Lifetime Cost of Care Simulation of Compensated Metabolic Dysfunction-Associated Steatohepatitis (MASH) Cirrhosis

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Introduction

- Metabolic dysfunction-associated steatohepatitis (MASH) is a progressive liver disease associated with substantial morbidity and a high risk of adverse outcomes, particularly in patients with compensated cirrhosis[1–5]
- The cost of care analysis includes health states spanning pre-cirrhosis fibrosis, compensated cirrhosis (F4c), decompensated cirrhosis (F4d), hepatocellular carcinoma (HCC), liver transplant (LT), and death

Objectives

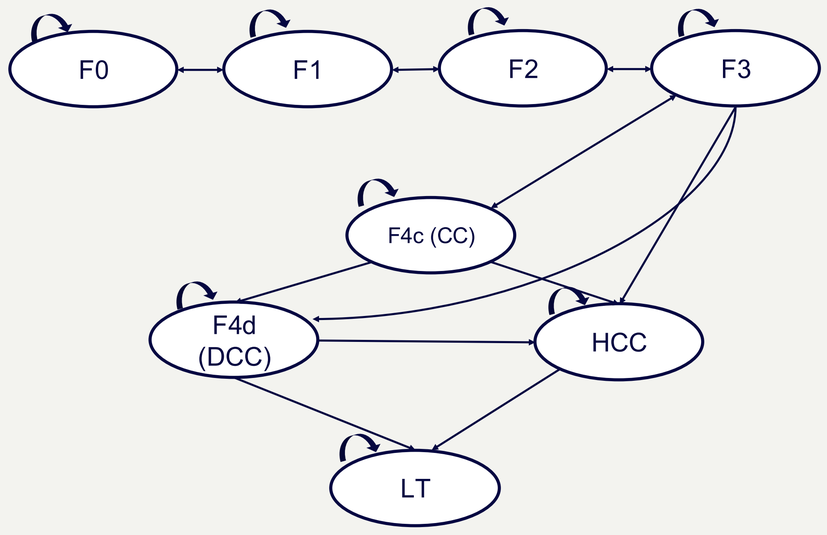
To quantify the **long-term clinical trajectory and economic burden** of patients entering the compensated cirrhosis health state due to MASH, including **progression to advanced liver outcomes, fibrosis regression, survival, and cumulative healthcare costs**.

Methods

Model structure

- A 9-state Markov cohort model – inclusive of pre-cirrhosis fibrosis states, advanced liver disease states, liver transplant, and death – was utilized to simulate the progression of a cohort of 100,000 patients in the United States **(Fig. 1)**
- All patients entered the model with MASH F4c and transitioned through health states in yearly cycles over a lifetime horizon (up to 40 years), using probabilities from published literature
- Costs incurred were associated with treatment, disease management, monitoring, cardiovascular events, liver-related events, and mortality, sourced from published literature. Costs were inflated to 2025 USD, as necessary, and a 3% annual discount rate was applied
- A scenario including concurrent semaglutide use for the treatment of comorbid T2DM and/or obesity for 50% of patients was included, which impacts clinical efficacy and costs **(Table 1)**

Figure 1: Markov cohort model flow chart.



All eight disease states can lead to death state (ninth state)

Model inputs and assumptions

Table 1: Assumptions used in Markov model.

Component	Assumptions
Population	In the base case, the model assumes all patients enter the model at F4c only at baseline
Clinical	ASCVD risk is informed by the risk equations sourced from Goff 2014 and applied in the base case
Costs	SOC is assumed to have $0 treatment costs in the base case (when GLP-1s are not applied); disease management costs by health states aligned with prior published cost-effectiveness analysis

Results

Health Outcomes

The cohort simulation demonstrated that **by Year 5, 68% of all patients were alive**, with 23% of all patients having progressed to more severe health states (18% decompensated cirrhosis, 3% hepatocellular carcinoma, and 1% liver transplantation); the proportion alive **decreased to approximately 50% by Year 9. Approximately 23% of patients regressed to pre-cirrhosis fibrosis states (i.e., F2-F3)**, over the lifetime horizon **(Fig. 2)**

Financial Burden

The lifetime cost of care for compensated cirrhosis due to MASH patients **(median of 9 years) was $240,400 per patient. The majority (94%) of the costs were driven by disease management, including liver-related events ($226,134);** the inclusion of semaglutide as concomitant baseline therapy within the model increased the total cost of care to $296,945 **(Fig. 3)**

Figure 2: Health State Occupancy for SOC for compensated cirrhosis due to MASH patients.

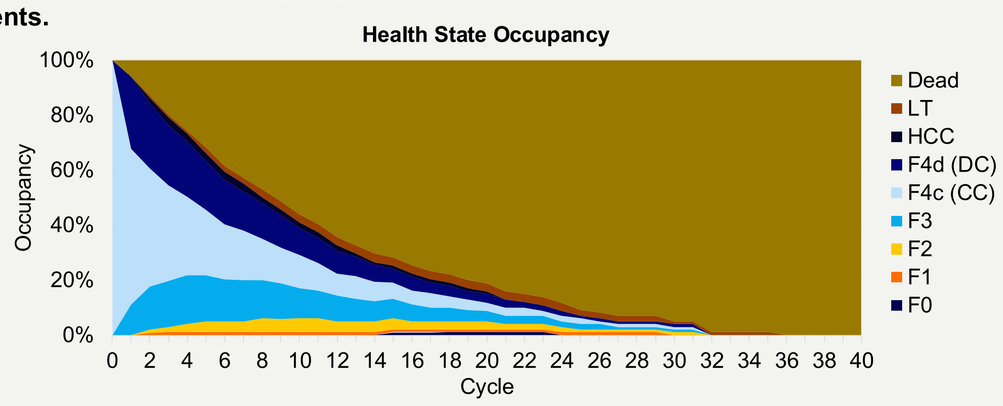
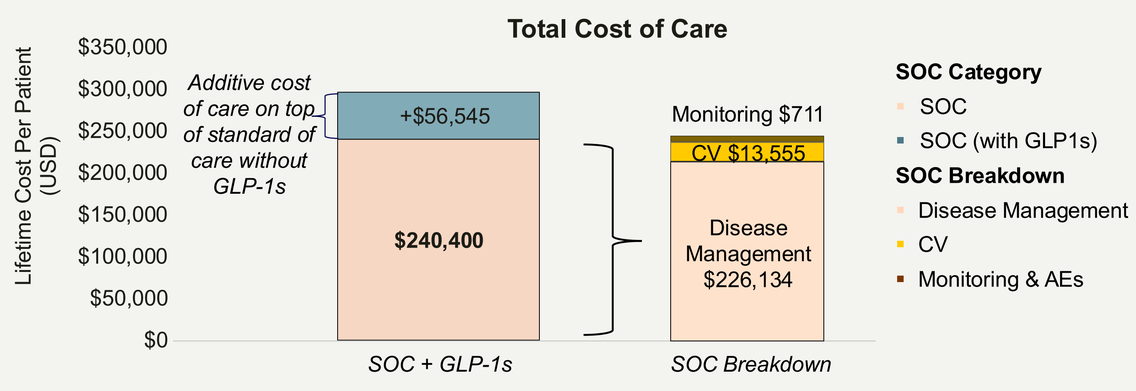


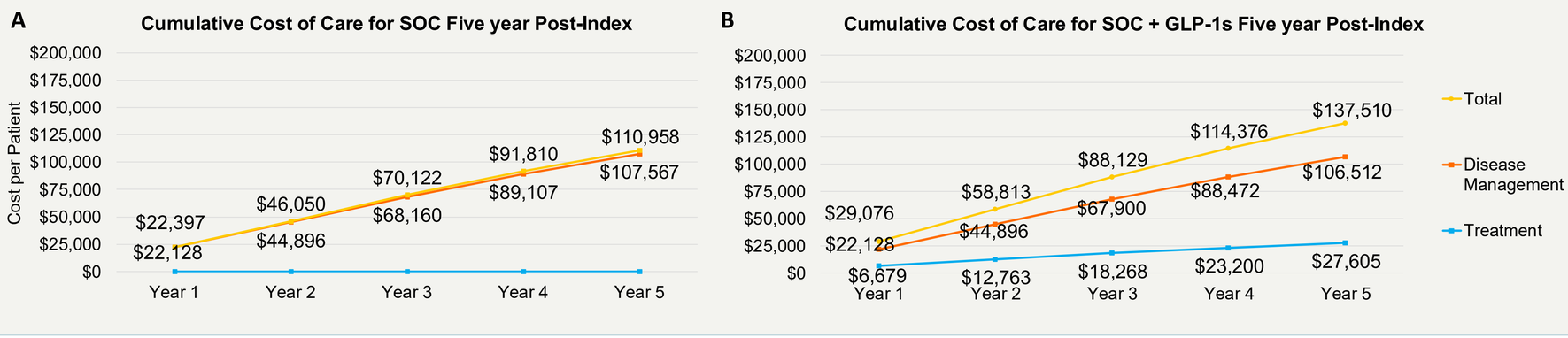
Figure 3: Lifetime cost of care for compensated cirrhosis due to MASH patients.



Financial Burden for SOC

- Across shorter time horizons, cost of care **were driven by medical visit costs attributable to MASH (disease management costs)**
- A smaller financial burden was driven by monitoring and costs of cardiovascular outcomes, and no associated treatment costs

Figure 4: Cost of care for cirrhosis due to MASH patients under (A) SOC and (B) SOC with GLP-1s over five years post-index



Discussion

- Most patients with compensated cirrhosis due to MASH progressed to more severe health states or death. **The steep survival decline illustrates the severity of compensated cirrhosis due to MASH and its rapid trajectory toward liver-related mortality once patients reach compensated cirrhosis**
- Although spontaneous fibrosis regression may occur, its incidence is very low. This suggests limited capacity for disease improvement without an effective disease-modifying intervention, reinforcing the largely progressive natural history of compensated cirrhosis due to MASH
- **Lifetime costs are high, driven by medical visit costs attributable to MASH,** with patients facing high clinical and economic burden
- Compensated cirrhosis due to MASH represents a high-burden stage of disease characterized by limited spontaneous regression, substantial progression and mortality, and high near- and long-term healthcare costs
- These findings highlight the need for interventions that can alter the clinical trajectory before patients progress to costly advanced liver outcomes

Limitations

- Lack of real-world evidence for model inputs, with published cost of care estimates varying widely
- 100% of patients entered the model at a compensated cirrhosis due to MASH baseline, which does not capture the heterogeneity of the disease
- Inclusion of semaglutide assumed a 50% uptake, whereas real-world utilization may differ
- This model did not capture humanistic or patient costs

Conclusion

This model indicates compensated cirrhosis due to MASH carries a **substantial clinical and economic burden, marked by high mortality, limited spontaneous regression, and substantial increasing costs over time.** These data underscore the need for more effective therapies for disease regression.

Abbreviations

AE, adverse event; ASCVD, atherosclerotic cardiovascular disease; CC, compensated cirrhosis; CV, cardiovascular; DC, decompensated cirrhosis; DCC, decompensated cirrhosis; EU5, France, Germany, Italy, Spain, and the United Kingdom; F0–F3, fibrosis stages 0–3; F4c, compensated cirrhosis; F4d, decompensated cirrhosis; GBD, Global Burden of Disease; GLP-1, glucagon-like peptide-1 (receptor agonist); HCC, hepatocellular carcinoma; LT, liver transplant; MASH, metabolic dysfunction-associated steatohepatitis; SOC, standard of care; US, United States; USD, United States dollars.

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Disclosures

YK, NA, and KP are employees and shareholders of Madrigal Pharmaceuticals, Inc. **AD, KP, RS** and **NH** are employees of Trinity Life Sciences, LLC, and have provided consulting services to Madrigal Pharmaceuticals, Inc., through their employment with Trinity. Trinity received funding from Madrigal Pharmaceuticals, Inc., for this study.

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