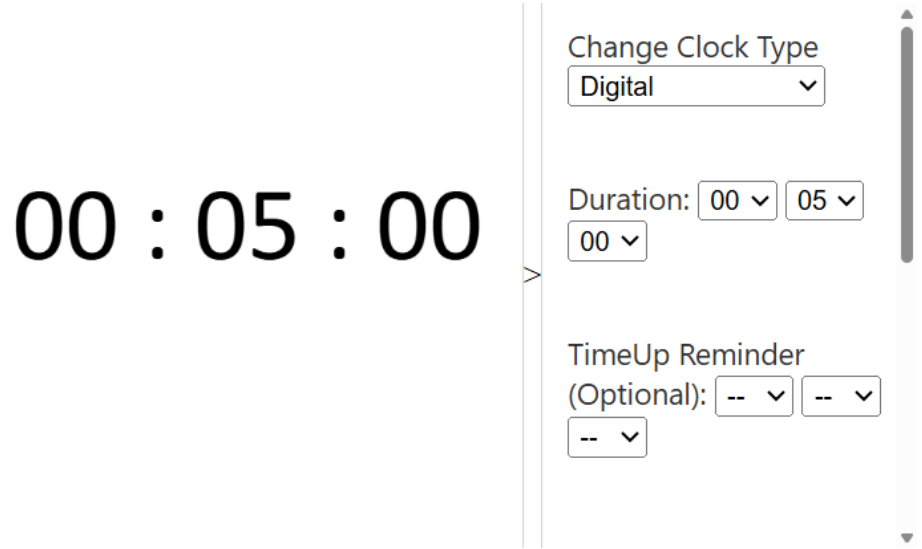
Jason Brett, MD
Principal Medical Head, Novo Nordisk Inc.

Dr. Jason Brett is a full-time employee at Novo Nordisk Inc.



Tracy Sims, MA
Executive Director, Corporate Affairs, Eli Lilly and Company

Tracy Sims is a full-time employee at Eli Lilly and Company.



Lunch

Meeting will resume at 12:45 PM ET

ICER
INSTITUTE FOR CLINICAL
AND ECONOMIC REVIEW

Voting Questions

Patient Population for all questions: Adults with obesity or adults with overweight in the presence of at least one weight-related comorbid condition, who are actively seeking medical management for weight loss; adults with established diabetes are excluded.

Clinical Evidence

1. Is the currently available evidence adequate to demonstrate that the net health benefit of injectable semaglutide added onto lifestyle modification is greater than that of lifestyle modification alone?

2. Is the currently available evidence adequate to demonstrate that the net health benefit of oral semaglutide added onto lifestyle modification is greater than that of lifestyle modification alone?

3. Is the currently available evidence adequate to demonstrate that the net health benefit of tirzepatide added onto lifestyle modification is greater than that of lifestyle modification alone?

4. Is the currently available evidence adequate to distinguish the net health benefit between tirzepatide and injectable semaglutide? If “Yes”, which has a greater net health benefit?

5. Is the currently available evidence adequate to distinguish the net health benefit between oral semaglutide and injectable semaglutide? If “Yes”, which has a greater net health benefit?

Benefits Beyond Health and Special Ethical Priorities

To help inform judgments of overall long-term value for money, please indicate your level of agreement with the following statements:

6. There is substantial unmet need despite currently available treatments.

7. This condition is of substantial relevance for people from a racial/ethnic group that have not been equitably served by the healthcare system.

To help inform judgments of overall long-term value for money, please indicate your level of agreement with the following statements:

8. Injectable semaglutide, compared with lifestyle modification alone, is likely to produce substantial improvement in caregivers' quality of life and/or ability to pursue their own education, work, and family life.

9. Oral semaglutide, compared with lifestyle modification alone, is likely to produce substantial improvement in caregivers' quality of life and/or ability to pursue their own education, work, and family life.

10. Tirzepatide, compared with lifestyle modification alone, is likely to produce substantial improvement in caregivers' quality of life and/or ability to pursue their own education, work, and family life.

11. Oral semaglutide offers a substantial opportunity to improve access to effective treatment by means of its mechanism of action or method of delivery.

Long-Term Value for Money

Given the available evidence on comparative clinical effectiveness and incremental cost effectiveness, and considering benefits beyond health and special ethical priorities…

12. What is the long-term value for money of injectable semaglutide added onto lifestyle modification compared to lifestyle modification alone at current pricing?

13. What is the long-term value for money of oral semaglutide added onto lifestyle modification compared to lifestyle modification alone at assumed pricing?

14. What is the long-term value for money of tirzepatide added onto lifestyle modification compared to lifestyle modification alone at current pricing?

Break

Meeting will resume at 2:20 PM ET

ICER
INSTITUTE FOR CLINICAL
AND ECONOMIC REVIEW

Policy Roundtable

Participant	Conflict of Interest
Jason Brett, MD Principal Medical Head, Novo Nordisk Inc.	Dr. Jason Brett is a full-time employee at Novo Nordisk Inc.
Pat Gleason, PharmD, FCCP, FAMCP, BCPS Assistant Vice President, Health Outcomes, Prime Therapeutics, LLC	Dr. Pat Gleason is a full-time employee at Prime Therapeutics.
Alyssa Guest, PharmD Associate Director, Clinical Pharmacy at IPD Analytics	Dr. Alyssa Guest is a full-time employee at IPD Analytics.
Melanie Jay, MD, MS Professor, Departments of Medicine and Population Health, NYU Grossman School of Medicine	No conflicts to disclose.
Joe Nadglowski President/CEO, Obesity Action Coalition	Joe Nadglowski has no personal relationships with industry. The Obesity Action Coalition receives 25% of financial support from health care companies including, Boehringer Ingelheim, Eli Lilly, Novo Nordisk, Amgen, Pfizer, AstraZeneca, Boston Scientific, Currax, Genentech, Intuitive, Kailera Therapeutics, Madrigal Pharmaceuticals, Medtronic, Regeneron, Rhythm Pharmaceuticals, Structure Therapeutics, Wave Life Sciences and Zealand Pharma.
Tracy Sims, MA Executive Director, Corporate Affairs, Eli Lilly and Company	Tracy Sims is a full-time employee at Eli Lilly and Company.
Michele Tedder, MSN, RN, BCC Director of Chronic Disease, Black Women's Health Imperative	Michele Tedder is an Obesity Action Coalition board member.
Alexa Triot, MD Clinical Director, Weight Management Programs, and Primary Care Physician, Healthcare Associates at Beth Israel Deaconess Medical Center	Alexa Triot's spouse works for Verve Therapeutics, a wholly owned subsidiary of Eli Lilly and Company.

New England CEPAC Council Reflections

Next Steps

- Meeting recording posted to ICER website next week
- Final Report published on or around December 16, 2025
    - Includes description of NE CEPAC votes, deliberation, policy roundtable discussion
- Materials available at: https://icer.org/assessment/obesity-2025

Adjourn

ICER
INSTITUTE FOR CLINICAL
AND ECONOMIC REVIEW