Factors Associated with Healthcare Costs and Disease Progression in Metabolic Dysfunction-Associated Steatohepatitis in the US Real-World Setting

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INTRODUCTION

- In the US, metabolic dysfunction-associated steatohepatitis (MASH) has been estimated to affect 3-6% of adults, with an increasing prevalence in recent years[1]
- Previous studies have reported that healthcare costs increase with comorbid type 2 diabetes,[2] disease severity, and are highest among individuals with advanced or end-stage liver disease (ESLD)[3,4]
- As the prevalence of MASH increases, there is a need to better understanding the factors associated with disease progression and higher healthcare costs

OBJECTIVE

- To model healthcare costs and progression to advanced or ESLD among adults with MASH

METHODS

Data Source and Study Population

- The Veradigm Network EHR linked to Komodo Health claims was used to identify adult patients (18+) with ≥1 inpatient claim or ≥2 outpatient claims/records (on different dates) with a diagnosis for MASH (ICD-10-CM: K75.81) between 07/01/2019-04/30/2025. The index date was the earliest MASH diagnosis **(Figure 1)**

Patient Characteristics

- Patient demographics were captured on the index date. Metabolic comorbidities, non-invasive tests, and baseline ESLD were captured in the 2-year baseline period
  - Metabolic comorbidities were identified by diagnosis codes, related treatment, or lab values as defined below:
    - Dyslipidemia: triglycerides ≥150mg/dL, HDL <40mg/dL for men or <50mg/dL for women
    - Hypertension: blood pressure ≥130/85 mmHg
    - Obesity: body mass index ≥30 kg/m2
    - Type 2 diabetes (T2D) or hyperglycemia: fasting blood glucose ≥100mg/dL)
  - Evidence of advanced liver disease or ESLD included diagnosis of cirrhosis[5], decompensated cirrhosis or lactulose treatment, other ascites, hepatic encephalopathy, unspecified encephalopathy, liver transplant, or hepatocellular carcinoma

Outcome Measures

- Progression to advanced liver disease or ESLD during following up was measured among those without baseline ESLD
- All-cause healthcare per-patient-per-year (PPPY) costs were examined across inpatient visits, outpatient visits, emergency department admissions, pharmacy, and total healthcare burden among patients with and without comorbid T2D

Modeling

- Progression to advanced liver disease or ESLD was modeled using a Cox proportional hazards model among patients without evidence for ESLD during baseline
  - Covariates included age, sex, race, baseline FIB-4 score (where available), and a composite flag for baseline T2D, obesity, or hypertension
- Total healthcare costs were modeled using a generalized linear model with a log link and gamma error distribution among patients with and without T2D
  - Covariates included age, sex, race, baseline FIB-4 score (where available), baseline advanced liver disease/ESLD, obesity, hypertension, dyslipidemia, and hypertension*dyslipidemia

RESULTS

FIGURE 1. Inclusion/Exclusion Criteria

≥1 inpatient claim or ≥2 outpatient claims/records (on separate dates) with a MASH diagnosis (ICD-10-CM: K75.81) between 07/01/2019 and 04/30/2025. Index date was the earliest MASH diagnosis
N = 585,725

↓

No missing age or sex data
N=585,449

↓

≥18 years on the index date
N=579,497

↓

≥2 years of continuous enrollment in medical and pharmacy claims prior to and including the index date (baseline period)
N=138,835

↓

≥1 year of continuous enrollment in medical and pharmacy claims after the index date (follow-up period)
N=97,610

↓

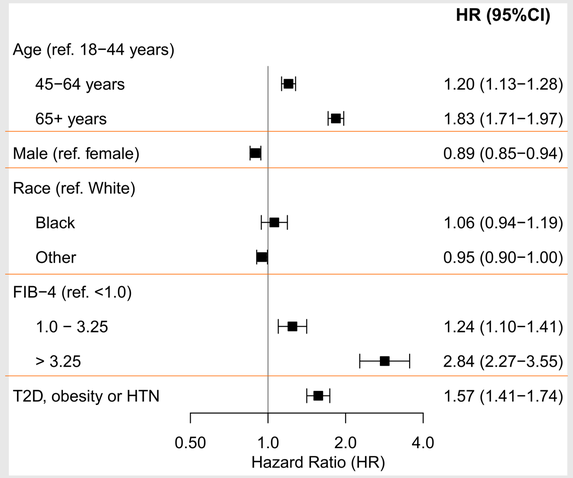
Excluded patients with a claim/record for resmetirom at any time during the study period
N=97,164

↓

Excluded patients with viral hepatitis, Wilson's disease, Gaucher's disease, lysosomal acid lipase deficiency, alcoholism/alcoholic liver disease, primary biliary/sclerosing cholangitis, hemochromatosis, autoimmune hepatitis, HIV, or heavy metal exposure at any time during the study period
N=68,209

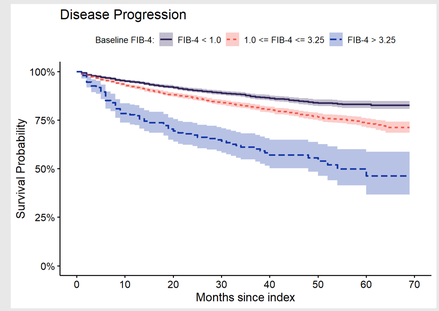
MASH: metabolic dysfunction-associated steatohepatitis.

FIGURE 2. Hazard of Disease Progression Among Patients Without Baseline Advanced or End-Stage Liver Disease



CI: confidence interval, FIB-4: fibrosis-4. HTN: hypertension, T2D: type 2 diabetes

FIGURE 3. Kaplan-Meier Plot of Disease Progression Among Patients Stratified by Baseline FIB-4 Score



. FIB-1: fibrosis-4

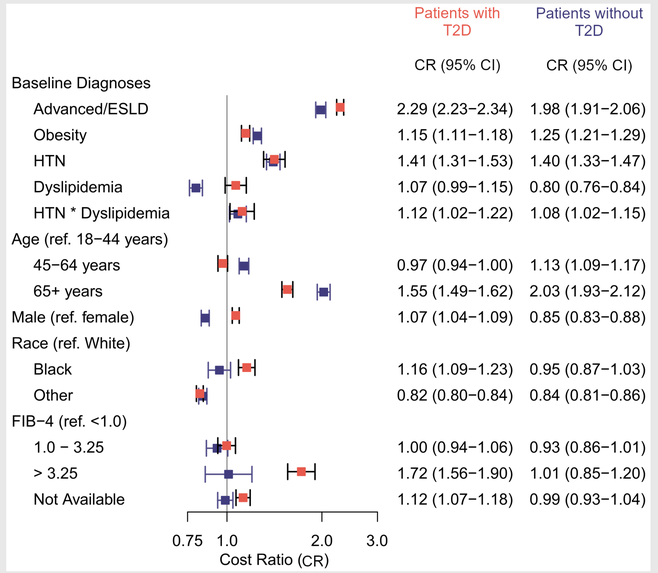
- The study included 68,209 adults with MASH (55.1 years and 63.3% female)
- Other metabolic conditions were common, and 19,741 patients had advanced/ESLD at index (Table 1)
- Among the 48,468 patients who did not have advanced/ESLD at index, 7,367 (15.2%) progressed during follow-up; follow-up averaged 2.8 [1.3] years
  - Factors significantly associated with an increased hazard of disease progression were older age, high baseline FIB-4 score, and presence of metabolic comorbidities at baseline (Figure 2 & 3)
  - Male sex was associated with a decreased hazard of disease progression
- Baseline advanced/ESLD was associated with roughly a doubling of healthcare costs for patients with and without T2D (Figure 4)
  - For patients without T2D, mean estimated costs increased from $19,360 (without baseline ESLD) to $38,396 (with baseline /ESLD)
  - For patients with T2D, mean estimated costs increased from $30,740 (without baseline ESLD) to $70,249 (with baseline /ESLD)
- Baseline obesity, hypertension and age ≥65 years were also associated with higher costs in both subgroups
  - There was a significant interaction between baseline hypertension and dyslipidemia associated with significantly higher costs among patients with both conditions.
- Directional effects of other factors, such as sex, race, FIB-4, and baseline dyslipidemia, differed between patients with and without T2D

TABLE 1. Baseline Patient Characteristics

	Patients with MASH N=68,209
Age, Index, mean (SD)	55.1 (14.0)
Sex, Female, N (%)	43,173 (63.3)
Race, N (%)	
Asian	2,883 (4.2)
African American/Black	2,570 (3.8)
White	40,034 (58.7)
Other	9,852 (14.4)
Unknown/Not Reported	12,870 (18.9)
FIB-4 Score, N (%)	10,600 (15.5)
FIB-4 < 1.0	4,390 (6.4)
1.0 <= FIB-4 <= 3.25	5,204 (7.6)
FIB-4 > 3.25	1,006 (1.5)
Advanced/ESLD	19,741 (28.9)
Metabolic Comorbidities, N (%)	
T2D	39,305 (57.6)
Obesity	49,851 (73.1)
Hypertension	52,490 (77.0)
Dyslipidemia	53,769 (78.8)
Follow-up Time, in years, mean (SD)	2.8 (1.3)

CI: confidence interval, ESLD: end-stage liver disease. FIB-4: fibrosis-4. MASH: metabolic-dysfunction-associated steatohepatitis, SD: standard deviation, T2D: type 2 diabetes

FIGURE 4. Follow-up Healthcare Costs Among Patients Stratified by T2D



CI: confidence interval, ESLD: end-stage liver disease. FIB-4: fibrosis-4. HTN: hypertension, T2D: type 2 diabetes

LIMITATIONS

- In this study, patients with MASH were identified with an ICD-10-CM diagnosis code, rather than with a liver biopsy
- As patients were required to have continuous claims enrollment for 3 years, the results of this study may not be generalizable to patients with less stable insurance or those who are uninsured
- Disease progression was determined by diagnosis code or condition specific procedure code or treatment not by results of a diagnostic test

CONCLUSIONS

- **Baseline advanced/ESLD was associated with higher costs while higher baseline FIB-4 was associated with a higher hazard of disease progression**
- **These models highlight factors associated with increased risk of disease progression and higher costs among patients with MASH, improving our understanding of this heterogeneous population**

DISCLOSURES AND ACKNOWLEDGEMENTS

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