# Evaluating long-term healthcare resource utilization in biopsy-confirmed MASLD: a retrospective longitudinal observational cohort study in Sweden

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Poster number: EE396

## Aims

- The aims of this study were to assess healthcare resource utilization (HCRU) and healthcare costs by fibrosis stage, to characterize patients with higher versus lower HCRU and to compare HCRU in patients with and without fibrosis progression.

## Introduction

- Metabolic dysfunction-associated steatotic liver disease (MASLD) is the most common liver disease globally – it is estimated to affect more than 1 in 3 individuals.[1]
- The MASLD spectrum ranges from isolated steatotic (fatty) liver to the more severe form, metabolic dysfunction-associated steatohepatitis (MASH), which is associated with progressive liver fibrosis, cirrhosis and hepatocellular carcinoma.[2]
  - MASLD is also associated with other conditions, including cardiovascular disease (CVD), obesity, type 2 diabetes (T2D), chronic kidney disease and extrahepatic cancers.[2–4]
- The economic burden of MASLD is substantial: costs in the USA and Europe are estimated to reach US$1 trillion and €334 billion, respectively, by 2026.[5]
  - By 2025 in the USA, MASH is expected to become the leading cause of liver transplantation, which is associated with considerable HCRU and healthcare costs.[6]
- However, there is limited evidence on factors contributing to long-term HCRU and healthcare costs associated with MASLD.

## Methods

### Data source and study design

- This longitudinal observational cohort study used medical records data collected between 1973 and 2020 from Karolinska University Hospital, Uppsala University Hospital and Linköping University Hospital in Sweden.
- The cohort is linked to several Swedish national registers, enabling analysis of both clinical and economic outcomes.
- Patients were followed up from index (date of first biopsy +30 days) until death or the date of their last database entry.

### Selection criteria

- All patients in the cohort had biopsy-defined MASLD or MASH.
- Patients with a history of other liver diseases were excluded, as were those with daily alcohol consumption exceeding 30 g for men or 20 g for women.
- Patients with a second biopsy recorded ≥6 months after the first were included in the progressors versus non-progressors analysis.
  - Fibrosis stages range from F0 (no fibrosis) to F4 (cirrhosis); therefore, patients with fibrosis stage F4 at first biopsy were excluded from this analysis only.

### Outcomes

- The following outcomes were compared between fibrosis stages and between progressors (those with worsening of fibrosis) and non-progressors (those without worsening of fibrosis):
  - mean annual numbers of hospitalizations and outpatient visits, and length of hospital stay, stratified by cause (all-cause and liver-related)
  - mean annual costs of hospitalizations, outpatient visits and prescriptions, converted to 2023 values.
- The characteristics of patients with higher and lower HCRU were compared; higher HCRU was defined as numbers of hospitalizations and outpatient visits in the ≥80th percentile.
- HCRU was presented as a mean across all patients, whereas costs were presented as a mean among all patients with the underlying resource use.

### Statistical methods

- Analyses of HCRU and healthcare costs were performed using negative-binomial regression models, adjusted for age, sex, body mass index (BMI), T2D and calendar time, and 95% confidence intervals (CIs) were calculated.
- Patient characteristics were summarized using descriptive statistics (means with standard deviations [SDs] for continuous variables, and numbers with percentages for categorical variables).
- Characteristics were compared using Wilcoxon signed-rank and Chi-squared tests for continuous and categorical variables, respectively. Adjusted mean annual HCRU and costs were compared using a Wald test.
- *p* values were calculated to assess statistical significance; *p* values <0.05 were considered significant.

## Results

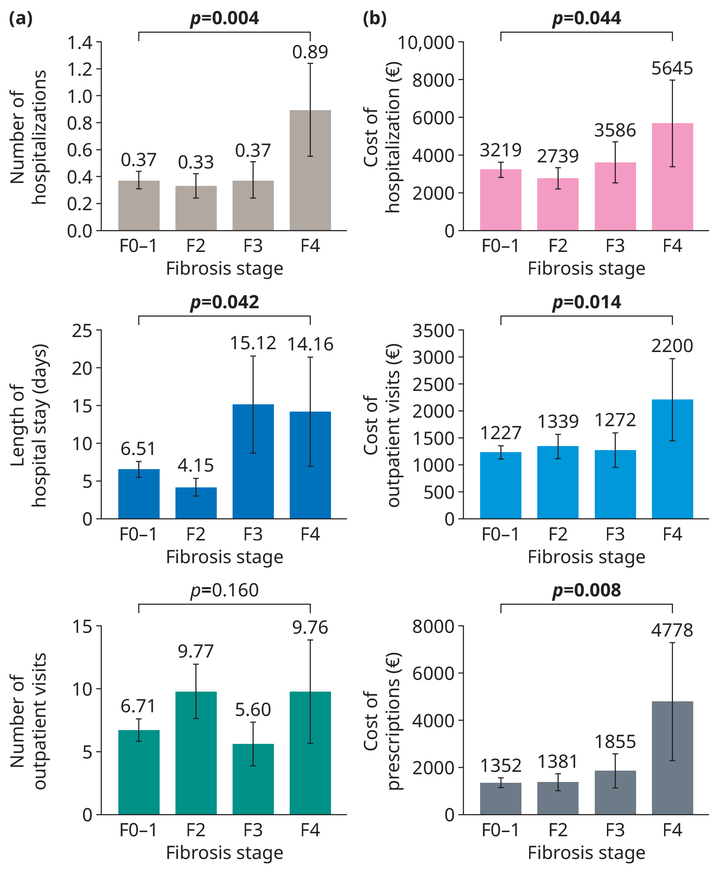
### Cohort characteristics

- Overall, 959 patients were included, 368 (38.4%) of whom were women. Mean age was 49.8 years (SD: 13.7).
- The proportion of patients with each fibrosis stage at baseline was as follows: F0 (23.1% of patients), F1 (38.8%), F2 (21.9%), F3 (10.4%) and F4 (5.7%).

### All-cause HCRU and healthcare costs by fibrosis stage

- Patients with cirrhosis (fibrosis stage F4) had significantly more annual hospitalizations compared with patients with early fibrosis (fibrosis stage F0–F1), and a significantly longer length of hospital stay (**Figure 1a**).
  - The number of outpatient visits was also greater in patients with cirrhosis compared with those with early fibrosis, but the difference was not statistically significant.
- Costs of hospitalization, outpatient visits and prescriptions were significantly higher for patients with cirrhosis than for those with early fibrosis (**Figure 1b**).

**Figure 1:** Annual per-patient all-cause HCRU (a) and healthcare costs (b) by fibrosis stage




*p* values are shown for the comparison between F0–1 and F4; *p* values <0.05 are in **bold**.
Error bars represent 95% CIs.
CI, confidence interval; HCRU, healthcare resource utilization.

### Liver-related HCRU and healthcare costs by fibrosis stage

- Patients with cirrhosis had a significantly longer length of hospital stay and significantly more outpatient visits compared with patients with early fibrosis (**Figure 2a**).
  - The number of hospitalizations was also greater in patients with cirrhosis compared with those with early fibrosis, but the difference was not statistically significant.
- Costs of outpatient visits were significantly higher for patients with cirrhosis than for those with early fibrosis, and although costs of hospitalizations were also higher, the difference was not statistically significant (**Figure 2b**).

### Characteristics of patients with higher versus lower HCRU

- Overall, 287 patients had higher HCRU (≥80th percentile) and 672 had lower HCRU (<80th percentile; **Table 1**).
  - Patients with higher HCRU were older than those with lower HCRU, and a greater proportion were women.
- Compared with the lower HCRU group, the higher HCRU group had lower proportions of patients with fibrosis stages F0–2, and greater proportions of patients with fibrosis stages F3–4 (**Table 1**).
  - Additionally, those with higher HCRU had greater BMI measurements, greater glycated haemoglobin ($HbA_{1c}$) levels and were more likely to have T2D or CVD.

### HCRU in progressors versus non-progressors

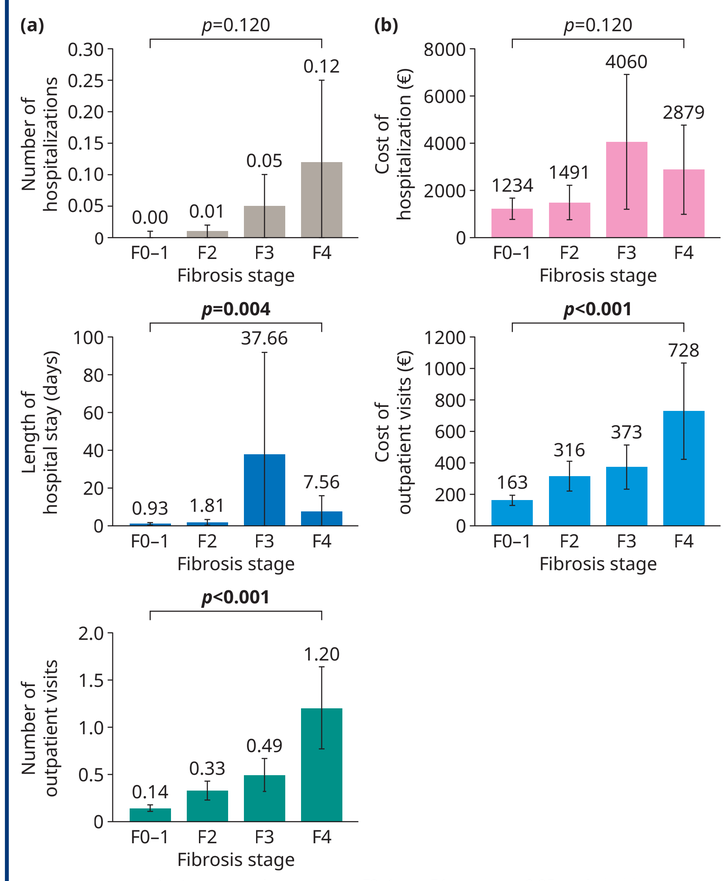
- In total, 49 patients without fibrosis stage F4 at index had data from a second biopsy to permit assessment of fibrosis progression, 24 of whom had worsening of fibrosis (progressors) and 25 who did not (non-progressors).
- Progressors had more all-cause hospitalizations and outpatient visits than non-progressors, and more liver-related outpatient visits, but CIs were wide owing to the limited sample size (**Figure 3**).
  - The same was true for liver-related hospitalizations (not shown in **Figure 3** owing to low values: progressors, 0.0000294; non-progressors, 0.0000053; *p*>0.99).

**Table 1:** Characteristics for patients with higher and lower HCRU

| Characteristic | Mean ± SD or n (%) | | *p* value |
|---|---|---|---|
| | Higher HCRU (≥80th percentile; n=287) | Lower HCRU (<80th percentile; n=672) | |
| Age, years | 51.2 ± 12.9 | 49.2 ± 14.0 | **0.035** |
| Women | 138 (48.1) | 230 (34.2) | **<0.001** |
| Fibrosis stage | | | **<0.001** |
| F0 | 52 (18.1) | 170 (25.3) | – |
| F1 | 110 (38.3) | 262 (39.0) | – |
| F2 | 54 (18.8) | 156 (23.2) | – |
| F3 | 39 (13.6) | 61 (9.1) | – |
| F4 | 32 (11.1) | 23 (3.4) | – |
| BMI, kg/m² | 30.0 ± 6.1 | 29.1 ± 4.3 | **0.031** |
| $HbA_{1c}$, mmol/mol | 54.6 ± 21.1 | 49.1 ± 16.5 | **<0.001** |
| Presence of T2D | 99 (34.5) | 141 (21.0) | **<0.001** |
| History of CVD | 36 (12.5) | 56 (8.3) | **0.043** |
| Presence of CKD | 16 (5.6) | 22 (3.3) | 0.094 |

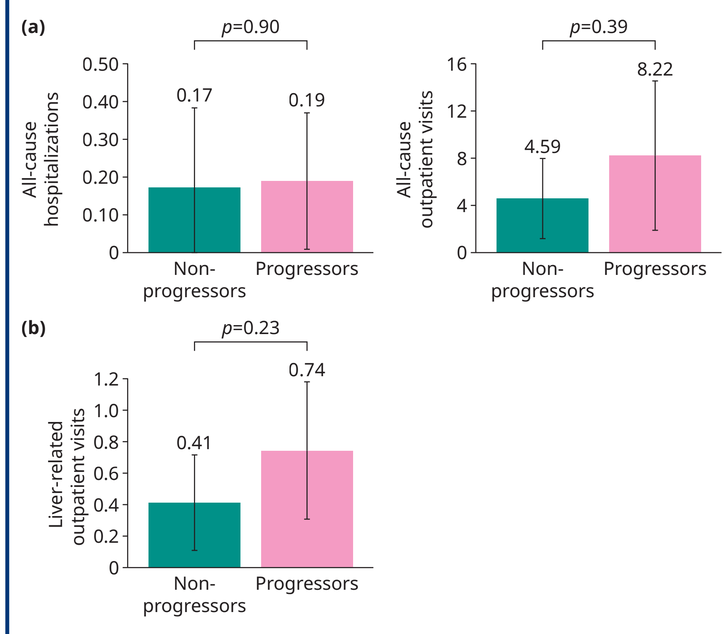
*p* values <0.05 are in **bold**.
BMI, body mass index; CKD, chronic kidney disease; CVD, cardiovascular disease; $HbA_{1c}$, glycated haemoglobin; HCRU, healthcare resource utilization; SD, standard deviation; T2D, type 2 diabetes.

**Figure 2:** Annual per-patient liver-related HCRU (a) and healthcare costs (b) by fibrosis stage




*p* values are shown for the comparison between F0–1 and F4; *p* values <0.05 are in **bold**.
Error bars represent 95% CIs.
CI, confidence interval; HCRU, healthcare resource utilization.

**Figure 3:** Annual per-patient all-cause (a) and liver-related (b) HCRU for progressors and non-progressors




*p* values are shown for the comparison between progressors and non-progressors.
Error bars represent 95% CIs.
CI, confidence interval; HCRU, healthcare resource utilization.

## Strengths and limitations

- The study population was large and well-characterized with a long follow-up, permitting analysis of factors contributing to long-term HCRU and healthcare costs in MASLD.
- Over 60% of patients had early-stage disease (fibrosis stage F0–1) at baseline, indicating reduced selection bias versus other studies with greater proportions of patients with advanced fibrosis; as such, the findings are expected to be more generalizable to real-world practice.
- The limited number of patients with repeat biopsy data impacted our ability to draw conclusions from the progression analysis.

## Conclusions

- Patients with more advanced fibrosis had increased HCRU and incurred greater costs, compared with those with earlier stages of fibrosis.
- Patients with higher HCRU were more likely to have advanced fibrosis, and were more likely to have higher BMI, elevated $HbA_{1c}$ levels, T2D or CVD, compared with those with lower HCRU.
- In the small subgroup of patients with repeat biopsy data, fibrosis progression was associated with numerically higher all-cause and liver-related hospitalizations and outpatient visits.
- These findings highlight the impact of worsening fibrosis stage on HCRU and healthcare costs in MASLD, and support the need for holistic treatments to manage both the disease itself and its cardiometabolic comorbidities.

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This study was funded by Novo Nordisk A/S. Medical writing support was provided by Oxford PharmaGenesis, Oxford, UK and was funded by Novo Nordisk A/S.

Presented at ISPOR Europe 2024, 17–20 November 2024, Barcelona, Spain.

**Disclosures:**
ETG is an employee of Quantify Research. KKM is an employee of Novo Nordisk Service Center India Pvt Ltd. and a shareholder of Novo Nordisk A/S. RO and MKW are employees and shareholders of Novo Nordisk A/S. YS reports no disclosures. HS is an employee of Quantify Research. JV reports advisory boards for Janssen and Novo Nordisk, and lecture fees for Gore and Norgine. ME reports advisory boards for AMRA Medical and Novo Nordisk. HH's institutions have received research funding from AstraZeneca, EchoSens, Gilead, Intercept, MSD, Novo Nordisk and Pfizer. He has served as a consultant on advisory boards for AstraZeneca, Bristol Myers Squibb, MSD and Novo Nordisk and has been part of hepatic events adjudication committees for Boehringer Ingelheim, GW Pharma and KOWA.

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