

# SOCIETAL BURDEN OF NON-ALCOHOLIC STEATOHEPATITIS (NASH) IN DENMARK – REAL-WORLD EVIDENCE FROM NATIONAL REGISTRIES

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## BACKGROUND

- Non-alcoholic fatty liver disease (NAFLD) is characterized by hepatic steatosis, diagnosed either by imaging or by histology, with no other causes for secondary hepatic fat accumulation.<sup>1</sup>
- Non-alcoholic steatohepatitis (NASH) is a progressive form of NAFLD defined by presence of histologically verified hepatic steatosis, inflammation, and with/without fibrosis.<sup>1</sup>
- NASH is associated with increased risk of cirrhosis, hepatocellular carcinoma, cardiovascular disease, and type 2 diabetes.<sup>2,3</sup>
- Burden of disease of NASH may be substantial, but further reliable evidence is needed.
- This is due to study design (e.g. survey studies), patient database studies without confirmation of NASH diagnosis, narrow healthcare sector perspectives on costs, and only small studies with biopsy-confirmed diagnosis.<sup>4-10</sup>
- Recently a need for more evidence on the excess costs of NASH was requested to better understand the public health burden and to fulfil healthcare planning needs.<sup>11</sup>

## OBJECTIVE

- Utilizing the population-based Danish national registers the aim of the present study was to examine the healthcare and societal costs related to patients with non-alcoholic fatty liver disease (NAFLD), including NASH.

## METHODS

### STUDY DESIGN AND DATA SOURCES

- Using real-world data from the nationwide Danish registers, patients (≥18 years) with a hospital diagnosis and a biopsy-confirmed NAFLD (≥18 years) were identified (1997–2021).
- Patients were identified in the National Patient Register<sup>12</sup> using the ICD-10 codes: K74.0, K74.6, K75.8, K76.0 or R74.0. Patients without a liver biopsy recorded in the Danish National Pathology Register<sup>13</sup> within six months registration of the ICD-10 code were excluded.
- Patients were classified in NASH (with/without fibrosis), simple steatosis or cirrhosis and were in each group matched 1:5 with a liver-disease free reference group (controls).
- Outcomes investigated in the national Danish registers were costs associated with healthcare services, home care, production loss (measured by wage differences in patients versus comparators), sick leave, unemployment and early retirement.

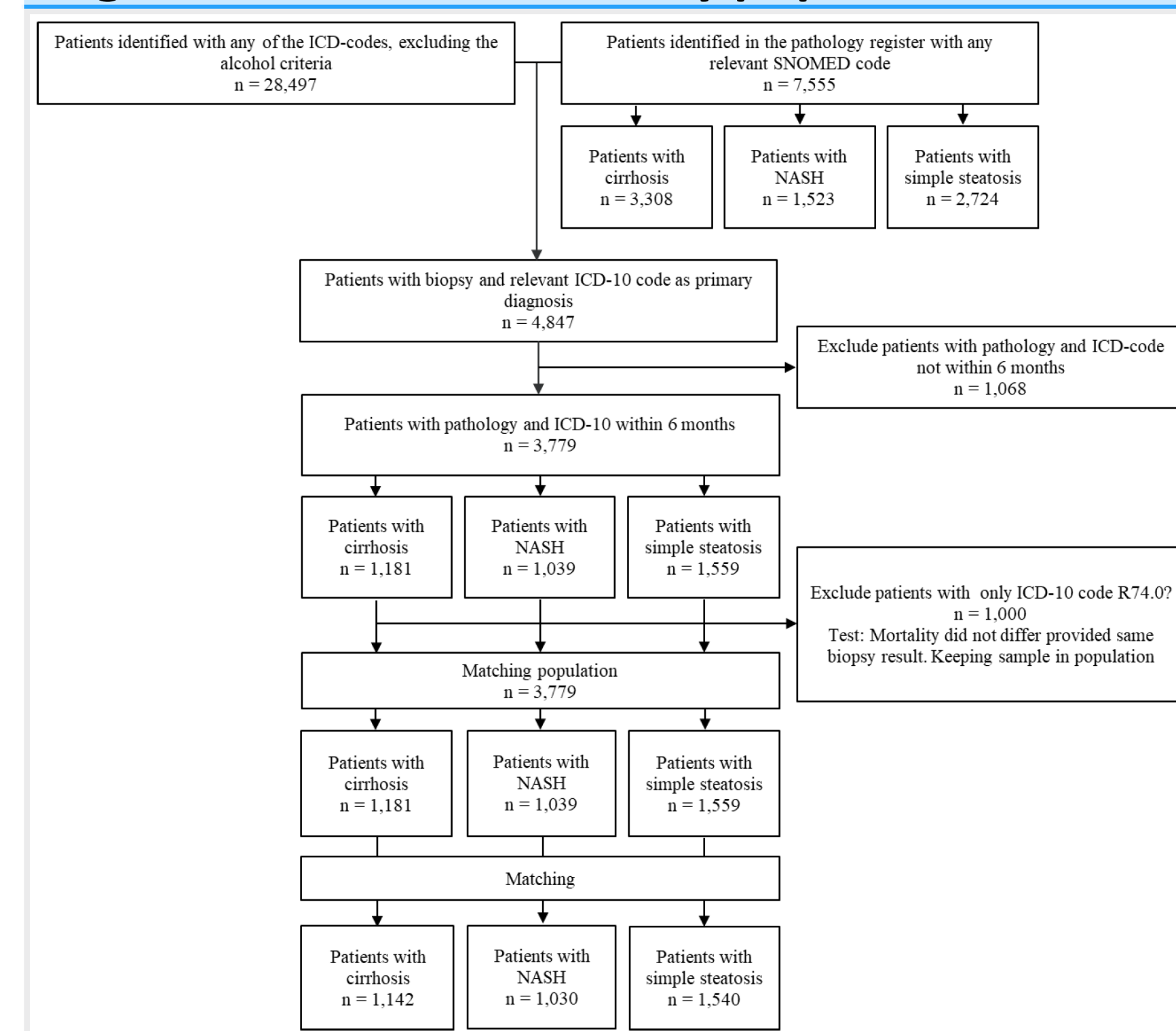
### STATISTICAL ANALYSIS

- Patients were followed in terms of outcomes for 16 years - five years before and 11 years after diagnosis.
- Healthcare and societal excess costs due to NASH/NAFLD diseases were calculated as the difference in mean costs for the disease group and the liver-disease free reference group.

## RESULTS

- 3,712 NAFLD patients were identified in the period 1997-2021 (Figure 1).
- Among these were 1,030 patients with NASH, 1,540 patients with simple steatosis and 1,142 patients with cirrhosis, which were all included in the analyses together with their matched liver-disease free reference groups.

**Figure 1. Flowchart of study populations**



- Median age for NASH and simple steatosis patients were 52 and 50 years with cirrhosis patients being older (63 years). Gender was evenly split, besides in cirrhosis (63% women).
- Cardiovascular disease was the predominant comorbidity in all three groups (Table 1).

**Table 1. Characteristics of study populations**

	Cirrhosis		NASH		Simple steatosis	
	Patient	Reference	Patient	Reference	Patient	Reference
N	1,142	5,682	1,030	5,119	1,540	7,650
Age, median (IQR)	63 (54, 70)	63 (54, 70)	52 (39, 62)	52 (39, 62)	50 (37, 59)	50 (37, 59)
Sex						
Male	490 (43%)	2,440 (43%)	500 (49%)	2,481 (48%)	775 (50%)	3,836 (50%)
Female	652 (57%)	3,242 (57%)	530 (51%)	2,638 (52%)	765 (50%)	3,814 (50%)
Comorbidity at baseline						
Chronic kidney disease (%)	31 (2.7%)	22 (0.4%)	10 (1%)	30 (0.6%)	16 (1%)	31 (0.4%)
Cardiovascular disease (%)	501 (43.9%)	612 (10.8%)	331 (32.1%)	522 (10.2%)	382 (24.8%)	608 (8.0%)
Hepatocellular carcinoma (%)	33 (2.9%)	0	<5	0	<5	0
Sleep apnoea (%)	34 (3%)	127 (2.2%)	117 (11.4%)	108 (2.1%)	100 (6.5%)	129 (1.7%)
Type 2 Diabetes (%)	401 (35.1%)	113 (2.0%)	258 (25.1%)	136 (2.7%)	137 (8.9%)	122 (1.6%)

### HEALTHCARE RESOURCE USE AND COSTS

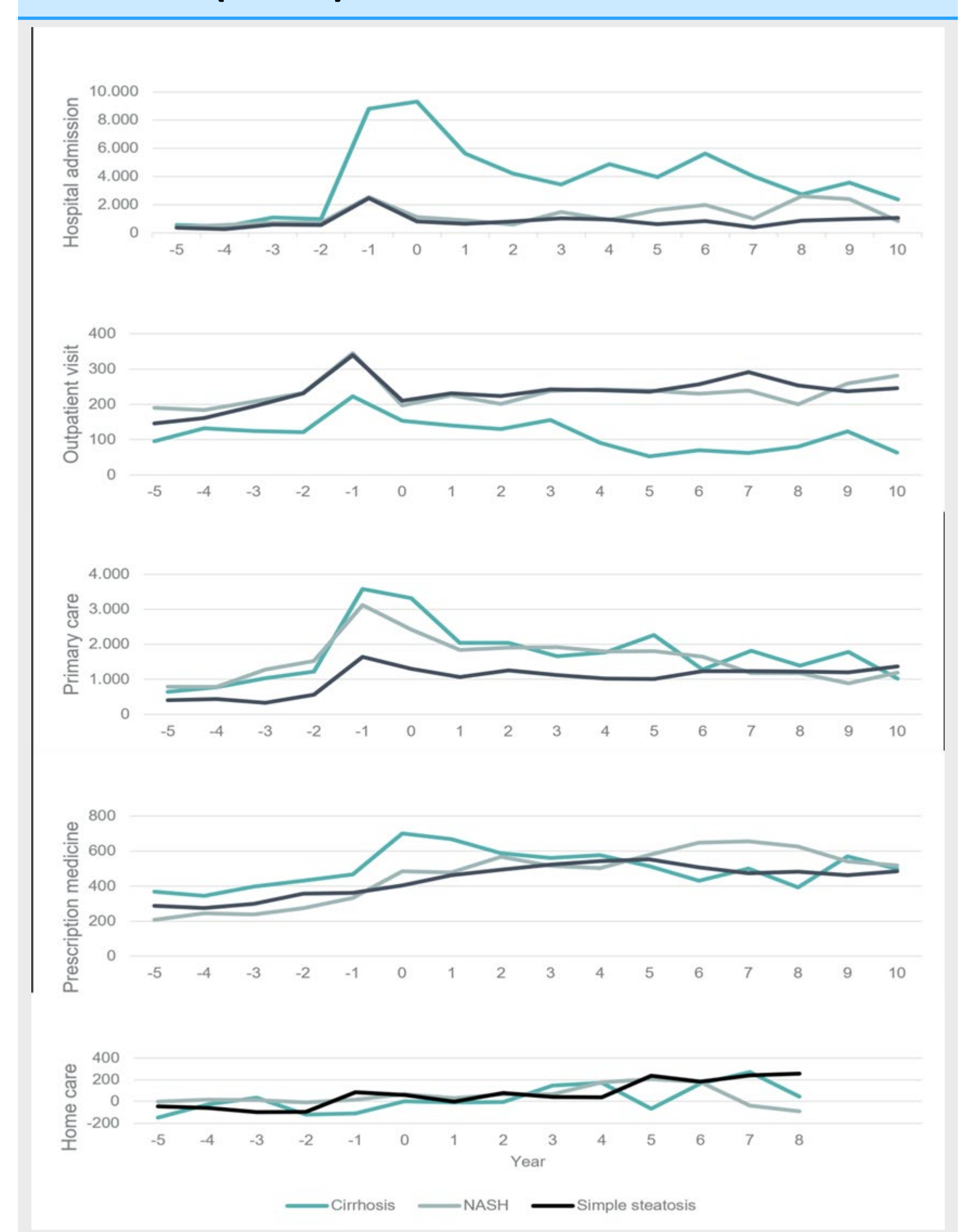
- Hospital admissions:** NASH and simple steatosis patients had twice as many admissions (0.76 and 0.9) as references the year before diagnosis and cirrhosis patients had 2.96 extra.
- Outpatient visits:** NASH and cirrhosis patients had around 9 excess contacts the year before diagnosis (7-8 times more), and simple steatosis patients had 7. Over a 10-year period excess contacts lowered a bit but were still high.
- Total healthcare costs:** Highest average total healthcare costs were found in the year leading up to diagnosis: cirrhosis €12,949 (6.2-fold higher), NASH €6,318 (4.1-fold) and simple steatosis €4,716 (3.1-fold) (Table 2).

**Table 2. Total healthcare costs per year (Euros)**

Period	Cirrhosis				NASH				Simple steatosis			
	Patient	Reference	Excess	Ratio	Patient	Reference	Excess	Ratio	Patient	Reference	Excess	Ratio
-1 to 0	15,431	2,478	12,949	6.23	8,384	2,042	6,318	4.11	7,181	2,291	4,716	3.13
-1 to 3	12,962	2,693	10,220	4.81	6,495	2,064	4,419	3.15	5,200	2,012	3,162	2.58
-1 to 8	12,217	3,009	9,183	4.06	6,463	2,140	4,325	3.02	5,176	2,136	3,011	2.42

- The mean annual excess cost of a NASH patient was €4,325 in a ten-year perspective (Table 2), i.e. approx. €43,000 in the 10-year period. For simple steatosis and cirrhosis, the annual excess cost was €3,011 and €9,183, respectively.
- For cirrhosis patients, inpatient contacts accounted for 68% of the excess costs, whereas outpatient contacts accounted for 49% of NASH patients' costs. Excess costs of NASH in the years after diagnosis were around 70% of excess costs in the year leading up to diagnosis.
- Figure 2 present detailed annual costs over the 16-year time period from year before diagnosis.

**Figure 2. Average annual individual excess healthcare costs for cirrhosis, NASH and simple steatosis (Euros)**



- Income loss:** NASH, simple steatosis and cirrhosis patients had significant lower income than the reference groups from year -5 to 8 (p<0.05). From the year before diagnosis and to year 8 annual difference of €6,757 to €13,568.
- Disability insurance:** A higher risk of early retirement due to disability was also found for all three groups, e.g. for NASH patients (HR: 4.37; 95% CI: 3.17–6.02).

## CONCLUSIONS

- The burden on healthcare and society caused by NAFLD diseases was considerable.
- The average NASH patient generated excess healthcare costs of €6,318 in the year leading up to diagnosis with the primary cost driver being hospital admissions.
- NAFLD patients, including NASH, had significant lower income compared to the general population, and significantly higher risk of receiving disability insurance.

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## DISCLOSURE OF INTEREST

JHP and JO were employees at EY, which is a paid vendor of Pfizer Denmark Aps. LLG, HG, MKJ, MV and PJ were paid by Pfizer Denmark Aps. for their work as members of the Study Steering Committee. PBP, NH, NTG and ABT were employees of Pfizer Denmark Aps. PBP, NH, and ABT owns shares from Pfizer Inc. The authors report no other conflicts of interest in this work.

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