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Institute for Clinical and Economic Review (ICER)
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RE: Public Comments on Draft Scope for 2025 Obesity Management Assessment

Eli Lilly and Company (Lilly) welcomes the opportunity to provide comments on ICER's Draft Scoping Document (DSD) for the recently announced review of select treatments for obesity management (OM).

For nearly 150 years, Lilly associates have worked tirelessly to develop and deliver safe, effective and accessible medications for people across the world. Today, we're at the forefront of transforming the treatment paradigm for people living with, or at risk of developing, many complex, multifactorial diseases, including obesity.

Approximately 75% of U.S. adults are living with overweight or obesity today,[i] fueling a growing public health crisis. Overweight and obesity are characterized by excess body weight, which can negatively impact physical, financial, mental, and/or social health and well-being. Obesity is a chronic, complex, and treatable disease, while overweight is a complex and treatable condition that increases the risk of progression to obesity.

Overweight and obesity are associated with serious health and economic consequences. People living with overweight or obesity are at an elevated risk of developing potentially debilitating weight-related comorbidities and complications,[ii] with excess body weight contributing to an estimated one in six U.S. deaths annually.[iii] Absent intervention, the total economic impact of overweight and obesity, inclusive of direct and indirect costs, is projected to exceed $1 trillion, or 3.8% of U.S. gross domestic product, within the next five years.[iv]

Lilly shares ICER's view that many recently approved and pipeline OM medications (OMMs), including tirzepatide (Zepbound®), have the potential to deliver broad health and economic benefits, not just for individual patients, but for the healthcare system and society at large. We agree with ICER's stance that Zepbound is both clinically efficacious and cost-effective,[v,vi] and we look forward to sharing existing and emerging clinical and economic data supporting its value.

Upon review of ICER's DSD, Lilly is aligned with many of the preliminary scoping choices; we are, however, seeking clarity and requesting more specificity in ICER's Revised Scoping Document (RSD) on certain elements. For ease of reference, Lilly's comments on the following pages are organized to correspond to specific sections in ICER's DSD.

Comments pertaining to the ***"Background"*** section of the DSD:

Terminology – Lilly appreciates the attention paid to the etiology, epidemiology, and pathophysiology of overweight and obesity in the DSD, which serves to highlight the complexities, urgency, and challenges of addressing this critical public health. In topical framing, we encourage ICER to be mindful of its use of non-person-first language in the DSD, and we encourage the consistent use of person-first language in future documents, including the RSD.

Treatments – In discussing the evolving treatment landscape, ICER may be unintentionally obscuring important distinctions between this assessment's intended interventions of interest. For clarity, each intervention should be introduced and discussed independently. As such, Zepbound should be described as the first and only dual glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide 1 (GLP-1) receptor agonist indicated in combination with a reduced-calorie diet and increased physical activity to: (1) reduce excess body weight and maintain weight reduction long-term in adults with obesity or adults with overweight in the presence of at least one weight-related comorbid condition; and/or (2) treat moderate to severe obstructive sleep apnea (OSA) in adults with obesity. Any reference to Zepbound's clinical outcomes should be cited and sourced directly from published trial results from the SURMOUNT phase 3 clinical development program. We strongly recommend that ICER avoid a 'bundling' approach whereby multiple interventions' mechanisms of action and outcomes are described jointly (i.e., "Both are weekly injections that mediate weight loss primarily through decreasing appetite." and "Not only are semaglutide and tirzepatide associated with substantial weight loss (mean 15-20%) but can also result in improvements in obesity-related complications.").

Comments pertaining to the ***"Scope of Clinical Evidence Review"*** section of the DSD:

Population – Lilly supports ICER's selection of "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" as the primary population of focus for this assessment. Until additional evidence emerges, we are aligned with ICER's decision to exclude adolescents and/or children (i.e., individuals under 18 years of age). In its RSD, Lilly respectfully requests that ICER reassess its decision to exclude "adults with established diabetes" from its clinical evaluation. In its 2022 OM assessment, ICER chose to incorporate data on the population with type 2 diabetes mellitus (T2DM) at baseline into its evidence review and synthesis exercises. We believe this was an appropriate and well-informed decision and, as such, encourage ICER to leverage evidence from Lilly's SURPASS phase 3 global clinical development program in its clinical evaluation.

Subpopulations – In accordance with ICER's Value Assessment Framework, Lilly respectfully requests that ICER provide both an a priori list of the subpopulations of interest and accompanying scientific rationale for evaluating each subpopulation.[vii] To expand on our comments above, Lilly believes that ICER should include clinical subpopulation analyses for: (1) adults with overweight or obesity and prediabetes; and (2) adults with overweight or obesity and T2DM. In its RSD, we ask that ICER: (1) clarify why age is not accounted for, given that this is a presumptive subpopulation for every review; and (2) specify which class-based body mass index (BMI) categorizations it plans to examine. Further, we recommend that ICER eliminate any planned subpopulation analyses that explore "use and intensity" of lifestyle modification (LSM) and, more specifically, may examine: (1) non-use of diet and exercise (i.e., standard LSM) as an adjunct to treatment with an OMM; and/or (2) the use of more intensive LSM as a precursor and/or adjunct to treatment with an OMM.

Comparators – Lilly recommends that ICER clarify that the primary comparator for each intervention plus standard LSM will be placebo plus standard LSM.

Outcomes – Lilly strongly recommends that ICER include specific, quantifiable measures within the RSD's list of outcomes of interest. For example, instead of listing "weight reduction" broadly, the outcome should be expanded to include: (1) mean percentage change in body weight from baseline; (2) percentage of patients achieving ≥5%, ≥10%, ≥15%, ≥20%, ≥25%, ≥30% body weight reduction from baseline; and (3) change in BMI from baseline. This standard should be applied to all of the listed outcomes of interest. Further, Lilly recommends that ICER incorporate metabolic markers (i.e., change from baseline in hemoglobin

A1c (HbA1c), fasting glucose, fasting insulin, triglycerides, free fatty acids, low-density lipoprotein (LDL), high-density lipoprotein (HDL), total cholesterol (TC), systolic blood pressure (SBP), diastolic blood pressure (DBP) and waist circumference) into its RSD, recognizing the importance of capturing both intermediate and long-term outcomes. To that end, Lilly urges caution in including an extensive, non-descript list of weight-related comorbidities and complications due to the paucity of direct, long-term evidence and longitudinal data from clinical trials of recently approved OMMs.

Timing – Given that many trials of recently approved or pipeline OMMs do not report outcomes at the 26-week timepoint, Lilly requests clarity on how ICER plans to assess outcomes at this interval, especially in instances where graphical digitization may not be possible. Further, we recommend that ICER's RSD address timepoints for each outcome, with strong consideration of the fact that extension data exists for some, but not all, interventions of interest. To that end, Lilly suggests that ICER anchor its NMAs at 52 weeks post titration to the highest maintenance dose (e.g., 72 weeks from baseline for tirzepatide 15mg, accounting for a 20-week titration period) since this is where most trials for new incretin-based OMMs converge in reporting outcome measures.

Comments pertaining to the **"*Scope of Comparative Value Analyses*"** section of the DSD:

Economic model – We request that ICER clarify how its economic model will account for weight-related comorbidities and complications, including specifics on: (1) whether the model will capture prevention, improvement, and/or regression; and (2) how potential incongruities between direct and indirect evidence will be addressed (e.g., the role and source of risk equations). For health states not accounted for in ICER's 2022 OM model, which is being adapted for this assessment, we recommend that ICER maintain precedent by conducting and publishing "Comorbidity X" scenario and sensitivity analyses. Further, ICER's base-case model should include common synergistic states that capture the additive detrimental impact of multimorbidity on patient outcomes and cost-effectiveness results.

Economic outcomes – Lilly recommends that ICER elaborate on its plan to incorporate "cost per key clinical outcome avoided (e.g., cost per cardiovascular event avoided)" into this assessment. ICER should provide a full list of outcomes and events they hope to capture, especially since a large number of weight-related comorbidities and complications were referenced in the DSD that extend far beyond just cardiovascular outcomes and associated adverse events.

Scenario analyses – We strongly recommended that ICER exclude any "Drug X" scenario analyses that model economic outcomes for inline or pipeline OMMs using inputs from ongoing or recently completed trials. If ICER is contemplating said analyses, the RSD should include the drug(s) name(s) and relevant trial(s) upon which inputs may be drawn; this will facilitate engagement in the process by the primary manufacturer(s) of said drug(s).

Budget impact – Lilly requests that ICER provide additional specificity as to which interventions it intends to include within its Budget Impact Analysis, with consideration of the fact that two of the three listed interventions included in the DSD will have been on market for more than two years by the time ICER's Final Evidence Report for this assessment is released.

We appreciate your consideration of these comments. Should you have any questions or require additional information, please reach out directly to Sean Grande from the Lilly Value & Access (LVA) team within Lilly USA.

Sincerely,

Kevin R. Hern
Senior Vice President, Market Access, LVA

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May 14, 2025

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Public comments to ICER Draft Scoping document for the assessment of the comparative effectiveness and value of Semaglutide (oral and injectable) and Tirzepatide for the treatment of obesity

Dear Sarah Emond:

Thank you for the opportunity to provide comments on the Draft Scoping document for the assessment of the comparative effectiveness and value of Semaglutide (oral and injectable) and Tirzepatide for the treatment of obesity.

The key to addressing obesity is the recognition that it is a chronic disease. The pathogenesis of obesity involves the interaction of genetic, environmental, and behavioral factors. Additionally, the consequences of increased prevalence of overweight and obesity not only include increased morbidity and mortality but also reduced quality of life, reduced economic productivity, and increased health expenditure. Therefore, in assessing the value of anti-obesity medications (AOMs), the cost of health services and indirect costs such as lost productivity, lost life years and reduced quality of life should be considered.

Please find below our comments on the draft scoping document. There are 3 key comments that we would like to highlight that may help this assessment:

Recommendations:

1- We advocate for a nuanced approach to obesity diagnosis where BMI serves as a screening tool and not a diagnostic one alone (The Lancet Diabetes Endocrinology, 2025). In addition, emerging evidence (Paccou and Compston, 2024) indicates that BMI does not appropriately distinguish between lean and fat mass. This is a particularly salient feature for the elderly and ethnic groups, where obesity manifestation varies and requires a comprehensive set of tools to assess an effective treatment.
While the proposed model captures utility gains from lowering BMI, it could benefit from incorporating broader quality of life endpoints and additional outcomes, such as:
   - Inclusion of improvement in physical functioning as an efficacy endpoint (Paccou and Compston, 2024)
   - Inclusion of falls and fractures as an outcome (Paccou and Compston, 2024)
   - Reduction in overall healthcare spending (Thorpe and Joski, 2024)

2- The model currently uses a single cohort with average characteristics. Incorporating more granular patient stratification based on factors such as age, gender, ethnicity, baseline comorbidities, and socioeconomic status could yield insights into how different

populations respond to treatments. This would allow for more tailored recommendations and better understanding of health disparities.

3- Weight regain on discontinuation of treatment is an important consideration which confirms the chronicity of obesity and suggests that ongoing treatment is required to maintain improvements in weight and health (Wilding et al., 2022). Thus, including components that simulate weight regain over time could provide a more realistic estimate of long-term outcomes and cost-effectiveness.

Thank you again for this opportunity to provide comments and we look forward to continuing this engagement. If you have any questions, please feel free to contact me.

Sincerely,

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Novo Nordisk Inc. (henceforth referred to as "NNI") is a global healthcare company committed to helping improve the lives of people with obesity by changing how the world sees, prevents, and treats obesity including development of effective medications for chronic weight management. As the manufacturer of Wegovy® (semaglutide) injection 2.4 mg, NNI appreciates the opportunity to provide comments to ICER regarding the *Semaglutide and Tirzepatide for Obesity Draft Background and Scope* document released on April 29, 2025. It is imperative that ICER evaluates semaglutide and tirzepatide using an evidence-driven approach, fully considering the context of obesity as a metabolic disease.

Obesity is a serious, complex, multifactorial chronic disease that poses a significant threat to public health,[1-4] and contributes to a substantial and increasing economic burden.[5] This burden was estimated to be $1.72 trillion for the US in 2016, equivalent to 9.3% of the US gross domestic product, consisting of $480.7 billion in direct healthcare costs and $1.24 trillion in indirect costs.[5] Without intervention, treatment of obesity-related diseases including heart disease, stroke, diabetes, and cancer is projected to increase by $48–$66 billion per year in the US by 2030.[6] In addition, people with obesity or overweight are at increased risk of developing and dying from cardiovascular disease (CVD).[7-9] Hence, when evaluating medications for obesity, it is essential to consider costs relating to obesity-related complications.

NNI has a continuing commitment to obesity research, as demonstrated by the STEP trials and the SELECT trial, with 14 clinical trials including more than 25,500 patients. In the STEP trials, weekly subcutaneous semaglutide 2.4 mg was consistently associated with statistically significant mean weight loss in patients with and without type 2 diabetes (T2D) and improvements in cardiometabolic risk factors, physical function, and quality of life.[10-22] In SELECT, the addition of weekly subcutaneous semaglutide 2.4 mg to standard care was superior to placebo in reducing the incidence of major adverse cardiovascular events (MACE). MACE was measured as a composite endpoint of death from cardiovascular causes, nonfatal myocardial infarction (MI), and nonfatal stroke.[23]

After conscientious review of the draft scope, NNI finds it vital to comment on several aspects of the draft scope, namely: (1) Subgroups for examination; (2) Included outcomes; (3) Inclusion of oral pipeline GLP-1 products; (4) Molecule-specific benefits across chronic metabolic conditions.

1. Subgroups for examination. ICER has listed patient subgroups for examination in the *Draft Background and Scope* with subgroups including sex at birth, race and ethnicity, body mass index (BMI) categories, use and intensity of lifestyle interventions, and prior bariatric surgery. Though not limited to the below, NNI believes that there are some additional subgroups that are extremely important and should be explicitly modeled. Notably, metabolic dysfunction-associated steatohepatitis (MASH), established CVD, and heart failure are comorbid conditions with high unmet need in patients with obesity or overweight.

Regarding MASH and CVD, in its FDA label, Wegovy® is indicated to reduce the risk of MACE (cardiovascular death, nonfatal MI, or nonfatal stroke) in adults with established CVD and obesity/overweight.[24] Furthermore, in April 2025, the FDA accepted the supplemental

New Drug Application (sNDA) and granted Priority Review for semaglutide injection 2.4 mg for MASH in adults with moderate to advanced fibrosis.[25] This follows the publication of results from the phase 3 ESSENCE trial that showed once-weekly semaglutide 2.4 mg improved liver histologic results.[26] In addition, the American Association for the Study of Liver Diseases (AASLD) guidelines recommend that semaglutide be considered for MASH improvement and cardiovascular benefits in patients with obesity/overweight.[27] The American College of Cardiology (ACC) guidelines also recommend semaglutide over liraglutide for patients with chronic coronary disease and obesity/overweight in whom pharmacologic therapy is warranted for further weight reduction.[28] Regarding heart failure, NNI notes that ICER has included it as an outcome in the list of cardiovascular events. NNI believes that ICER should include heart failure as a subgroup instead of an outcome, given the demonstrated results for patients with heart failure in SELECT, STEP HFpEF, and a pooled post-hoc analysis.[21,23,29] In line with these data and recommendations, ***NNI believes ICER should include MASH, established CVD, and heart failure as separate subgroups***.

2. Included outcomes. Within the *Patient-Important Outcomes* of interest for inclusion in the review, NNI notes that the broadly defined term *Cardiovascular events* has been listed under *Obesity-related complications*. Some cardiovascular events are listed separately: heart failure, hyperlipidemia requiring treatment, and hypertension requiring treatment. NNI is in favor of detailing named cardiovascular events separately in the list of outcomes because obesity is a well-established risk factor for specific cardiovascular events. ***NNI recommends the addition of more cardiovascular events to the list of outcomes in alignment with the SELECT trial,[23] including: death from cardiovascular causes, nonfatal MI, and nonfatal stroke.***

3. Inclusion of oral pipeline GLP-1 products. NNI acknowledges that ICER has included both subcutaneously administered semaglutide and subcutaneously administered tirzepatide in their list of interventions. NNI notes that ICER has also included oral semaglutide in the list - a pipeline product, that has not received FDA approval. In May 2025, the FDA accepted the New Drug Application (NDA) for oral semaglutide, and NNI is seeking approval for use in adults with obesity or overweight with one or more comorbid conditions and to reduce the risk of MACE in adults with obesity or overweight and established CVD. **NNI has not made any formal decisions regarding oral semaglutide including its place in therapy and commercial/access strategy.**

Oral semaglutide is not the only oral GLP-1 product in development; there are numerous pipeline products, with orforglipron being the closest to launch after oral semaglutide.[30] Like oral semaglutide, orforglipron is not FDA-approved and both products have available efficacy results for clinical trials in obesity/overweight.[31,32] If ICER intends to evaluate oral semaglutide, ***NNI strongly recommends that orforglipron is also evaluated.***

Furthermore, NNI wishes to note that if oral semaglutide is approved, it will become the first oral GLP-1 indicated for chronic weight management and the only treatment available in both injectable and oral routes of administration, that we are aware of. ***We anticipate the ICER review to describe the advantages that oral formulations offer to patients in terms of convenience, preference, and ease of use, as well as the advantage to patients in offering multiple routes of administration.***

4. Molecule-specific benefits across chronic metabolic conditions. Semaglutide is a GLP-1 analogue with 94% sequence homology to human GLP-1. It acts as a GLP-1 receptor agonist that selectively binds to and activates the receptor targeted by native GLP-1.[24] Its efficacy and tolerability have been extensively demonstrated in patients with chronic metabolic conditions

in both clinical trials and clinical practice. Clinician familiarity, established dosing and administration, and patient trust for semaglutide have developed over time.

Chronic metabolic diseases result from complex, interlinked pathophysiological processes; with each condition increasing the risk of others.[33,34] Weight gain, adiposity, and inflammation can initiate a decline in metabolic health.[33,35] Abnormal adipose tissue releases inflammatory mediators, causing low-grade systemic inflammation and potentially contributing to insulin resistance.[33,34] Adiposity and insulin resistance can promote hypertension and are associated with dyslipidemia and T2D, as well as inflammation – key risk factors for CVD.[36-39] Additionally, the association of T2D and obesity with other cardiovascular-kidney-metabolic diseases such as chronic kidney disease (CKD), MASH, and peripheral arterial disease (PAD) has been well documented.[35-39] We believe it is important for ICER to consider data that investigate the impact of semaglutide on metabolic conditions:

FDA-approved indications for Wegovy®	• Adults and pediatric patients aged 12+ with obesity[10-13,15,18] • Adults with overweight with ≥1 weight-related comorbidity[10-13,15] • Adults with obesity/overweight and established CVD[23]
Additional evidence in weight-related comorbidities	• Knee osteoarthritis[19] • Heart failure[21-23]
Additional metabolic diseases impacted by semaglutide	• MASH[26] • T2D[40] • T2D and established CVD[41,42] • T2D and CKD[43] • T2D with PAD[44]
Additional ongoing and completed clinical trials for semaglutide	• Early Alzheimer's disease[45,46] • Pediatric diabetes[47] • Pediatric obesity[48] • Prediabetes[20] • Primary prevention cardiovascular outcomes trial in T2D[49]

We encourage ICER to review the publications referenced in this letter. ***NNI believes that ICER should take a holistic view of the benefits of semaglutide and tirzepatide, given the nature of interlinked chronic metabolic conditions and the molecule-specific benefits that may be exhibited in these conditions.***

NNI appreciates the opportunity to provide input as the scope for this important review is further developed. We strive for an evidence-driven approach to the assessment and hope ICER will consider the substantial body of evidence across obesity and multiple metabolic conditions. We look forward to continuing engaging with ICER throughout this review.

Sincerely,

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Public Comment on ICER's Review of Semaglutide and Tirzepatide for Obesity
Submitted on behalf of the Black Women's Health Imperative

Thank you for the opportunity to submit comments on the Institute for Clinical and Economic Review's (ICER) draft report assessing the clinical effectiveness and value of semaglutide and tirzepatide for the treatment of obesity.

For over 40 years, The Black Women's Health Imperative (BWHI) has driven change through evidence-based wellness programs, policy and advocacy and research translation. As an organization committed to eliminating health disparities across chronic diseases—particularly obesity, diabetes, and cardiovascular disease—we recognize the critical importance of evaluating emerging treatments with both scientific rigor and an equity-centered lens.

Addressing Low-Value Care in Obesity Treatment
Far too many individuals, especially Black women, continue to receive low-value, ineffective, or stigmatizing care for obesity. These practices include:

- Reliance on BMI alone, which fails to reflect the full scope of an individual's metabolic health.
- Recommending lifestyle changes in isolation, without access to comprehensive medical support.
- Delaying access to anti-obesity medications until after the development of comorbidities.
- Weight-centric care that does not address trauma, structural inequities, or mental health.
- Failure to broach the subject of weight or weight-loss options all together.

These approaches contribute to worsening outcomes and deepen the mistrust and disengagement many patients already feel within the healthcare system. Black women, in particular, are more likely to encounter weight stigma from healthcare providers and less likely to be offered comprehensive obesity treatment options, including medication or surgical referral, even when clinically appropriate [1,2].

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The Promise of Semaglutide and Tirzepatide
Semaglutide and tirzepatide represent a significant advancement in evidence-based treatment for obesity. Clinical trials have shown meaningful and sustained weight reduction, alongside improvements in cardiometabolic risk factors, physical function, and quality of life.

These medications offer new opportunities to:
- Interrupt the progression of obesity-related diseases.
- Provide options for patients who have historically lacked effective treatment.
- Support the shift away from harmful, one-size-fits-all models of obesity care.

Centering Equity in Value Assessment
Any evaluation of obesity therapies must explicitly consider equity. Black women face disproportionately high rates of obesity—nearly 57% of non-Hispanic Black women have obesity, compared to 44% of white women [3]. Despite this, Black women are underrepresented in clinical trials for anti-obesity medications and less likely to be prescribed AOMs, reflecting long-standing systemic barriers in access to care [4,5].

We urge ICER to integrate the following into its final review:
1. A health equity adjustment factor that accounts for the historic under-treatment and unique barriers faced by marginalized communities.
2. Patient-centered metrics, including improvements in mobility,energy, sleep, and self-perception—**not just weight loss.**
3. Access considerations for Medicaid and underserved populations, who are least likely to access these treatments without intentional policy action.

Recommendations:
BWHI strongly encourages ICER to:

- Acknowledge the full value of semaglutide and tirzepatide beyond weight loss, including their preventive potential and psychosocial impact.
- Avoid outdated cost-effectiveness thresholds that penalize innovation and reinforce delayed treatment models.

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- Recommend fair coverage and reimbursement practices that prioritize early, equitable access.

Conclusion

The science is clear: obesity is a chronic disease requiring comprehensive, evidence-based care. Semaglutide and Tirzepatide are not luxury treatments—they are necessary tools in closing persistent health equity gaps.

As ICER completes its review, we urge the committee to recognize the real-world benefit these medications offer to communities that have been marginalized, stigmatized, and underserved for far too long.

Sincerely,

Black Women's Health Imperative

www.bwhi.org

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May 19, 2025

Institute for Clinical and Economic Review
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Electronically delivered to: publiccomments@icer.org

Re: Semaglutide and Tirzepatide for Obesity: Draft Background and Scope

Dear ICER,

The Obesity Action Coalition (OAC) is the leading national non-profit organization dedicated to serving people living with the disease of obesity through awareness, support, education, and advocacy. Our vision is to create a society in which all individuals are treated with respect and without discrimination or bias regardless of their size or weight. We strive for those affected by the disease of obesity to have the right to access safe and effective treatment options. OAC has a strong and growing membership of more than 85,000 individuals across the United States.

We deeply appreciate the ongoing opportunities ICER has provided for the OAC and our members to share the lived experiences and perspectives of people affected by obesity. These opportunities have allowed us to ensure that patient voices are meaningfully included in key assessments and recommendations that impact access to care. We value this collaboration and look forward to continuing to work together to promote equitable, patient-centered approaches to obesity treatment.

We commend the ICER for recognizing obesity as a chronic disease, "that affects both physical and mental health, and can result in an increased risk for other conditions such as diabetes, hypertension, liver disease, sleep apnea, cancer, and cardiovascular disease." Treating obesity as a chronic disease is essential for fostering a comprehensive understanding of its complexities and long-term management. Patients living with a chronic disease should have access to medications that treat their disease. We provide these written comments as feedback and perspectives from the lived experience.

Reducing Weight Bias and Stigma

We appreciate ICER's acknowledgement that "Obesity can start in childhood and thus can have lifelong effects on an individual's education, work, and social interactions." It is well established that reducing weight-related bias and stigma is essential for promoting equitable and compassionate care for individuals living with obesity. Weight bias is often rooted in stereotypes that portray people with obesity as lazy, undisciplined, or lacking willpower can lead to discrimination in healthcare, employment, education, and social settings. This stigma not only harms psychological well-being but also discourages individuals from seeking medical care, contributing to poorer health outcomes.

By addressing and eliminating these biases, we can create more supportive environments that focus on evidence-based treatment, respect individual experiences, and empower patients to engage in their health without fear of judgment. Reducing stigma is a critical step toward improving both the quality of care and overall health equity. OAC recommends removing the term "anti" when referring to obesity medications. The term "anti" can be stigmatizing and perpetuate bias. Professional associations and patient advocacy groups in the obesity space have made this change.

Importance of People-First Language

Person-first language is crucial when discussing individuals living with obesity, as it emphasizes their identity beyond a medical condition and fosters dignity and respect. By placing the person before the condition—referring to them as "individuals living with obesity" rather than labeling them with a term that can carry stigma—OAC advocates for a more compassionate and understanding perspective. This approach not only acknowledges the complexities of their experiences but also encourages a supportive dialogue that focuses on overall health and well-being. Using person-first language helps to combat stereotypes, reduce discrimination, and promote acceptance, ultimately valuing people for who they are, rather than how they look. Specifically, we encourage ICER to update references of "obese" to "living with obesity."

Outcome Measures for Obesity

OAC appreciates that the field of obesity science is quickly evolving. While we support the outcomes of interest and patient-important outcomes listed in the scoping document we would like to share additional resources to take into consideration as ICER continues to build out the obesity treatment model. OAC also encourages broader consideration using all obesity medications in future assessments.

OAC participated in a project to develop a Patient-Centered Outcome Measures for Adults living with Obesity with the International Consortium for Health Outcomes Measurement (ICHOM). The ICHOM Adult Obesity Measure Set included outcomes under the following domains:

- Physical Health and Clinical Outcomes
- Wellbeing
- Health Behaviors
- Body Functioning
- Adverse Outcomes
- Surgery Specific Adverse Events
- Obstetric and Gynecological Outcomes

We encourage ICER staff to visit the ICHOM link above to review specific outcome measures and the related assessment tools. OAC would be happy to discuss the ICHOM project and patient-centered outcomes.

OAC appreciates the opportunity to provide input on this important draft background and scope document and recommends additional updates. With questions please contact Dr. Tracy Zvenyach, PhD, Director of Policy Strategy at tzvenyach@obesityaction.org.

Sincerely,

Joe Nadglowski
President & CEO
Obesity Action Coalition

Dear ICER,

For your CY2025 assessment of semaglutide and tirzepatide for obesity management, please kindly consider adding the comparative cost-effectiveness of oral anti-obesity medications (e.g., phertermine, bupropion/naltrexone). This would allow payers to consider formulary strategies to additionally add these agents where they have been traditionally excluded for weight-loss benefits.

Thank you,

Sarah Yoon, PharmD

Re: ICER Semaglutide and Tirzepatide for Obesity Draft Background and Scope

To Whom It May Concern:

Thank you for providing an opportunity to comment on your scoping document. Our feedback is shared below.

The scope does not seem to include investigation of the appropriateness and/or effect of discontinuing GLP-1 therapy. Understanding whether and when it is safe or beneficial to stop GLP-1 therapy directly affects its value proposition. If discontinuation leads to rapid weight regain, loss of glycemic control, or other adverse outcomes, the long-term cost-effectiveness of the therapy may be significantly reduced. Conversely, if sustained use is not essential and short-term use provides lasting benefits, then this may increase cost-effectiveness. Clinicians need evidence-based guidance on tapering or stopping treatment. Without such data, they may continue treatment unnecessarily or stop it prematurely, risking harm or reduced effectiveness. Some patients may experience side effects or wish to stop treatment due to costs or lifestyle reasons. Understanding what happens after discontinuation helps support shared decision-making and individualized care.

The scope does not seem to include investigating causes or accounting for medication non-adherence or dose-optimization when evaluating efficacy of GLP-1 therapy. Clinical trials often report ideal outcomes under controlled conditions. In practice, non-adherence and suboptimal dosing can significantly reduce the actual benefits seen in patients. If non-adherence or incorrect dosing is not considered, conclusions about a drug's efficacy may be misleading—either overstating its effectiveness or misattributing poor outcomes to the drug itself rather than to how it was used. Understanding why patients do not adhere—whether due to cost, side effects, complexity, or expectations—can inform strategies to improve adherence, leading to better outcomes. Dose optimization ensures patients get the most benefit at the lowest effective dose, reducing side effects and costs, which is critical for long-term therapy management. Non-adherence is often linked to social determinants of health. Ignoring it may obscure disparities in treatment outcomes among different populations.

It would be valuable for the analysis to explore the cost-effectiveness of different dosing strategies, potentially including scenarios that evaluate the "least effective dose." Given the significant cost of these medications and reported variability in patient response, including "hyper-responders," an evaluation of initiating and maintaining treatment at lower-than-maximum approved doses for certain patient profiles could reveal more cost-effective approaches for achieving meaningful, albeit potentially not maximal, weight loss. This could also have implications for tolerability and long-term adherence, which are critical factors in lifelong disease management.

The draft scope's use of "lifestyle modification" as a comparator and subgroup element would benefit from greater specificity for a robust cost-effectiveness analysis. To accurately assess value, it's crucial to define whether this refers to general approach or a structured, intensive lifestyle intervention program incorporating elements like medical nutrition therapy (MNT)

delivered by a registered dietitian, a prescribed exercise plan, and formal behavioral counseling. The composition, intensity, and associated costs of such a structured program significantly impact both the effectiveness of the "lifestyle modification alone" arm and the incremental benefit attributed to the AOMs when used in combination, thereby influencing the overall cost-effectiveness conclusions.

Clinical relevance of the selected outcomes of interest is not sufficiently addressed or explained. Outcomes should reflect real-world health benefits (e.g., reduced complications, improved quality of life) rather than just surrogate markers. Without this connection, it is unclear whether the results truly matter to patients and clinicians. Clinicians rely on relevant outcomes to determine how a therapy will impact patient care. If outcomes are not clearly linked to clinical benefits, they cannot support evidence-based decisions. Without justification, the choice of outcomes may appear arbitrary or biased, reducing trust in the findings and limiting their usefulness in broader populations. Outcomes should reflect what matters to patients, like functional improvements or reduced symptom burden, not just diagnostic endpoints. Of course, these outcomes should be investigated to determine whether they provide long-term value of therapy—such as reduced hospitalizations or disease progression.

Finally, while comparisons between semaglutide, tirzepatide, and lifestyle modification are essential, the current scope notably omits comparisons with other established, non-GLP-1 anti-obesity medications (AOMs) like phentermine-topiramate or naltrexone-bupropion. As the document itself notes clinical experts offer these when GLP-1 RAs are cost-prohibitive, a direct cost-effectiveness comparison against these older, less expensive agents would provide crucial context for payers and clinicians. Understanding the incremental cost-effectiveness ratio of GLP-1 RAs over these existing, generally less potent, alternatives is vital for formulary decisions and for situations where access to newer agents is limited.

Treating obesity with GLP-1 agents is an incredibly complex and nuanced endeavor due to a range of clinical, behavioral, and systemic factors. We appreciate the chance to engage with ICER on this very important topic.

Sincerely,
CVS Health

To: ICER

From: Harold Bays MD

RE: Semaglutide and Tirzepatide for Obesity Draft Background and Scope APRIL 29, 2025

Thank you for the opportunity to review this latest ICER report. You may recall I was involved in an earlier ICER report: **What about that 2022 ICER report on anti-obesity medications?** https://www.sciencedirect.com/science/article/pii/S2667368122000298.

The following are my current comments:

OVERALL ASSESSMENT: I found this to be a thoughtful and very well written draft document.

QUOTE: "There are multiple modalities for treating obesity including lifestyle modifications (e.g., diet, physical activity, and behavioral modifications)"
COMMENT: Instead of the word "diet," many prefer the term "healthful nutrition"

QUOTE: "Clinical experts stated that although some individuals may respond to older, cheaper medications, those are not as effective as GLP-1 RAs and thus are mainly offered when GLP-1 RAs are cost-prohibitive or when they are not available."
COMMENT: The term "they" may be misinterpreted. Might be best to rephrase: " . . . or when GLP-1 Ras are not available"

QUOTE: "Finally, we heard that there is excitement about the use of GLP-1 RAs for treatment for diseases other than obesity and Type 2 diabetes, including substance use disorder and Alzheimer's disease."
COMMENT: Might change to: "Finally, we heard that there is excitement about the use of GLP-1 RAs for treatment for diseases other than obesity and Type 2 diabetes, including cardiovascular disease, thromboembolic disease, heart failure, sleep apnea, osteoarthritis, fatty liver, kidney disease, substance use disorder and Alzheimer's disease."

QUOTE: "This project will evaluate the health and economic outcomes of semaglutide (subcutaneous and oral) and tirzepatide for individuals with obesity, excluding those with established type 2 diabetes, who are seeking medical management for weight loss."
COMMENT: While indicated to treat type 2 diabetes, oral GLP-1 RA (i.e., oral semaglutide) do not yet have an indication to treat obesity

QUOTE: Interventions The full list of interventions is as follows: • Semaglutide, subcutaneous administered weekly • Semaglutide, oral administered daily • Tirzepatide, subcutaneous administered weekly
COMMENT: Again, while oral semaglutide 25 mg is undergoing FDA review for treatment of obesity, and while many other oral GLP-1 RA are in development, no oral GLP-1 RA is approved to treat obesity

QUOTE: Obesity-related complications, including but not limited to:
COMMENT: Some of the most common and costly adverse consequences of obesity that often improve with GLP-1 RA, and which are not listed, include osteoarthritis, thromboembolic disease (including stroke), and congestive heart failure.

QUOTE: Identification of Low-Value Services ICER includes in its reports information on wasteful or lower-value services in the same clinical area that could be reduced or eliminated to create additional resources in health care budgets for higher-value innovative services (for more information, see ICER's Value Assessment Framework). These services are ones that would not be directly affected by semaglutide or tirzepatide (e.g., CPAP for OSA treatment), as these services will be captured in the economic model. Rather, we are seeking services used in the current management of obesity beyond the potential offsets that arise from a new intervention. ICER encourages all stakeholders to suggest services (including treatments and mechanisms of care) that could be reduced, eliminated, or made more efficient.

COMMENT: Regarding efficiency, once a patient has been prescribed a highly effective AOM, and once the patient experiences a robust response to treatment, then the priorities of nutritional intervention are best redirected from a focus on weight reduction, to a focus on improving the quality and healthfulness of the nutritional intervention. This includes a specific emphasis on (1) adequate protein (to help mitigate loss of lean body mass), (2) adequate micronutrient intake (with the risk of mineral and vitamin deficiencies increased with greater and more prolonged weight reduction) and (3) need for hydration (with dehydration common among recipients of GLP-1 RA due to decreased thirst, nausea, vomiting, and reduced water content in foods due to decreased food intake). All are important with respect for cost. For example, a failure to adequately emphasize hydration during treatment with GLP-1 RA can result in (and has resulted in) ER visits and hospitalization due to acute kidney injury. Analogous cost-saving and health enhancing examples likewise apply to ensuring adequate protein and micronutrient intake. Thus, to maximize efficiency, improve health, and reduce costs among those treated with GLP-RA, dietitians might best redirect their priorities from dietary caloric quantity to improved nutritional quality.

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