Cost-Effectiveness of Semaglutide 2.4 mg Compared with Resmetirom and Standard of Care for Metabolic Dysfunction-Associated Steatohepatitis (MASH) in the U.S. Using Most-Favored-Nation (MFN) Pricing

EE219

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Aim

This model was developed to estimate the clinical and economic outcomes of semaglutide 2.4 mg, at the MFN price, with standard of care (SoC) and resmetirom.

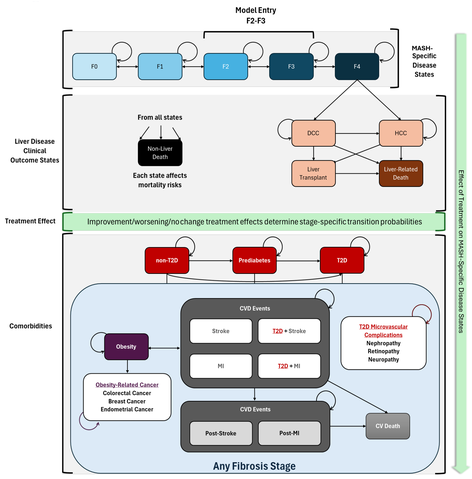
Introduction

- Although underdiagnosed, the prevalence of MASH is rising in U.S. adults, elevating the risk of serious clinical events such as decompensated cirrhosis (DCC), hepatocellular carcinoma (HCC), liver transplant (LT), and death.[1]
- Current evidence supports the significant association between MASH with other chronic metabolic conditions, including prediabetes, type 2 diabetes (T2D), cardiovascular disease (CVD), and obesity.[2]
- Following its FDA approval for MASH in August 2025, semaglutide is available at a more accessible price under MFN pricing.[8]
- With the introduction of semaglutide as a treatment for MASH, it is critical to evaluate the clinical and economic implications of a new treatment compared to other existing treatment strategies, including SoC and resmetirom.

Methods

- A cost-effectiveness model (**Figure 1**) was built using a Markov cohort structure to project fibrosis progression, comorbidity status, and associated clinical events in adults with MASH.

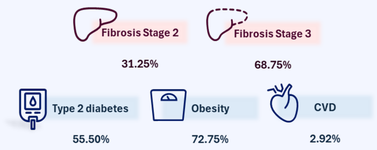
Figure 1: Markov Model Diagram



See bottom right for abbreviations.

- Disease progression was modeled with mutually exclusive health states: F0 (no fibrosis) through F4 (compensated cirrhosis (CC)), DCC, HCC, LT, and death.

Figure 2: Baseline Population Distributions of Fibrosis Stage and Associated Comorbidities



- The baseline population characteristics were based on the demographic and clinical characteristics of the ESSENCE trial[3] population.
- Patients were in either F2 or F3 health states at baseline. Fibrosis stage and comorbidity distributions are described in **Figure 2**.
- The baseline age of the model cohort was 56 years, and 42.9% were male. The baseline BMI was 34.6 kg/m^2.

Table 1: Model Overview

Parameter	Value
Time Horizon	Lifetime
Cycle Length	1-year
Perspectives	U.S. Healthcare Payer (Commercial Payers, Medicaid, and Medicare)
Discount Rate	3% annually for costs and outcomes
Interventions	Semaglutide 2.4 mg once-weekly SC injection, resmetirom 80 mg PO once daily, and resmetirom 100 mg PO once daily
Comparator	SoC[†]
Inputs	Medical costs, monitoring costs, event costs and utility values by health state across MASH and other comorbidities (CVD, prediabetes, T2D, and obesity), treatment acquisition costs, treatment-related clinical inputs, disease-related clinical inputs, adverse events, discontinuation, all-cause and disease-associated mortality
Outputs	Drug Costs; Total Costs; Total LY, QALY, and evLY; Incremental Results (Costs, LYG, QALYG, evLYG); Incremental Cost-Effectiveness Ratios (ICER per LYG, ICUR per QALYG, ICER per evLYG)
Sensitivity Analyses	One-way sensitivity analysis (OWSA), probabilistic sensitivity analysis (PSA), and cost-effectiveness plane

[†]SoC includes lifestyle modifications (i.e. diet, exercise, weight loss);
[‡]Serious adverse events reported in the trials were included in the base case and assumed to require hospitalization;
See bottom right for abbreviations.

- Clinical and cost inputs were sourced from clinical trials (e.g. REGENERATE, ESSENCE, MAESTRO-NASH)[3-5] and published literature on MASH progression.
- Risks of CVD and T2D were estimated using a custom adaptation of a QRisk3 model calibrated to patients with MASH.[6]
- The WAC for treatments was obtained from Micromedex RED BOOK.[7] Semaglutide was assumed to be available at the MFN price of $350.[8]

Results

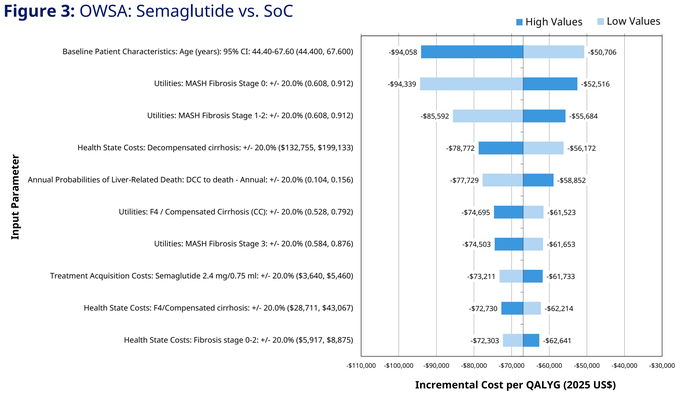
Table 2: Base-Case Results vs. Standard of Care (SoC)

Measures	SoC	Semaglutide 2.4 mg	Resmetirom 80 mg	Resmetirom 100 mg
Drug Cost	$0	$50,488	$534,042	$365,163
Total Cost	$552,763	$441,736	$967,514	$798,503
LYs	13.59	15.37	14.87	14.93
QALYs	9.34	11.00	10.54	10.58
evLYs	9.34	11.25	10.73	10.78
Incremental Results: SoC vs. Other Options				
Incr. Costs	—	-$111,027	$414,751	$245,740
Incr. LYs	—	1.78	1.28	1.34
Incr. QALYs	—	1.66	1.20	1.24
Incr. evLYs	—	1.91	1.39	1.44
Incremental Cost-Effectiveness and Cost-Utility Ratios				
ICER (per LYG)	—	Dominant	$324,024	$183,388
ICUR (per QALYG)	—	Dominant	$345,626	$198,177
ICER (per evLYG)	—	Dominant	$298,382	$170,653

All results were discounted and reported in 2025 US Dollar.
Green indicates a dominant strategy (less costly and more effective than SoC).
See bottom right for abbreviations.

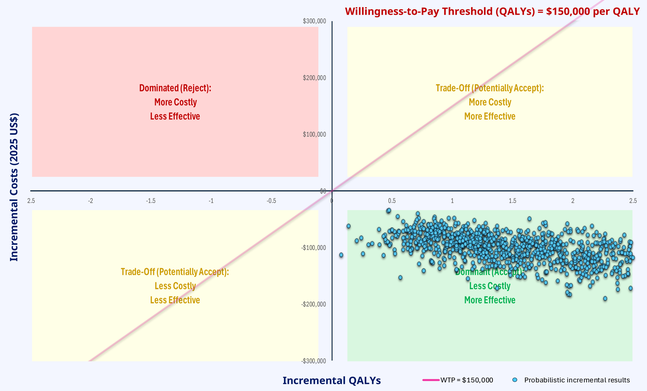
- From the base-case results, shown in **Table 2**, semaglutide provided greater health effects at lower total costs compared with SoC
- Semaglutide demonstrated greater LYs (+1.78), QALYs (+1.66), and evLYs (+1.91) than SoC.
- Resmetirom 80 mg and 100 mg also demonstrated a higher benefit in LYs, QALYs, and evLYs at higher total costs than SoC.
- Semaglutide was the dominant strategy versus SoC across all three cost-effectiveness metrics (ie; ICER per LYG, ICUR per QALYG, ICER per evLYG). Resmetirom 80 mg and 100 mg were more costly and more effective than SoC with ICURs of $345,626 and $198,177 per QALY gained respectively (higher than a WTP threshold of $150,000).

Figure 3: OWSA: Semaglutide vs. SoC



- The OWSA result shown in **Figure 3** presents the top drivers for cost-effectiveness in semaglutide compared with SoC.
- Baseline age, utility values across MASH health states, DCC costs, liver-related death, and semaglutide acquisition costs were the primary drivers in ICUR compared with SoC.

Figure 4:
Probabilistic Cost-Effectiveness Plane at WTP $150,000: Semaglutide vs. SoC



- Probabilistic sensitivity analysis (PSA) results are presented in **Figure 4**.
- There was a 99.9% probability of dominance, demonstrating greater effectiveness (QALYs) achieved at a lower total costs with semaglutide compared with SoC.

Limitations

- Natural history transitions and event risks are based on trial data, which may not capture real-world heterogeneity.
- Treatment effects on fibrosis are assumed constant over time with no treatment-effect waning following discontinuation, potentially overstating long-term benefits.
- The model extrapolates beyond trial follow-up using parametric survival models, which introduces uncertainty, particularly without long-term real-world data.

Conclusion

- Under the MFN price, semaglutide was associated with lower costs and superior health outcomes compared to SoC from the U.S. healthcare payer perspective.
- These findings suggest favorable cost-effectiveness for semaglutide in current treatment strategies, including SoC.

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Abbreviations: CC, compensated cirrhosis; CVD, cardiovascular disease; DCC, decompensated cirrhosis; evLY(G), equal value life-year (gained); F0-F4, fibrosis stage 0 (no fibrosis) to stage 4 (compensated cirrhosis); HCC, hepatocellular carcinoma; ICER, incremental cost-effectiveness ratio; ICUR, incremental cost-utility ratio; LT, liver transplant; LY(G), life-year (gained); MASH, metabolic dysfunction-associated steatohepatitis; MFN, Most-Favored-Nation; MI, myocardial infarction; OWSA, one-way sensitivity analysis; PO, per os (oral); PSA, probabilistic sensitivity analysis; SoC, standard of care; SC, subcutaneous; T2D, type 2 diabetes; QALY(G), quality-adjusted life-year (gained); WAC, wholesale acquisition cost; WTP, willingness-to-pay

References: (**1**) Taylor et al. Gastroenterology, 2020; 158: 1611-25; (**2**) Estes et al. Hepatology 2018; 67: 123-33; (**3**) Sanyal et al. N Engl J Med. 2025:5;392(21): 2089–2099; (**4**) Younossi et al. Lancet 2019; 394(10215): 2184-2196; (**5**) Harrison et al. N Engl J Med. 2024; 390 (6): 497-509; (**6**) HEOR Ltd and Novo Nordisk. Parametric cardiovascular risk equations. Final Report. January 2025. (**7**) RED BOOK online. IBM Micromedex. 2025; (**8**) Fact Sheet. The White House Washington. 6 Nov 2025;