The natural history and clinical progression of MASH in a U.S. adult patient cohort: A claims-based analysis of Optum's® De-identified Market Clarity Data

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INTRODUCTION

- **Metabolic dysfunction-associated steatohepatitis** (MASH) is a progressive liver disease, that can advance to compensated cirrhosis (CC), decompensated cirrhosis (DC), hepatocellular carcinoma (HCC), or liver transplant (LT).[1] Progression is associated with increased morbidity, mortality, and healthcare costs.[2] With the recent approval of resmetirom (Rezdiffra),[3] understanding the untreated natural history of MASH is critical to contextualize treatment impact and guide future decisions.

OBJECTIVE

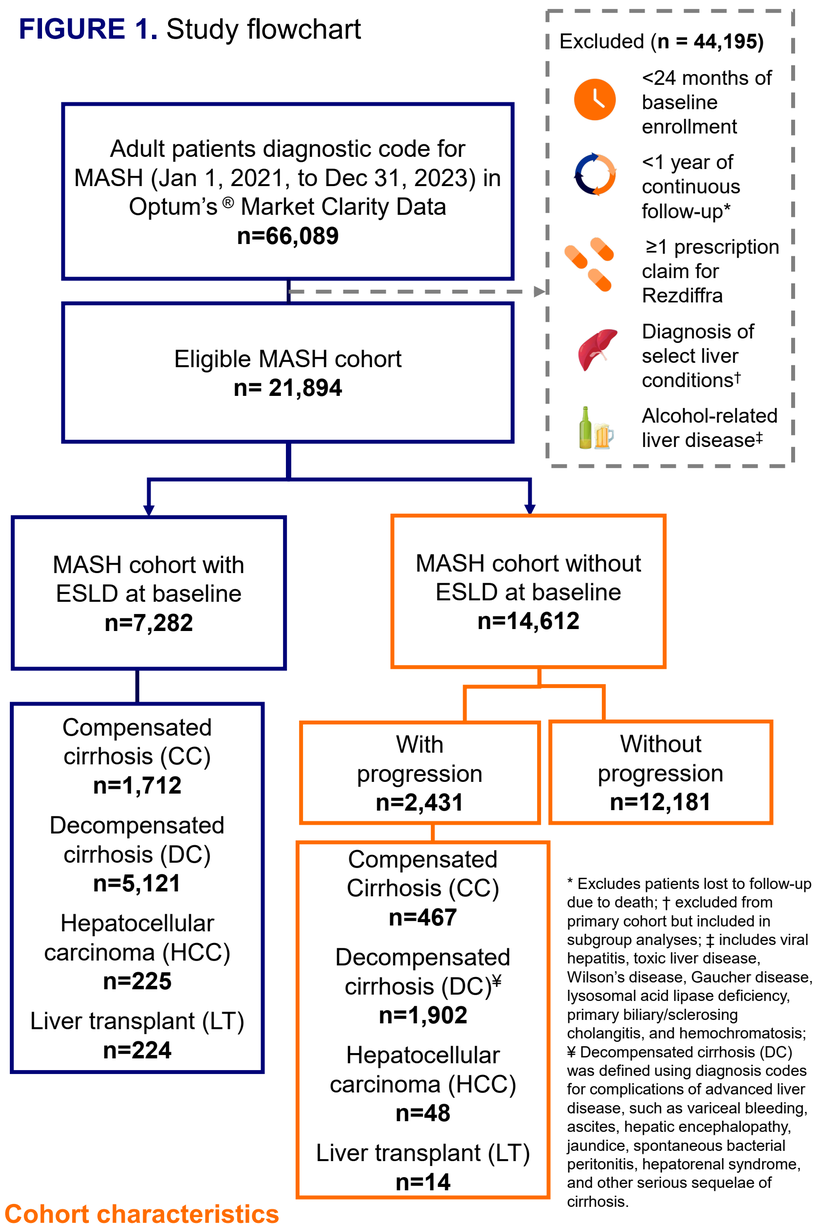
- To characterize patients with MASH and assess progression to CC, DC, HCC, LT or death over follow-up, as well as healthcare costs and resource use by ESLD and progression status.

METHODS

- **Design & data source:** Retrospective cohort study using Optum's® De-identified Market Clarity Data (January 1, 2019, to December 31, 2024).
- **Population:** Adults with ≥1 inpatient or ≥2 outpatient diagnoses of MASH (ICD-10: K75.81, K74.02) on separate dates.
  - We excluded patients with <24 months of baseline enrollment, <1 year of follow-up, Rezdiffra prescriptions, select liver conditions, or alcohol-related liver disease (**Figure 1**).
- **Index date:** First recorded MASH diagnosis between January 1, 2021, to December 31, 2023.
- **Lookback period:** 2 years pre-index to identify baseline ESLD (CC, DC, HCC, LT) via diagnosis/procedure codes.
- **Outcomes:** Disease progression (CC, DC, HCC, or LT) among patients without ESLD at baseline. Composite outcome: first occurrence of CC, DC, HCC, LT, or death during follow-up. Healthcare resource utilization and annual healthcare costs by progression status.
- **Statistical analyses:** Clinical progression analyzed using modified Poisson (relative risks [RR]) and Cox models (hazard ratios [HR]). HCRU counts modeled with negative binomial regression; costs with two-part models, both reported as adjusted marginal means.

RESULTS

FIGURE 1. Study flowchart



* Excludes patients lost to follow-up due to death; † excluded from primary cohort but included in subgroup analyses; ‡ includes viral hepatitis, toxic liver disease, Wilson's disease, Gaucher disease, lysosomal acid lipase deficiency, primary biliary/sclerosing cholangitis, and hemochromatosis; ¥ Decompensated cirrhosis (DC) was defined using diagnosis codes for complications of advanced liver disease, such as variceal bleeding, ascites, hepatic encephalopathy, jaundice, spontaneous bacterial peritonitis, hepatorenal syndrome, and other serious sequelae of cirrhosis.

Cohort characteristics

- After exclusions, 21,894 adults with MASH were identified (**Figure 1**).
- At baseline, 7,282 (33.3%) had end-stage liver disease (ESLD), most commonly DC (n = 5,121). The remaining 14,612 (66.7%) without ESLD comprised the primary analytic population and were followed for progression.
- Patients with progression were older (41.2% ≥65 years), had higher comorbidity burden (mean weighted Elixhauser Index: 4.0 vs 3.0; unweighted: 3.3 vs 1.3) and more metabolic risk factors (hypertension, dyslipidemia, obesity, type 2 diabetes mellitus).

TABLE 1. Baseline characteristics of MASH patients without ESLD at index by progression status (n=14,612)

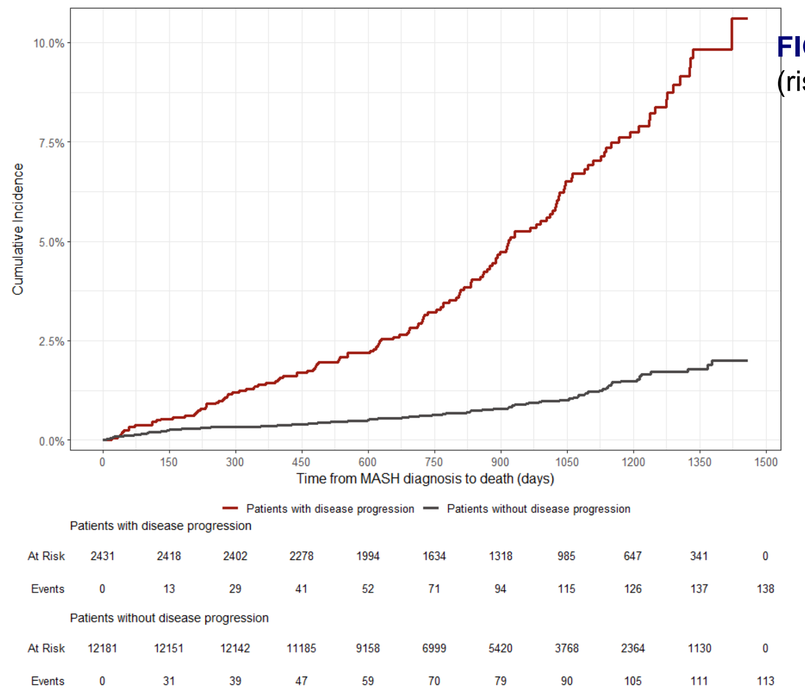
Characteristic	With progression n = 2,431	Without progression n = 12,181
Age at index (years), n (%)		
18-44	338 (13.9)	2,509 (20.6)
45-64	1,092 (44.9)	6,417 (52.7)
≥ 65	1,001 (41.2)	3,255 (26.7)
Sex, n (%)		
Female	1,474 (60.6)	6,818 (56.0)
Male	956 (39.3)	5,354 (44.0)
Unknown	1 (0.0)	9 (0.1)
Race, n (%)		
White	1,875 (77.1)	8,903 (73.1)
Black	103 (4.2)	562 (4.6)
Asian	75 (3.1)	450 (3.7)
Other/Unknown	378 (15.5)	2,266 (18.6)
Geographic region at index, n (%)		
Northeast	492 (20.2)	2,836 (23.3)
Midwest	813 (33.4)	3,914 (32.1)
South	775 (31.9)	3,602 (29.6)
West	253 (10.4)	1,417 (11.6)
Unknown	98 (4.0)	412 (3.4)
Metabolic risk factors, n (%)		
Metabolic syndrome*	946 (38.9)	4,638 (38.1)
Hypertension	1,597 (65.7)	6,888 (56.5)
Dyslipidemia	1,922 (79.1)	9,454 (77.6)
Obesity	1,733 (71.3)	8,393 (68.9)
Type 2 diabetes mellitus	1,194 (49.1)	4,543 (37.3)
≥ 2 metabolic conditions	2,073 (85.3)	9,880 (81.1)
≥ 3 metabolic conditions	1,610 (66.2)	7,166 (58.8)
Elixhauser Comorbidity Index		
Weighted		
Mean (SD)	4.0 (2.4)	3.0 (2.0)
Median (IQR)	4.0 (4.0)	3.0 (2.0)
Unweighted		
Mean (SD)	3.3 (7.9)	1.3 (6.6)
Median (IQR)	2.0 (0.0)	0.0 (0.0)

*Metabolic syndrome was defined using ICD-10-CM code E88.810 or the presence of abnormal biometric values (elevated fasting glucose, triglycerides, blood pressure, BMI/waist circumference, or reduced HDL-c).

Non-invasive testing (NIT) at diagnosis

- Among patients without baseline ESLD (n=12,181), fewer than one-third (29.8%) underwent ≥1 NIT within 30 days of diagnosis. Among those tested, abdominal ultrasound was most common (53%), followed by CT scan (30%).
- Notably, no patients received Enhanced Liver Fibrosis (ELF) and <0.1% received LiverMultiScan at diagnosis.

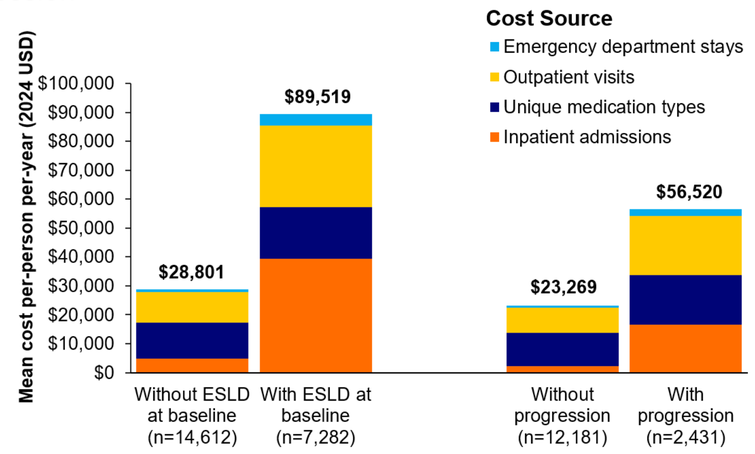
FIGURE 2. Cumulative incidence of death by progression status among patients with MASH without ESLD at baseline



Progression characteristics and mortality

- Among those without ESLD at baseline, 2,431 (16.6%) progressed during follow up: 467 (19.2%) to CC, 1,902 (78.2%) to DC, 48 (2.0%) to HCC, 14 (0.6%) to LT.
- Mortality was higher in patients with progression (138 deaths; 5.7%) compared to those without progression (113 deaths; 0.9%) (**Figure 2**).

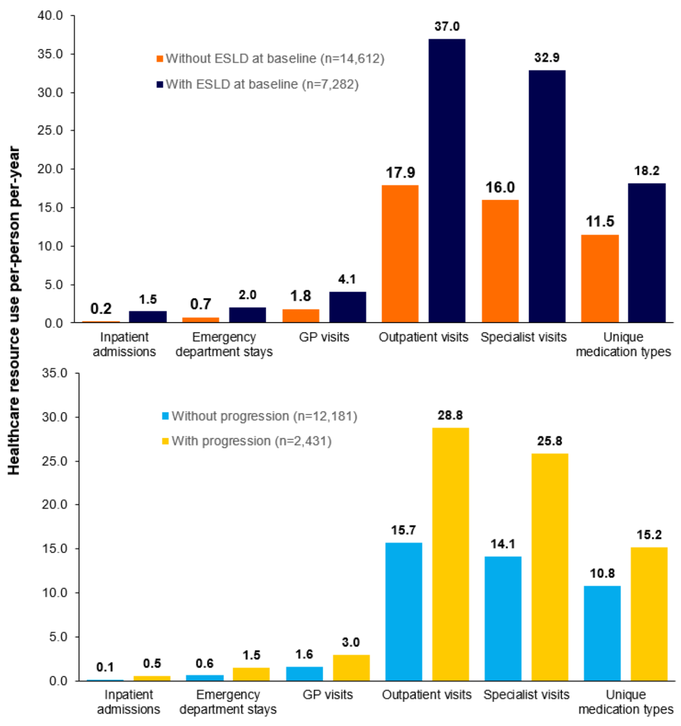
FIGURE 3. Mean annual per-person healthcare costs by ESLD status and progression



Healthcare utilization and resource use (HCRU) and cost outcomes

- Patients with ESLD at baseline incurred over 3x higher annual costs compared to those without ESLD ($89,519 vs. $28,801), driven primarily by inpatient admissions.
- Disease progression also significantly increased annual costs, with progressed patients averaging $56,520 per year vs. $23,269 for those without progression (**Figure 3**).
- Patients with ESLD at baseline and those who progressed also had substantially higher HCRU across all service types (**Figure 4**).

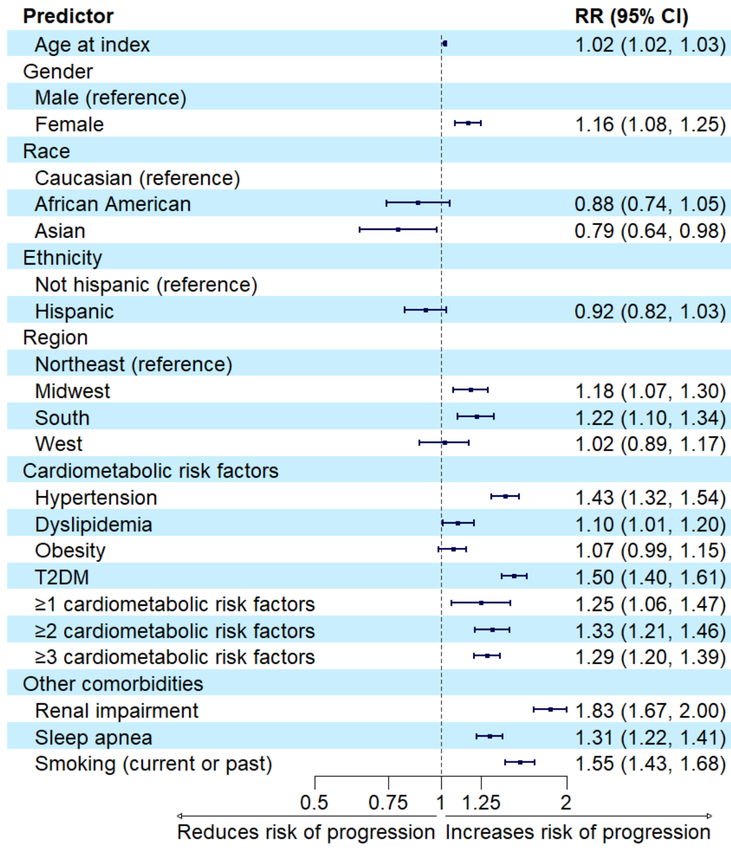
FIGURE 4. Healthcare resource use by ESLD status and progression



Predictors of disease progression

- Higher risk of disease progression was associated with older age, female sex, residence in the Midwest or South, cardiometabolic conditions (especially hypertension), renal impairment, sleep apnea, and smoking (**Figure 5**).

FIGURE 5. Unadjusted predictors of disease progression (risk ratios [RR], 95% CI)



Strengths:
- Use of a large, well-validated database extensively applied in research on clinical outcomes and disease progression.[4]
- Diverse data sources (claims, EHR) provide a comprehensive view of patients' natural disease history and progression.

Limitations:
- Data accuracy dependent on the quality and completeness of administrative claims.
- Primarily represents commercially insured U.S. patients, limiting generalizability to other populations and healthcare systems.
- Given the study period, findings may be influenced by confounding related to the COVID-19 pandemic.

CONCLUSION

In this large real-world cohort of patients with MASH, a notable proportion progressed to advanced liver outcomes over a relatively short follow-up period. These findings highlight the need for early identification and targeted management strategies to prevent ESLD progression, potentially reducing inpatient utilization and related healthcare costs.

FUNDING & DISCLOSURES

This study was funded by Madrigal Pharmaceuticals, inc. YK and JOD are employees of Madrigal Pharmaceuticals. RF, KJ, RS, MB, RM and AK are employees of Broadstreet HEOR, which received funds from Madrigal Pharmaceuticals for this work. AD has received consulting fees from Petauri, Novo Nordisk, and Madrigal.

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