

# The cost of care among patients with nonalcoholic steatohepatitis, with versus without cirrhosis: A US cohort study

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## Background

- Nonalcoholic steatohepatitis (NASH) is characterized by an accumulation of fat in the liver accompanied by inflammation.<sup>1</sup> The prolonged inflammation and liver damage of NASH can result in scarring of the liver and progress to cirrhosis.<sup>2</sup>
  - Cirrhosis includes both an asymptomatic phase (compensated cirrhosis [CC]), followed by decompensated cirrhosis (DCC), which is defined by the development of symptoms and complications.<sup>3</sup>
  - Based on the clinical literature, it is estimated that 20% of patients with NASH are expected to progress to CC within two years of diagnosis; and 20% of patients with CC progress to DCC over the same time period<sup>4</sup>
- Previous studies have highlighted high healthcare costs among those with NASH, and increasing direct medical costs with advancing stages of NASH;<sup>5,6</sup> however, how costs differ among NASH patients with versus without cirrhosis in the United States (US) is unclear.

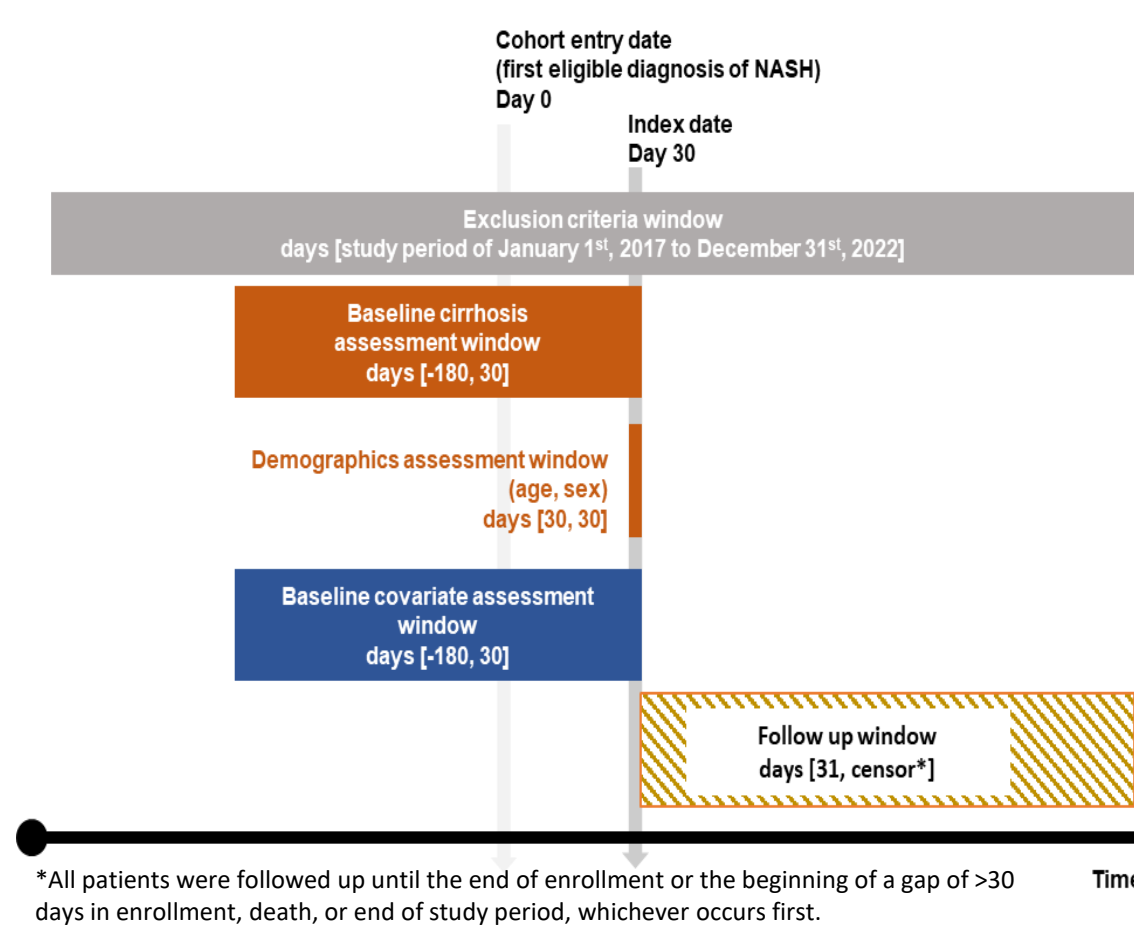
## Objective

- To compare health-care related annual costs among NASH patients with versus without cirrhosis in the US.

## Methods

- Eligible adults with ≥1 inpatient or ≥ claims for NASH (ICD-10-CM K75.81) were identified from Optum's de-identified Clinformatics® Data Mart Database (CDM; 10/2015-12/2022) (Figure 1).

Figure 1: Study design overview



- Detailed inclusion and exclusion criteria are outlined in Figure 2.

- Patient demographics and baseline comorbidity burden were summarized categorically and continuously using summary statistics.

- Mean annual total costs per person were summarized, along with components including inpatient admission, outpatient visits, and medication, descriptively and compared using student's T test. In addition, users, for procedures and visits of particular interest to the NASH population, were also estimated. All costs were adjusted to 2022 US dollars (USD).

- Generalized linear models (GLM) with a gamma distribution were used to compare annual costs per patient between those with vs. without cirrhosis. Annual costs per patient over each year of follow-up were modeled using gamma generalized linear mixed models (GLMM), accounting for within-patient time correlations and adjusting for death during follow-up.
  - Both models adjusted for sex, age (categorical), race, region, comorbidities of cardiovascular diseases, type 2 diabetes mellitus, and obesity, and baseline costs per person.

- All analyses were performed within the Optum De-identified Data Workspace using the Jupyter Notebook.

## References

1. Sheka AC, Adeyi O, Thompson J, et al. JAMA. 2020;323(12):1175-1183. 2. Estes C, Anstee QM, Arias-Loste MT, et al. J Hepatol. 2018;69(4):896-904. 3. Samonakis DN, Koulentaki M, Coucououtsis C, et al. World J Hepatol. 2014;6(7):504-512. 4. Loomba R, Adams LA. Hepatology. 2019;70(6):1885-1888. 5. Tapper EB, Bonafede M, Fishman J, et al. J Med Econ. 2023;26(1):348-356. 6. Wong RJ, Kachru N, Martinez DJ, et al. J Clin Gastroenterol. 2021;55(10):891-902. 7. Optum. <https://www.optum.com/business/life-sciences/real-world-data/claims-data.html>. Accessed 14/08/2023. 8. Welliver C, Feinstein L, Ward JB, et al. Int J Urol Nephrol. 2022;54(11):2797-2803.

## Results

- Patients with cirrhosis were older at baseline (mean [SD] age, 67.1 [10.8] years) and had a shorter mean follow-up (2.5 years) compared to those without cirrhosis (age: 59.8 [13.4] years; follow-up: 3.2 years; Table 1)

Figure 2: Two NASH cohorts were defined: those with (n=9,157) and without (n=19,419) cirrhosis

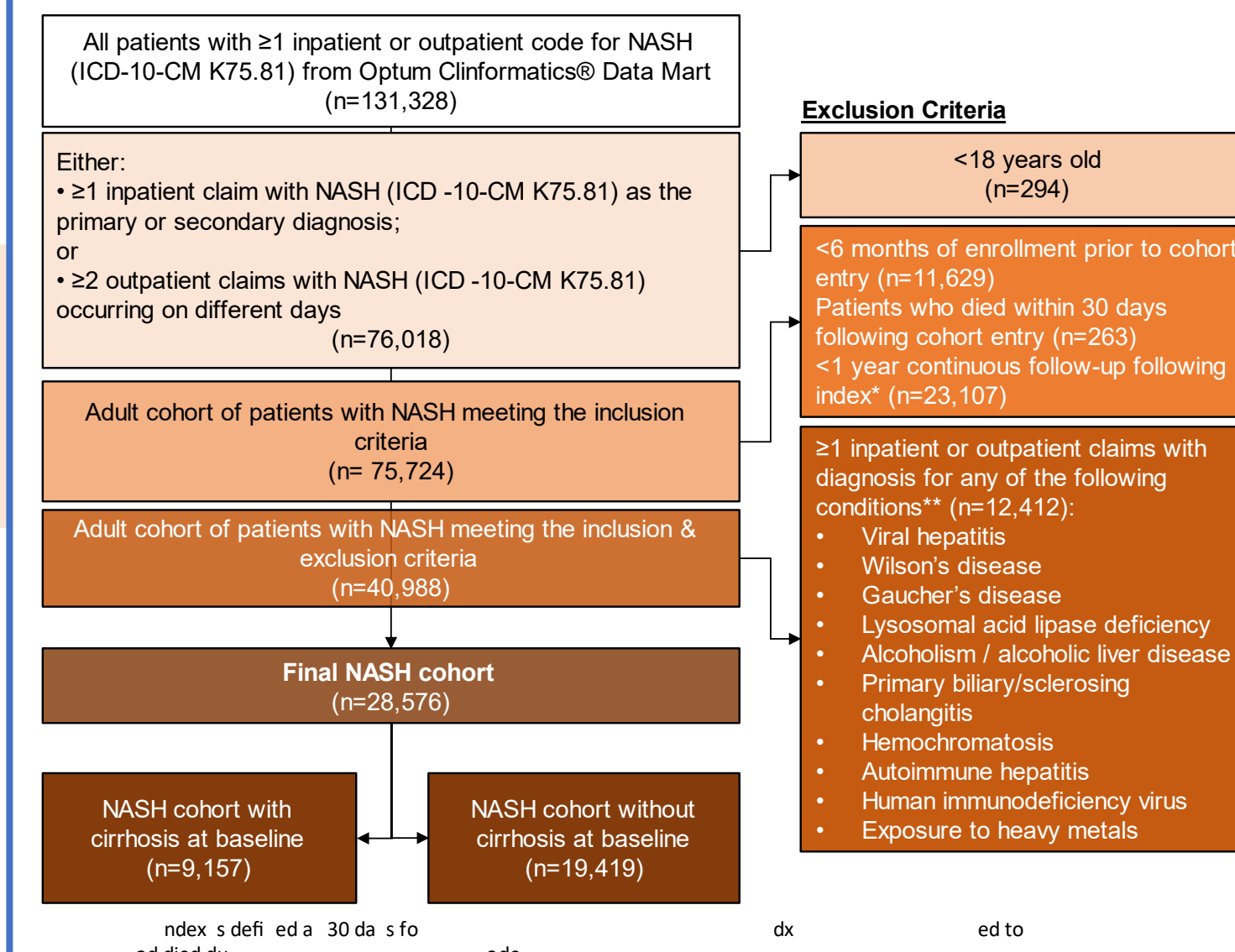


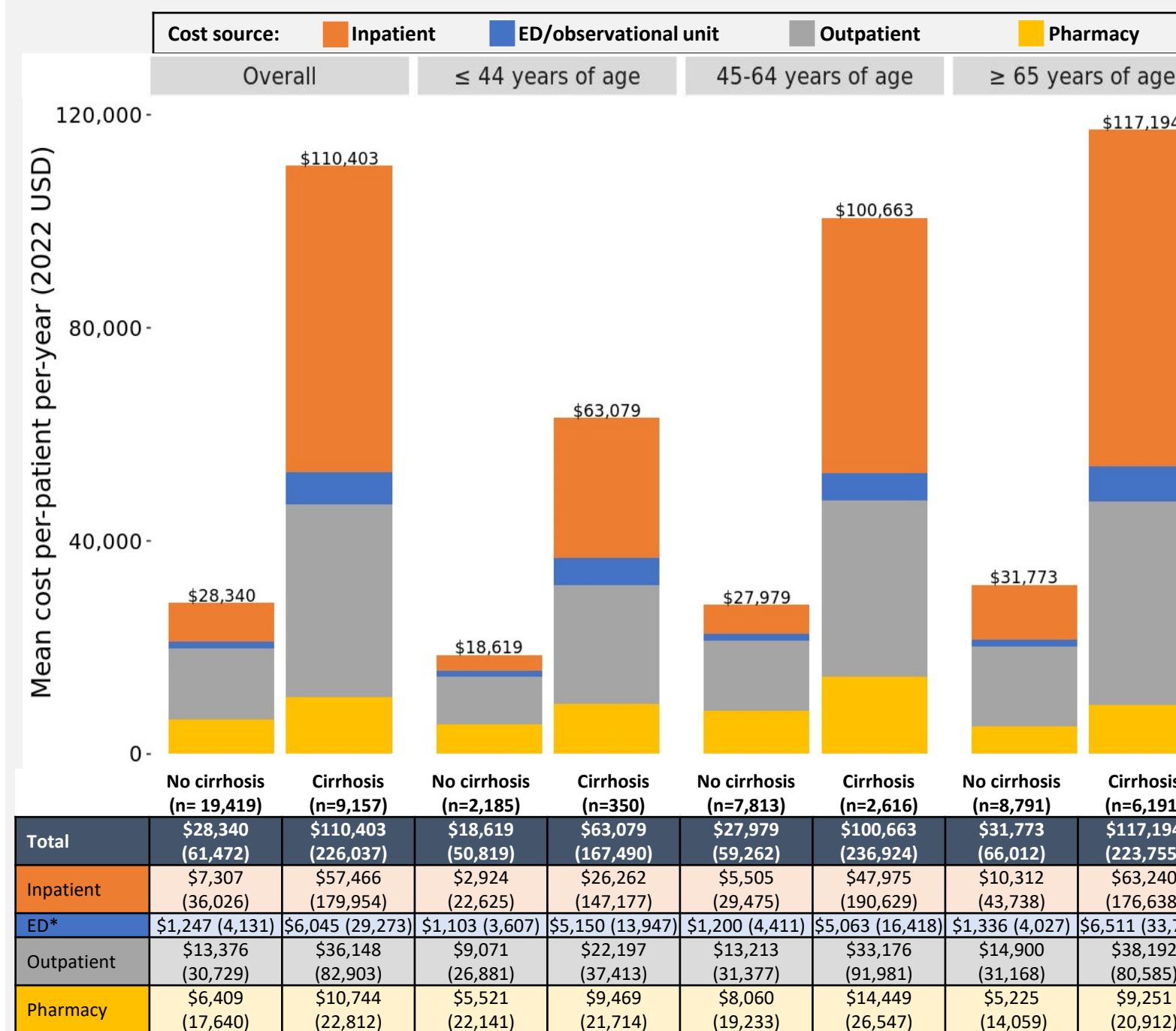
Table 1: Baseline demographics

Measured within the baseline covariate assessment window	With cirrhosis (n= 9,157)	Without cirrhosis (n= 19,419)
Total follow-up per person, years, mean (SD)	2.5 (1.6)	3.2 (1.5)*
Age at index, years, mean (SD)	67.1 (10.8)	59.8 (13.4)*
Male sex, n (%)	3,158 (34.5)	7,982 (41.1)*
Race, n (%)		
Asian	171 (1.9)	871 (4.5)*
Black	654 (7.1)	1,380 (7.1)*
Hispanic	1,376 (15.0)	3,648 (18.8)*
White	6,447 (70.4)	12,647 (65.1)*
Unknown	509 (5.6)	873 (4.5)*
Insurance, n (%)		
MAPD dual (Medicaid/Medicare)	393 (11.1)	418 (8.6)*
MAPD LIS	455 (12.9)	523 (10.8)*
Other	2,379 (67.4)	3,445 (70.8)*
Unknown	304 (8.6)	477 (9.8)*
Comorbidities, n (%)		
Cardiovascular disease	7,798 (85.2)	13,141 (67.7)*
Type 2 diabetes mellitus	5,203 (56.8)	5,893 (30.3)*
Obesity	3,725 (40.7)	5,753 (29.6)*
Cost, 2022 USD PPPY, mean (SD)	87,239 (121,782)	26,581 (52,976)

Abbreviations: Q1, first quartile; Q3, third quartile; PPPY, per-person per-year, SD, standard deviation, USD, United States dollars. \*P<0.01 when using two-tailed Student's T-Test to compare the means between the cohorts with vs. without cirrhosis cohorts.

- Total annual costs per patient were significantly higher among patients with cirrhosis (\$110,403 vs. \$28,340; p<0.01) and this trend persisted across age stratifications (Figure 3)
  - Among patients with at least one resource use, costs of specialists and procedures related to NASH were estimated (Table 2)

Figure 3: Mean annual costs per patient with and without cirrhosis, stratified by age at index



\*ED/observational unit. Notes costs are presented as mean (SD) 2022 USD. Abbreviations: ED, emergency department; SD, standard deviation; USD, United States dollars.

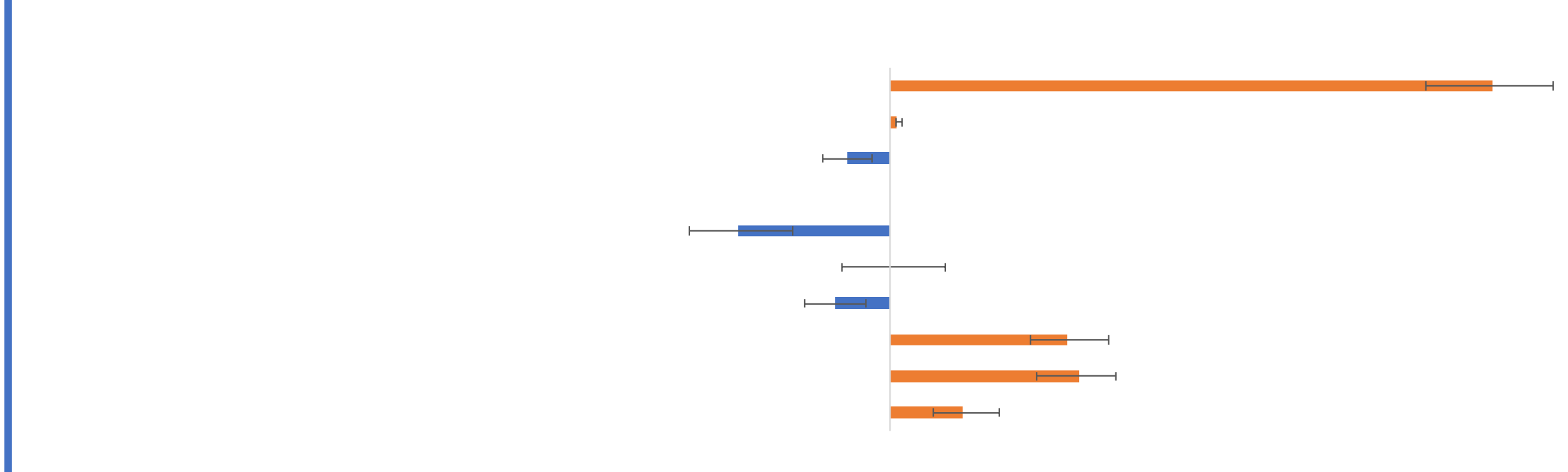
Table 2: Mean annual costs per patient, among users

Category, annual costs among users (patients with ≥1 resource use in each category)	With cirrhosis (n= 9,157)	Without cirrhosis (n= 19,419)
Gastroenterologists*, n(%)	6,165 (67.3)	9,833 (50.6)
Mean (SD)	\$665 (\$1,445)	\$383 (\$1,943)
Fibrosis staging related procedures, all, n(%)	7,588 (82.9)	10,856 (55.9)
Mean (SD)	403 (1,277)	260 (804)
Liver biopsies, n(%)	545 (6.0)	998 (5.1)
Mean (SD)	\$1,903 (\$4,105)	\$1,654 (\$2,036)
FibroScans, n(%)	656 (7.2)	1,922 (9.9)
Mean (SD)	\$87 (\$105)	\$79 (\$105)
Abdominal ultrasounds, n(%)	5,729 (62.6)	6,371 (32.8)
Mean (SD)	\$342 (\$464)	\$161 (\$157)
CT's, n(%)	5,243 (57.3)	6,424 (33.1)
Mean (SD)	\$1,037 (\$2,668)	\$582 (\$952)
MRI's, n(%)	1,887 (20.6)	1,337 (6.9)
Mean (SD)	\$1,082 (\$1,370)	\$519 (\$563)

\*Including hepatologists. Abbreviations: CT, computerized tomography; MRI, magnetic resonance imaging; SD, standard deviation.

- Total annual costs remained significantly higher (risk ratio=1.99 [95% confidence interval=1.88-2.09]) when adjusted for demographics, and baseline comorbidities and costs (Figure 4)

Figure 4: GLM estimates of total annual costs per patient, based on the final NASH cohort of 28,576 patients



Note: region, Elixhauser index, and costs per person per year were also adjusted in the model but not presented due to space limitations. \*Relative to an intercept of \$7,059.58 (6,258.61, 7,963.06) per patient. Abbreviations: CI, confidence interval; CVD, cardiovascular disease; T2D, type 2 diabetes mellitus; GLM, generalized linear model.

- Compared to year 1, total annual costs/person increased by 3% in year 2 and 21% in year 6 among those with cirrhosis; and by 1% and 34% among those without cirrhosis over the same time period (Table 3)

Table 3: GLMM estimates of total annual cost per patient, over the first six years of follow-up

Variable	Cirrhosis cohort			Non-cirrhosis cohort		
	Estimate	95% CI	P-value	Estimate	95%CI	P-value
Intercept	19,510.71	(16,673.94, 22,830.09)	<0.01	4,533.95	(4,159.08, 4,942.61)	<0.01
Years since index (vs. Year 1)						
Year 2	1.03	(1.00, 1.06)	0.08	1.01	(0.99, 1.04)	0.15
Year 3	1.12	(1.07, 1.16)	<0.01	1.06	(1.04, 1.09)	<0.01
Year 4	1.17	(1.11, 1.24)	<0.01	1.12	(1.08, 1.15)	<0.01
Year 5	1.14	(1.06, 1.23)	<0.01	1.24	(1.20, 1.30)	<0.01
Year 6	1.21	(1.07, 1.37)	<0.01	1.34	(1.25, 1.42)	<0.01
Death	4.17	(3.95, 4.40)	<0.01	4.80	(4.42, 5.21)	<0.01
Age	1.00	(1.00, 1.00)	0.10	1.01	(1.01, 1.01)	<0.01
Sex (Male vs. Female)	0.92	(0.88, 0.97)	<0.01	0.76	(0.73, 0.78)	<0.01
Race (vs. White)						
Asian	0.94	(0.80, 1.10)	0.43	0.68	(0.63, 0.73)	<0.01
Black	0.94	(0.87, 1.03)	0.17	1.04	(0.98, 1.11)	0.18
Hispanic	0.88	(0.83, 0.94)	<0.01	0.86	(0.82, 0.89)	<0.01
Baseline CVD	1.38	(1.30, 1.47)	<0.01	1.35	(1.30, 1.39)	<0.01
Baseline T2D	1.22	(1.17, 1.28)	<0.01	1.25	(1.21, 1.30)	<0.01
Baseline obesity	1.21	(1.15, 1.27)	<0.01	1.11	(1.07, 1.15)	<0.01

Note: region, Elixhauser index, and costs per person per year were also adjusted in the model but not presented due to space limitations. Abbreviations: CI, confidence interval; CVD, cardiovascular disease; T2D, type 2 diabetes mellitus; GLMM, generalized linear mixed model. Note: green highlighting signifies variables with a significant association with decreasing annual costs and orange for increasing.

## Discussion

- Total medical costs of care of NASH in the US are substantially higher among patients with cirrhosis than without (\$110,403 vs. \$28,340 per patient, p <0.01), with adjusted annual costs being twice as high among NASH patients with cirrhosis.

- This is consistent with a US database study from 2006-2016 that similarly reported high costs among NAFLD/NASH patients; and that patients with advanced liver events had higher annual medical costs compared to those without (\$29,078-\$197,392 vs. \$23,860).<sup>6</sup>

- In the current study, while patients without cirrhosis had lower costs overall, the longitudinal analyses suggest they would experience greater increases in costs over time.

- The generalizability of the findings is restricted to the population enrolled within Optum's CDM. However, these data include >77 million patients and it is a widely-used and validated research environment.<sup>7,8</sup>

- Findings from this study show that the costs of caring for NASH are substantial, and significantly greater among NASH patients with cirrhosis. Therapies that slow progression to cirrhosis may help alleviate the financial burden of managing NASH.

