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ORIGINAL RESEARCH

The Relative Value of Anti-Obesity Medications Compared to Similar Therapies

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Purpose: To demonstrate a need for improved health insurance coverage for anti-obesity medications (AOMs) by comparing clinical and economic benefits of obesity treatments to covered medications for selected therapeutic areas.

Methods: Using a grey literature search, we identified and prioritized therapeutic areas and treatment analogues for comparison to obesity. A targeted literature review identified clinical and economic outcomes research across the therapeutic area analogues. Associated comorbidities, clinical evidence, indirect costs (ie, absenteeism and productivity loss), and direct medical costs were evaluated to determine the relative value of treating obesity.

Results: Four therapeutic areas/treatment analogues were selected for comparison to obesity: smoking cessation (varenicline), daytime sleepiness (modafinil), migraines (erenumab), and fibromyalgia (pregabalin). Obesity was associated with 17 comorbidities, more than migraine (9), smoking (8), daytime sleepiness (5), and fibromyalgia (2). Economic burden was greatest for obesity, followed by smoking, with yearly indirect and direct medical costs totaling $676 and $345 billion, respectively. AOMs resulted in cost savings of $2586 in direct medical costs per patient per year (PPPY), greater than that for varenicline at $930 PPPY, modafinil at $1045 PPPY, and erenumab at $468 PPPY; pregabalin utilization increased costs by $924 PPPY. AOMs were covered by 10–16% of United States health insurance plans, compared to 45–59% for the four comparators.

Conclusion: Compared to four therapeutic analogues, obesity represented the highest economic burden and was associated with more comorbidities. AOMs provide greater cost savings compared to selected analogues. However, AOMs have limited formulary coverage. Improved coverage of AOMs may increase access to these treatments and may help address the clinical and economic burden associated with obesity and its comorbidities.

Keywords: obesity, anti-obesity drugs, health care costs, cost savings, health insurance

Plain Language Summary

Obesity is a chronic disease affecting over 40% of United States adults. It can lead to serious health risks and substantial medical costs. Although prescription anti-obesity medications (AOMs) can be effective for treating obesity and are recommended by medical guidelines, most health insurance plans do not cover them. We conducted a targeted literature review of published studies and reports to compare the relative value of AOMs to treatments for smoking, daytime sleepiness, migraines, and fibromyalgia (a condition that causes pain all over the body). We found that AOMs resulted in greater direct medical cost savings than the treatments for the other conditions. However, AOMs were covered by fewer health insurance plans than the other treatments.

Introduction

Obesity is highly prevalent in the United States (US), affecting over 40% of the adults,[1] with prevalence rates expected to increase to nearly 50% by 2030.[2] It is associated with significant disease burden by increasing the risk for many comorbidities including cancer, stroke, osteoarthritis, sleep apnea, type 2 diabetes, and other cardiometabolic conditions.[3–7] Additionally, obesity poses considerable economic burden, both in direct medical costs[8–12] and indirect

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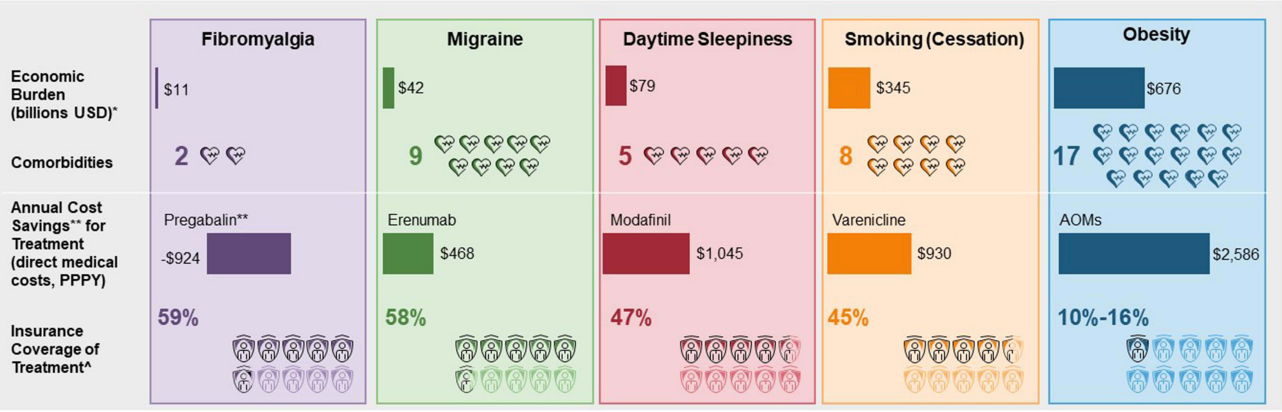
Graphical Abstract



costs including absenteeism and productivity loss.[13–18] Obesity-related complications accounted for almost half of the medical and productivity costs of chronic diseases in the US as of 2016, totaling $1.72 trillion.[19]

Sustained weight loss of at least 5% body weight is recommended by obesity treatment guidelines[20,21] and is associated with a significant reduction in the development and delayed onset of type 2 diabetes, hypertension, hyperlipidemia, and osteoarthritis.[22,23] Additionally, weight loss has been shown to reduce healthcare costs.[24,25] However, weight loss is difficult to maintain over time.[26–28] Pharmacotherapy, as recommended by treatment guidelines,[20,29] can be effective in managing obesity.[30–33] Anti-obesity medications (AOMs), as an adjunct to a reduced calorie diet and increased physical activity, can provide greater weight loss than lifestyle changes alone.[34–37]

Although AOMs have been shown to be cost-effective[38–41] and cost-saving,[24,25,42] less than 2% of eligible patients have been prescribed AOMs.[43–48] Low use of AOMs may be due to many reasons including lack of, or limited, health insurance coverage.[48–52] Coverage of AOMs is currently lower than treatments for other chronic conditions such as migraine and fibromyalgia, for which over 50% of the commercial, Medicare, and Medicaid health plans provide formulary coverage.[53] Increased coverage for AOMs may lead to substantial societal value, as demonstrated by a simulation model by Kabiri et al.[54]

The objective of this study is to demonstrate a need for improved health insurance coverage for AOMs by comparing clinical and economic benefits of obesity treatments to medications for other comparable chronic diseases. We conducted a literature review to identify the most appropriate therapeutic areas to compare to obesity and evaluated these across key economic factors.

Methods

Study Design

The study was conducted in three steps: 1) grey literature review to identify treatment areas similar to obesity and of concern for US payers and employers, 2) prioritization of therapeutic area and treatment analogues, and 3) targeted literature review to compare the relative value of AOMs to other therapies. Clinical outcomes, patient-reported endpoints, associated comorbidities, direct medical costs, and indirect costs (absenteeism and productivity loss) were evaluated for the selected analogues to assess the relative value compared to obesity.

Analogue Identification

We conducted a grey literature search to create a list of candidate therapeutic areas. A preliminary list was developed using information on US medication spending and utilization trends from resources including IQVIA Institute databases and reports from the pharmaceutical industry, health plans, employer organizations, and the Centers for Disease Control and Prevention

(CDC).[55–63] Twenty-five therapeutic areas were selected and screened based on pre-specified criteria including healthcare cost spending, relevance to obesity, type of indication, and duration of treatment (Table S1).

Analogue Prioritization

The list of 25 therapeutic areas were further evaluated; 16 were eliminated due to having primarily generic options in the market, acute nature of the condition or episodes, falling outside medical/pharmacy budgets (eg, dental care and vision care), and overlapping with obesity (eg, diabetes, and hypercholesterolemia) (Table S2). The remaining nine therapeutic areas were selected for further analysis and prioritization: daytime sleepiness, asthma/chronic obstructive pulmonary disease (respiratory), dermatology, fibromyalgia, gastrointestinal, hypoactive sexual desire disorder, smoking cessation, vaccines (human papillomavirus), and migraine. These therapeutic areas were assessed using seven dimensions: population size, reimbursement type/history, cost evolution, type of therapies, benefit to patients, barriers, and lifestyle indication. See Table S3 for more information about each dimension.

We characterized each therapeutic area based on the prioritization criteria using secondary research including academic, peer-reviewed, business, and scientific reports and databases. The top four areas were selected based on their ranking and included the following therapeutic areas and one analogue/representative product each: smoking cessation (varenicline [Chantix]), daytime sleepiness (modafinil [Provigil]), migraine (erenumab [Aimovig]), and fibromyalgia (pregabalin [Lyrica]) (Table 1). These were included in the targeted literature review (Figure 1).

Targeted Literature Review

We conducted a targeted literature review of published studies available in online databases or accessible via Google or PubMed. This was not meant to be an exhaustive review, but rather aimed to identify the most relevant, current, and high-quality evidence. The study considered MEDLINE and Embase using combinations of keywords, indexing terms, and Boolean operators based on predefined PICOS (Population, Intervention, Comparator, Outcomes, and Study Design) criteria for the therapeutic area analogues (Table S4).

The search strategy was developed in collaboration with an experienced information specialist/medical librarian. We searched for published materials in the English language without geographic limits. Publications were limited to the past 5 years. Supplemental Google searches were conducted to identify older, seminal studies (eg, used for health technology assessment and reimbursement decisions). A total of 2956 articles were identified. See Tables 5–8 for the search strategies for each analogue.

References were screened in an Excel workbook and marked for inclusion/exclusion for consideration for full-text review. Filters were applied to reduce the list of articles, removing duplicates and studies outside the relevant geography (ie, US). The 89 articles meeting the eligibility criteria were included in the full-text screening, data extraction, and synthesis. Data extraction included study population, data source, study setting, study design, outcomes, year/age of data, sample size, and stakeholder relevance (eg, employer, payer, clinician).

The full-text review yielded 39 articles considered most relevant in terms of time frame, stakeholder representation, granularity of data, and cost details. Nine of these articles were discarded due to lack of information or relevance regarding geography (eg, nationwide vs regional), type of data (eg, claims, real-world studies), and comparators considered in our analysis. Nine references for obesity were previously compiled and based on the same parameters regarding recency, geography, as well as the outcomes and study design PICOS criteria. Clinical and patient-reported endpoints were reported for subcutaneous semaglutide 2.4 mg (Wegovy). However, due to the recency of this medication's approval by the Food and Drug Administration (FDA) for the treatment of obesity, analysis of economic burden of obesity and formulary coverage were based on research examining other FDA-approved prescription AOMs for long-term treatment of overweight and obesity. Cost savings of AOMs was based on assumptions of 10–20% weight reduction in a cohort of patients at 1 year and the direct medical cost impact and direct medical cost impact,[25] which is consistent with 15% weight loss seen in the STEP 4 68-week clinical trial evaluating weekly subcutaneous semaglutide.[64]

Relative Value Analysis

The results of the 39 articles included in the analysis were summarized and tallied descriptively (eg, range of values) and qualitatively. The relative value analysis started with the collection of clinical and financial outcomes (clinical trials,

Table 1 Detailed Prioritization Matrix and Prioritized Treatment Areas

Therapeutic Area (Drug)	US Prevalence	Coverage[a] (% Plans)	Coverage	Cost Evolution[b]	Types of Therapy[c]	Number of Products Available	Benefit to Patients[d]	Payer Perception	Monthly WAC ($)[e]	Duration[f]	Opt-in Required[g]
Obesity (Saxenda)	35%[1]	16%	Not covered	2.19%	Oral, injectable	3–5 products	Large Improvement	Lifestyle indication	1367.00	Chronic	X
Daytime sleepiness (Provigil)	23%[65]	47%	Generally covered with restrictions	5.00%	Oral	5–7 products	Large Improvement	Lifestyle indication	1563.00	Episodic	
Smoking cessation (Chantix)	14%[93]	45%	Generally covered with restrictions	10.02%	Oral, injectable	3–5 products	Minor / No improvement	Lifestyle indication	673.90	Short course	X
Migraine (Aimovig)	17%[92]	58%	Generally covered with restrictions	22.48%	Oral, injectable	>10 products	Minor / No improvement	Lifestyle indication	682.10	Chronic	
Fibromyalgia (Lyrica)	4%[94]	59%	Covered	9.03%	Oral	3–5 products	Mild improvement	Lifestyle indication	694.50	Chronic	

Notes: [a]Percentage of commercial, Medicare, and Medicaid plans that cover the product as preferred (IQVIA SMART). [b]Cost variations in response to innovative treatments entry or other relevant events in the disease area (IQVIA SMART, 2015–2021). [c]Represents the routes of administration that account for 60–70% of the share. [d]Qualitative rating summarizing the improvement on key endpoints; Data from package insert by product. [e]IQVIA MIDAS, last reported price; Price RX; Monthly cost calculated based on prescribing information, each product label. [f]Based on product label. Short-term <1 year; Mid-term 1–3 years; Long-term >3 years. [g]Based on GoodRx coverage by insurance; X = Employer's opt-in required at current state.

Abbreviation: WAC, wholesale acquisition cost.

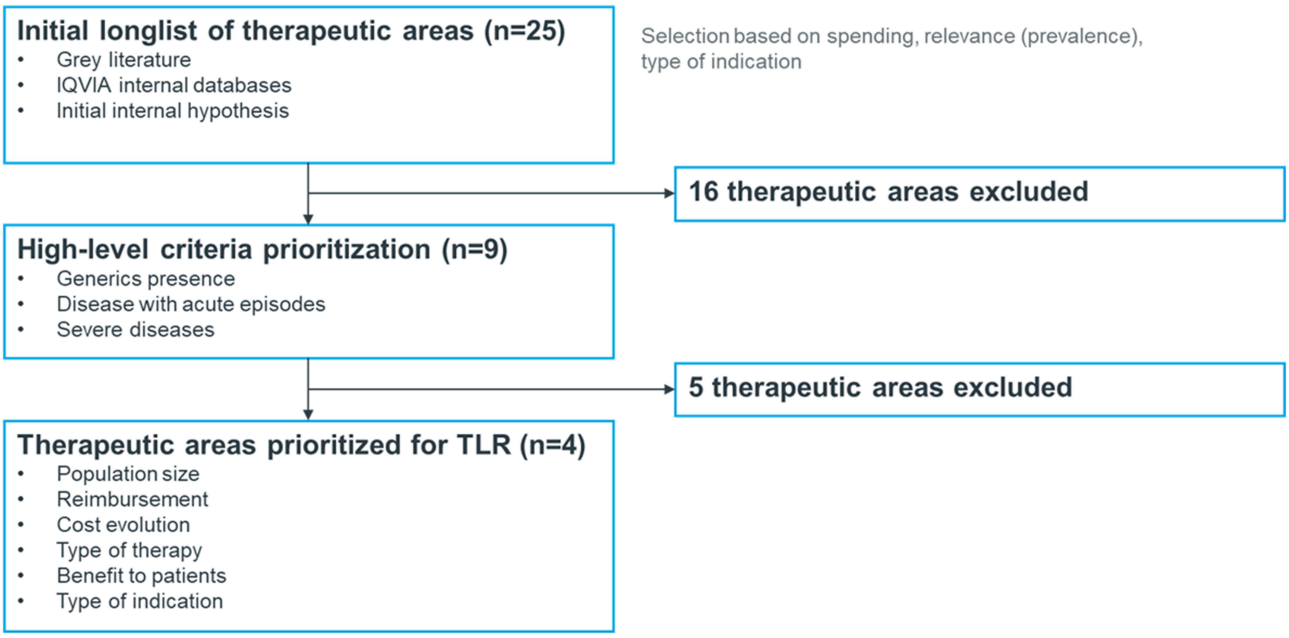


Figure 1 Therapeutic area analogue identification flow chart.
Abbreviation: TLR, targeted literature review.

claims databases, real-world studies). After identifying the most comparable endpoints and outcomes, results were compared against obesity to assess the relative value of treating obesity versus other treatment areas with covered products. To assess the broader impact of each condition, we identified comorbidities from the literature for obesity and for each of the four selected therapeutic analogues.

Results

Comparison of Analogues to Anti-Obesity Medications

Smoking cessation, daytime sleepiness, migraines, and fibromyalgia were selected as analogues based on similarities to AOMs including healthcare cost spending, chronicity, type of indication, and duration of treatment. Daytime sleepiness is defined as excessive sleepiness during the daytime stemming from causes such as obstructive sleep apnea.[65] Migraines are characterized by recurrent headaches that can last from 4 to 72 hours and are often accompanied by other disabling symptoms such as nausea, vomiting, and/or photophobia.[66] Fibromyalgia is a cause of widespread musculoskeletal pain and is often accompanied by irregular sleep patterns, fatigue, and substantial limitations in physical function and daily living.[67] Treatment analogues were selected due to their clinical efficacy,[68–77] coverage challenges at launch,[78–85] and/or cost-effectiveness.[86–91]

Clinical Burden and Formulary Coverage

Prevalence of the four analogue conditions ranged from 4% to 23%,[65,92–94] lower than that of obesity.[1] Obesity was associated with 17 comorbidities,[5] migraine was associated with 10,[95] smoking with 8,[96] daytime sleepiness with 5,[97] and fibromyalgia with 2[98] (Table S9). The economic impact of obesity-related comorbidities ranged from $486 for dyslipidemia to $1665 for pulmonary embolism, for an estimated total of $139 million in a population of 100,000 individuals.[5]

The new generation of AOMs (subcutaneous semaglutide 2.4 mg) demonstrated significant improvement in four clinical outcomes, compared to improvement in one clinical endpoint for each of the four treatment analogues.[64] Benefits provided by therapies for daytime sleepiness, migraine, and fibromyalgia were based more on patient-reported outcomes (Table S10).[99–102] Insurance coverage among commercial, Medicare, and Medicaid plans ranges from 45% for varenicline, 47% for modafinil, 58% for erenumab, and 59% for pregabalin; coverage for liraglutide 3.0 mg and subcutaneous semaglutide 2.4 mg is 16% and less than 10%, respectively (Table 1).[103]

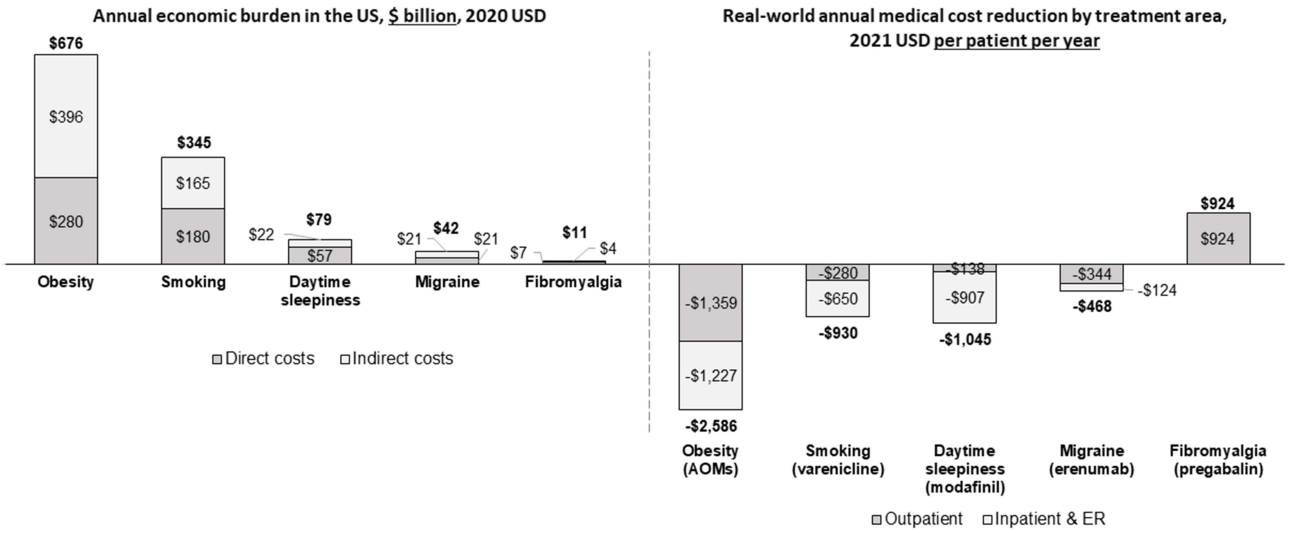


Figure 2 Annual economic burden in the US and real-world annual medical cost reduction by treatment area.
Notes: Direct costs are medical and pharmacy costs attributable to the burden of the disease. Indirect costs are costs not directly associated with treatment but are produced by the disease (eg, productivity loss).
Abbreviations: AOMs, anti-obesity medications; ER, emergency room.

Economic Burden and Direct Medical Savings

Across the areas evaluated, obesity accounted for the largest total economic burden (direct and indirect costs) at $676 billion[8,104] annually, followed by smoking at $345 billion[87] (Figure 2). Total economic burden was lower for the other conditions, ranging from $11 billion for fibromyalgia,[105,106] $42 billion for migraine,[107,108] and $79 billion for daytime sleepiness.[109,110] Indirect costs primarily included absenteeism and productivity loss as these were the most common and consistent indirect cost measures for comparison across therapeutic areas. Direct and indirect costs for each therapeutic area are presented in Figure 2.

Weight loss medications accounted for almost $2600 savings in direct medical costs per patient per year (PPPY) assuming 15% weight loss,[25,64] compared to approximately $1000 PPPY for smoking (varenicline)[87] and daytime sleepiness (modafinil),[111] and $468 PPPY for migraine (erenumab)[112] (Figure 2). The main drivers of these cost savings were reductions in outpatient, inpatient, and emergency room (ER) costs. There was an increase of $924 PPPY in medical costs for fibromyalgia (pregabalin), primarily due to increased physician visits for dose titration and monitoring.[113] Obesity and smoking treatments provided the greatest reduction in critical healthcare resource use utilization (eg, hospitalizations and ER admissions).[25,87] AOMs showed the greatest cost reduction potential, as they can be attributed to a decrease in inpatient and outpatient visits for musculoskeletal, digestive, and circulatory disorders.[25]

Productivity Loss

To understand the financial implications in an average mid-size company defined as having 100 to 999 employees,[114] we calculated indirect costs by multiplying the number of yearly average additional absenteeism days for each condition by the prevalence in an average mid-size company (assuming 500 employees), using the 2021 US national average hourly wage.[115] The annual workday loss was highest for obesity and daytime sleepiness, resulting in >520 days for an average mid-sized employer, and approximately $130,000 in annual productivity loss for both conditions (Table 2).

Discussion

Obesity contributes a significant burden on the US healthcare system. Although diet, exercise, and bariatric surgery are available to address obesity, they are not viable and effective options for every person living with obesity. AOMs offer another treatment option in adjunct to diet and exercise to help patients achieve their obesity treatment goals. Despite demonstrated clinical efficacy of AOMs[22,23,30–33] and reduced costs associated with weight loss,[24,25] payers have been slow to include

Table 2 Annual Workday Loss Associate with the Disease, for a Mid-Sized Company

Therapeutic Area	Average Additional Absenteeism (Per Person Per Year)	Prevalence in an Average Mid-Size Company (Number of Employees)	Annual Workday Loss (Days)	Annual Productivity Loss Due to Absenteeism (USD)
Obesity	3.0 days[13]	175	525	129,000
Smoking	2.3 days[120]	70	161	40,000
Daytime sleepiness	4.6 days[121]	115	529	130,000
Migraine	1.7 days[122]	85	145	36,000
Fibromyalgia	13 days[123]	20	260	93,000

Notes: Baseline of annual average absenteeism is 2.34 days in workers with normal weight.[13] Annual workday loss was calculated using the assumption of 500 employees for an average mid-size employer and reported prevalence rates for each condition. Productivity loss to absenteeism assumes the US national average hourly wage, US Bureau of Labor and Statistics 2021.
Abbreviation: USD, United States Dollar.

AOMs on their formularies. To better understand the potential value of increased health insurance coverage of AOMs, we compared AOMs to treatment analogues which have broad formulary coverage. Smoking cessation, daytime sleepiness, migraine, and fibromyalgia were deemed appropriate comparators due to factors such as their chronicity.

In our study, we found that obesity is associated with the greatest number of comorbidities as compared to the other health conditions evaluated. Each comorbidity related to obesity also contributes its own economic burden to the US healthcare system.[5] Our analysis showed that among the therapeutic areas evaluated, the greatest economic burden was seen for obesity at $676 billion annually,[8,104] nearly twice that of smoking,[87] 9 times that of daytime sleepiness,[109,110] 16 times that of migraine,[108] and 61 times that of fibromyalgia.[106] When considering the impact of all chronic diseases associated with obesity, the economic burden is even greater, estimated at $1.72 trillion in 2016, 72% of which was indirect costs due to lost productivity.[19] Our research also demonstrated that AOMs have greater direct medical cost savings than the therapeutic analogues.

Treatments for obesity, smoking cessation, daytime sleepiness, migraine, and fibromyalgia all provide clinical and economic benefits.[5,25,68–71,73,75,76,86–91,112] In addition to decreasing the risk for many obesity-related comorbidities[64] and recommended by clinical guidelines,[20,29] weight loss among patients with obesity is likely to decrease inpatient, outpatient, and ER visits, thus reducing the disease burden overall.[24,25] Furthermore, this may contribute to fewer absenteeism days that may improve overall productivity.[13] In a large study of patients treated to lose weight, Bilger et al found that weight loss of >5% could lead to an annual reduction of 3 days of absenteeism, translating to potential cost savings of $2.1 million.[116] In 2019, the societal value of increased access to currently available and next-generation AOMs was estimated at $1.9 to $2.5 trillion, varying by the level of uptake ranging from 15% to 30% of the patients eligible for chronic weight management.[54] AOMs offer benefits to payers and employers and may also have a positive impact on patients.[117]

Treatment of obesity demonstrates greater potential for a return on investment in decreasing comorbidity costs, all-cause medical expenditure, and absenteeism as compared to the four analogues studied. However, as of today, AOMs are only covered by 10–16% of health insurance plans, whereas the associated medications for the four analogues have at least 45% coverage.[118] Acknowledging the benefits of AOMs, the National Institute for Health and Care Excellence (NICE) in the United Kingdom recently recommended that subcutaneous semaglutide 2.4 mg be available to eligible patients as a weight management option.[119] Similar to the other treatments evaluated, coverage and adoption of AOMs may be a gradual process in the US, but our research demonstrates that broader coverage and increased utilization of AOMs can potentially reduce the economic burden associated with obesity.

This study consisted of a targeted literature review and was thus not a comprehensive review of the available literature for obesity and the four therapeutic area analogues. The analysis was limited to publicly available data. The data for daytime sleepiness is specific to sleep apnea based on available information in the literature; information on daytime sleepiness due to other reasons such as narcolepsy was not assessed. Data available in the literature and secondary sources were analyzed qualitatively; indirect comparisons were made from the extracted data, without any adjustments or meta-analysis. Data

analyzed in this study to assess the economic burden of obesity were based on treatments approved by the FDA prior to 2021; thus, newer generation AOMs with greater weight loss effects were not considered, which could underestimate the economic benefits of treatment. Lastly, in-depth analysis of formulary positioning was not evaluated due to limited public information available to perform this comparison. This study estimated healthcare cost savings from weight loss of 15% which was recently reported in the STEP 4 clinical trial comparing weekly subcutaneous semaglutide against placebo. AOMs may not be suitable for all patients and may not produce weight loss of 15% in real-world populations. AOMs may not be suitable for patients with liver and kidney issues, and Ding et al excluded patients with cirrhosis and patients undergoing dialysis from their study on healthcare costs associated with weight loss.[25] AOMs and the comparator treatments included in our analysis can have negative side-effects in some patients, and these negative side-effects could be associated with increased healthcare costs. This study did not capture costs that could be associated with negative side effects of AOMs or any of the comparator treatments. Further work is needed to evaluate how all-cause healthcare costs may be affected by weight loss specifically attributable to AOMs. Further work is needed to evaluate long-term effects of AOMs on health and healthcare costs.

Conclusions

The treatment of obesity showed a substantial potential for a return on investment by decreasing comorbidity costs, all-cause medical expenditure, and absenteeism. Ensuring increased patient access to obesity treatment options, including AOMs, may help address the obesity epidemic and decrease the overall disease burden of obesity, which will benefit patients, payers, and employers.

Abbreviations

US, United States; AOMs, anti-obesity medications; PPPY, per patient per year; ER, emergency room, CDC, Centers for Disease Control and Prevention; PICOS, Population, Intervention, Comparator, Outcomes, and Study Design; FDA, Food and Drug Administration; NICE, National Institute for Health and Care Excellence.

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Author Contributions

A Ruseva, A Ramasamy, C Blanchette, N Kim, and C Burudpakdee were responsible for study conception and design. J Estrada and I Chow were responsible for data analysis. All authors were responsible for analysis and interpretation of the data. All authors took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Novo Nordisk Inc. funded the study and had a role in the study design, data collection, analysis, and interpretation of data, as well as writing support of the manuscript.

Disclosure

Aleksandrina Ruseva, Abhilasha Ramasamy, and Christopher M. Blanchette are employees of Novo Nordisk. Nina Kim and Chakkarin Burudpakdee were employees of Novo Nordisk, Inc. at the time the study was conducted. Isabella Chow is an employee of IQVIA, Inc., which received funding to conduct the research. Joaquin Estrada was an employee of IQVIA, Inc. at the time the study was conducted. The authors report no other conflicts of interest in this work.

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