The Natural History and Economic Burden of Metabolic Dysfunction-associated Steatohepatitis in the US Real-World Setting

Yestle Kim, PharmD[1], Ni Zeng, PhD[2], Jessamine P. Winer-Jones, PhD[2], Maryam Ajose, MPH[2], Machaon Bonafede, PhD, MPH[2], John O'Donnell, PhD[1], Taylor Ryan, MHI[2]

Madrigal Pharmaceuticals, Inc., West Conshohocken, PA, USA[1]; Veradigm, Chicago, IL, USA[2]

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 disease severity and are highest among individuals with advanced or end-stage liver disease (ESLD)[2,3]
- As the prevalence of MASH increases, there is a need to better understanding the clinical significance and economic burden that may be affected by the presence of cirrhosis

OBJECTIVE

- The aim of this retrospective study was to describe the clinical characteristics and economic burden of MASH patients by evidence or absence of baseline ESLD, and to assess the time to progression to ESLD in the US real-world setting

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)**
- Patients were stratified by evidence of ESLD (diagnosis of cirrhosis[5], decompensated cirrhosis or lactulose treatment, other ascites, hepatic encephalopathy, unspecified encephalopathy, liver transplant, or hepatocellular carcinoma) on or anytime prior to the index date (baseline period) up to 30 days post-index

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

↓

Patients with ≥1 claim/record for any ESLD event in baseline
Baseline ESLD: N=19,741

Patients with no claims/records for any ESLD events in baseline
No baseline ESLD: N=48,468

Patient Characteristics

- Patient demographics were captured on the index date. Clinical comorbidities, body mass index (BMI), and non-invasive tests (NITs) were captured in the 2-year baseline period, upon data availability
- Progression to cirrhosis, decompensated cirrhotic events (decompensated cirrhosis or lactulose treatment, other ascites, hepatic encephalopathy, unspecified encephalopathy), liver transplant, and hepatocellular carcinoma was captured post-index (follow-up period)
- All-cause healthcare per-patient-per-year (PPPY) costs were examined across inpatient visits, outpatient visits, emergency department admissions, pharmacy, and total healthcare burden

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RESULTS

TABLE 1. Patient Characteristics, Baseline

	Baseline ESLD N=19,741	No Baseline ESLD N=48,468
Age, Index, mean (SD)	59.6 (13.6)	53.3 (13.7)
Sex, Female, N (%)	13,079 (66.3%)	30,094 (62.1%)
Race, N (%)		
Asian	645 (3.3%)	2,238 (4.6%)
African American/Black	721 (3.7%)	1,849 (3.8%)
White	12,437 (63.0%)	27,597 (56.9%)
Other	2,738 (13.9%)	7,114 (14.7%)
Unknown/Not Reported	3,200 (16.2%)	9,670 (20.0%)
Payer Type, N (%)		
Commercial	6,900 (35.0%)	26,533 (54.7%)
Medicare	8,458 (42.8%)	11,097 (22.9%)
Medicaid	4,359 (22.1%)	10,779 (22.2%)
Other/Unknown	24 (0.1%)	59 (0.1%)
≥1 BMI value[1], N (%)	1,881 (9.5%)	4,248 (8.8%)
BMI[1], mean (SD)	33.7 (5.8)	33.5 (5.7)
Type 2 diabetes, N (%)	14,229 (72.1%)	25,076 (51.7%)
Obesity, N (%)	15,405 (78.0%)	34,446 (71.1%)
Hypertension, N (%)	17,278 (87.5%)	35,212 (72.7%)
Dyslipidemia, N (%)	16,405 (83.1%)	37,364 (77.1%)

BMI: body mass index. ESLD: end-stage liver disease. SD: standard deviation
[1]BMI was captured amongst patients with ≥1 BMI value in their medical record

TABLE 2. Disease Progression, Follow-Up

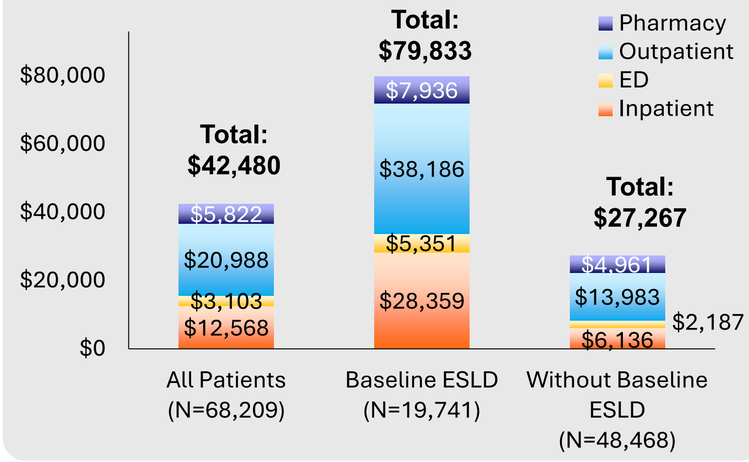
	No Baseline ESLD N=48,468
Any disease progression[1], N (%)	7,367 (15.2%)
Time to progression[2], months, mean (SD)	17.3 (14.0)
Cirrhosis, N (%)	2,803 (5.8%)
Time to progression[2], months, mean (SD)	16.7 (14.1)
Decompensated cirrhotic events[3], N (%)	5,935 (12.3%)
Time to progression[2], months, mean (SD)	18.6 (14.3)
Liver transplant, N (%)	60 (0.1%)
Time to progression[2], months, mean (SD)	16.9 (13.5)
Hepatocellular carcinoma, N (%)	130 (0.3%)
Time to progression[2], months, mean (SD)	21.8 (15.0)

ESLD: end-stage liver disease. SD: standard deviation
[1]Any disease progression was defined as a diagnosis of cirrhosis or any other end-stage liver progression events. [2]Time to progression was defined as time to first evidence of progression. [3]Decompensated cirrhotic events include a diagnosis for decompensated cirrhosis or lactulose treatment, other ascites, hepatic encephalopathy, or unspecified encephalopathy [3]Patients with cirrhosis were identified using a validated algorithm proposed by Khalifa et al[5]

Results

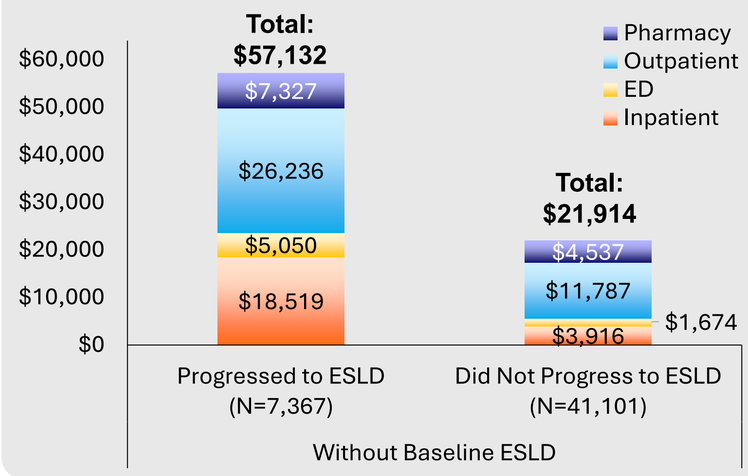
- This study included 68,209 patients with MASH, of which, 19,741 (28.9%) had evidence of baseline ESLD **(Figure 1)**
- Overall, patients were, on average, 55.1 (SD: 14.0) years old, majority female (63.3%), and White (58.7%)
- Among 6,129 patients overall with ≥1 BMI value in their medical record in baseline, mean baseline BMI was 33.6 (SD: 5.7) kg/m^2 **(Table 1)**
- During the baseline period, metabolic comorbidities were most commonly documented in those with baseline ESLD vs. without: type 2 diabetes (72.1% vs. 51.7%) obesity (78.0% vs. 71.1%), hypertension (87.5% vs. 72.7%), dyslipidemia (83.1% vs. 77.1%)
- Similarly, for patients with baseline ESLD vs. without, NITs were more commonly used across abdominal ultrasound (63.8% vs. 49.3%), computed tomography (56.4% vs. 27.2%), liver biopsy (14.9% vs. 8.9%), and MRI (14.8% vs. 5.2%)

FIGURE 2. Mean Costs by Service Type, PPPY: Overall Population and Stratified by Baseline ESLD



ED: emergency department. ESLD: end-stage liver disease. PPPY: per-person per-year

FIGURE 3. Mean Costs by Service Type, PPPY: Stratified By ESLD Progression Amongst Those Without Baseline ESLD



ED: emergency department. ESLD: end-stage liver disease. PPPY: per-person per-year

Results (cont'd)

- Over the mean 2.8 (SD: 1.3) year follow-up period, 15.2% (n=7,367) of patients without baseline ESLD progressed, most often to decompensated cirrhotic events (n=5,935, 12.3%) or cirrhosis (n=2,803, 5.8%) within 18.6 (SD: 14.3) and 16.7 (SD: 14.1) months, respectively **(Table 2)**
- Mean (SD) PPPY costs were highest among patients with baseline ESLD ($79,833 [SD: $470,608]) than without ($27,267 [SD: $98,384]) **(Figure 2)**
- For patients without baseline ESLD, those who progressed had higher PPPY costs ($57,132 [SD: $208,634] vs. $21,914 [SD: $58,520]) **(Figure 3)**
- Among the 683 patients with the highest PPPY costs (top 1%), 467 (68.4%) had baseline ESLD and 123 (18.0%) did not but later progressed during follow-up

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

CONCLUSION

- **In this retrospective, observational study, in patients without baseline ESLD who later progressed, a higher proportion of progression to decompensated cirrhotic events was observed, possibly reflecting an underdiagnosis or underreporting of compensated cirrhosis and MASH**
- **On average, time to progression was 17 months, characterizing the need for health systems in the US to risk stratify patients earlier**
- **While patients without baseline ESLD in this analysis had lower PPPY healthcare costs, those who later progressed incurred 2.6x costs than those who did not**
- **This study highlights the need for earlier identification and management to slow disease progression and reduce the economic burden**

NOTES

This study identified patients with cirrhosis in electronic health records using a validated algorithm proposed by Khalifa et al[5]

DISCLOSURES

This study was funded by Madrigal Pharmaceuticals. Y Kim, and J O'Donnell are employees of Madrigal Pharmaceuticals. N Zeng, JP Winer-Jones, M Ajose, M Bonafede, and T Ryan are employees of Veradigm, which received fees from Madrigal Pharmaceuticals related to this work.

REFERENCES

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