From:	BRITTANY MICHELLE GALUSHA
To:	ETF SMB Board Feedback
Cc:	Sieg, Tricia - ETF
Subject:	Reconsidering Antiobesity Medication Coverage
Date:	Monday, July 8, 2024 8:26:17 AM
Attachments:	Reconsidering coverage of antiobesity medication.pdf

Dear Ms. Sieg and Board Members,

I hope this message finds you well. My name is Brittany Galusha and I am an internal medicine physician with additional certification from the American Board of Obesity Medicine. I am reaching out to introduce myself and present a letter urging the Group Insurance Board/ETF to reconsider coverage of antiobesity medications.

Recent developments and research have highlighted the necessity of these medications in the effective management of obesity, which is recognized as a complex chronic disease that has been escalating at an alarming rate over the last several decades. It is abundantly clear that we need better treatment strategies in order to reverse this epidemic, improve the health of our population, and reduce healthcare costs related to obesity. The attached document further outlines the importance of coverage for these medications and the positive impact this change will have in each of these areas.

I look forward to discussing this issue further and exploring how the Group Health Insurance Program can move forward to implement this much needed change in coverage.

Thank you for your attention to this matter.

Warm regards,

Brittany Galusha, MD
Internal Medicine Physician
American Board of Obesity Medicine Diplomate

Dear Board Members,

My name is Brittany Galusha. I am a diplomate of the American Board of Obesity Medicine and a board-certified internal medicine physician. I have worked extensively with patients facing a variety of serious and extremely costly obesity related conditions over this period and despite ongoing efforts to promote more effective treatments, including systematic changes to improve our management of obesity, multiple obstacles continue to impede progress within this crucial field of medicine. One such obstacle is the lack of coverage for antiobesity medicines (AOMs) and I am disappointed that despite consensus from leading medical organizations, the Group Insurance Board/ETF declined to expand coverage for all its covered public employee health plans.

I understand that you have taken the important step to reconsider this benefit in light of the increasingly serious obesity epidemic across the nation and here in Wisconsin, including among the hundreds of thousands of WRS covered employees, many of whom are my patients. As you are likely aware, other states' employee health plans, including neighbors in the Midwest, provide coverage for eligible patients meeting certain criteria, some with mandatory wraparound support such as nutritional counseling and exercise monitoring to ensure adherence.

While lifestyle interventions are foundational for obesity management, AOMs are also an essential component of a comprehensive weight management plan for many individuals with obesity. Many of my patients have tried various diet and exercise programs for years without success and they, along with millions of others, are at serious risk of catastrophic future complications. AOMs are evidence-based therapies and a standard of care in obesity medicine, intended as an adjunct to lifestyle-based therapies for individuals with a BMI ≥ 30 or 27-29.9 with a weight related complication.[5] These treatments are safe and effective when used appropriately, per guideline recommendations (society guidelines are included on the reference page that follows). We need to have access to all appropriate evidence-based treatments to adequately address this complex disease process and halt the escalating epidemic of obesity. In terms of a direct impact on the ETF population, a healthy and productive public workforce also means safer streets, better schools, and a more efficient and responsive government that all of us rely on.

Reconsidering approval of AOMs is crucial in the context of several recent developments, namely the FDA label expansion (for major adverse cardiovascular events) of Zepbound (tirzepatide) and the compelling results of the widely publicized SELECT trial confirming the long-term effectiveness of AOMs beyond their use in Type 2 Diabetes, specifically for comorbid outcomes related to obesity and cardiac disease. Importantly, this study showed a 20% reduction in major adverse cardiovascular events over a 3-year period in more than 17,000 adults who had pre-existing cardiovascular disease and overweight or obesity, without diabetes.[8] The American Gastroenterological Association and American College of Endocrinology guidelines also recommend prioritization of GLP-1 agonists, such as semaglutide or tirzepatide, for individuals with comorbid nonalcoholic fatty liver disease (NAFLD) due to the magnitude of clinical benefit with these treatments.[4,6]

While cost considerations cannot be ignored, the Board and ETF must take a more comprehensive and precise approach in measuring not just short-term costs, but also the

longterm value of AOMs for patients who are truly in need of these treatments. Obesity is one of the most significant drivers of healthcare expenditures, costing the U.S. health care system nearly $173 billion a year. [3] Cardiovascular disease and cancer, two obesity-related comorbidities, are the costliest chronic conditions and leading causes of death in the United States. In terms of cancer, it is important to note that obesity not only increases a person's risk for developing cancer (4-8% of all cancers can be attributed to obesity, of which post-menopausal breast cancer and colon cancer are the most common), it also increases the risk of recurrence and is associated with a 17% increased risk of cancer-specific mortality.[9] Cancer related expenditures are expected to exceed $240 billion by 2030. Although this is an extraordinary number, it still falls below the $251 billion that our health care system incurs each year due to heart disease.[3]

Other notable obesity-related comorbidities include, but are not limited to, diabetes, NAFLD, osteoarthritis, chronic kidney disease, and sleep apnea. Beyond direct health care costs, obesity and its comorbid conditions have a significant economic impact due to related job absenteeism and lost productivity. Modeling from the 2001 to 2016 Medical Expenditure Panel Survey (MEPS) estimated an average annual productivity loss of $541.58 per worker due to obesity and the extent of productivity loss correlated with the class of obesity, with an increase to $1,286.54 for those with class 3 obesity (BMI > 40).[2] Employers experience excess obesityrelated costs in terms of covered medical, sick day, short-term disability, and workers' compensation claims and employees with severe obesity are estimated to cost more than twice that of employees without obesity ($8067 vs. $3830 in 2011 $US).[10]

The good news is we have effective treatments for obesity and successful weight loss for employees translates to significant cost savings for insurers and our healthcare system as a whole. The key is expanding access to these treatments and appropriately matching treatment modalities to our patient population.

Thorpe, et. al (2021), estimated the cost savings associated with various levels of weight loss (from 5% to 20% BMI reduction) among commercially insured adults with obesity and one or more chronic conditions. This population was followed over a 2-year period and found to have statistically significant savings in annual medical expenditures for people with diabetes, hypertension, mental health disorders, arthritis, and back pain. These cost savings varied by condition and were greatest for those with diabetes and hypertension; for each 1 BMI unit (kg/m^2) reduction, people with diabetes saved an estimated $752 and those with hypertension saved $367. The greater the weight loss, the greater the savings. The higher the baseline BMI, the greater the savings for similar levels of weight loss.

A whitepaper published by USC's Schaeffer Center for Health Policy Economics in 2023 modeled the impact of improved access to AOMs for Medicare beneficiaries and potentially other Americans as well. They considered a variety of scenarios (summary in Table 1 of the reference page that follows) for U.S. residents ages 25 and older in 2023 including an initial population of 68.4 million Medicare beneficiaries. Their simulation projected $176 billion in cost offsets to Medicare in the first 10 years of expanded coverage and over $700 billion in cost offsets after 30 years. These savings are accounted for by a healthier population with less utilization of various healthcare services including fewer hospitalizations, surgeries, physician visits, medications, nursing home admissions, etc. After just 10 years of Medicare coverage for AOMs, they estimate an average BMI reduction of 3.1 points and more than 4 points if private insurances were to expand coverage as well. The model predicts that the prevalence of diabetes would decrease by

7.7% after 30 years of Medicare coverage for AOMs and diabetes would decrease even further, to 24%, if private insurers were to also provide coverage for these therapies. (1)

Understandably, I recognize that there are questions about adherence and utilization management given the current costs of AOMs and patient population, but I think there are potential coverage structures that could prioritize patients who would benefit most and increase the likelihood that they will continue with treatment under close supervision by their medical team. Such strategies could include embedded requirements for concurrent nutritional counseling and exercise monitoring in addition to a tiered approach for prescribing of specific AOMs. The older, less expensive AOMs may be appropriate for individuals with lower BMIs and those without extensive comorbid conditions or contraindications to these medications. The more costly GLP-1 agonists, such as semaglutide and tirzepatide, could initially be restricted to patients with a BMI > 35 (class 2 obesity or greater) and those with concomitant cardiovascular disease, obesity-related cancer diagnoses, or NAFLD. These are just a few examples, but there are many other filtering mechanisms to consider that could help to ensure patients with the greatest potential clinical benefit and cost savings are prioritized.

Overall, we need an “all of the above”, patient focused strategy versus what seems to be the current "all or nothing" approach to the AOM coverage policy that enables medical professionals like me to leverage the latest proven technologies for our patients while also understanding that it may be a phased implementation approach as more FDA approved AOMs enter the market, likely lowering overall costs and improving health outcomes on an increasingly larger scale.

Thank you for your consideration on this important matter and I look forward to hearing from you soon.

Sincerely,

Brittany Galusha, MD
Internal Medicine Physician
American Board of Obesity Medicine Diplomate

Key Figures and References

Summary of approach to prescribing FDA-approved antiobesity medications

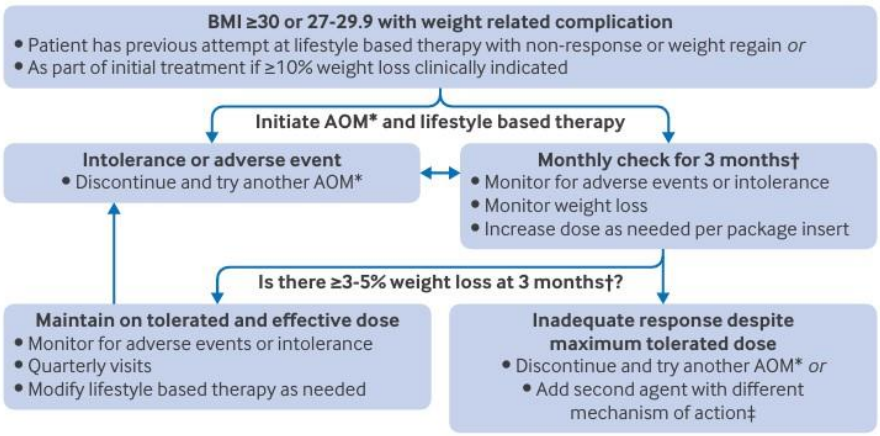


Fig 1 | A guideline informed strategy for antiobesity medication prescribing. AOM=antiobesity medication. *After factoring in patient comorbidities, preferences, and affordability/insurance coverage, clinicians could consider prioritizing based on expected weight loss, such as: - GLP-1 receptor agonist (semaglutide/liraglutide (semaglutide produces more weight loss on average than liraglutide)) or dual agonist (tirzepatide) - Phentermine-topiramate extended release - Bupropion-naltrexone sustained release - Phentermine monotherapy or similar (if patient is an appropriate candidate and in concordance with regulations and guidelines in your institution or location) - Orlistat (if patient is unable to take other, more effective drugs) †Depending on tolerability, some drug treatments can take longer than three months to reach full dosing. In these cases, longer monitoring for weight loss and adverse events is indicated. ‡Current guidelines do not specifically advise this additive approach to pharmacotherapy; however, the approach could be reasonable with individual patients under the care of an obesity medicine specialist (provided that the second agent is well tolerated, affordable, sustainable and appears to benefit the patient). Further research is needed in this area to guide general practice

FDA-approved Antiobesity Medications

Table 1 | Overview of antiobesity medications approved by the Food and Drug Administration

Generic name (year approved, approval type*)	Mechanism of action	Route of administration	Placebo subtracted % weight loss (95% CI) at 12-24 months	Proportion of patients achieving 5% weight loss at 12-24 months, %	Other weight loss estimates	Side effects	Contraindications	Cost for 1 month supply, $†	Ideal use case (special benefits)
Phentermine (1959, short term use, DEA schedule IV)	Sympathomimetic amine; increases norepinephrine (primarily), dopamine, serotonin in hypothalamic nuclei that regulate hunger	Oral; options for daily or three times daily dosing	Unknown	Unknown	5-15% total weight loss at 6 months[29-32] (uncontrolled studies) 7.2% average total weight loss at 24 months[33] (observational cohort) 32-80% of patients lose at least 5% over 3 months[29 33-37]	**Common**: Dry mouth, insomnia, constipation, anxiety, headache; **Possible/ rare**: elevated blood pressure, tachyarrhythmia; **Theoretical**: cardiovascular events such as myocardial infarction, stroke	Cardiovascular disease including arrhythmia, history of substance use disorder, hyperthyroidism, poorly controlled hypertension, cardiac valvulopathy	5-20	Young or middle aged patient with no cardiovascular disease history and for whom affordability of drug treatments is a concern (**Affordability**)
Orlistat (1999, long term use)	Reversible inhibitor of gastric and pancreatic lipases; inhibits absorption of dietary fats	Oral; three times daily ingestion with meals	3.2 (95% CI 2.8-3.5)[12]	49.7[12]	2.8% (95% CI 2.4-3.2)[10] placebo subtracted % weight loss up to 4 years	**Common**: flatulence, oily stools, fecal urgency, fecal incontinence. **Rare/theoretical**: liver failure	Pregnancy, chronic malabsorption syndrome (eg, celiac disease, inflammatory bowel disease, previous bariatric surgery), cholestasis	0-60	Patient for whom cost is a concern but who is not worried about gastrointestinal adverse effects or is adhering to a very low fat diet‡ (**Few contraindications**)
Phentermine-topiramate extended release (2012, long term use, DEA schedule IV)	Phentermine: as above; topiramate: GABAergic agent used for epilepsy, carbonic anhydrase inhibitor	Oral; once daily dosing	7.9 (95% CI 6.7-9.3)[12]	74.4[12]	7.8-9.8% total weight loss at 12 months and 9.3-10.5% total weight loss at 24 months (depending on dose)[38 39]	**Common**: Same as phentermine + paresthesias, dysgeusia, cognitive dysfunction **Possible/ rare**: same as phentermine + glaucoma, nephrolithiasis§	Same as phentermine + pregnancy category X (topiramate); consider avoiding in patients with glaucoma, nephrolithiasis	100-150	Young or middle aged patient with no cardiovascular disease history, with history of migraine headache and no risk of becoming pregnant (**Migraine prophylaxis**)
Naltrexone-bupropion sustained release (2014, long term)	Naltrexone pure opioid antagonist. Bupropion: weakly inhibits neuronal reuptake of dopamine and norepinephrine Mechanism leading to weight loss not fully understood	Oral; twice daily dosing	4.1[12] (95% CI 3.0-5.2)	64.6[12]	3.0% (95% CI 2.5-3.5)[10] Placebo subtracted % weight loss at 56 weeks	**Common**: headache, dizziness, nausea, vomiting, depression, initial increase in blood pressure that resolves by 12 weeks in RCTs. **Rare**: seizure, cholecystitis, suicidal ideation	Seizure disorder or high risk of seizures; opioid use; uncontrolled hypertension; hepatic cirrhosis; current or recent (<14 days) use of monoamine oxidase inhibitor, pregnancy	500	Patient with alcohol use disorder, tobacco use disorder, and/ or depression and no history of hypertension, who would be willing to take two separate pills if cost was a concern (**Alcohol use disorder, depression, tobacco cessation**)
Liraglutide (2014, long term)	GLP-1 receptor agonist; acts centrally to improve satiety and slows gastric emptying	Subcutaneous injection; daily	4.7 (95% CI 4.1-5.3)[12]	64[12]	Average total weight loss 8.0% +/- 6.7 (SD) at 56 weeks[40]	**Common**: nausea, vomiting, constipation **Possible/rare**: pancreatitis	Family history of MEN type 2 syndrome; personal history of medullary thyroid cancer	1090	Patient with type 2 diabetes whose insurance will not cover weekly injectables (**Type 2 diabetes**)
Setmelanotide (2020, long term use)	Melanocortin-4 receptor agonist for monogenic obesity syndromes	Subcutaneous injection; daily	Unknown	Unknown	Average total weight loss 5-20%, 45-80% achieved a 10% reduction at 1 year depending on gene defect[41]	**Common**: hyperpigmentation, injection site reactions, gastrointestinal upset, headache, sexual adverse reactions	None	20 904	Individuals with an approved monogenic obesity indication (***POMC*, *PCSK1*, or *LEPR* deficiency, Bardet-Biedl syndrome**)

Table 1 | Continued

Generic name (year approved, approval type*)	Mechanism of action	Route of administration	Placebo subtracted % weight loss (95% CI) at 12-24 months	Proportion of patients achieving 5% weight loss at 12-24 months, %	Other weight loss estimates	Side effects	Contraindications	Cost for 1 month supply, $†	Ideal use case (special benefits)
Semaglutide (2021, long term use)	GLP-1 receptor agonist; acts centrally to improve satiety and slows gastric emptying	Subcutaneous injection; once weekly dosing	11.4 (95% CI 10.3-12.5)[12]	78.1[12]	Average total weight loss 14.9% at 68 weeks[42]	**Common**: nausea, vomiting, constipation **Possible/rare**: pancreatitis	Family history of MEN type 2 syndrome; personal history of medullary thyroid cancer	1100	Patient with at least 10% weight loss clinically indicated, with cardiovascular disease, or diabetes/insulin resistance who cannot take a phentermine-containing agent (**Type 2 diabetes; cardiovascular-disease; substantial weight loss**)
Tirzepatide (2023, long term)	Dual agonist to GLP-1 and glucose dependent insulinotropic polypeptide receptors; and slows gastric emptying	Subcutaneous injection; once weekly dosing	11.9 (95% CI 10.4-13.4) to 17.8[43] (95% CI 16.3-19.3) depending on dose	85-91 depending on dose	Average total weight loss 15-21% at 72 weeks (depending on dose)	**Common**: nausea, vomiting, constipation **Possible/rare**: pancreatitis	Family history of MEN type 2 syndrome; personal history of medullary thyroid cancer	1060	Patient with at least 10% weight loss clinically indicated and diabetes or insulin resistance who cannot take a phentermine containing agent. (**Type 2 diabetes; substantial weight loss**)

CI=confidence interval; DEA=Drug Enforcement Administration; GABA=γ-aminobutyric acid; GLP-1=glucagon-like peptide-1; MEN=multiple endocrine neoplasia; RCT=randomized controlled trial; SD=standard deviation.
*Short term indicates three months; long term indicates 12 months or longer.
†In US dollars, 2023 reported average wholesale prices (does not account for potential insurance coverage).
‡Also recommended to prescribe a daily multivitamin with orlistat owing to resulting malabsorption of fat soluble vitamins.
§In clinical trials, no difference in serious adverse event rate was observed for active drug participants compared with placebo.

Table 1. American Gastroenterological Association Recommendations on Pharmacological Interventions for Management of Obesity

Recommendation	Strength of recommendation	Quality of evidence
1. In adults with obesity or overweight with weight-related complications, who have had an inadequate response to lifestyle interventions, the AGA recommends adding pharmacological agents to lifestyle interventions over continuing lifestyle interventions alone. Implementation considerations: • AOMs generally need to be used chronically, and the selection of the medication or intervention should be based on the clinical profile and needs of the patient, including, but not limited to, comorbidities, patients' preferences, costs, and access to the therapy.	Strong	Moderate
2. In adults with obesity or overweight with weight-related complications, the AGA suggests using semaglutide 2.4 mg with lifestyle modifications, compared with lifestyle modifications alone. Implementation considerations: • Given the magnitude of net benefit, semaglutide 2.4 mg may be prioritized over other approved AOMs for the long-term treatment of obesity for most patients. • Semaglutide has glucoregulatory benefits and is also approved for the treatment of T2DM • Semaglutide may delay gastric emptying with adverse effects of nausea and vomiting. Gradual dose titration may help mitigate these adverse effects. • GLP-1 RAs have been associated with increased risk of pancreatitis and gallbladder disease.	Conditional	Moderate
3. In adults with obesity or overweight with weight-related complications, the AGA suggests using liraglutide 3.0 mg with lifestyle modifications, compared with lifestyle modifications alone. Implementation considerations: • Liraglutide has glucoregulatory benefits and is also approved for the treatment of T2DM • Liraglutide may delay gastric emptying with adverse effects of nausea and vomiting. Gradual dose titration may help mitigate these adverse effects. • Liraglutide has been associated with an increased risk of pancreatitis and gallbladder disease	Conditional	Moderate
4. In adults with obesity or overweight with weight-related complications, the AGA suggests using phentermine-topiramate ER with lifestyle modifications, compared with lifestyle modifications alone. Implementation considerations: • Because topiramate is effective for treating migraine headaches, phentermine-topiramate ER may be preferentially used in patients with comorbid migraines. • Phentermine-topiramate ER should be avoided in patients with a history of cardiovascular disease and uncontrolled hypertension. • Topiramate is teratogenic. Women of childbearing potential should be counseled to use effective contraception consistently. • Blood pressure and heart rate should be monitored periodically while taking medications with phentermine.	Conditional	Moderate
5. In adults with obesity or overweight with weight-related complications, the AGA suggests using naltrexone-bupropion ER with lifestyle modifications, compared with lifestyle modifications alone. Implementation Considerations: • Naltrexone-bupropion ER may be considered for the treatment of overweight or obesity in patients who are attempting smoking cessation, and in patients with depression. • Naltrexone-bupropion ER should be avoided in patients with seizure disorders and used with caution in patients at risk of seizures. • Naltrexone-bupropion ER should not be used concomitantly with opiate medications. • Blood pressure and heart rate should be monitored periodically while taking naltrexone-bupropion ER, especially in the first 12 weeks of treatment.	Conditional	Moderate

Table 1. Continued

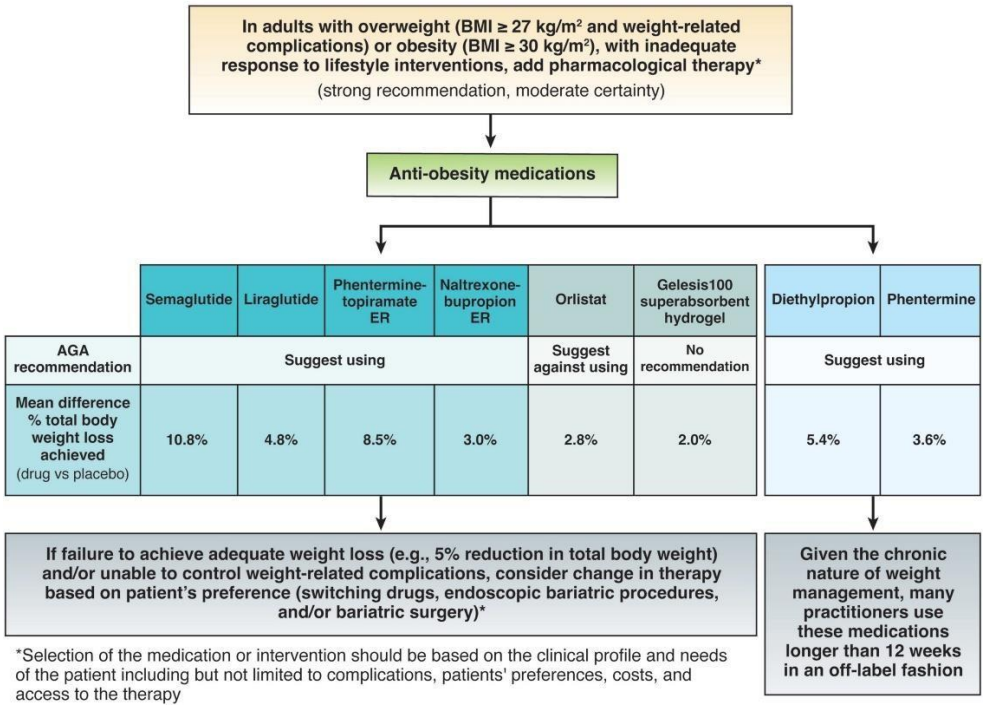
Recommendation	Strength of recommendation	Quality of evidence
6. In adults with obesity or overweight with weight-related complications, AGA suggests against the use of orlistat. *Comment:* Patients who place a high value on the potential small weight loss benefit and low value on GI adverse effects may reasonably choose treatment with orlistat. Implementation Considerations: • Patients using orlistat should take a multivitamin daily. Vitamins should contain fat-soluble vitamins (A, D, E, K) and should be taken 2 hours apart from orlistat.	Conditional	Moderate
7. In adults with obesity or overweight with weight-related complications, the AGA suggests using phentermine with lifestyle modifications, compared with lifestyle modifications alone. Implementation Considerations: • Phentermine monotherapy is approved by the FDA for short-term use (12 weeks). However, given the chronic nature of weight management, many practitioners use phentermine longer than 12 weeks in an off-label fashion. • Phentermine should be avoided in patients with a history of cardiovascular disease. • Blood pressure and heart rate should be monitored periodically while taking phentermine.	Conditional	Low
8. In adults with obesity or overweight with weight-related complications, the AGA suggests using diethylpropion with lifestyle modifications, compared with lifestyle modifications alone. Implementation considerations: • Diethylpropion monotherapy is approved by the FDA for short-term use (12 weeks). However, given the chronic nature of weight management, many practitioners use diethylpropion longer than 12 weeks in an off-label fashion. • Diethylpropion should be avoided in patients with a history of cardiovascular disease. • Blood pressure and heart rate should be monitored periodically while taking diethylpropion.	Conditional	Low
9. In adults with BMI between 25 and 40 kg/m^2, the AGA recommends using Gelesis100 oral superabsorbent hydrogel only in the context of a clinical trial.	No recommendation	Knowledge gap

Table 4. Evidence Profile for Supporting the Use of Pharmacologic Interventions for the Treatment of Obesity

Outcomes	No. of participants (studies), follow-up	Certainty of the evidence (GRADE)	Relative effect, RR (95% CI)	Anticipated absolute effects (risk difference with treatment)
Semaglutide 2.4 mg				
%TBWL	4352 (8 RCTs)	⨁⨁⨁⨁ High	—	MD 10.76% more (8.73 more to 12.8 more)
Treatment discontinuation due to adverse events	4353 (8 RCTs)	⨁⨁⨁⨁ High[a]	2.10 (1.54 to 2.86)	34 more per 1000 (from 17 more to 57 more)
Liraglutide 3.0 mg				
%TBWL	5968 (8 RCTs)	⨁⨁⨁⨁ High	—	MD 4.81% lower (5.39 lower to 4.23 lower)
Treatment discontinuation due to adverse events	6362 (10 RCTs)	⨁⨁⨁⨁ High[a]	2.31 (1.85 to 2.88)	91 more per 1000 (69 more to 120 more)
Phentermine-topiramate ER				
%TBWL	3141 (3 RCTs)	⨁⨁⨁⨁ High[b]	—	MD 8.45% higher (7.89 higher to 9.01 higher)
Treatment discontinuation due to adverse events	3141 (3 RCTs)	⨁⨁⨁⨁ High[a,b]	2.08 (1.71 to 2.52)	91 more per 1000 (from 60 more to 129 more)
Naltrexone-bupropion ER				
%TBWL	12659 (5 RCTs)	⨁⨁⨁◯ Moderate[c]	—	MD 3.01% lower (3.54 lower to 2.47 lower)
Treatment discontinuation due to adverse events	12839 (5 RCTs)	⨁⨁⨁⨁ High[d]	2.39 (1.69 to 3.37)	129 more per 1000 (64 more to 219 more)

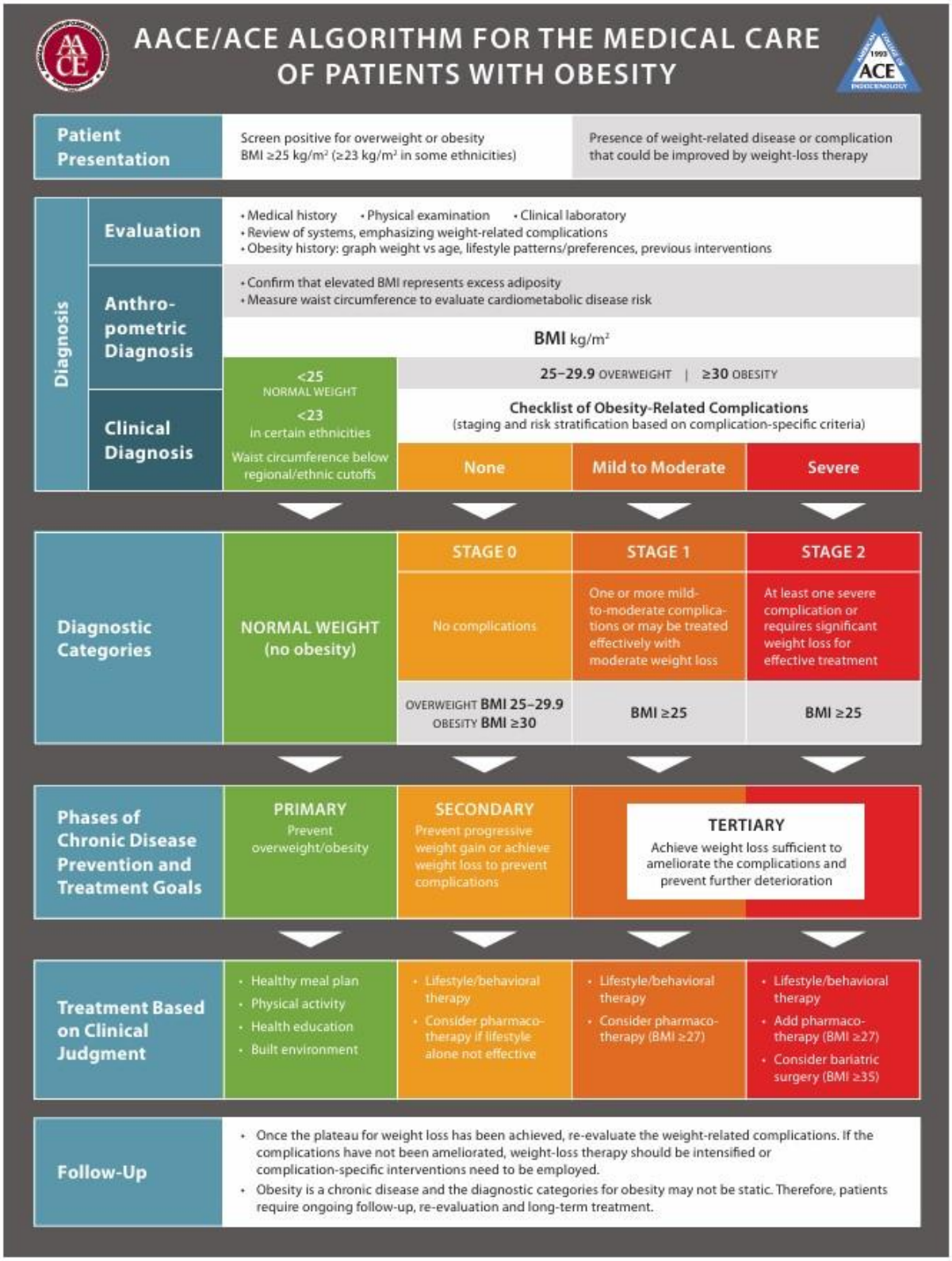
[a]Serious imprecision in the SAE outcome because the absolute risk crosses threshold of 1%, which was the predetermined MID threshold. Thus, the overall certainty of evidence for this pharmacotherapy was moderate.
[b]Low event rate leading to serious imprecision in both %TBWL ≥15% and SAE.
[c]MID or clinically important threshold below which there is no clear benefit of the intervention in discussion with the guideline panel and technical review team was determined to be 3 kg (or approximately 3%). We noted serious imprecision as the lower confidence limit crosses the MID for benefit.
[d]Low event rate leading to serious imprecision in SAE outcome.

Clinical Decision Support Tool
Pharmacological Interventions for Adults With Obesity



*Selection of the medication or intervention should be based on the clinical profile and needs of the patient including but not limited to complications, patients' preferences, costs, and access to the therapy

American College of Endocrinology Guidelines for Obesity Management



AACE/ACE Obesity CPG, Endocr Pract. 2016;22

CLINICAL COMPONENT OF THE MEDICAL DIAGNOSIS OF OBESITY

Evaluation of a checklist of weight-related complications. Candidates for weight-loss therapy can present with either excess adiposity (i.e., the anthropometric component) or weight-related complications (i.e., the clinical component)

Patients Present with Overweight or Obesity (Anthropometric Component)	Candidates for Weight Loss Therapy	Patients Present with Weight-Related Disease or Complication (Clinical Component)
Patients present with BMI ≥25 kg/m², or ≥23 kg/m² in certain ethnicities, and excess adiposity	Evaluate for weight-related complications →	Prediabetes
		Metabolic Syndrome
		Type 2 Diabetes
		Dyslipidemia
		Hypertension
		Cardiovascular Disease
		Nonalcoholic Fatty Liver Disease
	← Evaluate for overweight or obesity	Polycystic Ovary Syndrome
		Female Infertility
		Male Hypogonadism
		Obstructive Sleep Apnea
		Asthma/Reactive Airway Disease
		Osteoarthritis
		Urinary Stress Incontinence
		Gastroesophageal Reflux Disease
		Depression

WHEN TO INITIATE WEIGHT-LOSS MEDICATIONS IN PATIENTS WITH OVERWEIGHT/OBESITY

INITIATE LIFESTYLE THERAPY

1. No Complications.
Patients with overweight or obesity who have no clinically significant weight-related complications (secondary prevention)

2. Mild to Moderate Complications.
- Patient with mild to moderate weight-related complications when lifestyle therapy is anticipated to achieve sufficient weight loss to ameliorate the complication (tertiary prevention)
- Note: weight-loss medications may also be indicated based on clinical judgment

INITIATE WEIGHT LOSS MEDICATION AS AN ADJUNCT TO LIFESTYLE THERAPY

1. Failure to lose weight.
Add medication for patients who have progressive weight gain or who have not achieved clinical improvement in weight-related complications on lifestyle therapy alone.

2. Weight Regain on Lifestyle Therapy.
Add medication for patients with overweight (BMI 25 to 29.9 kg/m²) or obesity who are experiencing weight regain following initial success on lifestyle therapy alone.

3. Presence of Weight-Related Complications.
Initiate medication concurrent with lifestyle therapy for patients with overweight (BMI to 29.9 kg/m²) or obesity who have weight-related complications, particularly if severe, in order to achieve sufficient weight loss to ameliorate the complication (tertiary prevention).

AACE/ACE Obesity CPG, Endocr Pract. 2016;22

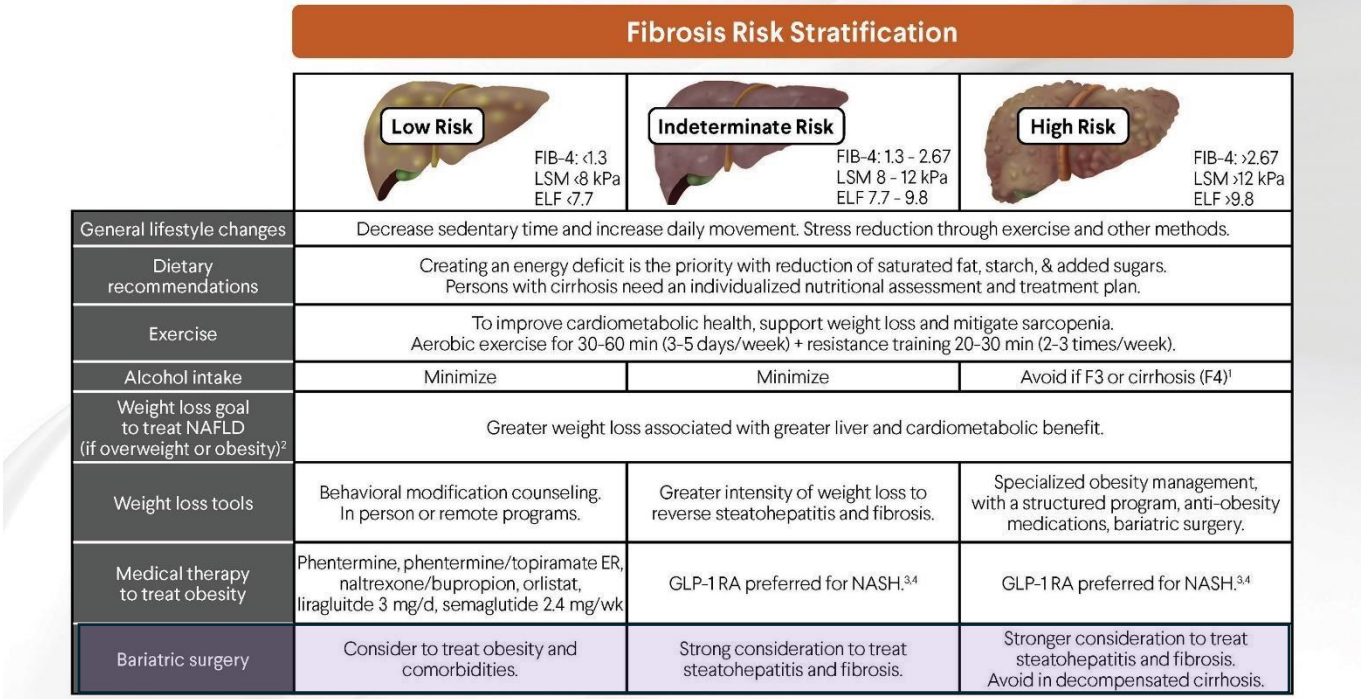
TREATMENT GOALS BASED ON DIAGNOSIS IN THE MEDICAL MANAGEMENT OF PATIENTS WITH OBESITY

	DIAGNOSIS		TREATMENT GOALS	
	Anthropometric Component	Clinical Component	Intervention/ Weight-Loss Goal	Clinical Goals
PRIMARY PREVENTION				
Primordial Prevention	BMI ≤25 (≤23 in certain ethnicities)	Obesogenic environment	• Public education • Built environment • Access to healthy foods	Decreased incidence of overweight/obesity in populations
Primary Prevention	BMI ≤25 (≤23 in certain ethnicities)	High-risk individuals or subgroups based on individual or cultural behaviors, ethnicity, family history, biomarkers, or genetics	• Annual BMI screening • Healthy meal plan • Increased physical activity	Decreased incidence of overweight/obesity in high-risk individuals or identifiable subgroups
SECONDARY PREVENTION				
Overweight	BMI 25–29.9 (BMI 23–24.9 in certain ethnicities)	No clinically significant or detectable weight-related complications	• Prevent progressive weight gain or • Weight loss	• Prevent progression to obesity • Prevent the development of weight-related complications
Obesity	BMI ≥30 (≥25 in certain ethnicities)	No clinically significant or detectable weight-related complications	• Weight loss or • Prevent progressive weight gain	Prevent the development of weight-related complications
TERTIARY PREVENTION				
Overweight or Obesity	BMI ≥25 (≥23 in certain ethnicities)	Metabolic syndrome	10%	Prevention of T2DM
		Prediabetes	10%	Prevention of T2DM
		T2DM	5-15% or more	• Reduction in A1C • Reduction in number and/or doses of glucose-lowering medications • Diabetes remission especially when diabetes duration is short
		Dyslipidemia	5-15% or more	• Lower triglycerides • Raise HDL-c • Lower non-HDL-c
		Hypertension	5-15% or more	• Lower systolic and diastolic BP • Reductions in number and/or doses of antihypertensive medications
		Nonalcoholic fatty liver disease: Steatosis	5% or more	Reduction in intrahepatocellular lipid
		Nonalcoholic fatty liver disease: Steatohepatitis	10-40%	Reduction in inflammation and fibrosis
		Polycystic ovary syndrome	5-15% or more	• Ovulation • Regularization of menses • Reduction in hirsutism • Enhanced insulin sensitivity • Reduced serum androgen levels
		Female infertility	10% or more	• Ovulation • Pregnancy and live birth
		Male hypogonadism	5-10% or more	Increase in serum testosterone
		Obstructive sleep apnea	7-11% or more	• Improved symptomatology • Decreased apnea-hypopnea index
		Asthma/reactive airway disease	7-8% or more	• Improvement in forced expiratory volume at 1 second • Improved symptomatology
		Osteoarthritis	• ≥10% • 5-10% or more when coupled with exercise	• Improved symptomatology • Increased function
		Urinary stress incontinence	5-10% or more	Reduced frequency of incontinence
		Gastroesophageal reflux disease	10% or more	Improved symptomatology
		Depression	Uncertain	• Improved symptomatology • Improvement in depression scores

Abbreviations: A1C = hemoglobin A1c; BMI = body mass index; BP = blood pressure; HDL-c = high-density lipoprotein cholesterol; T2DM = type 2 diabetes mellitus.

AACE/ACE Obesity CPG, Endocr Pract. 2016;22

Weight Management in NAFLD



Abbreviations: GLP-1 RA = Glucagon-like peptide-1 receptor agonists, HCC = Hepatocellular carcinoma, NASH = Nonalcoholic steatohepatitis

1. Persons with confirmed cirrhosis based on biopsy or high likelihood based on LSM >13.6kPa from vibration controlled transient elastography (FibroScan®), ELF ≥9.8 or >5.0 kPa on MRE) should undergo HCC surveillance. Varices screening is recommended if LSM >20 kPa or platelet count of <150,000/mm^3.
2. These goals should only be taken as a broad guidance. NAFLD/NASH may also improve by changes in macronutrient content, exercise and other factors beyond magnitude of weight loss. All high-quality studies available limited to a maximum of 12 month duration.
3. No high-quality evidence for pharmacotherapy in persons with NASH cirrhosis. Treatment should be individualized and used with caution only by liver specialists.
4. Among GLP-1 RAs, semaglutide has the best evidence of benefit in persons with steatohepatitis and fibrosis.

Algorithm Figure 3

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Table 2

Gender-specific summary of cancer risk for each 5 kg per m^2 increase in BMI for major cancers with strong evidence of relationship with obesity.

Type of Cancer	Number of Cohorts	Relative Risk (95% Confidence Interval)	
		Women	Men
Endometrial cancer [4]	19	1.59 (1.50–1.68)	NA
Gallbladder cancer [4]	4	1.59 (1.02–2.47)	1.09 (0.99–1.21)
Esophageal adenocarcinoma [4]	5	1.51 (1.31–1.74)	1.52 (1.33–1.74)
Kidney cancer [4]	12	1.34 (1.25–1.43)	1.24 (1.15–1.34)
Postmenopausal breast cancer [4]	34	1.12 (1.08–1.16)	NA
Hpatocellular cancer [19]	9	1.12 (1.03–1.22)	1.19 (1.09–1.29)
Pancreatic adenocarcinoma [23]	23	1.10 (1.04–1.16)	1.13 (1.04–1.22)
Colon cancer [4]	29	1.09 (1.05–1.13)	1.24 (1.20–1.28)
Ovarian cancer [77]	34	1.06 (1.00–1.12)	NA
Stomach cancer [4]	8	1.04 (0.90–1.20)	0.97 (0.88–1.06)
Rectal cancer [4]	29	1.02 (1.00–1.05)	1.09 (1.06–1.12)
Later stage prostate cancer [73]	23	NA	1.08 (1.04–1.12)

Table 3

Relationship between obesity and overall survival and cancer-specific survival in some major solid-organ cancers.

Type of Cancer [27]	Number of Cohorts	Overall Survival (HR, 95%CI)	Number of Cohorts	Cancer-Specific Survival (HR, 95%CI)
Breast	59	1.26 (1.20–1.33)	36	1.23 (1.15–1.32)
Colorectal cancer	30	1.22 (1.14–1.31)	13	1.24 (1.16–1.33)
Pancreas	6	1.36 (0.95–1.93)	3	1.28 (1.05–1.57)
Endometrial cancer	12	1.20 (1.04–1.38)	6	1.02 (0.75–1.39)
Prostate cancer	12	1.07 (0.91–1.25)	15	1.26 (1.08–1.47)
Gastroesophageal cancer	7	1.08 (0.77–1.52)	2	0.83 (0.58–1.16)
Bladder cancer	3	1.08 (0.98–1.20)	3	1.36 (0.96–1.93)
Hepatobiliary cancer	5	1.06 (0.89–1.25)	1	0.79 (0.50–1.24)
Ovarian cancer	4	1.03 (0.75–1.41)	4	1.06 (0.82–1.37)

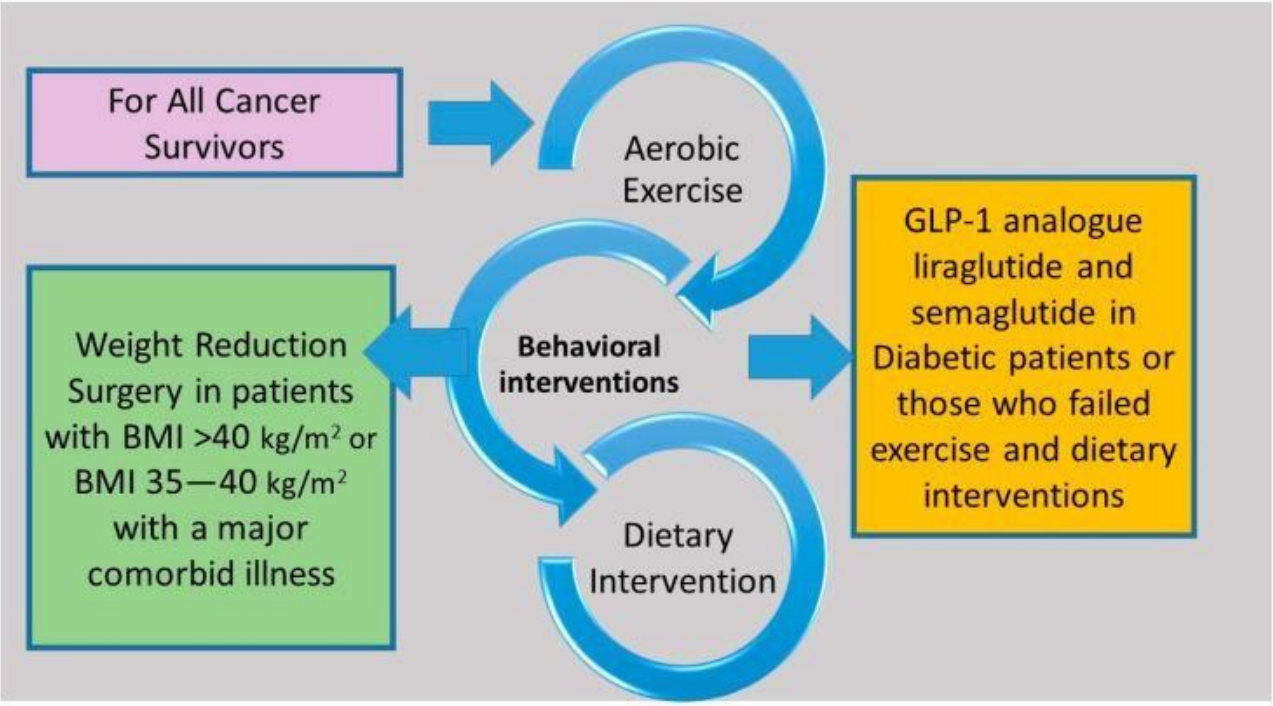


Figure 2

Structured exercise in combination with dietary support and behavior therapy are effective interventions for all cancer survivors. Treatment with glucagon-like peptide-1 analogues and bariatric surgery can be considered in selected cancer survivors.

TABLE 2. Marginal Effect of an Additional Unit of BMI on Individual Work Loss Days and Productivity at National and State Level

	Work Loss Days	Productivity (Full Day Expenditure Estimates)	Productivity (Half Day Expenditure Estimates)
U.S., 2001–2016 (n = 50,789)	0.24 (0.15, 0.33)	42.64 (26.96, 58.31)	21.32 (13.38, 29.16)
2001–2005 (n = 17,064)	0.26 (0.16, 0.35)	44.99 (28.62, 61.36)	22.50 (14.31, 30.68)
2006–2010 (n = 15,380)	0.25 (0.15, 0.34)	43.29 (26.83, 59.75)	21.65 (13.42, 29.88)
2011–2016 (n = 18,345)	0.22 (0.14, 0.31)	40.05 (25.16, 54.94)	20.03 (12.58, 27.47)
California (n = 8554)	0.20 (0.04, 0.35)	35.55 (7.51, 63.59)	17.77 (3.75, 31.79)
Texas (n = 5732)	0.22 (0.06, 0.39)	35.82 (10.42, 61.22)	17.91 (5.21, 30.61)
Florida (n = 2708)	0.24 (−0.07, 0.54)	40.66 (−12.24, 93.56)	20.33 (−6.12, 46.78)
New York (n = 2619)	0.20 (−0.16, 0.56)	40.00 (−30.33, 110.34)	20.00 (−15.17, 55.17)
Illinois (n = 1961)	0.22 (−0.15, 0.59)	42.73 (−24.01, 109.46)	21.36 (−12.00, 54.73)
Michigan (n = 1691)	0.75 (−0.37, 1.87)	148.8 (−39.51, 337.12)	74.4 (−19.76, 168.56)
New Jersey (n = 1616)	0.37 (−0.23, 0.97)	87.47 (−47.97, 222.9)	43.73 (−23.99, 111.45)
Pennsylvania (n = 1551)	0.05 (−0.15, 0.25)	9.12 (−26.8, 45.05)	4.56 (−13.4, 22.52)
Georgia (n = 1546)	0.15 (−0.34, 0.64)	24.06 (−41.49, 89.60)	12.03 (−20.75, 44.80)
North Carolina (n = 1264)	0.40 (−1.23, 2.02)	66.16 (−170.33, 302.65)	33.08 (−85.16, 151.32)
Virginia (n = 1246)	0.21 (0.01, 0.40)	43.92 (4.10, 83.74)	21.96 (2.05, 41.87)
Wisconsin (n = 1038)	0.24 (0.01, 0.46)	41.33 (2.64, 80.01)	20.66 (1.32, 40.01)
Missouri (n = 897)	0.24 (−0.16, 0.65)	42.67 (−25.41, 110.75)	21.33 (−12.71, 55.37)
Kentucky (n = 831)	0.90 (−1.56, 3.37)	151.59 (−223.79, 526.96)	75.79 (−111.89, 263.48)

Data are from the 2001 to 2016 MEPS. Marginal effect estimates of BMI are from an IV two-part model and productivity loss is expressed in 2017 USD. The full day estimate for productivity loss is based on the assumption that the individual missed the full workday due to illness or injury. The half day estimate is based on the assumption that only half the day was missed. 90% confidence intervals in parenthesis are adjusted for the complex design of the MEPS.

BMI, body mass index; IV, instrumental variable; MEPS, Medical Expenditure Panel Surveys; U.S., United States; USD, United States Dollar.

TABLE 3. Average Marginal Effect of Obesity on Individual Work Loss Days and Productivity at National and State Level

		Work Loss Days		Productivity (Full Day Expenditure Estimates)		Productivity (Half Day Expenditure Estimates)	
		Normal Weight	Obesity	Normal Weight	Obesity	Normal Weight	Obesity
U.S.	Predicted	2.34	5.34	424.41	965.99	212.20	483.00
(n = 50,789)	mean	(1.98, 2.71)	(4.62, 6.06)	(359.98, 488.84)	(832.26, 1099.73)	(179.99, 244.42)	(416.13, 549.86)
	Average marginal effect	–	3.00 (1.95, 4.04)	–	541.58 (350.46, 732.71)	–	270.79 (175.23, 366.35)
California	Predicted	2.23	4.68	416.25	859.91	208.12	429.96
(n = 8554)	mean	(1.62, 2.84)	(3.24, 6.12)	(303.99, 528.50)	(587.72, 1132.11)	(152.00, 264.25)	(293.86, 566.05)
	Average marginal effect	–	2.45 (0.51, 4.39)	–	443.67 (84.77, 802.57)	–	221.83 (42.38, 401.28)
Texas	Predicted	1.71	4.53	282.12	738.87	141.06	369.44
(n = 5732)	mean	(1.09, 2.33)	(3.27, 5.79)	(184.15, 380.09)	(526.95, 950.80)	(92.08, 190.05)	(263.47, 475.40)
	Average marginal effect	–	2.82 (1.05, 4.59)	–	456.75 (164.25, 749.25)	–	228.38 (82.13, 374.62)
Florida	Predicted	2.45	5.50	417.03	938.51	208.51	469.26
(n = 2708)	mean	(1.19, 3.71)	(2.89, 8.12)	(196.78, 637.27)	(494.96, 1382.07)	(98.39, 318.64)	(247.48, 691.03)
	Average marginal effect	–	3.06 (−0.50, 6.62)	–	521.48 (−82.63, 1125.59)	–	260.74 (−41.31, 562.80)
New York	Predicted	2.77	5.30	565.10	1083.12	282.55	541.56
(n = 2619)	mean	(1.57, 3.97)	(2.17, 8.43)	(336.92, 793.27)	(405.27, 1760.97)	(168.46, 396.63)	(202.63, 880.48)
	Average marginal effect	–	2.53 (−1.70, 6.77)	–	518.02 (−362.46, 1398.50)	–	259.01 (−181.23, 699.25)
Illinois	Predicted	2.18	4.96	423.31	967.20	211.65	483.60
(n = 1,961)	mean	(1.03, 3.33)	(2.53, 7.38)	(199.35, 647.26)	(492.34, 1442.06)	(99.67, 323.63)	(246.17, 721.03)
	Average marginal effect	–	2.77 (−0.59, 6.13)	–	543.89 (−110.60, 1198.39)	–	271.95 (−55.30, 599.19)
Michigan	Predicted	0.98	9.82	201.11	2,024.56	100.56	1012.28
(n = 1,691)	mean	(0.23, 1.73)	(3.53, 16.10)	(43.45, 358.77)	(681.92, 3367.21)	(21.72, 179.39)	(340.96, 1683.61)
	Average marginal effect	–	8.84 (1.93, 15.75)	–	1,823.45 (362.50, 3284.41)	–	911.73 (181.25, 1642.20)
New Jersey	Predicted	2.50	6.95	599.51	1,681.90	299.75	840.95
(n = 1,616)	mean	(0.79, 4.21)	(2.07, 11.83)	(187.16, 1011.86)	(488.74, 2875.06)	(93.58, 505.93)	(244.37, 1437.53)
	Average marginal effect	–	4.45 (−1.87, 10.78)	–	1,082.39 (−452.20, 2616.98)	–	541.20 (−226.10, 1308.49)
Pennsylvania	Predicted	4.22	4.87	754.82	872.83	377.41	436.42
(n = 1,551)	mean	(2.52, 5.91)	(3.46, 6.29)	(463.30, 1046.33)	(631.95, 1113.71)	(231.65, 523.16)	(315.98, 556.86)
	Average marginal effect	–	0.66 (−1.97, 3.28)	–	118.02 (−352.78, 588.81)	–	59.01 (−176.39, 294.41)
Georgia	Predicted	2.07	3.92	351.45	661.33	175.72	330.66
(n = 1,546)	mean	(0.44, 3.71)	(1.14, 6.70)	(98.82, 604.07)	(151.53, 1171.12)	(49.41, 302.04)	(75.77, 585.56)
	Average marginal effect	–	1.84 (−2.44, 6.13)	–	309.88 (−436.52, 1056.28)	–	154.94 (−218.26, 528.14)
North Carolina	Predicted	1.53	6.09	257.24	1,027.20	128.62	513.60
(n = 1,264)	mean	(−0.63, 3.70)	(−2.89, 15.07)	(−110.97, 625.46)	(−402.91, 2457.30)	(−55.49, 312.73)	(−201.45, 1228.65)
	Average marginal effect	–	4.56 (−6.30, 15.42)	–	769.96 (−983.78, 2523.70)	–	384.98 (−491.89, 1261.85)
Virginia	Predicted	2.05	4.78	446.96	1,033.50	223.48	516.75
(n = 1,246)	mean	(0.92, 3.18)	(3.26, 6.30)	(208.22, 685.70)	(687.26, 1379.73)	(104.11, 342.85)	(343.63, 689.86)
	Average marginal effect	–	2.73 (0.30, 5.16)	–	586.53 (55.95, 1117.11)	–	293.27 (27.98, 558.56)
Wisconsin	Predicted	2.06	4.92	373.21	883.56	186.60	441.78
(n = 1,038)	mean	(1.52, 2.60)	(2.74, 7.10)	(269.98, 476.43)	(491.59, 1275.54)	(134.99, 238.22)	(245.79, 637.77)
	Average marginal effect	–	2.86 (0.45, 5.27)	–	510.36 (76.20, 944.51)	–	255.18 (38.10, 472.25)
Missouri	Predicted	2.36	5.48	434.30	1,004.27	217.15	502.13
(n = 897)	mean	(0.68, 4.04)	(2.57, 8.38)	(120.56, 748.05)	(496.88, 1511.65)	(60.28, 374.02)	(248.44, 755.82)
	Average marginal effect	–	3.11 (−1.25, 7.48)	–	569.96 (−223.90, 1363.83)	–	284.98 (−111.95, 681.92)
Kentucky	Predicted	1.52	9.22	281.19	1,712.11	140.59	856.05
(n = 831)	mean	(0.15, 2.88)	(1.01, 17.42)	(19.46, 542.92)	(225.76, 3198.45)	(9.73, 271.46)	(112.88, 1599.23)
	Average marginal effect	–	7.70 (−1.53, 16.93)	–	1,430.92 (−248.14, 3109.98)	–	715.46 (−124.07, 1554.99)

Data are from the 2001 to 2016 MEPS. Average marginal effect estimates of obesity are from an IV two-part model and productivity loss is expressed in 2017 USD. The full day estimate for productivity loss is based on the assumption that the individual missed the full workday due to illness or injury. The half day estimate is based on the assumption that only half the day was missed. Estimates of total productivity loss are inflated using MEPS sample weights to reflect productivity loss attributable to obesity for all employed adults aged 18 to 64. 90% confidence intervals in parenthesis are adjusted for the complex design of the MEPS.

IV, instrumental variable; MEPS, Medical Expenditure Panel Surveys; U.S., United States; USD, United States Dollar.

TABLE 4. Aggregate Full-Day and Half-Day Productivity Loss due to Obesity Among Employed Adults by Payment Type at National and State Level (Expressed in Billions of 2017 USD)

	Obesity		Class 1 obesity		Class 2 obesity		Class 3 obesity	
	Full-Day Productivity	Half-Day Productivity	Full-Day Productivity	Half-Day Productivity	Full-Day Productivity	Half-Day Productivity	Full-Day Productivity	Half-Day Productivity
U.S. (n = 50,789)								
2016	26.84 (16.57, 37.12)	13.42 (8.28, 18.56)	10.97 (6.95, 14.98)	5.48 (3.47, 7.49)	8.73 (5.21, 12.26)	4.37 (2.60, 6.13)	8.79 (4.03, 13.56)	4.40 (2.01, 6.78)
2001–2016 Avg.	21.96 (14.38, 29.54)	10.98 (7.19, 14.77)	9.48 (6.57, 12.38)	4.74 (3.28, 6.19)	6.50 (4.09, 8.91)	3.25 (2.05, 4.45)	6.86 (3.53, 10.20)	3.43 (1.76, 5.10)
Comparison of average trends								
2001–2005 Avg. (1)	21.41 (13.81, 29.01)	10.70 (6.90, 14.51)	9.36 (6.43, 12.38)	4.68 (3.21, 6.15)	6.09 (3.70, 8.47)	3.04 (1.85, 4.24)	6.74 (3.33, 10.15)	3.37 (1.67, 5.07)
2006–2010 Avg. (2)	22.58 (14.40, 30.77)	11.29 (7.20, 15.38)	9.91 (6.68, 13.15)	4.96 (3.34, 6.57)	6.52 (3.93, 9.11)	3.26 (1.96, 4.56)	6.86 (3.47, 10.25)	3.43 (1.73, 5.13)
2011–2016 Avg. (3)	21.89 (14.45, 29.33)	10.95 (7.23, 14.66)	9.21 (6.35, 12.06)	4.60 (3.18, 6.03)	6.83 (4.39, 9.27)	3.42 (2.20, 4.63)	6.97 (3.57, 10.36)	3.48 (1.78, 5.18)
(3)-(1)	0.48 (−2.23, 3.19)	0.24 (−1.11, 1.60)	-0.16 (−1.52, 1.21)	-0.08 (−0.76, 0.60)	0.74 (−0.24, 1.72)	0.37 (−0.12, 0.86)	0.23 (−1.00, 1.45)	0.11 (−0.50, 0.73)
(3)-(2)	−0.69 (−3.14, 1.75)	−0.35 (−1.57, 0.88)	−0.70 (−1.90, 0.49)	−0.35 (−0.95, 0.24)	0.31 (−0.60, 1.22)	0.16 (−0.30, 0.61)	0.11 (−1.00, 1.21)	0.05 (−0.50, 0.60)
California (n = 8554)								
2016	1.64 (0.26, 3.02)	0.82 (0.13, 1.51)	0.76 (0.17, 1.36)	0.38 (0.08, 0.68)	0.51 (0.02, 1.01)	0.26 (0.01, 0.50)	0.46 (−0.08, 1.00)	0.23 (−0.04, 0.50)
2001–2016 Avg.	2.27 (0.52, 4.03)	1.14 (0.26, 2.01)	1.10 (0.33, 1.87)	0.55 (0.16, 0.94)	0.65 (0.10, 1.21)	0.33 (0.05, 0.61)	0.62 (−0.07, 1.31)	0.31 (−0.03, 0.65)
Texas (n = 5,732)								
2016	4.17 (1.53, 6.82)	2.09 (0.76, 3.41)	1.77 (0.76, 2.78)	0.88 (0.38, 1.39)	0.78 (0.17, 1.39)	0.39 (0.09, 0.69)	1.91 (0.08, 3.74)	0.95 (0.04, 1.87)
2001–2016 Avg.	2.66 (0.99, 4.33)	1.33 (0.50, 2.16)	1.15 (0.54, 1.75)	0.57 (0.27, 0.88)	0.77 (0.25, 1.28)	0.38 (0.13, 0.64)	0.72 (−0.03, 1.47)	0.36 (−0.01, 0.74)
Florida (n = 2708)								
2016	2.78 (−0.34, 5.90)	1.39 (−0.17, 2.95)	1.30 (−0.05, 2.65)	0.65 (−0.02, 1.32)	1.05 (−0.34, 2.45)	0.53 (−0.17, 1.22)	0.27 (−0.22, 0.75)	0.13 (−0.11, 0.38)
2001–2016 Avg.	1.52 (−0.24, 3.29)	0.76 (−0.12, 1.64)	0.67 (−0.01, 1.35)	0.34 (0.00, 0.67)	0.46 (−0.18, 1.10)	0.23 (−0.09, 0.55)	0.47 (−0.33, 1.27)	0.24 (−0.16, 0.64)
New York (n = 2,619)								
2016	2.01 (−1.32, 5.34)	1.00 (−0.66, 2.67)	0.90 (−0.51, 2.31)	0.45 (−0.26, 1.15)	0.71 (−0.74, 2.18)	0.36 (−0.37, 1.08)	0.38 (−0.40, 1.16)	0.19 (−0.20, 0.58)
2001–2016 Avg.	1.20 (−0.80, 3.20)	0.60 (−0.40, 1.60)	0.53 (−0.27, 1.33)	0.26 (−0.14, 0.66)	0.37 (−0.35, 1.10)	0.19 (−0.17, 0.55)	0.40 (−0.51, 1.32)	0.20 (−0.26, 0.66)
Illinois (n = 1,961)								
2016	0.80 (−0.15, 1.74)	0.37 (−0.07, 0.81)	0.27 (−0.03, 0.57)	0.13 (−0.02, 0.28)	0.45 (−0.13, 1.02)	0.16 (−0.05, 0.37)	0.17 (−0.16, 0.51)	0.09 (−0.08, 0.27)
2001–2016 Avg.	1.10 (−0.21, 2.40)	0.51 (−0.10, 1.11)	0.43 (0.00, 0.87)	0.21 (0.00, 0.43)	0.38 (−0.10, 0.86)	0.14 (−0.04, 0.31)	0.35 (−0.45, 1.16)	0.19 (−0.24, 0.61)
Michigan (n = 1691)								
2016	4.47 (0.57, 8.37)	2.23 (0.28, 4.18)	1.40 (0.20, 2.61)	0.70 (0.10, 1.30)	1.80 (−0.34, 3.94)	0.90 (−0.17, 1.97)	2.16 (−1.44, 5.76)	1.08 (−0.72, 2.88)
2001–2016 Avg.	3.60 (0.92, 6.28)	1.80 (0.46, 3.14)	1.18 (0.54, 1.82)	0.59 (0.27, 0.91)	1.62 (0.05, 3.19)	0.81 (0.03, 1.59)	1.32 (−0.78, 3.43)	0.66 (−0.39, 1.72)
New Jersey (n = 1616)								
2016	2.09 (−1.03, 5.20)	1.04 (−0.51, 2.60)	1.12 (−0.35, 2.58)	0.56 (−0.18, 1.29)	0.52 (−0.46, 1.50)	0.26 (−0.23, 0.75)	0.72 (−1.82, 3.27)	0.36 (−0.91, 1.63)
2001–2016 Avg.	1.48 (−0.66, 3.61)	0.74 (−0.33, 1.80)	0.83 (−0.25, 1.90)	0.41 (−0.12, 0.95)	0.38 (−0.26, 1.02)	0.19 (−0.13, 0.51)	0.32 (−0.52, 1.17)	0.16 (−0.26, 0.58)
Pennsylvania (n = 1551)								
2016	0.22 (−0.70, 1.15)	0.11 (−0.35, 0.57)	0.09 (−0.27, 0.46)	0.05 (−0.14, 0.23)	0.05 (−0.15, 0.25)	0.02 (−0.08, 0.12)	0.09 (−0.44, 0.62)	0.05 (−0.22, 0.31)
2001–2016 Avg.	0.24 (−0.74, 1.22)	0.12 (−0.37, 0.61)	0.09 (−0.27, 0.45)	0.05 (−0.13, 0.23)	0.08 (−0.26, 0.42)	0.04 (−0.13, 0.21)	0.08 (−0.29, 0.45)	0.04 (−0.14, 0.23)
Georgia (n = 1546)								
2016	0.59 (−0.80, 1.99)	0.30 (−0.40, 0.99)	0.31 (−0.32, 0.48)	0.15 (−0.16, 0.45)	0.13 (−0.23, 0.48)	0.06 (−0.11, 0.24)	0.10 (−0.27, 0.47)	0.05 (−0.14, 0.23)
2001–2016 Avg.	0.51 (−0.72, 1.74)	0.26 (−0.36, 0.87)	0.22 (−0.25, 0.52)	0.11 (−0.12, 0.34)	0.14 (−0.24, 0.52)	0.07 (−0.12, 0.26)	0.19 (−0.54, 0.93)	0.10 (−0.27, 0.26)

TABLE 4. (*Continued*)

	Obesity		Class 1 obesity		Class 2 obesity		Class 3 obesity	
	Full-Day Productivity	**Half-Day Productivity**	**Full-Day Productivity**	**Half-Day Productivity**	**Full-Day Productivity**	**Half-Day Productivity**	**Full-Day Productivity**	**Half-Day Productivity**
North Carolina (n = 1264)								
2016	2.21	1.11	1.13	0.56	0.33	0.17	0.80	0.40
	(−1.84, 6.27)	(−0.92, 3.13)	(−0.40, 2.65)	(−0.20, 1.33)	(−0.73, 1.39)	(−0.36, 0.69)	(−2.80, 4.40)	(−1.40, 2.20)
2001–2016 Avg.	1.46	0.73	0.67	0.34	0.45	0.22	0.39	0.20
	(−1.45, 4.37)	(−0.72, 2.19)	(−0.32, 1.67)	(−0.16, 0.83)	(−0.83, 1.72)	(−0.41, 0.86)	(−1.42, 2.21)	(−0.71, 1.10)
Virginia (n = 1246)								
2016	0.56	0.28	0.15	0.08	0.22	0.11	0.29	0.15
	(0.02, 1.09)	(0.01, 0.55)	(0.02, 0.29)	(0.01, 0.14)	(−0.06, 0.50)	(−0.03, 0.25)	(−0.11, 0.69)	(−0.06, 0.35)
2001–2016 Avg.	0.68	0.34	0.31	0.15	0.16	0.08	0.20	0.10
	(0.10, 1.26)	(0.05, 0.63)	(0.06, 0.55)	(0.03, 0.28)	(0.00, 0.33)	(0.00, 0.16)	(−0.02, 0.42)	(−0.01, 0.21)
Wisconsin (n = 1038)								
2016	1.05	0.49	0.47	0.23	0.25	0.09	0.35	0.18
	(−0.08, 2.18)	(−0.04, 1.01)	(−0.04, 1.99)	(−0.02, 0.48)	(−0.05, 0.56)	(−0.02, 0.21)	(−0.12, 0.82)	(−0.06, 0.43)
2001–2016 Avg.	0.55	0.26	0.22	0.11	0.21	0.08	0.17	0.09
	(0.09, 1.02)	(0.04, 0.47)	(0.02, 0.43)	(0.01, 0.21)	(0.04, 0.39)	(0.01, 0.14)	(0.00, 0.34)	(0.00, 0.18)
Missouri (n = 897)								
2016	0.84	0.42	0.24	0.12	0.47	0.24	0.12	0.06
	(−0.37, 2.04)	(−0.18, 1.02)	(−0.07, 0.55)	(−0.03, 0.27)	(−0.34, 1.28)	(−0.17, 0.64)	(−0.18, 0.42)	(−0.09, 0.21)
2001–2016 Avg.	0.70	0.35	0.25	0.12	0.22	0.11	0.28	0.14
	(−0.25, 1.64)	(−0.12, 0.82)	(−0.05, 0.54)	(−0.02, 0.27)	(−0.10, 0.54)	(−0.05, 0.27)	(−0.27, 0.83)	(−0.13, 0.42)
Kentucky (n = 831)								
2016	0.51	0.25	0.12	0.06	0.17	0.08	0.47	0.24
	(0.05, 0.96)	(0.03, 0.48)	(0.01, 0.22)	(0.01, 0.11)	(0.03, 0.31)	(0.02, 0.15)	(−0.62, 1.56)	(−0.31, 0.78)
2001–2016 Avg.	1.02	0.51	0.29	0.14	0.36	0.18	0.57	0.28
	(−0.21, 2.25)	(−0.10, 1.13)	(0.09, 0.49)	(0.05, 0.24)	(−0.27, 0.98)	(−0.13, 0.49)	(−0.67, 1.80)	(−0.34, 0.90)

Data are from the 2001 to 2016 MEPS. Average marginal effect estimates of obesity are from an IV two-part model and productivity loss is expressed in 2017 USD. The full day estimate for productivity loss is based on the assumption that the individual missed the full workday due to illness or injury. The half day estimate is based on the assumption that only half the day was missed. Estimates of total productivity loss are inflated using MEPS sample weights to reflect productivity loss attributable to obesity for all employed adults aged 18 to 64. 90% confidence intervals in parenthesis are adjusted for the complex design of the MEPS. Classes of obesity are defined as follows, class 1—30 $kg/m^2 \leq$ BMI $<$ 35 kg/m^2; class 2—35 $kg/m^2 \leq$ BMI $<$ 40 kg/m^2; class 3—BMI $\geq$ 40 kg/m^2.

Avg., average; BMI, body mass index; IV, instrumental variable; kg, kilogram; MEPS, Medical Expenditure Panel Surveys; U.S., United States; USD, United States Dollar.

TABLE 2. Reduction in Healthcare Expenditures Associated with Weight Loss

Condition	*N*	Total Medical Expenditures (Baseline) Mean, SD	Condition-Specific Medical Expenditures (Baseline) Mean, SD	Decrease in Total Healthcare Expenditures for Each Decrease in 1 BMI unit (kg/m^2)		Direction of Statistically Significant Covariate Effect				
				$	*P* value	Female Gender (relative to males)	Race (Relative to Non-Hispanic White)	Age (Relative to 24–34 yr olds)	Education (Relative to High School Grads)	Marital Status (Relative to Unmarried)
Diabetes	1967	$9127 ($22,005)	$2303 ($4607)	−$752	0.05	+0.04	−Black and Hispanic 0.03	ns	ns	+0.045
Hyperlipidemia	3584	$7054 ($17,576)	$777 ($1137)	−$238	0.1	+<0.001	−Non-Hispanic Other and Hispanic 0.004	ns	ns	ns
Hypertension	5335	$6736 ($16,143)	$650 ($1638)	−$367	0.004	+0.01	−Black and Hispanic 0.001	ns	ns	+0.005
Mental health disorders	3660	$7943 ($17,420)	$1216 ($3022)	−$306	0.02	ns	ns	ns	ns	+<0.001
Pulmonary disease	1101	$7331 ($12,431)	$1132 ($1808)	−$306	0.07	ns	ns	+45–64 yr <0.001	ns	ns
Arthritis	2742	$8681 ($14,595)	$1874 ($6609)	−$209	<0.001	+<0.001	−Black and Hispanic 0.02	+45–64 yr 0.008	ns	+0.04
Back pain	2582	$7,81 ($15,502)	$1663 ($5225)	−$289	0.04	+0.009	ns	ns	ns	+0.007

BMI, body mass index.

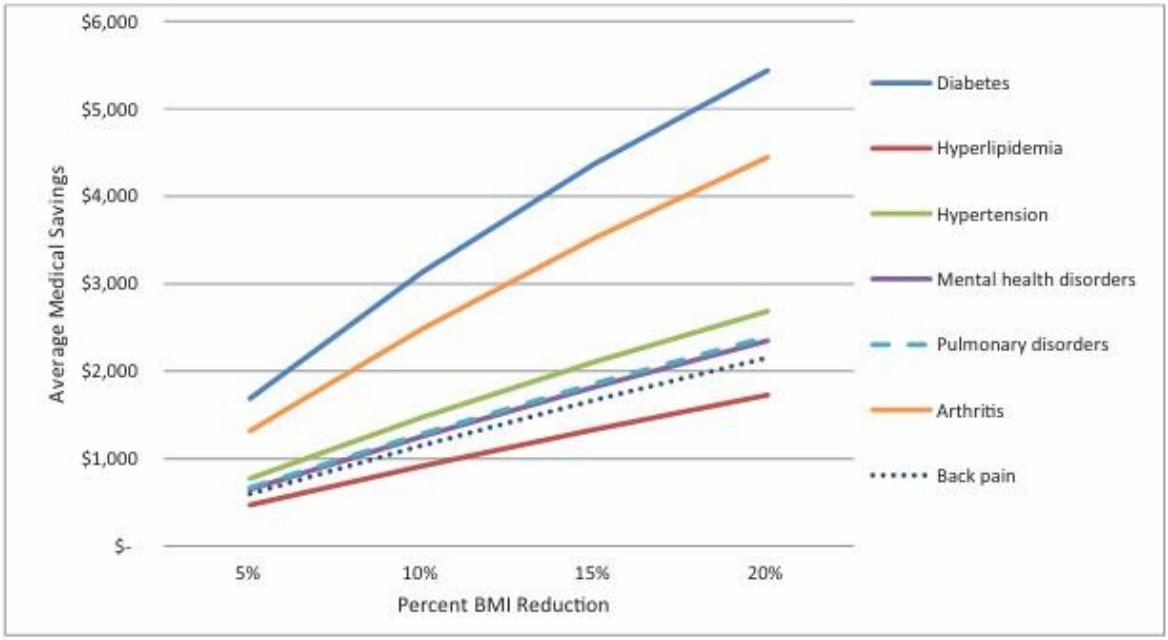


FIGURE 1. Predicted reductions in average annual healthcare expenditures per person associated with 5% to 20% reduction in BMI by chronic condition. BMI, body mass index.

Table 3. Value to Medicare From Covering and Treating Obesity (Difference From Status Quo)

	10 Years		20 Years		30 Years	
	Medicare	Medicare & Private	Medicare	Medicare & Private	Medicare	Medicare & Private
Cumulative Cost Offsets						
Total Medicare cost offsets	$175.6B	$245.1B	$479.0B	$832.2B	$704.3B	$1,494.6B
Part A	$107.1B	$146.3B	$293.5B	$482.8B	$425.9B	$845.5B
Part B	$61.5B	$87.0B	$169.2B	$303.9B	$258.4B	$564.5B
Part D	$6.9B	$11.8B	$16.3B	$45.4B	$20.0B	$84.7B
Cumulative Health Benefits						
Value of Added QALYs ($150K/QALY)	$770B	$927B	$1,971B	$2,535B	$3,131B	$4,595B
Social benefit	$1,002B	$1,269B	$2,597B	$3,743B	$3,997B	$6,743B

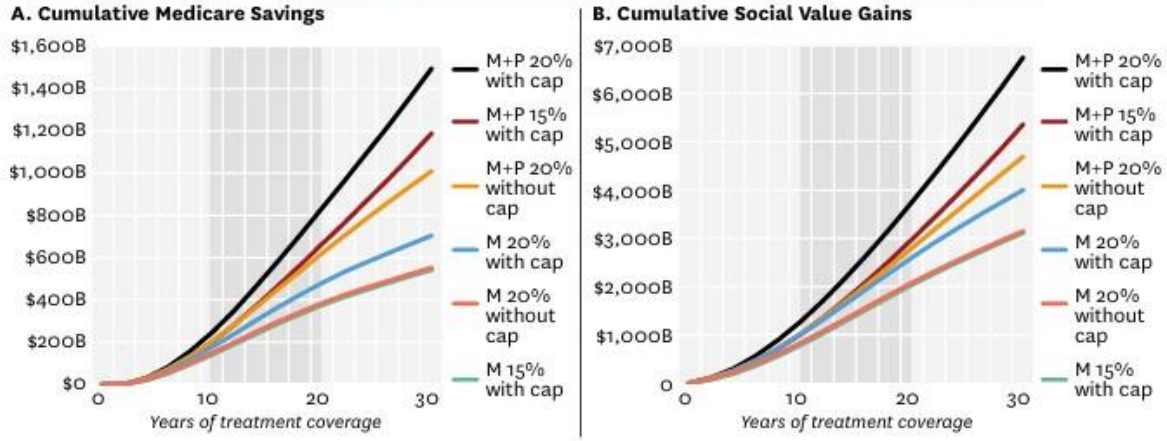
Notes: Medicare population simulation results. Treatment costs are not included in benefit calculations. We assumed 100% uptake and adherence. Social value is measured as the sum of the value of QALYs, medical expenditure cost offsets and disability expenditure savings.

Table 4. Medicare Population Health Impacts From Treating Obesity

	10 Years			20 Years			30 Years		
	SQ	Medicare	M+P	SQ	Medicare	M+P	SQ	Medicare	M+P
Population Average (Change from Status Quo for Medicare and M+P)									
Average BMI	29.0	-3.1	-3.6	29.2	-3.2	-3.8	29.8	-3.4	-4.1
Population Prevalence (Percent Change from Status Quo for Medicare and M+P)									
Obese (≥30)	0.40	-53.3%	-61.5%	0.42	-49.3%	-59.7%	0.45	-47.0%	-61.0%
BMI 30-34	0.20	-41.9%	-47.9%	0.20	-36.1%	-43.7%	0.21	-31.4%	-42.6%
BMI 35-39	0.11	-60.4%	-69.8%	0.12	-55.7%	-67.6%	0.13	-53.7%	-70.1%
BMI 40+	0.08	-71.0%	-83.4%	0.09	-69.1%	-83.5%	0.11	-69.1%	-84.9%
Diabetes	0.28	-5.5%	-8.9%	0.32	-7.7%	-17.3%	0.35	-7.7%	-23.8%
Hypertension	0.67	-1.2%	-2.3%	0.72	-1.7%	-4.6%	0.75	-1.5%	-6.7%
Heart disease	0.36	-1.7%	-2.6%	0.39	-2.1%	-5.2%	0.41	-2.3%	-8.4%
Stroke	0.13	1.2%	1.2%	0.15	1.4%	0.9%	0.16	1.7%	-0.7%
Cancer	0.24	-0.9%	-1.3%	0.25	-1.1%	-1.8%	0.25	-0.9%	-2.0%
Disability	0.43	-3.0%	-4.7%	0.47	-3.3%	-6.5%	0.49	-3.3%	-8.3%

Note: SQ stands for status quo. SQ prevalence for each disease is shown in decimal format and represents the percent of the Medicare population with the disease in the baseline scenario."; M+P stands for Medicare and private insurance coverage.

Figure 1. Medicare Cost Offsets and Social Benefits From Alternative Scenarios



M stands for Medicare, P for Private insurance coverage.

REFERENCES

1. Alison Ward et al, Benefits of Medicare Coverage for Weight Loss Drugs, USC Schaeffer Center for Health Policy Economics(2023). DOI: 10.25549/4rf9-kh77

2. Cawley, John PhD; Biener, Adam PhD; Meyerhoefer, Chad PhD; Ding, Yuchen PhD; Zvenyach, Tracy PhD, NP; Smolarz, B. Gabriel MD, MS; Ramasamy, Abhilasha MS. Job Absenteeism Costs of Obesity in the United States: National and State-Level Estimates. Journal of Occupational and Environmental Medicine 63(7):p 565-573, July 2021. | DOI: 10.1097/JOM.0000000000002198

3. Centers for Disease Control and Prevention. (2024). Fast Facts: Health and Economic Costs of Chronic Conditions. Retrieved from https://www.cdc.gov/chronic-disease/data-research/facts-stats/index.html

4. Cusi K, Isaacs S, Barb D, Basu R, Caprio S, Garvey WT, Kashyap S, Mechanick JI, Mouzaki M, Nadolsky K, Rinella ME, Vos MB, Younossi Z. American Association of Clinical Endocrinology Clinical Practice Guideline for the Diagnosis and Management of Nonalcoholic Fatty Liver Disease in Primary Care and Endocrinology Clinical Settings: Co-Sponsored by the American Association for the Study of Liver Diseases (AASLD). Endocr Pract. 2022 May;28(5):528-562. doi: 10.1016/j.eprac.2022.03.010. PMID: 35569886.

5. Garvey WT, Mechanick JI, Brett EM, Garber AJ, Hurley DL, Jastreboff AM, Nadolsky K, Pessah-Pollack R, Plodkowski R; Reviewers of the AACE/ACE Obesity Clinical Practice Guidelines. AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND AMERICAN COLLEGE OF ENDOCRINOLOGY COMPREHENSIVE CLINICAL PRACTICE GUIDELINES FOR MEDICAL CARE OF PATIENTS WITH OBESITY. Endocr Pract. 2016 Jul;22 Suppl 3:1-203. doi: 10.4158/EP161365.GL. Epub 2016 May 24. PMID: 27219496.

6. Grunvald E, Shah R, Hernaez R, Chandar AK, Pickett-Blakely O, Teigen LM, Harindhanavudhi T, Sultan S, Singh S, Davitkov P; AGA Clinical Guidelines Committee. AGA Clinical Practice Guideline on Pharmacological Interventions for Adults With Obesity. Gastroenterology. 2022 Nov;163(5):1198-1225. doi: 10.1053/j.gastro.2022.08.045. Epub 2022 Oct 20. PMID: 36273831.

7. Henderson Lewis K, Sloan C E, Bessesen D H, Arterburn D. Effectiveness and safety of drugs for obesity BMJ 2024; 384 :e072686 doi:10.1136/bmj-2022-072686

8. Lincoff AM, Brown-Frandsen K, Colhoun HM, Deanfield J, Emerson SS, Esbjerg S, Hardt-Lindberg S, Hovingh GK, Kahn SE, Kushner RF, Lingvay I, Oral TK, Michelsen MM, Plutzky J, Tornøe CW, Ryan DH; SELECT Trial Investigators. Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes. N Engl J Med. 2023 Dec 14;389(24):2221-2232. doi: 10.1056/NEJMoa2307563. Epub 2023 Nov 11. PMID: 37952131.

9. Pati S, Irfan W, Jameel A, Ahmed S, Shahid RK. Obesity and Cancer: A Current Overview of Epidemiology, Pathogenesis, Outcomes, and Management. Cancers (Basel). 2023 Jan 12;15(2):485. doi: 10.3390/cancers15020485. PMID: 36672434; PMCID: PMC9857053.

10. Thorpe K, Toles A, Shah B, Schneider J, Bravata DM. Weight Loss-Associated Decreases in Medical Care Expenditures for Commercially Insured Patients With Chronic Conditions. J Occup Environ Med. 2021 Oct 1;63(10):847-851. doi: 10.1097/JOM.0000000000002296. PMID: 34138824; PMCID: PMC8478295.

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July 12, 2024

Dr. Brittany Galusha
bgalusha@medicine.wisc.edu

Dear Dr. Galusha,

Thank you for your email to the Group Insurance Board (Board) regarding coverage for anti-obesity medicines (AOMs).

The Board choose not to cover weight-loss drugs through the Group Health Insurance Program (GHIP) for 2025 but directed continuous monitoring of AOMs relative to the program's Triple Aim Framework measured by program affordability (cost), program quality (quality/experience) and quality of life (health). The Board Chair stated at the May 2024 meeting that any potential future AOM benefit changes would not be voted on outside of the annual benefit changes and rate setting cycle, which occurs each year in February and May.

While the Board and the Department of Employee Trust Funds (ETF) acknowledge that these drugs can be effective for some patients, the challenge in covering these in our program is the cost, both short term and long term, without substantial long-term evidence of the AOMs health benefits or complications to estimate offsetting costs, quality, and health outcomes.

The Centers for Medicare and Medicaid (CMS), who oversee the Medicare Part D program, do not allow plan sponsors such as the Board to offer weight-loss drug coverage on Medicare Part D formularies due to Federal Statute 42 USC 1395W-102, which prohibits CMS from including such coverage.
Wis. Stat. § 40.03(6)(c) only allows the Board to add benefits to the GHIP if the addition is mandated by law or if a savings greater than the cost of adding coverage can be demonstrated. If neither of these provisions are met, the Board must reduce benefits to allow for the addition of new benefits.

There is not a state mandate in place to cover weight loss drugs. ETF would need to prove cost savings or reduce benefits in order comply with state law.

Prior to the February 2024 meeting, the Board asked their actuary, Segal, to conduct a cost/savings analysis for covering weight loss drugs under the Board's pharmacy benefit for commercial members. The cost analysis found that if 7,406 members, which

is 25% of GHIP members with a Body Mass Index (BMI) of 35 or higher, in 2025 were prescribed weight-loss drugs, including Zepbound, it would cost the Board just over $21 million. That analysis can be found on the bottom of page 3 at https://etf.wi.gov/boards/groupinsurance/2024/02/21/gib7c/direct. Also, included in the memo are links to 2022 and 2023 Board memos regarding the coverage of weight-loss drugs.

The Board, ETF, Segal (the Board's actuary), and Navitus Health Solutions (the Board's Pharmacy Benefits Manager), continue updating their analyses as new information becomes available. For example, at the August 14, 2024, Board meeting the Board will hear an informational presentation about current research, legalities and actions taken among peer state group health insurance programs regarding AOMs.

Again, thank you for your email. If you have any other questions, comments, concerns, or have any research you would like to share with me please do not hesitate to contact me.

Sincerely,

Tricia Sieg
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