Progression to Advanced Liver Disease Trajectories in Metabolic Dysfunction-Associated Steatohepatitis: Real-World Transition Estimates for Economic Modeling

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INTRODUCTION

- Metabolic dysfunction-associated steatohepatitis (MASH) is a progressive liver disease that can advance to compensated cirrhosis (CC), decompensated cirrhosis (DCC), hepatocellular carcinoma (HCC), liver transplantation, and death.[1-3]
- Economic models of MASH burden require robust estimates of progression to advanced liver disease; however, real-world progression trajectories remain limited.
- Characterizing the timing and frequency of progression to advanced liver disease using large-scale longitudinal real-world data sources can help inform disease modeling estimates.

OBJECTIVE

- To characterize progression to advanced liver disease among patients with MASH in England using time-to-event analyses and generate real-world transition estimates to inform future economic models.

METHODS

- Retrospective cohort study using Clinical Practice Research Datalink (CPRD) Aurum primary care electronic health records linked to Hospital Episode Statistics (HES) secondary care reimbursement and Office for National Statistics mortality data.
- Adults diagnosed with MASH between 2011 and 2020 were followed longitudinally for progression to CC, DCC, HCC, liver transplantation, and death. Landmark analysis was used to reduce inclusion of delayed recognition of prevalent progression, with patients who had progression events occurring before or within 90 days after MASH diagnosis excluded.
- Kaplan-Meier (KM) analyses were used to estimate progression trajectories, restricted mean time free from progression, and survival probabilities.
- Progression events were summarized according to timing following diagnosis (<1 year, 1–2 years, and >2 years).
- Observed transition proportions were calculated as the proportion of patients with MASH who progressed to each state during follow-up.

RESULTS

- A total of 2,696 patients with MASH were included (mean follow-up, 4 years).

Advanced Liver Disease Progression

- During follow-up, 356 patients progressed to ≥1 advanced liver disease state, corresponding to an overall disease progression incidence of 30.9 per 1,000 person-years.
- Progression most commonly occurred to CC (n=234), followed by DCC (n=174) and HCC (n=18).
- Progression incidence was highest among patients with type 2 diabetes mellitus (43.9 per 1,000 person-years) and cardiovascular disease (42.4 per 1,000 person-years). Similar patterns were observed for progression to CC, DCC, and HCC (**Table 1**).

TABLE 1. Progression to Advanced Liver Disease States Following MASH Diagnosis

Source cohort	Progression state/prior state	Patients at risk (N)	Patients progressed N (%)	Incidence (per 1,000 PY)
All patients with MASH	Any Advanced State	2,696	356 (13.2)	30.9
	CC	2,696	234 (8.7)	20.3
	DCC	2,696	174 (6.5)	15.1
	HCC	2,696	18 (0.7)	1.6
Patients with DCC	Prior CC	174	54 (31.0)	-
Patients with HCC	Prior CC	18	11 (61.1)	-

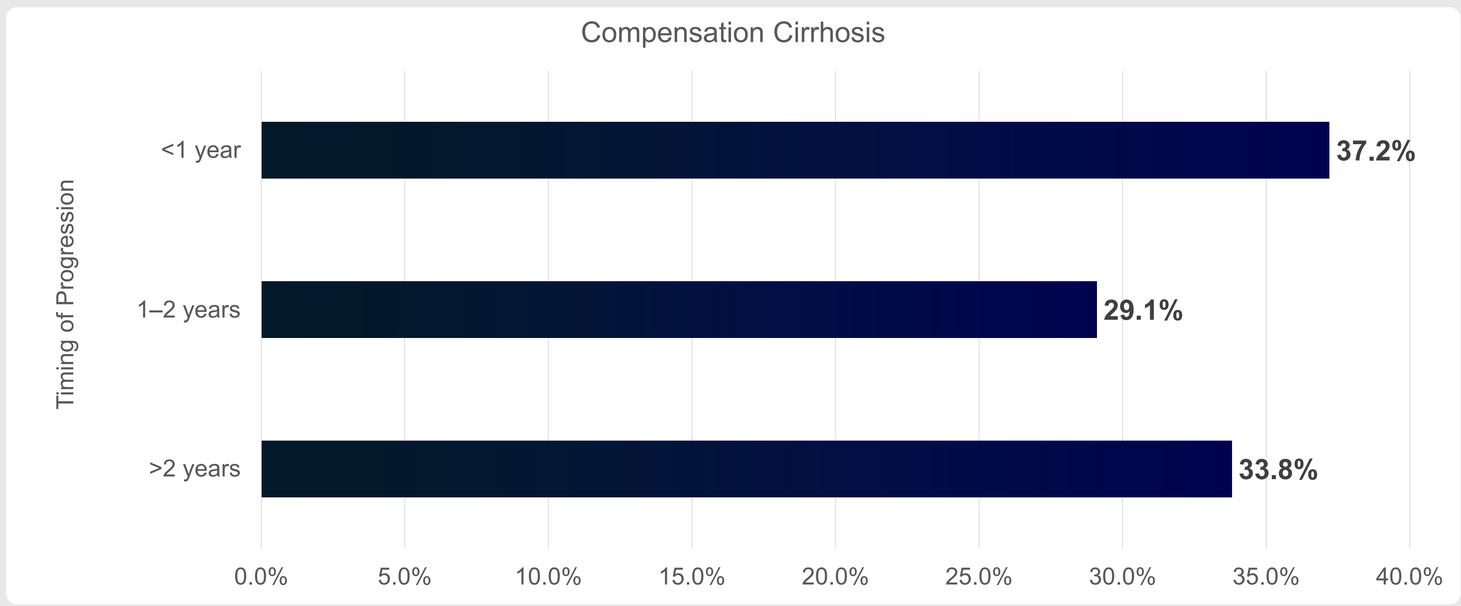
Abbreviations: CC = compensated cirrhosis; DCC = decompensated cirrhosis; HCC = hepatocellular carcinoma; MASH = metabolic dysfunction-associated steatohepatitis; PY = person-year

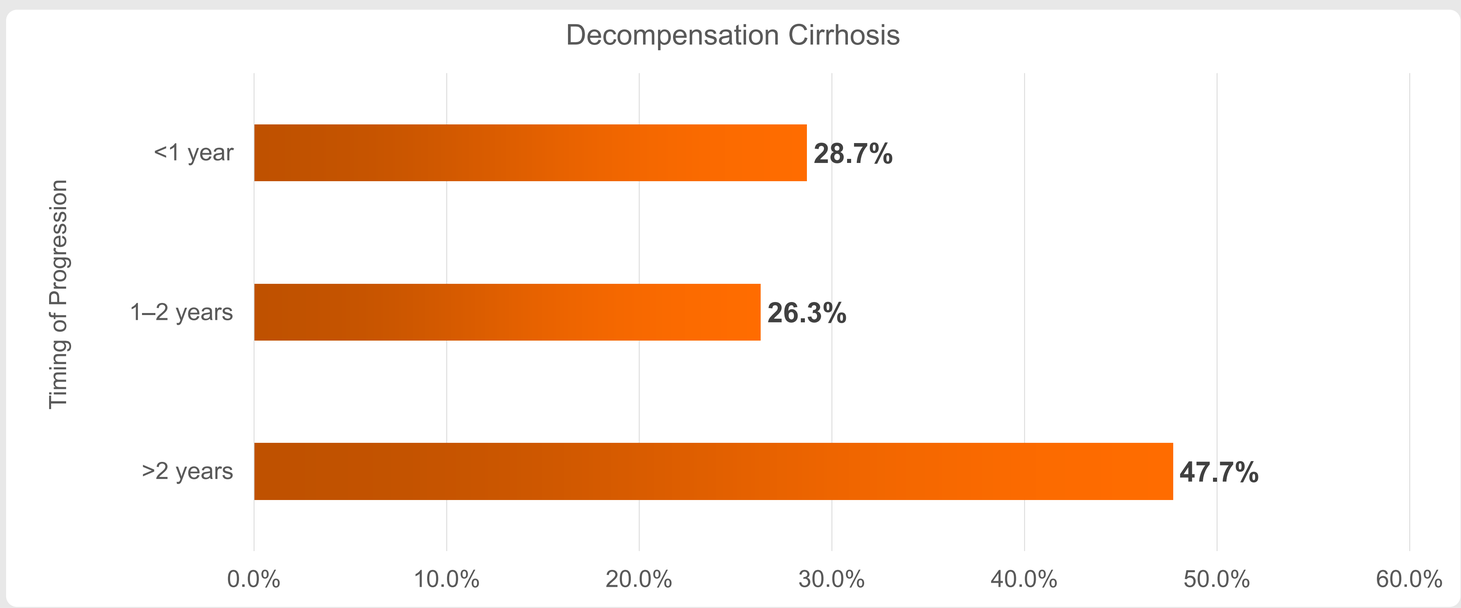
RESULTS (CON'T)

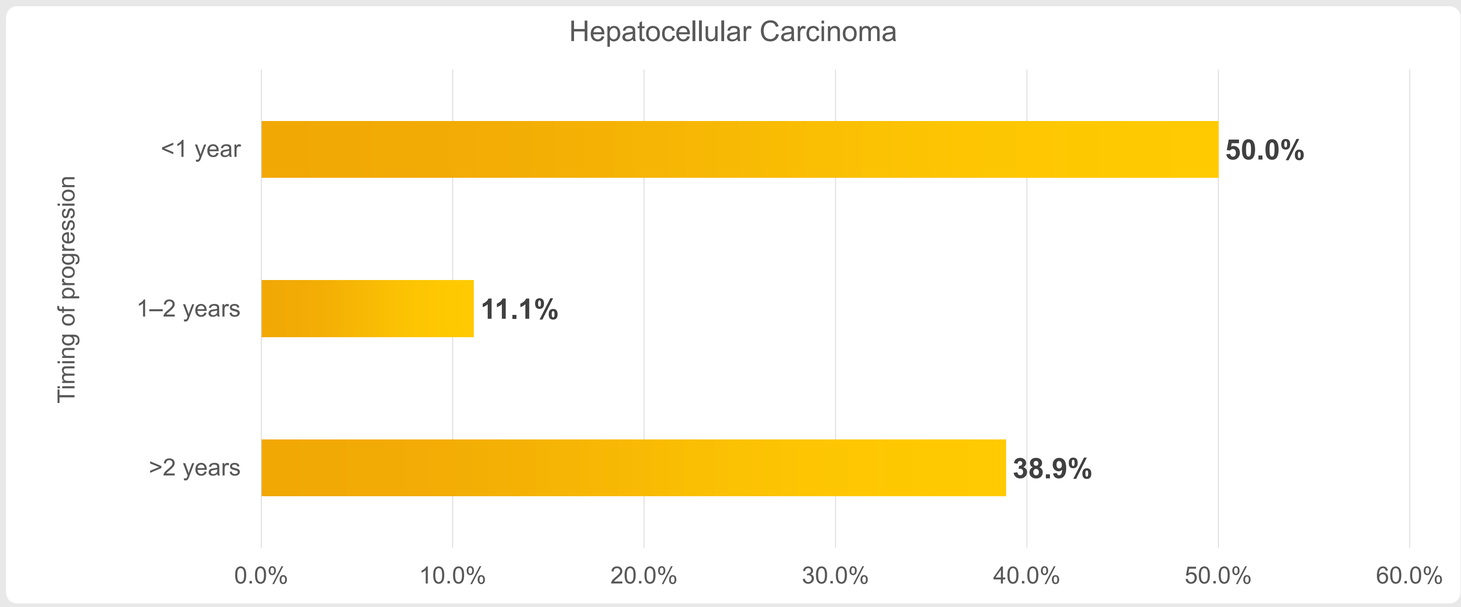
Timing of Progression

- Observed progression to CC occurred relatively early following MASH diagnosis, with the majority in ≤2 years (37.2% of events occurring <1 year, 29.1% during years 1 and 2, and 33.8% ≥2 years after diagnosis).
- Progression to DCC occurred over a slightly longer period, with just over half progressing ≤2 years (28.7% of DCC events occurred <1 year, 23.6% during years 1 and 2), and 47.7% of events occurred >2 years after diagnosis.
- Half of the patients (n=9) who progressed to HCC experienced progression in <1 year of follow-up.
- Among patients who progressed, median time to progression was 1.43 years for CC, 1.74 years for DCC, and 1.11 years for HCC (**Figure 1**).
- Among patients with known prior CC, progression was high: 31.0% (n=54) subsequently progressed to DCC and 61.1% (n=11) progressed to HCC (**Table 1**).

FIGURE 1. Timing of Progression to Compensated and Decompensated Cirrhosis Following MASH Diagnosis







Abbreviation: MASH = metabolic dysfunction-associated steatohepatitis

CONCLUSION

- **This study provides real-world progression trajectories from MASH to advanced liver disease states based on routinely collected healthcare data with clinically coded diagnoses.**
- **Among patients who progressed, outcomes were observed within a relatively short time after MASH diagnosis. This may reflect true progression, delayed recognition of advanced liver disease, or a combination of both. The 90-day landmark analysis was included to reduce the influence of prevalent advanced disease identified shortly after diagnosis or acting as a trigger for MASH diagnosis.**
- **Interpretation should be cautioned as this dataset did not provide data on fibrosis stage and small sample sizes were observed in the advanced liver disease cohorts, which may limit generalizability.**

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