Cost-effectiveness of semaglutide for the treatment of metabolic dysfunction-associated steatotic liver disease in the United States

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Background and objective

- Metabolic dysfunction-associated steatotic liver disease (MASLD) is one of the most prevalent chronic liver diseases globally, affecting 25-30% of the adult population[1].
- MASLD management is primarily focused on the lifestyle modifications and treatment of metabolic comorbidities[2].
- The economic value of semaglutide in the US is still uncertain though it has demonstrated the improved metabolic and liver-related outcomes in patients with MASLD[3,4].
- This study evaluated the cost-effectiveness of semaglutide vs usual care for MASLD patients with moderate or advanced hepatic fibrosis (F2 to F3) from a U.S. healthcare system perspective.

Methods

- A state-transition Markov model[5] were adapted to assess the cost-effectiveness of semaglutide compared to usual care for MASLD treatment over a lifetime horizon.
- This analysis was modeled after a hypothetical U.S. cohort of MASLD patients with moderate or advanced hepatic fibrosis from a healthcare system perspective.
- Multiple health states including fibrosis (F1-F3), cirrhosis (F4; compensated and decompensated), hepatocellular carcinoma (HCC), liver transplantation, post-transplantation and death were considered (**Figure 1**).
- Semaglutide treatment was defined according to the recent ESSENCE Phase-3 trial (once-weekly subcutaneous semaglutide at a dose of 2.4 mg)[4].
- Usual care, defined as weight loss through lifestyle changes as reflected in the current standard of care for MASLD[5].
- Semaglutide significantly increased the resolution of steatohepatitis with no worsening of liver fibrosis (62.9% vs 34.3%) compared to placebo, yielding an RR of 1.84 (95%CI: 1.54 - 2.20) in patients with F2-F3 fibrosis [4].
- The cost of semaglutide was considered based on the wholesale acquisition cost in the base-case analysis, and a scenario analysis was conducted based on the federal supply schedule cost (Veteran affairs service cost)[6,7].
- No indirect cost was considered in the analysis.
- All cost parameters were adjusted to the 2024 US dollars ($) using the Medical Care component of the US Consumer Price Index.
- Both cost and outcome were discounted at an annual rate of 3%.
- Quality-adjusted life years (QALYs), cost (2024 USD), and incremental cost-effectiveness ratios (ICERs) for cost per QALY were estimated.
- A Cost-effectiveness Acceptability Curve illustrated the probability of being cost-effective across willingness-to-pay (WTP) thresholds.
- A series of sensitivity analyses were performed to assess the robustness of the findings.

Methods

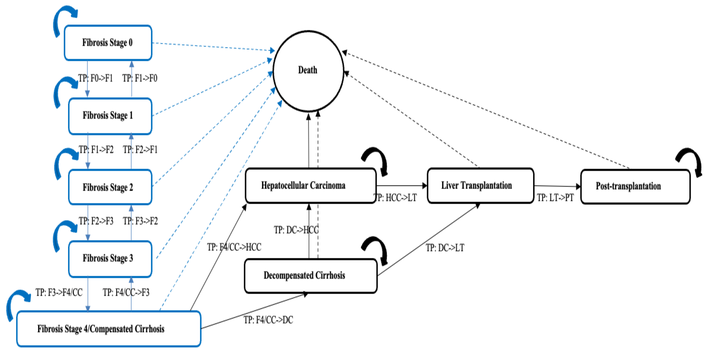

Figure 1: The transition model describing the disease progression in MASLD

Category	Parameter	Base-case Value
Population	Target population Starting age	Adults with MASH (F2–F3)[4] 60 years[4]
Progression probabilities	F2 → F3 F3 → F4 F4→ DC F4 → HCC HCC → Death	11.54% per year[8] 9.10% per year[8] 6.6% per year[8] 3.8% per year[8] 13.1% per year[8]
Regression probabilities	F1 → F0 F2 → F1 F3 → F2 F4 → F3	7.10% per year[8] 7.90% per year[8] 7.90% per year[8] 5.2% per year[8]
Treatment effectiveness	Fibrosis improvement Reduction in progression	RR = 1.84[4] 28.7%[4]
Cost (2024 USD)	Semaglutide cost	$19,200/year[6,7]
Utilities	MASLD F2, F3 CC DC HCC	0.85[8] 0.84[8] 0.8[8] 0.6[8] 0.5[8]

Table 1: The key input parameters
(a representative subset of the full set of model inputs)

Results

- In the base case analysis, semaglutide treatment is projected to prevent 252 decompensated cirrhosis cases and 131 HCC cases per 10,000 patients over the lifetime.
- Treatment with semaglutide was associated with an additional 0.21 QALYs compared to usual care with an incremental cost of $18,135; resulting in an ICER of $87,776 per QALY (**Table 2**).
- Semaglutide had a 63% probability of being cost-effective at a WTP of $100,000 per QALY, with corresponding probabilities of 89% and 95% at $150,000 and $200,000 per QALY, respectively
- The PSA results showed a mean incremental ICER of $69,252/QALY (CrI: $25821 to $264624), with 99.8% probability of being cost-effective at $100,000/QALY. (**Figure 2**).

Outcomes	Usual care	Semaglutide
LYs	15.366	15.582
QALYs	12.976	13.185
Total Cost	$55,045	$73,361
LYs Gained	0.22	
QALYs Gained	0.21	
Incremental Costs	$18,315.56	
ICER/QALY	$87,776 (CrI: 25,821 - 264,624)	

Table 2: Base-case analysis

Results

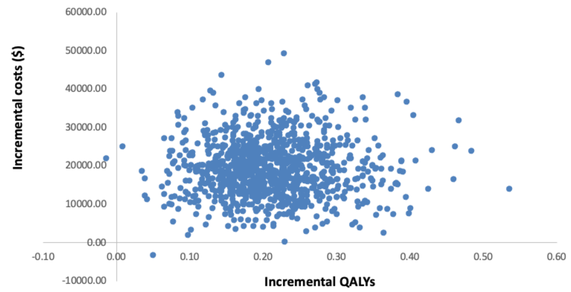

Figure 2: Cost-effectiveness plane from probabilistic sensitivity analysis

Discussion and Conclusion

- Semaglutide is likely to be cost-effective in MASLD patients with moderate or advanced hepatic fibrosis under most accepted U.S. thresholds.
- The cost-effectiveness of semaglutide is largely driven by its ability to slow fibrosis progression, leading to further cost savings by reducing hepatic complications such as liver-related hospitalizations and transplantation[8,9].
- These findings align with prior evidence that interventions which delay chronic liver disease progression can provide good value for money by preventing costly and life-threatening liver-related complications[5,6,10-13].
- The sensitivity and scenario analyses indicates that, longer horizons, lower discounting, lower drug costs, larger effectiveness, and younger age improved cost-effectiveness. This was in line with a recent meta-analysis of economic evaluation of semaglutide[13].
- Current study support the early use of semaglutide in the high risk MASLD patients and provide the evidence for future clinical guidelines and reimbursement decision.

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