

# Characterizing the management of patients with NASH (with versus without cirrhosis) in real-world clinical practice – Low utilization of gastroenterology and hepatology specialty care

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## Background

- Nonalcoholic steatohepatitis (NASH), also known as metabolic dysfunction-associated steatohepatitis (MASH), affects 3-6% of US adults.<sup>1</sup>
- Guidelines recommend patients with NASH undergo regular assessment and follow-up by specialists, particularly gastroenterologists/hepatologists (GIH),<sup>2</sup> to ensure adequate care and monitor for complications. Patients with cirrhosis should be assessed annually, versus every 2-3 years for those without cirrhosis.<sup>2</sup>
- Additionally, while liver biopsy remains the reference standard for staging of NASH, noninvasive tests (NITs) are increasingly used for monitoring.<sup>2,3</sup>

## Objective

- This analysis aimed to characterize the management of patients with NASH in real-world clinical practice and describe the patient care pathway, considering those with vs. without cirrhosis.

## Methods

- Optum's de-identified Clinformatics® Data Mart Database (CDM) (01Oct2015-31Dec2022) was used to identify adults with ≥1 inpatient claim for NASH (ICD-10-CM K75.81) or ≥2 outpatient claims for NASH; patients with other causes of liver diseases, HIV, or exposure to heavy metals were excluded.
- Index date was defined as 30 days following first diagnosis of NASH, to allow for delays in cirrhosis reporting at baseline. Two cohorts of patients were defined based on the presence of cirrhosis, classified by ≥1 code for cirrhosis, DCC, LT, or HCC, in the baseline period (6 months before and 1 month after index date).
  - This additional one-month window beyond index date was used to account for cirrhosis reporting delays at the time of NASH diagnosis.
- Patients were followed for ≥12 months (death was exempted), until end of follow-up defined by the first of: death, loss of follow-up, or study end.
- Demographics, comorbidities, and the per-year-per-person (PYPP) frequency of specialist visits (including GIH visits) and diagnostic procedures were estimated for patients with vs. without cirrhosis.
  - Specialists include all physicians with a specialty that is not for primary care; including GIH, as identified using provider category in CDM.
  - Diagnostic procedures performed to examine fibrosis level included liver biopsy, FibroScan®, abdominal ultrasound, computed tomography (CT) and magnetic resonance imaging (MRI) including magnetic resonance elastography.
  - Results were stratified by presence of baseline metabolic syndrome (MetS), defined as either an ICD-10 code for MetS (E. E88.81) OR 3 of the following 4 comorbidities: obesity/severe obesity, hypercholesterolemia/ hyperlipidemia, hypertensive disease, or type II diabetes mellitus (T2DM)
- Kaplan Meier analyses were run for time to and between visits and diagnostic procedures stratified by specific patient profiles based on patient demographics and metabolic comorbidities.
- All statistical analyses were performed within Optum's De-identified Data Workspace using the Jupyter Notebook.

## Results

- A total of 9,157 patients with and 19,419 patients without cirrhosis were followed for a median of 2.2 years and 3.0 years, respectively (Table 1). Patients with cirrhosis were older, had shorter median follow-up, and a higher comorbidity burden.

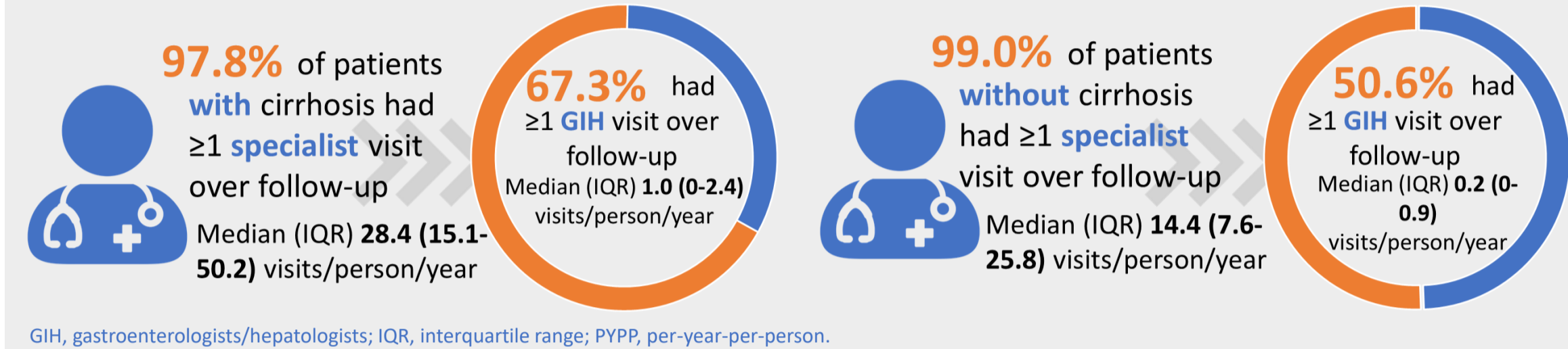
Table 1. Characteristics of NASH patients with versus without cirrhosis

|   | With cirrhosis (n=9,157) | Without cirrhosis (n=19,419) |
|---|--------------------------|------------------------------|
| Length of follow-up, median (IQR) years                   | 2.2 (1.3-3.4)            | 3.0 (2.0-4.3)                |
| Age, median (IQR) years                                   | 68.0 (62.0-74.0)         | 62.0 (51.0-70.0)             |
| Female sex, n (%)   | 5,999 (65.5)             | 11,431* (58.9)               |
| Elixhauser Comorbidity Index over follow-up, median (IQR) | 5.0 (0-15.0)             | 0 (0-0)                      |
| Baseline comorbidities for MetS definition, n (%)         |                          |                              |
| Obesity/severe obesity                                    | 4,844 (52.9)             | 8,419 (43.4)                 |
| Hypercholesterolemia                                      | 6,396 (69.8)             | 13,580 (69.9)                |
| Hyperlipidemia  | 35 (0.4)                 | 114 (0.6)                    |
| Hypertension  | 7,581 (82.8)             | 13,154 (67.7)                |
| T2DM  | 5,209 (56.9)             | 5,899 (30.4)                 |

CVD, cardiovascular disease; IQR, interquartile range; T2DM, type 2 diabetes mellitus. \*sex missing from 6 patients.

- Despite having regular specialist visits (median[interquartile range (IQR)], 28.4[15.1-50.2] PYPP with cirrhosis vs. 14.4[7.6-25.8] without cirrhosis), GIH visits occurred less frequently (1.0[0-2.4] PYPP with cirrhosis and 0.2[0-0.9] without cirrhosis (Figure 1)).

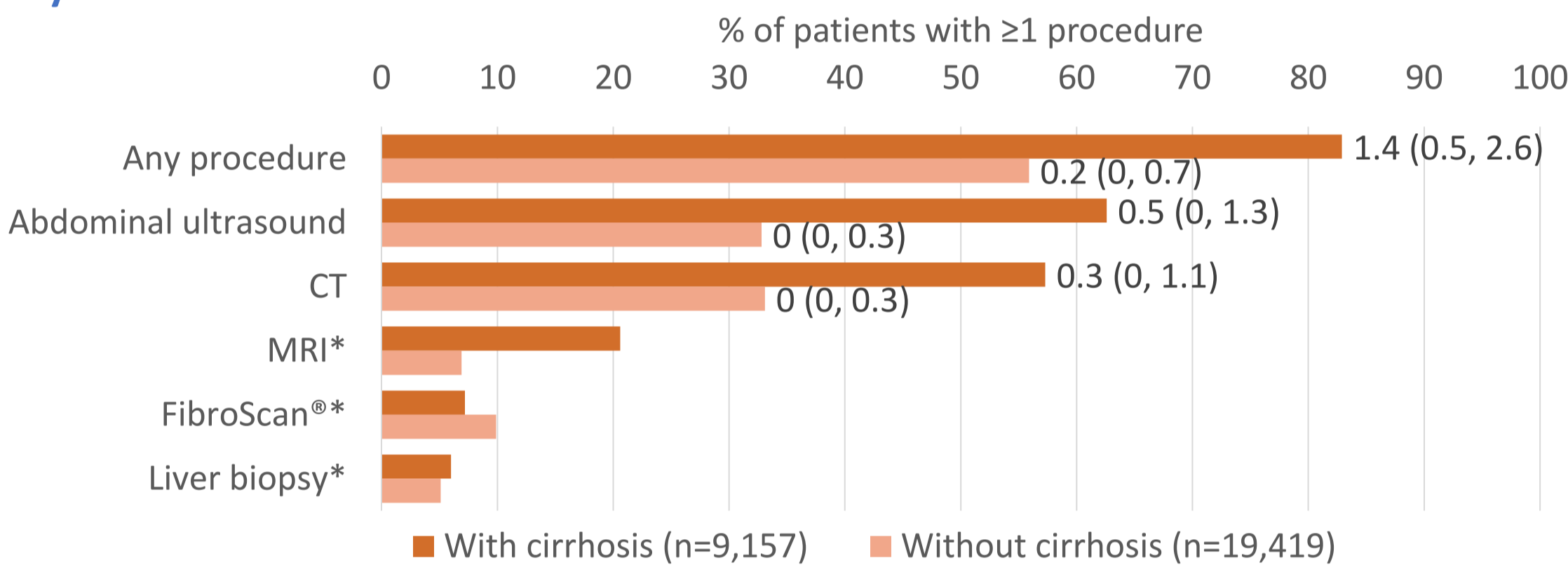
Figure 1. The percentage (%) of NASH patients with specialist and GIH visits over follow-up, and median (IQR) frequency PYPP, stratified by baseline cirrhosis status



- Liver biopsy was rarely performed even among patients with cirrhosis (Figure 2).

- Among imaging NITs, abdominal ultrasound and CT were most frequently used. A median of 0.5 abdominal ultrasounds and 0.3 CTs were performed PYPP with cirrhosis, and 0 PYPP without cirrhosis for both NITs.

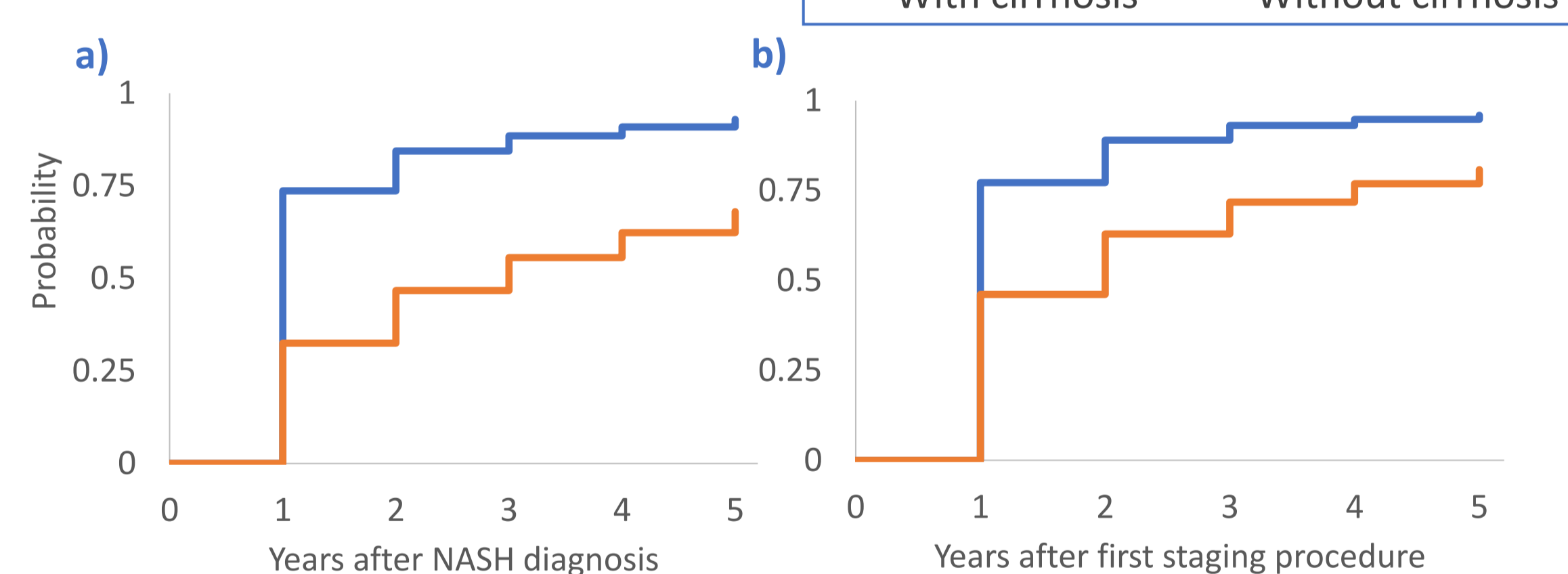
Figure 2. The percentage (%) of NASH patients receiving fibrosis staging related diagnostic procedures over follow-up, and (median [IQR]) frequency PYPP, stratified by baseline cirrhosis status



CT, computed tomography; IQR, interquartile range; MRI, magnetic resonance imaging; PYPP, per-year-per-person. Liver biopsy Current Procedural Terminology (CPT) codes: 37200, 47100, 47001, 47562, 47379, 47000; fibrosis scan CPT: 91200; abdominal ultrasound CPT: 76700, 76705; computed tomography (CT) CPT: 74150, 74160, 74170, 74174, 74175, 74176, 74177, 74178, 74179; MRI (including magnetic elastography of the abdomen) CPT: 74181, 74182, 74183, 74185. Note: median estimates represent annual frequency of specialist visits per person.

- Those with cirrhosis had a higher probability of receiving their first fibrosis staging related diagnostic procedure during the first year after NASH diagnosis compared to those without cirrhosis (0.73 vs. 0.33; Figure 3). Those with cirrhosis also had a higher probability of a second staging procedure occurring sooner than among those without cirrhosis.

Figure 3. Probability of a) first and b) second fibrosis staging procedure occurring each year during follow-up



## Discussion

- Findings from this retrospective claims analysis suggest that a substantial proportion of NASH patients are not being adequately followed up and assessed, even among those with cirrhosis.
  - Despite regular specialist visits, patients with cirrhosis had a median of 1.0 GIH visit PYPP indicating ≥25% were not being followed up at the recommended frequency of once per year.<sup>2</sup>
  - Those without cirrhosis had only a median of 0.2 GIH visits PYPP, indicating ≥50% were being assessed less frequently than every 2-3 years, as recommended.<sup>2</sup>
  - The median estimate of 1.4 diagnostic procedures PYPP with cirrhosis suggests that ≥50% were assessed for HCC less frequently than the recommended twice a year,<sup>2</sup> highlighting a potential gap in HCC monitoring.
  - Liver biopsy was rarely performed, even among patients with cirrhosis (6.0%), indicating underutilization of this diagnostic procedure and likely reflecting the increased reliance on NITs.
  - Patients who were older, female, or with a high comorbidity burden had more frequent visits and diagnostic procedures, but still at a lower rate than recommended; suggesting a need to emphasize specialist follow-up care for NASH patients who are younger, male, and those with or without MetS.
- Entries in specialty fields in CDM reflect healthcare provider training; not necessarily the type of service provided. For example, internists practicing as GIH would not be identified as a GIH visit.
  - Likely relatedly, visits to hepatologists, a subspecialty of gastroenterologists, were infrequently identified (<1% of patients saw a hepatologist).
  - Nonetheless, the overall numbers of GIH available in CDM are comparable to those reported previously,<sup>4,5</sup> and confirm that the GIH visits captured in this study are likely representative of visits to specialists with specific GIH training. The findings of this study should be interpreted with this context.
- An additional limitation is that while stratification by severity of fibrosis and frequency of fibrosis-4 (FIB-4) testing may help better elucidate clinical practice in the real world, such clinical data were not available for the entire study population.
- Despite limitations in being able to measure some aspects of the care pathway for NASH, our findings suggest how patients with NASH are managed in routine clinical practice in the US is only partially aligned with clinical guidelines.

## References

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