RTI (h)(s) Health Solutions

EE471

Identifying the Value Drivers in Obesity Treatment: A Targeted Review of Weight Loss Effects on Health Economic Outcomes

Naoko Ronquest, PhD[1]; Yiwei Zhang, PhD[1]; Kyle Paret, PhD[1]; Shannon Armstrong, MSc[2]; Lisa Mostovoy, PharmD[2]; Roy Berggren, MD[2]

[1]RTI Health Solutions, Research Triangle Park, NC, United States; [2]Metsera, New York, NY, United States

BACKGROUND

- Obesity is a multifaceted disease with implications for multiple organ systems and significant health and economic burdens.[1-2]
- To model the value of various weight loss treatments, published models have used complex decision-analytic modeling structures to account for interdependence between patient characteristics and obesity-related complications.
- Interpretation of results of such models can be clarified by a review of real-world evidence on value drivers of cost-effectiveness.

OBJECTIVE

- This study aims to elucidate the value drivers of obesity treatment and identify potential gaps and inconsistencies in existing economic analyses.

METHODS

- We conducted a targeted review of economic models and real-world evidence estimating prevalence and costs of obesity-related complications by following 3 steps (**Figure 1**).

Figure 1. Targeted Literature Review Process

HTA = health technology assessment.

RESULTS

Economic Models

- The majority of cost savings due to weight loss are from delayed or avoided onsets of chronic complications, such as type 2 diabetes (T2D), cardiovascular diseases (CVD), and liver diseases (**Table 1**).
- Baseline weight and diabetes diagnoses were key clinical characteristics influencing weight loss benefits.

Real-World Evidence

Key Obesity-Related Complications

- Over 25 obesity-related complications were reported in a pooled, prospective database analysis of 114,657 adults in Finland and 499,357 adults in the UK.[1]
- Another study of electronic health records of 204,921 patients in a US hospital reported associations between weight loss and onset of obesity complications.[8]
- **Table 2** presents the effect of 10% weight loss over 5 years on onset of each of the top 8 obesity-related complications and conditions, with the highest effect of weight loss (odds ratio [OR] < 0.5).
- The prevalent complications influenced by weight loss were T2D, obstructive sleep apnea (OSA), osteoarthritis of the knee, metabolic dysfunction–associated fatty liver disease/metabolic dysfunction–associated steatohepatitis (MAFLD/MASH), and CVD (HF and hypertension).

High Cost Complications

- **Figure 2** reports costs of key obesity-related complications. Although costs of OSA and hypertension were relatively low, they may be important to account for as it is prevalent in patients with obesity; an onset of OSA can be substantially influenced by weight loss.

Comparison of Modeled Outcomes and Drivers Identified in the Literature

- Although most key obesity-related complications were modeled in published HTA submission models, MAFLD/MASH were not modeled (**Table 3**).

Table 1. Summary of Reviewed Economic Models

Author (year)	Country	Model type (modeled population)	Obesity-related complications and events considered	Reported key CE drivers
CADTH[3]	**Canada**	Cohort multi-state Markov model (BMI ≥ 30 kg/m² or ≥ 27 kg/m² with at least 1 weight-related comorbidity)	Prediabetes, T2D, ACS, stroke, cancer (colon, breast, endometrial), OSA, and knee replacement	Utility benefit of weight reduction; delay of onset of prediabetes and T2D; drug price
NICE[4]	**UK**	Cohort multi-state Markov model (BMI ≥ 30 kg/m² with at least 1 weight-related comorbidity)	Non-diabetic hyperglycemia, T2D, ACS, stroke, OSA, osteoarthritis (knee replacement)	Baseline BMI; the outcomes discount rate; weight reduction size at year 2 with diet and exercise
NICE[5]	**UK**	Cohort multi-state Markov model (BMI ≥ 35 kg/m² and prediabetes and high risk of cardiovascular disease)	Onset of T2D, OSA, cardiovascular events, knee replacement, cancer (colon, breast, endometrial)	Probability of remission from prediabetes; weight reduction size at year 2; HbA_{1c} level post T2D onset; smoking status; baseline BMI; mortality from stroke and angina; cost of prediabetes
ICER[6]	**US**	Cohort multi-state Markov model (80% female with average age of 45 years, BMI of 38 kg/m², SBP of 125 mm Hg, and HbA_{1c} of 5.5%)	CVD, stroke, MI, HF, DM	Health state utility; weight loss drug efficacy; HbA_{1c} level post T2D onset, and baseline HbA_{1c}
Nuijten et al.[7]	**US**	Decision tree model (BMI > 30 kg/m²)	MI, angina pectoris, chronic HF, stroke, hypertension, DM, osteoarthritis, arthrosis hip/knee, dorsopathy, cancer, gall bladder disease, back pain, asthma, pulmonary embolism, coronary artery disease	Baseline BMI; costs of T2D; costs of obesity-related complications, obesity treatments; model time horizon

ACS = acute coronary syndrome; BMI = body mass index; CE = cost-effectiveness; CVD = cardiovascular disease; DM = diabetes mellitus; HbA_{1c} = glycated hemoglobin; HF = heart failure; ICER = incremental cost-effectiveness ratio; MI = myocardial infarction; NICE = National Institute for Health and Care Excellence; OSA = obstructive sleep apnea; SBP = systolic blood pressure; T2D = type 2 diabetes; UK = United Kingdom; US = United States.

Table 2. Key Obesity-Related Complications

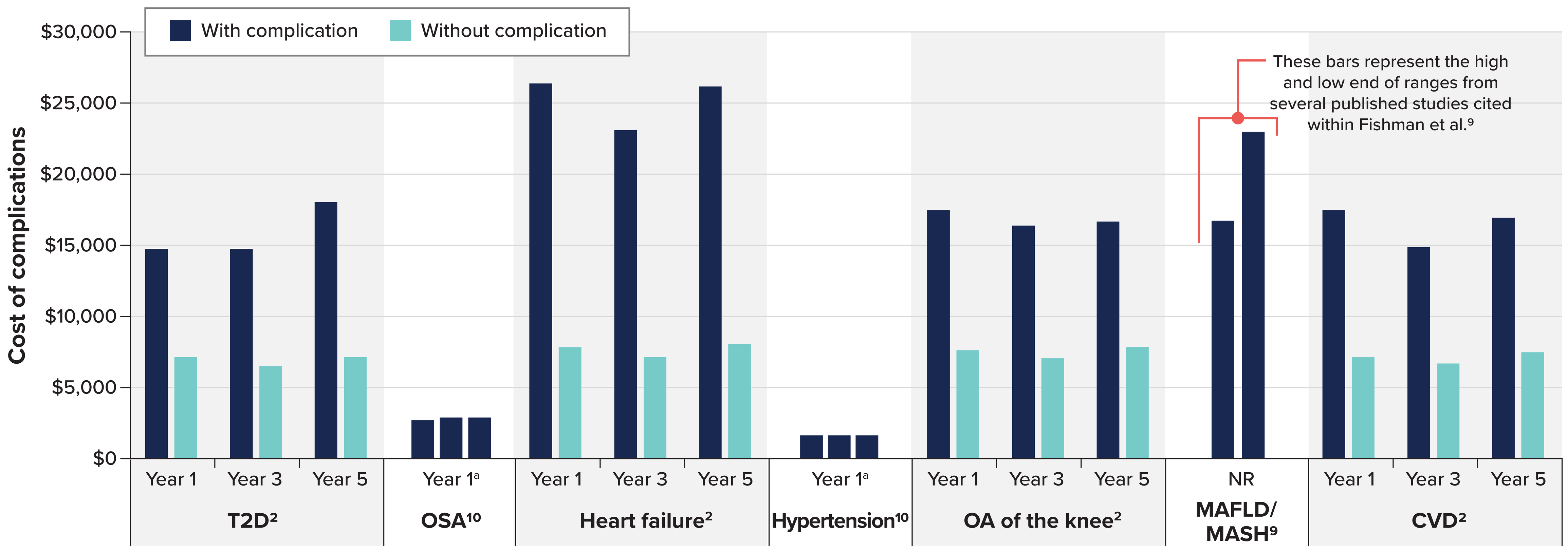
Complication	Effect of obesity[a] on complication (hazard ratios)[1]	Impact of ≥ 10% weight loss over 5 years on onset of complication (OR)[8]	To investigate costs for selection of key complications?
T2D	12.14	0.39	✓ High prevalence and weight loss impact
OSA	6.27	0.28	✓ High prevalence and weight loss impact
Gout	4.31	NR	✗ Impact of weight loss on onset of gout is not reported. Likely substantially overlapping with T2D
HF	4.17	0.84	✓ High prevalence and weight loss impact
Hypertension	3.20	0.47	✓ High prevalence and weight loss impact
OA of the knee	2.71	0.63	✓ High prevalence and weight loss impact
MI	1.52	1.05	✓ This is part of the CVD listed below
Stroke	1.41	1.10	✗ Weight loss impact not substantial
Eating disorder	NR	0.21	✗ Often recognized as a psychiatric disorder vs. an obesity-related complication[1]
MAFLD/MASH	NR	0.41	✓ Prevalence is not reported; high weight loss impact[9]
CVD	NR	0.82	✓ Miriam et al.[8] estimate for CVD includes HF and MI

A higher HR = a higher impact of obesity (vs. normal weight) on the incidence of the corresponding complication

A lower OR = a higher impact of weight loss (vs. no weight loss) on the complication onset

MAFLD = metabolic dysfunction–associated fatty liver disease; MASH = metabolic dysfunction–associated steatohepatitis; NR = not reported (dropped from consideration due to little evidence on the effect of weight loss); OR = odds ratio.
[a] Obesity (BMI ≥ 30 kg/m²) vs. normal weight.

Figure 2. Reported Costs of Key Obesity-Related Complications



Note: Rezdiffra was not available when this study was completed and is not accounted for in the cost estimate.
[a] Bars represent costs for patients with BMI ≥ 25: 1st bar = 30.0 kg/m²–34.9 kg/m²; 2nd bar = 35.0 kg/m²–39.9 kg/m²; 3rd bar = ≥ 40.0 kg/m².
Sources: Pearson-Stuttard et al.,[2] in 2019 US dollars; Fishman et al.,[9] currency year not reported; Divino et al.,[10] in 2017 US dollars.

Table 3. Anticipated Top Cost Drivers of Obesity Treatment, Mapped to Previous Cost-Effectiveness Modeling Approaches

Complications	Modeled in HTA-submitted cost-effectiveness models or the ICER model? If not, why?
T2D	✓ CADTH (2022),[3] NICE (2021),[4] NICE (2019),[5] ICER (2022)[6]
OSA	✓ CADTH (2022),[3] NICE (2021),[4] NICE (2019)[5]
CVD	✓ CADTH (2022),[3] NICE (2021),[4] NICE (2019),[5] ICER (2022)[6]
OA of the knee	✓ CADTH (2022),[3] NICE (2021),[4] NICE (2019)[5]
MAFLD/MASH	✗ Reasons not reported in reports: A substantial overlap between T2D and MAFLD/MASH may have contributed to the exclusion of MAFLD/MASH as a separate condition.[9] Additionally, MAFLD/ MASH is not well diagnosed due to non-specific symptoms. The diagnostic coding for this complication was only introduced in October 2023 with no available treatments until 2024.[11]

DISCUSSION AND CONCLUSIONS

- This study confirmed a strong association between obesity and complications that impose significant health and economic burdens on both patients and healthcare systems.
- Previous economic models of weight loss interventions may have underestimated the benefits of weight loss by omitting some prevalent obesity-related complications with high costs, such as MAFLD/MASH, and by ignoring the complex multimorbidity of patients with obesity.
- Although cancers were included in some of the economic models, the evidence to support the impact of weight loss on cancer diagnoses is lacking.[1]
- Where evidence shows that obesity increases the risk of comorbidities, further research is needed to clarify how weight loss impacts risk reduction or remission of these conditions to provide greater confidence in the value of treating obesity.
- Despite strong evidence of the relationship between obesity and poor health, the value of treating obesity is questioned in health systems around the world; it is critical to develop additional analytic, time-bound, population-based tools to support rational coverage decisions that enable improvement in global health and reduction in obesity-related healthcare costs.

References

1. Kivimäki M, et al. Lancet Diabetes Endocrinol. 2022 Apr;10(4):253-63.
2. Pearson-Stuttard J, et al. Int J Obes (Lond). 2023 Dec;47(12):1239-46.
3. CADTH. CADTH Reimbursement Review Semaglutide (Wegovy). December 2022.
4. NICE. Single Technology Appraisal Semaglutide for managing overweight and obesity [ID3850]. Committee Papers. July 2021.
5. NICE. Single Technology Appraisal Liraglutide for managing overweight and obesity [ID740] Committee Papers. June 2019.
6. ICER. Medications for obesity management: effectiveness and value. Evidence Report. 31 August 2022.
7. Nuijten M, et al. J Med Econ. 2018;21(9):835-44.
8. Mariam A, et al. Diabetes Obes Metab. 2021 Dec;23(12):2804-13.
9. Fishman J, et al. Curr Med Res Opin. 2023 Sep 22:1-5.
10. Divino V, et al. J Manag Care Spec Pharm. 2021 Feb;27(2):210-22.
11. FDA approves first MASH drug. Nat Biotechnol. 2024 Apr;42:540.

Contact Information

Shannon Armstrong
Metsera

3 World Trade Center
New York, NY 10007

shannon.armstrong@metsera.com

Scan the QR code for the full version of the poster

Presented at: ISPOR Europe 2024; 17-20 November 2024; Barcelona, Spain