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Development of a Markov model for assessing the cost-effectiveness of chronic weight management interventions

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Background

- Obesity affects 42% of the United States (US) population,[1] resulting in preventable premature death, increased risk of comorbidities,[2] and over 260 billion dollars in direct medical costs.[3]
- Since 2021, two new glucagon-like peptide-1 receptor agonists (GLP-1 RA) have gained approval for chronic weight management, demonstrating the significant potential for weight loss as supported by numerous phase-three clinical trials and initial real-world data.[4-11]
- A comprehensive model for cost-effectiveness analysis is crucial for comparing cardiovascular outcomes across novel weight management strategies. This will aid stakeholders in making informed choices about clinical applications, coverage, and reimbursement.

Objective

To create a Markov model for assessing the cost-effectiveness of chronic weight management interventions in a commercially insured adult population in the US from the payor perspective.

Methods

- The study adapted the Core Obesity Model (COM) to facilitate the evaluation of chronic weight management interventions from a large US payer's perspective.[12-14]
- Revised model parameters were derived from a retrospective cohort analysis of GLP-1 RA naive adults in the Healthcare Integrated Research Database (HIRD®), which contains geographically diverse medical and pharmacy claims with integrated clinical data for over 50 million US lives.
- Eligible patients had a body mass index (BMI) ≥30 kg/m^2 between 01 January 2016 and 30 November 2022 (first observed = index date) and ≥12 months of continuous health plan enrollment, no diagnosis of type 1 diabetes, no prescriptions for any GLP-1 RA, and no bariatric surgery prior to index.
- Base-case clinical characteristics were described over the 12-month pre-index period, and transition probabilities and costs were described over the post-index period (i.e., index date until 30 November 2023, death, or health plan disenrollment, whichever came first). Risk equations and hazard ratios (HR) were derived using Cox Proportional Hazard Models. Base-case treatment effects were extrapolated from publicly available clinical trial data.

Results

Figure 1. Structure of Adapted COM

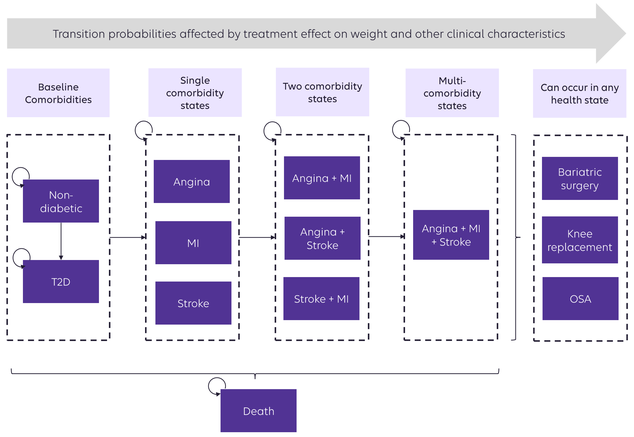

Table 1. Baseline characteristics of eligible patients

	All eligible	Without T2D	With T2D
N, (%)	1,209,646 (100%)	1,072,030 (89%)	137,616 (11%)
Age in years			
Mean (SD)	46 (13.6)	45 (13.5)	56 (10.4)
Sex, %			
Male	43%	42%	50%
Female	57%	58%	50%
Race/ethnicity, %			
Asian, non-Hispanic (NH)	2%	2%	2%
Black, NH	13%	12%	17%
Hispanic	6%	6%	6%
White, NH	75%	76%	71%
Other/unknown	4%	4%	4%
BMI in kg/m^2 category, %			
30-34.9 (obesity class I)	60%	60%	48%
35-39.9 (obesity class II)	23%	23%	27%
≥40 (obesity class III)	17%	17%	25%
Comorbidities, %			
Angina	3%	2%	7%
MI	2%	1%	4%
Stroke	3%	2%	6%
Excessive alcohol consumption	1%	1%	1%
Smoking treatment	2%	1%	2%
Systolic blood pressure in mmHg			
Mean (SD)	130 (15.1)	129 (14.9)	134 (16.0)
Diastolic blood pressure in mmHg			
Mean (SD)	81 (9.6)	81 (9.6)	80 (9.7)
Abnormal lab values, %			
High blood pressure	22%	22%	22%
Low high-density lipoprotein	41%	39%	51%
High triglycerides	36%	34%	46%
Abnormal fasting glucose	2%	18%	37%

Note: Blood pressure data available for ~70% of patients. High-density lipoprotein and triglyceride data available for ~30% of patients. Fasting glucose data available for ~1% of patients.

- The COM is a closed cohort Markov model that encompasses mutually exclusive obesity-related health states, including prediabetes, type 2 diabetes (T2D), angina, myocardial infarction (MI), stroke, and cancer. Patients enter the model with prespecified baseline characteristics. Integrated via risk equations, treatment effects dictate how patients move through the model.
- The adapted model retains the original structure of the COM with the following variations **(Figure 1):**
  - Excluded cancer and prediabetes and added obstructive sleep apnea (OSA) as health states.
  - Revised population characteristics reflect eligible patients enrolled in the health plan.
  - Revised risk equations to incorporate new significant treatment effects (i.e., GLP-1 RAs effect on diastolic blood pressure, triglycerides, and fasting glucose). The covariates in the model vary by outcome to ensure best fit among eligible patients enrolled in the health plan. The likelihood ratio, which signifies how many times more likely the data are under the full model compared to the intercept only, was used to indicate the model's fit.
  - Used a shorter base case time horizon of two years to represent the duration of interest to the health plan. The first year uses three-month cycles, while the subsequent year applies a one-year cycle.
- Patients in the population of interest (N = 1,209,646) are 43% male, with a mean age of 46 years and a mean BMI of 36 kg/m^2. Upon entering the model, 11% had T2D, and 7% had a history of any cardiovascular disease ((CVD) i.e., angina, MI, or stroke) **(Table 1)**. 44% of CVD is angina, 36% is MI, and 20% is stroke.
- In 2023 adjusted US dollars, the incremental cost per patient per month was $1,413 (T2D), $3,324 (angina), $5,365 (post-MI), $4,084 (post-stroke), and $1,274 (OSA), and the average per-event cost was $46,260 (bariatric surgery) and $46,229 (knee replacement).
- Risk equations, which determine how patients transition through the model, included novel static characteristics (i.e., alcohol consumption, smoking treatment) and dynamic characteristics (i.e., triglycerides, blood pressure, and fasting glucose; **Table 2-3**).
- Abnormal lab results in these models were defined as follows: High blood pressure: systolic>130 and diastolic >85 mmHg or on an antihypertensive medication. Low high-density lipoprotein: men <40 mg/dL, women <50 mg/dL. High triglycerides: >150 mg/dL. Abnormal glucose: 100-125 mg/dL.

Table 2. Relative hazard of transition to T2D by patient characteristics

	HR	95% LCI	95% UCI
Age (reference: <50)			
50-64	1.53	1.24	1.90
≥65	1.46	1.00	2.13
Male (reference: female)	1.05	0.86	1.28
Race (reference: White, NH)			
Asian, NH	1.28	0.68	2.42
Black, NH	1.64	1.23	2.20
Hispanic	1.53	1.17	2.01
Other/unknown	1.14	0.74	1.76
BMI in kg/m^2 (reference: 30-34.9)			
35-39.9	1.87	1.48	2.36
≥40	2.34	1.83	3.00
Low high-density lipoprotein	1.43	1.17	1.74
Abnormal fasting glucose	1.55	1.26	1.9
Systolic blood pressure	1.01	1.01	1.02

Note: Valid N: 4,457. Likelihood Ratio: 144.296 (p<0.0001).

Table 3. Relative hazard of transition to incident and subsequent CVD by patient characteristics

	Incident CVD			Subsequent CVD		
	HR	95% LCI	95% UCI	HR	95% LCI	95% UCI
Age (reference: <50)						
50-64	2.38	2.25	2.50	1.33	1.25	1.42
≥65	4.84	4.49	5.23	1.71	1.58	1.84
Male (reference: female)	1.50	1.43	1.57	1.37	1.30	1.43
Race (reference: White, NH)						
Asian, NH	0.95	0.81	1.13	1.13	0.96	1.33
Black, NH	1.04	0.98	1.11	1.01	0.94	1.08
Hispanic	1.01	0.93	1.10	0.90	0.81	0.99
Other/unknown	0.97	0.87	1.09	0.93	0.83	1.04
BMI in kg/m^2 (reference: 30-34.9)						
35-39.9	1.09	1.04	1.15	-	-	-
≥40	1.15	1.08	1.22	-	-	-
Excessive alcohol consumption	1.51	1.26	1.81	1.15	0.98	1.34
Smoking cessation intervention	1.94	1.69	2.23	1.46	1.31	1.63
T2D	1.52	1.45	1.6	1.13	1.08	1.19
Low high-density lipoprotein	1.21	1.16	1.27	1.24	1.19	1.30
High triglycerides	1.16	1.11	1.22	-	-	-
High blood pressure	1.06	1.01	1.12	-	-	-

Note: Incident CVD - Valid N: 177,593. Likelihood Ratio: 3162.638 (p<0.0001). Subsequent CVD – Valid N: 22,141. Likelihood Ratio: 600.623 (p<0.0001).

Limitations

- Administrative claims may have coding inaccuracies and may not accurately reflect actual medication adherence. Cost estimates from medical and pharmacy claims exclude most rebates or adjustments and may not accurately portray value-based contracts.
- Literature-derived inputs may not wholly represent the US payer population of interest.

Conclusions

The adapted model provides a comprehensive framework to understand and quantify the value of chronic weight management interventions over time from the payer perspective. The intended uses encompass an assessment of the relative cost-effectiveness of chronic weight management interventions using real-world data.

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