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ESTIMATING REAL WORLD CLINICAL AND ECONOMIC IMPLICATIONS OF GLP-1 PERSISTENCE AND DOSING IN METABOLIC DYSFUNCTION-ASSOCIATED STEATOHEPATITIS (MASH)

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INTRODUCTION

Recent studies estimate that metabolic dysfunction-associated steatohepatitis (MASH) cases in the United States are expected to increase 82.6% by 2039.[1] MASH has significant ramifications in liver related sequelae (cirrhosis, cancer, decompensation) and cost burden.[2-4] Real world data (RWD) shows lower attainment of ESSENCE trial's semaglutide 2.4mg dose[5,8,9] and higher premature discontinuation.[6-8] Cost per optimal dose responder wastage modeling based on RWD can identify disparities within estimated clinical outcomes and consequential economic impact of MASH treatment.

AIM

To elucidate the estimated clinical effects of semaglutide dependent on real world dose exposure, persistence, and consequential economic impact.

METHOD

- A MASH treatment cost per optimal dose responder wastage model using a Markov state-transition framework was developed to estimate the number of clinical responders, progressors, treatment discontinuations, and economic wastage outcomes from the use of Wegovy (semaglutide) in a MASH population.
- Model optimal dose responders were defined as patients who reached and maintained persistence on the 2.4mg dose (utilized for clinical endpoints in ESSENCE trial) by 72 weeks and achieved fibrosis improvement without steatohepatitis worsening.[9]
- Dose exposure and treatment persistence were informed by RWD.[8]
- Economic wastage impact was defined as total excess medical and pharmacy costs experienced by a commercial health plan for MASH patients treated with semaglutide who did not achieve fibrosis improvement at 2.4mg by 72 weeks to yield one optimal 2.4mg dose responder.
- Probabilistic and deterministic sensitivity analyses were conducted to evaluate uncertainty of key model parameters.

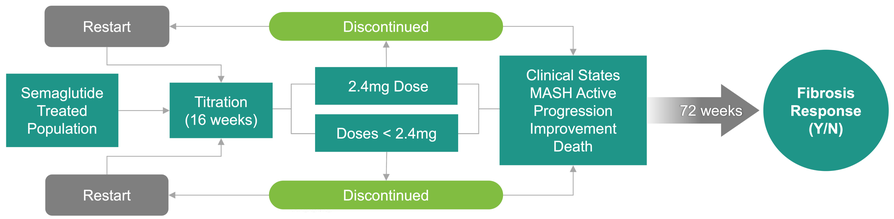


Figure 1. Model Architecture

Clinical States

MASH Active: This clinical state represents patients with F2/F3 MASH who remain in the same fibrosis stage over the modeled interval.

Progression (Fibrosis Progression): This clinical state in which a patient with F2/F3 MASH experiences worsening fibrosis over the modeled interval.

Improvement (Fibrosis Improvement): The clinical state in which a patient with F2/F3 MASH demonstrates a reduction in fibrosis severity by at least one stage with no evidence of worsening steatohepatitis.

Death: This clinical state is terminal state in which a patient is permanently exits the modeled population due to mortality from any cause.

RESULTS

In a modeled commercial population of 80,000 members, an estimated ~100 patients will be diagnosed and eligible (F2/F3) for MASH treatment with semaglutide.

- Of the 100 patients, 24 remain persistent at 72 weeks of which:
  - 9 response eligible patients will achieve 2.4 mg and maintain persistent at 72 weeks.
  - 3.2 patients will achieve fibrosis improvement without worsening steatohepatitis on 2.4mg defined as optimal dose responders.
- Additionally, 29 patients will experience fibrosis progression (20 new F4 and 9 new F3).

It is estimated that a commercial health plan would experience:

- Economic wastage impact of $1.1M in non-responder spend (pharmacy and medical) to yield one 2.4mg optimal dose responder.

Modeled Population	Total Medical and Pharmacy Cost	Number of 2.4mg Dose Responders	Economic Wastage Cost Per 2.4mg Dose Responder
Non-Responder Population (MASH Active and Progression)	**$3,670,790**	**~3.2**	**$1,147,865**

Table 1. Commercial Health Plan (n=80,000). Non-Responder Costs Per Optimal Dose Responder

Markov Model Clinical State Distribution at 72-Week Horizon

MASH Active	Fibrosis Improvement	Fibrosis Progression	Death
• 45 Total Patients • On and Off Semaglutide Therapy	• 24 Total Patients • On and Off Semaglutide Therapy • **ONLY ~3.2 Patients on 2.4mg Dose**	• 29 Total Patients • On and Off Semaglutide Therapy • **(20) F3 → F4** • **(9) F2 → F3**	• **2 Patients**

*Figure 2. Clinical States at End of 72-week horizon for 80,000 Commercial Plan (N=100 Treated Patients) * Numbers rounded.*

CONCLUSIONS

Our MASH treatment cost per optimal dose responder wastage model demonstrates that the combined low persistence with those achieving an optimal dose of semaglutide (2.4mg) in the real-world environment, compared to clinical trial, results in high number of progressors, low number of responders, and significant economic impact to be experienced by commercial health plans.

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CONTACT INFORMATION

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