USC Schaeffer
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for Health Policy & Economics

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Congressional Budget Office
441 D St SW
Washington, DC 20024

Re: CBO Blog Posted by Phill Swagel on October 5, 2023:
"A Call for New Research in the Area of Obesity"

Dear Congressional Budget Office Staff:

We read with great interest your October 5, 2023 blog post, "A Call for New Research in the Area of Obesity," outlining the current state of the research on anti-obesity medications (AOMs) and seeking help from the research community to address unmet needs.

As researchers at the University of Southern California's Schaeffer Center for Health Policy & Economics with experience in this topic, we would like to suggest several research strategies for addressing these needs and enhancing CBO's analysis of policies affecting the use of AOMs.[1] In your blog post, CBO called for new research on "factors affecting AOM use, such as take-up rates, patients' adherence to drugs currently on the market, and expectations about the prices and effectiveness of AOMs that are being developed." CBO also called for "research on near- and long-term clinical impacts of AOMs (including health benefits or complications associated with them) and their effects on patients' use of, and spending on, other medical services."

For fourteen years, researchers at the USC Schaeffer Center have been conducting data-driven analyses to measurably improve value in health through evidence-based policy solutions, research excellence, and private and public-sector engagement. Schaeffer Center experts have studied the burden of obesity and projected future health and economic impacts of the obesity epidemic.[1-4] We have modeled the value of innovative obesity treatments and developed drug pricing and payment models to encourage broader access to new therapies.

We believe we can help CBO enhance its analysis of AOMs in several ways:

- Summarizing the serious limitations and biases of current real-world data on AOMs.
- Outlining the best methods for producing unbiased estimates of the value of current and future AOM treatments
- Highlighting existing evidence to help address remaining analysis gaps

Limitations of real-world evidence on AOMs.

The CBO blog highlights a lack of research using real-world data to estimate the impacts of new AOMs on various outcomes, including total medical spending. Yet real-world data are typically non-randomized and available over relatively short time horizons. Semaglutide (Wegovy), the popular new AOM, was only approved to treat obesity in 2021, limiting the availability of real-world data about its use. Insurance claims are the only timely data source that would capture AOM usage in 2022 or later, but insurance coverage for AOMs remains low and many users of semaglutide and other GLP-1 agonists for obesity management pay cash.[5] Moreover, the average tenure of patients in private health insurance

[1] The views expressed in this letter are those of the authors and do not necessarily reflect the views of the USC Schaeffer Center or the University of Southern California (USC).

plans is only 4 years.[6] To capture both the insurance and cash-pay markets for AOMs, and to reliably follow patients who switch insurers, researchers would need a data source such as the Medical Expenditure Panel Survey (MEPS). Yet the most recent MEPS files cover 2021; true follow-up data on AOM usage in MEPS won't be available for years.

A recent analysis by USC Schaeffer Center shows that treating obesity would reduce the incidence of many costly, comorbid conditions like diabetes and heart disease.[1] However, these complications do not arise immediately. Treating patients today will not necessarily reduce spending on these comorbid diseases in the same calendar year. Instead, it will prevent and delay future cases of disease which will generate savings over the coming decades. USC's analysis shows that the Medicare cost-offsets and the social value from treating obesity grow significantly from 10-20 years and from 20-30 years. An accurate assessment of the societal health benefits from AOMs would require decades of follow-up. But any current analyses using real-world data would necessarily apply only to short time horizon, thus missing the majority of the benefits associated with treatment and understating the eventual value to payers, patients, and society.

Not only are real-world data on AOMs limited to short-term use in the insurance market, they also suffer from selection bias. Claims data are not generated via a random assignment of patients to AOM usage. Instead, patients opt into AOM treatment based on factors that are unobserved in the insurance claims data but that may impact health and spending outcomes. On the one hand, patients deciding to take AOMs may be more likely to benefit. On the other hand, they may be less severely ill with lower expected benefits, but instead higher income and access to care. Thus, it is difficult to assess *a priori* the direction of the selection bias. There are many other unobserved characteristics that could drive this tendency towards medical spending such as a physician's propensity to prescribe treatments, patients' willingness to adhere to therapy, or differences in patients' overall health.

These unobserved variables that impact both whether a patient is taking AOMs and his/her medical spending will confound any claims analysis and lead to biased results that mischaracterize the potential cost savings associated with treatment. In fact, the unpublished claims analysis of GLP-1 usage mentioned in the CBO blog and cited in the popular press demonstrates the obvious selection bias for AOMs.[7] The study shows that the baseline annual medical costs for patients selecting into AOM treatment was almost $800 (7%) higher than the non-AOM cohort. The authors calculate the difference in medical costs in the year before AOM treatment initiation and the costs in the first year with treatment. They compare the change in costs for the AOM cohort to those of patients not taking AOMs. Although this differences-in-differences methodology is an attempt to account for selection issues, the authors have not accounted for unobserved variables that impact the selection into AOMs in the first place and can impact the change in medical spending year-over-year. For example, if a patient changes to a new physician who is more likely to prescribe medical treatments, this could impact both whether or not the patient takes AOMs and the patient's overall medical spending. The difference and difference model would incorrectly attribute the increases in spending to the AOM use. In practice, it is almost impossible to control for enough variables to ensure AOM use is independent of medical spending.

Despite the limitations of real-world data in estimating the health and spending impacts of AOMs, these data may be a good source for measuring drug adherence. However, any current analyses must consider how drug shortages have impacted the results. We know from Novo Nordisk that there have been supply shortages for Wegovy starting in March of 2022 and persisting today.[8] The popular press has also disseminated stories of discontinuation forced by shortages. The claims analysis cited in CBO's blog followed patients initiating treatment in 2021 for a year, meaning they may have been affected by supply shortages. This may partially explain the poor AOM adherence found in the study. Additionally, Wegovy was not approved until June 2021; earlier treatment initiation may have been with the predecessor GLP-1, Saxenda, which is less effective than Wegovy for weight loss, according to

clinical trials. Analyses that consider adherence across multiple AOMs should account for the possibility that adherence may depend on the relative efficacies across treatments.

Unbiased approaches to estimating the medical impacts of AOMs

The best approach for estimating the medical impacts of AOMs would be a randomized controlled trial that follows patients over multiple decades. The key is to randomly assign patients into a group receiving new AOM treatments and a group receiving a placebo, and then to track health and economic outcomes over a decade or more. Although a randomized trial would eliminate concerns over selection bias, we realize that such a trial is infeasible in the short-term, and that CBO is looking for more immediate estimates to inform Congress. Thus, we believe that a simulation approach is the best method to generate long-term, unbiased estimates of the impacts of treating obesity with new AOMs. The simulation approach allows researchers to use current data on the relationship between BMI and health and economic outcomes to project future outcomes under different scenarios. Essentially, simulation methods can be used to mimic a clinical trial by estimating patient outcomes under both a treatment scenario and a placebo scenario. Additionally, with the right assumptions around future health and population trends, the simulation can predict outcomes decades into the future. In fact, simulation methods have become a priority at the Food and Drug Administration (FDA), and a working group was established in 2016 to "support the implementation of modeling and simulation in the regulatory review process."

Researchers at the Schaeffer Center used the Future Adult Model (FAM) to estimate of the benefits of Medicare coverage for new AOMs. FAM is a well-established, economic-demographic microsimulation model that combines data from several large, nationally representative surveys to simulate lifetime health, medical spending, social services use and economic outcomes using transition probabilities across health and economic states (e.g., incidence of diabetes) in two-year cycles. We believe FAM is the appropriate simulation model to answer CBO's research questions for several reasons. First, FAM uses real versus synthetic cohorts from nationally representative survey data. The model simulates outcomes at the individual level and connects various health states and financial outcomes to *policy outcomes* such as taxes, medical care costs, pension benefits paid, and disability benefits. Additionally, FAM models all adults age 25+ in the US and predicts everyone's insurance coverage, which allows the simulation to uniquely model different AOM coverage scenarios.

Using FAM, we predict that Medicare coverage of new AOMs would generate $175-245 billion in savings to Medicare in the first 10 years alone (not counting for the costs of the drugs).[1] These cost offsets to Medicare would grow to $704 billion - $1.5 trillion after 30 years of coverage, which highlights the importance of longer-term analyses. In addition to the large Medicare cost-offsets, we predict that the U.S. could save over $7 trillion in medical spending over 30 years if everyone has access to AOMs.

Existing Evidence Gaps

Although simulation models have shown the tremendous value of treating patients with obesity, many policy makers and researchers remain solely focused on the price and potential uptake rates of AOMs. In fact, several studies have published budget impact estimates for covering new AOMs, but none of them account for the dynamic nature of net prices over the lifetime of a drug. For example, the Institute for Clinical and Economic Review (ICER) released a report on medications for obesity management in August of 2022 that made several assumptions on drug pricing that don't reflect real world price dynamics.[9] First, ICER estimated a net price for semaglutide that is similar to its list price in 2023 and does not account for the drug's 48% average rebate from SSR health data.[10] Second, ICER assumed the price of semaglutide would be constant over patients' (average age of 45) in their simulation model. This constant-price assumption fails to account for the impact of branded price competition and

the eventual generic competition that will dramatically lower prices when the patent for semaglutide expires. Similarly, a perspective published in the *New England Journal of Medicine* adopted ICER's assumptions on drug pricing and generated budget estimates including 100% uptake among the Medicare population with obesity using these higher prices.[11] These unrealistic pricing assumptions distort the conversation on the true benefits of weight loss drugs.

Recent analysis of SRR health data suggests that the new GLP-1 agonists in diabetes and obesity have average rebates ranging from 48-79% off list prices.[10] Not only are these rebates significantly larger than those assumed in previously published cost-benefit analyses, but they are also likely to increase as more drugs are approved and competition for formulary placement intensifies. In fact, the FDA is expected to approve Tirzepatide (Mounjaro) for obesity treatment later this year, which should impact net prices for Wegovy.

Expensive, innovative drugs are not a new phenomenon, and CBO should look to the price trajectories of earlier examples to understand how prices will evolve as branded competitors enter, followed by the eventual introduction of cheap generics. A study of brand-name-drug prices between 2011-2019 found that the introduction of branded competition was associated with an 18.5 percent reduction in projected spending.[12] Even though list prices increased for many drugs, the branded competition for formulary placement resulted in lower net prices. We also have examples of previous blockbuster drugs that fell in price as competition increased. HIV treatments cost more than $1000 per month in 1998; generic versions now sell for $69 per month or less. Similar price trajectories were seen with innovative treatments for hypertension, cholesterol, HCV and other diseases. After years of real-world treatment, we recognize the immense value generated by these treatments that dwarfs their initial costs. However, in too many instances, access to new drugs is initially restricted and patients suffer.

Finally, CBO also noted concerns over future AOMs: "The new drugs might be more effective, have fewer side effects, or be taken less frequently or more easily than current medications. Those improvements could translate to higher prices for AOMs in the future, even if prices decline for drugs that exist today." We respectfully point out that the next-generation, more effective AOMs that CBO anticipates will also generate more cost offsets and more value to society. In fact, this is the nature of all innovation, whether it is in the pharmaceutical space or elsewhere: Better technology that improves the quality and/or quantity of life sells for a premium. The relevant question for CBO's analysis is the current and future cost of the current treatments, compared to the value they generate. Our analysis shows that Medicare coverage alone for current AOMs could generate $1 trillion in social benefits over the next 10 years. This estimate suggests that there is roughly $100 billion per year in social benefits just among Medicare beneficiaries. Although initial prices for AOMs may be high, our results clearly show there is plenty of economic surplus to be divided among taxpayers, Medicare beneficiaries, and AOM manufacturers.

We commend CBO for recognizing the existing gaps in the understanding of how AOMs will impact future medical spending, and for seeking input from the research community about how to fill them. While there are significant data and methodological challenges to be overcome, there are better alternatives to simplistically extrapolating from the real-world data on AOM use that is currently available.

Sincerely,

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