

Increasing Healthcare Resource Utilization (HCRU) and Costs Associated With Advanced Liver Disease – A Multivariate Analyses of Real-World Medicare Nonalcoholic Fatty Liver Disease/Nonalcoholic Steatohepatitis (NAFLD/NASH) Patients

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Background

- The projected increase in the prevalence of NAFLD/NASH has potential for profound impact on HCRU and healthcare costs in the US.^{1,2,3,4}
- However, data on HCRU and healthcare costs among NAFLD/NASH patients are limited, especially in patients with progression to end-stage liver disease (ESLD).^{5,6}

Aim

- To evaluate the impact of NAFLD/NASH on HCRU and healthcare costs in Medicare NAFLD/NASH patients.

Study Design and Methods

- Design: this was a retrospective, observational cohort study.
- Data source: 20% US Medicare sample with fee-for-service coverage. Data maintained by the Centers for Medicare and Medicaid Services (CMS), which insures 97% of US population ≥65 years.

- Inclusion criteria:
 - NAFLD/NASH diagnosed patients (patients with ≥ 1 claim of ICD-9-CM [571.8, 571.9] or ICD-10-CM [K76.0, K75.81] diagnosis codes for NAFLD/NASH) aged ≥18 years between 1/1/2008 and 11/30/2015.
 - Among NAFLD/NASH patients, 5 study cohorts identified: (1) NAFLD/NASH only (patients with no further liver disease progression), (2) compensated cirrhosis (CC), (3) decompensated cirrhosis (DCC), (4) hepatocellular carcinoma (HCC), (5) and liver transplant (LT).
 - The first NAFLD/NASH or advanced liver disease (CC, DCC, HCC, LT) diagnosis marked the index date. Cohorts were not mutually exclusive.
 - Patients required to have ≥6 months coverage prior to each cohort index date to assess baseline comorbidities and minimum of one month of follow-up post-index for each cohort.
 - Eligible patients followed from index date of each diagnosis to earliest of 6 months, end of Medicare coverage, 31 December 2015, index for more severe disease, or death.

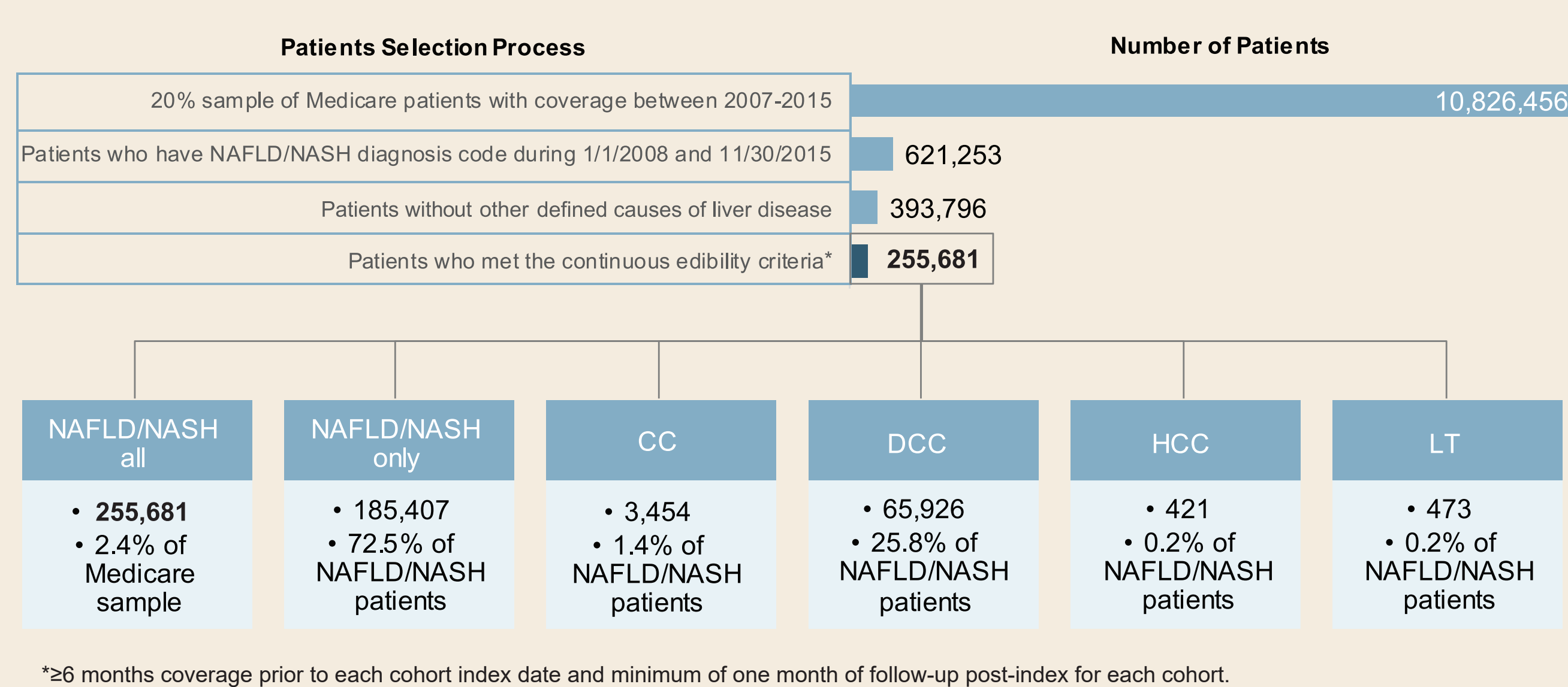
- Exclusion criteria:
 - Patients with other defined causes of liver disease were excluded (alcoholism, alcoholic liver disease, viral hepatitis, mumps hepatitis, HIV, Wilson's disease, autoimmune hepatitis, chronic toxic hepatitis, Gaucher, lysosomal acid lipase deficiency, primary biliary cholangitis, hemochromatosis and primary sclerosing cholangitis).

- Outcomes - the following were reported for each severity cohort:
 - Covariates: baseline demographics and comorbidities
 - HCRU and total all-cause healthcare costs (total visits, inpatient, outpatient, physician [visits, services, and tests ordered by physician at locations including physician office, hospital, and skilled nursing facility], and number of pharmacy fills)
 - per-member-per-month values annualized to 2015 dollars

- Statistical analysis:
 - Student's t-tests and chi-square test of independence were used to determine if mean costs and sample proportions were significantly different between cohorts.
 - Generalized linear model (GLM) to evaluate relative cost per patient adjusting for patients' demographics, comorbidities, and severity of liver disease.
 - P-values < 0.05 were deemed significant.

Results

Figure 1. Patient Selection Flowchart and Disease Severity Groups



- 2.4% of the Medicare patients in the study had NAFLD/NASH.
- At the time of first cirrhosis diagnosis, 93% were first identified with a decompensation event (DCC).

Results

Table 1. NAFLD/NASH Patient Demographics by Disease Severity

	NAFLD/NASH only (n=185,407)	CC (n=3,454)	DCC (n=65,926)	HCC (n=421)	LT (n=473)
Female, %	60.1%	63.4%*	59.5%*	53.7%*	49.5%
Age mean (SD)	66.7 (11.7)	66.7 (10.9)	70.5 (12.4)**	72.5 (9.6)**	67.0 (11.7)
Age group, %					
18-64	27.2%	30.9%*	22.8%**	15.2%**	26.4%*
65-69	33.4%	29.0%*	19.9%**	21.2%**	28.8%*
70-74	19.8%	20.4%*	20.0%**	27.1%**	23.5%*
75-79	10.8%	11.4%*	16.1%**	16.2%**	12.9%*
80+	8.9%	8.3%*	21.2%**	20.4%**	8.5%*
Race, %					
White	84.4	87.1*	86.4**	81.5**	86.5
Black	7.2	4.5*	7.3**	6.4**	6.1
Other	8.4	8.4	6.3	12.1	7.4

*P<.05 vs. NAFLD/NASH; **P<.05 vs. CC. Note: NAFLD/NASH only (patients with no further liver disease progression)

- Patients' age ranged from 66.7 for NAFLD/NASH only to 72.5 for HCC patients. DCC (70.5) and HCC (72.5) patients were significantly older than CC (66.7) and NAFLD/NASH (66.7) only patients.
- Across disease severity groups, patients were primarily white (81.5 – 87.1%) and about 60% of CC and DCC patients were female.

Table 2. NAFLD/NASH Patient Comorbidities by Disease Severity

	NAFLD/NASH only (n=185,407)	CC (n=3,454)	DCC (n=65,926)	HCC (n=421)	LT (n=473)
CVD, n (%)	120,093 (64.8)	2,539 (73.5)*	57,635 (87.4)**	349 (82.9)**	392 (82.9)**
Diabetes mellitus, n (%)	100,098 (54.0)	2,412 (69.8)*	41,806 (63.4)**	286 (67.9)*	339 (71.7)*
Dysrhythmia, n (%)	53,566 (28.9)	1,222 (35.4)*	36,707 (55.7)**	220 (52.3)**	260 (55.0)**
Hyperlipidemia, n (%)	156,254 (84.3)	2,988 (86.5)*	58,039 (88.0)**	369 (87.6)*	403 (85.2)
Hypertension, n (%)	156,116 (84.2)	3,086 (89.3)*	60,890 (92.4)**	386 (91.7)*	432 (91.3)*
Renal impairment, n (%)	39,299 (21.2)	986 (28.5)*	29,748 (45.1)**	188 (44.7)**	236 (49.9)**
Smoking, n (%)	46,792 (25.2)	1,069 (30.9)*	25,911 (39.3)**	157 (37.3)**	215 (45.5)**
Diabetes mellitus AND hypertension AND hyperlipidemia, n (%)	85,535 (46.1)	2,110 (61.1)*	38,032 (57.7)**	256 (60.8)**	292 (61.7)*
Diabetes mellitus OR hypertension OR hyperlipidemia, n (%)	176,073 (95.0)	3,329 (96.4)*	64,126 (97.3)**	411 (97.6)*	460 (97.3)*

*P<.05 vs. NAFLD/NASH; **P<.05 vs. CC.

- NAFLD/NASH patients had a high metabolic comorbidity burden across all disease severity groups: 64.8 – 87.4% with CVD, 54.0 – 71.7% with diabetes mellitus, and 84.3 – 88.0% with hyperlipidemia.
- At least 58% of patients with CC or more severe liver disease also had all three comorbidities of diabetes mellitus and hypertension and hyperlipidemia.
- DCC and CC patients had significantly higher rates of comorbidities than NAFLD/NASH only patients, including CVD, diabetes mellitus, hyperlipidemia, hypertension, and renal impairment.

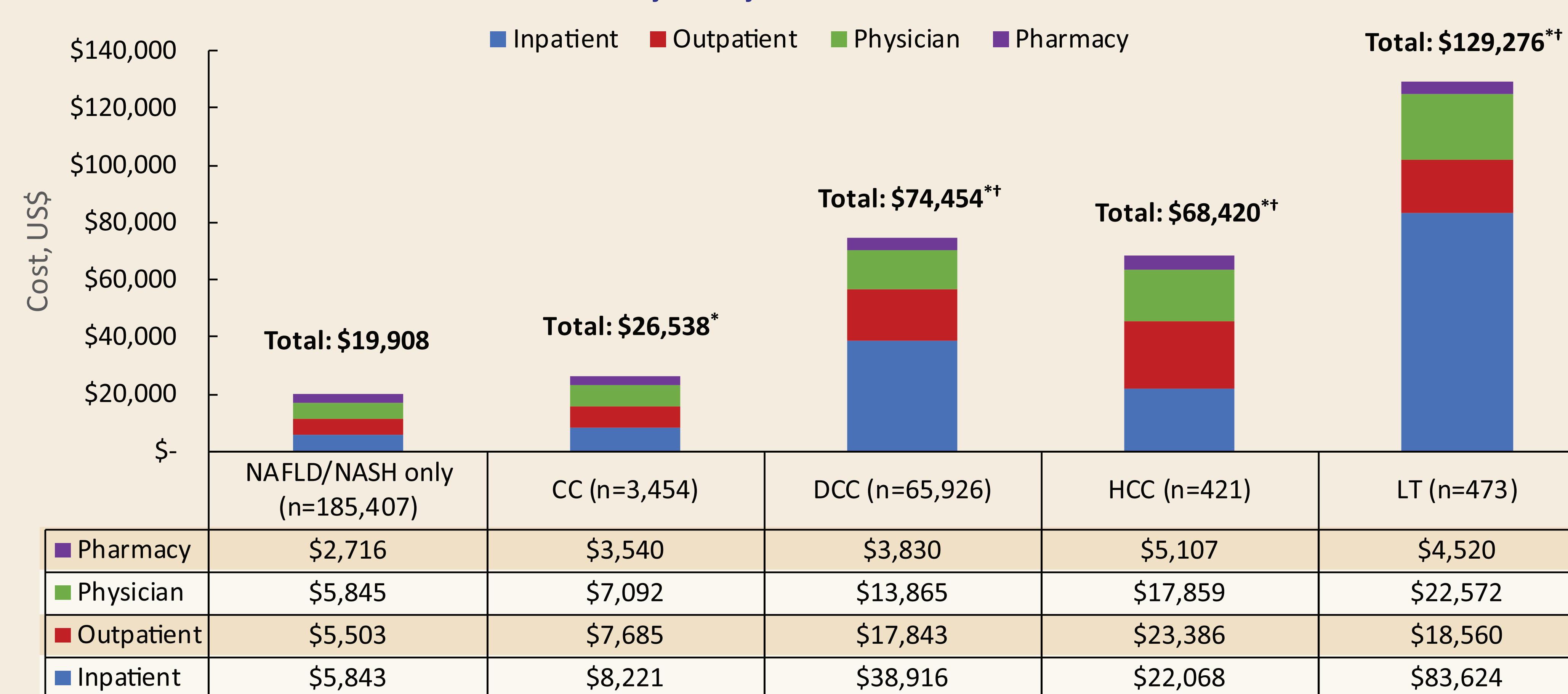
Table 3. Annual Mean All-cause Healthcare Resource Utilization for NAFLD/NASH Patients by Severity of Liver Disease

	NAFLD/NASH only (n=185,407)	CC (n=3,454)	DCC (n=65,926)	HCC (n=421)	LT (n=473)
All visits, Mean (SD)	32.1 (25.0)	37.3 (29.6)*	59.8 (54.4)**	59.3 (54.7)**	74.1 (59.7)**
Inpatient stays, Mean (SD)	0.5 (1.5)	0.7 (2.1)*	2.0 (3.8)**	1.7 (4.9)**	3.2 (4.2)**
Outpatient visits, Mean (SD)	7.3 (8.8)	8.9 (10.2)*	10.9 (12.9)**	12.5 (15.9)**	16.9 (18.9)**
Physician visits, Mean (SD)	24.2 (19.9)	27.7 (23.4)*	46.9 (48.3)**	45.1 (44.1)**	54.1 (51.2)**
Pharmacy fills, Mean (SD)	17.7 (20.6)	20.9 (23.3)*	23.9 (25.4)**	19.0 (22.8)**	24.0 (23.2)**

*P<.05 vs. NAFLD/NASH; **P<.05 vs. CC.

- Annual mean number of all healthcare visits was significantly higher in patients with more severe liver disease, rising from 32.1 for NAFLD/NASH only patients to 37.3 for CC patients, 59.8 for DCC patients, 59.3 for HCC patients, and 74.1 for patients undergoing LT. Similarly, the annual mean number of all visits was significantly higher in patients with DCC, HCC, and LT compared with CC patients.
- Annual mean hospital admissions significantly increased from 0.5 for those with NAFLD/NASH only to 0.7 for CC and 3.2 for LT.

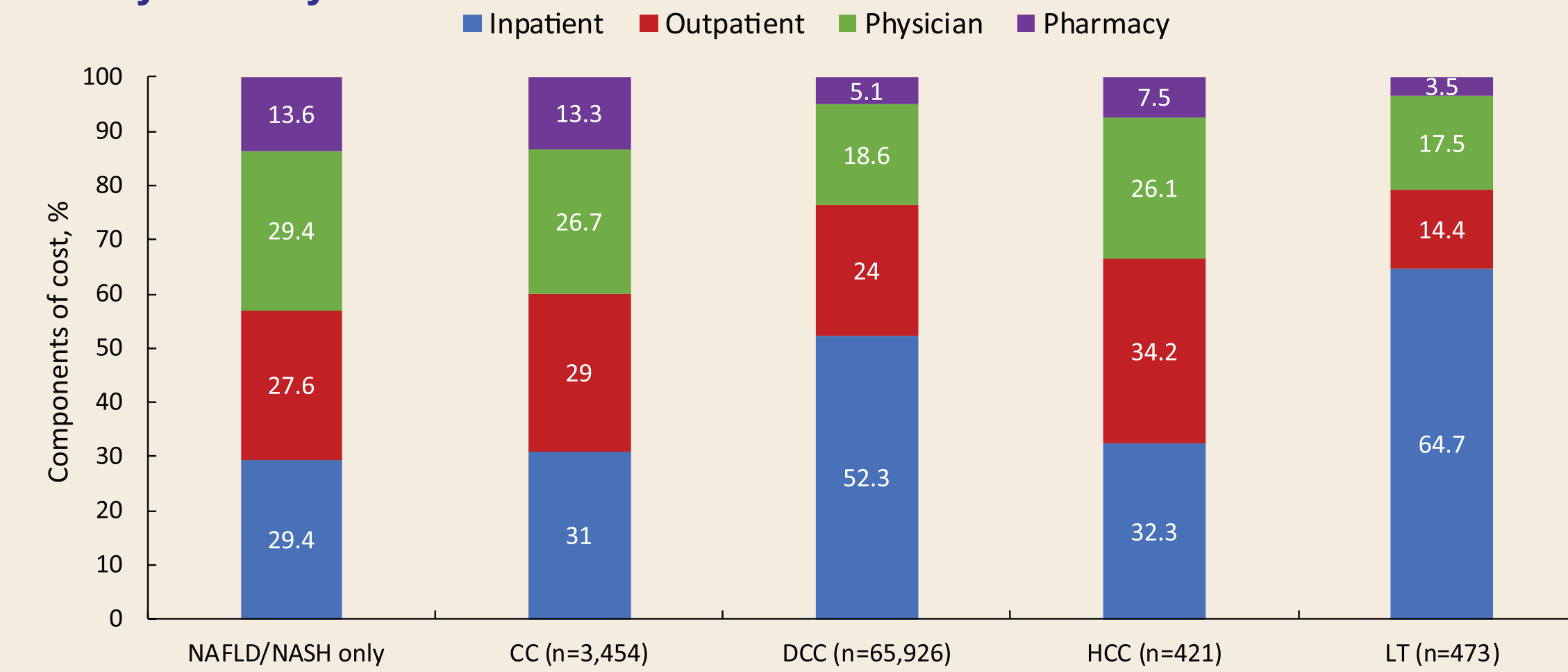
Figure 2. Annual Mean All-cause Healthcare Costs for NAFLD/NASH Patients by Severity of Liver Disease



*P<.05 vs. NAFLD/NASH; **P<.05 vs. CC. P<.05 for all comparisons of cost components for CC/DCC/HCC/LT vs. NAFLD/NASH. P<.05 for all comparisons of cost components for DCC/HCC/LT vs. CC except DCC pharmacy. CC, compensated cirrhosis; DCC, decompensated cirrhosis; HCC, hepatocellular carcinoma; LT, liver transplant; NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis; SD, standard deviation; US, United States.

- Healthcare costs significantly increased in patients with more advanced stages of liver disease, including costs associated with inpatient, outpatient, physician, and pharmacy services.
- Specifically, total annual mean healthcare costs were significantly lower for those with NAFLD/NASH only at \$19,908 compared with those with advanced liver disease at \$26,538 for CC, \$74,454 for DCC, \$68,420 for HCC, and \$129,276 for LT. In addition, total annual costs for patients with CC were significantly less than total costs for patients with DCC, HCC, and LT.

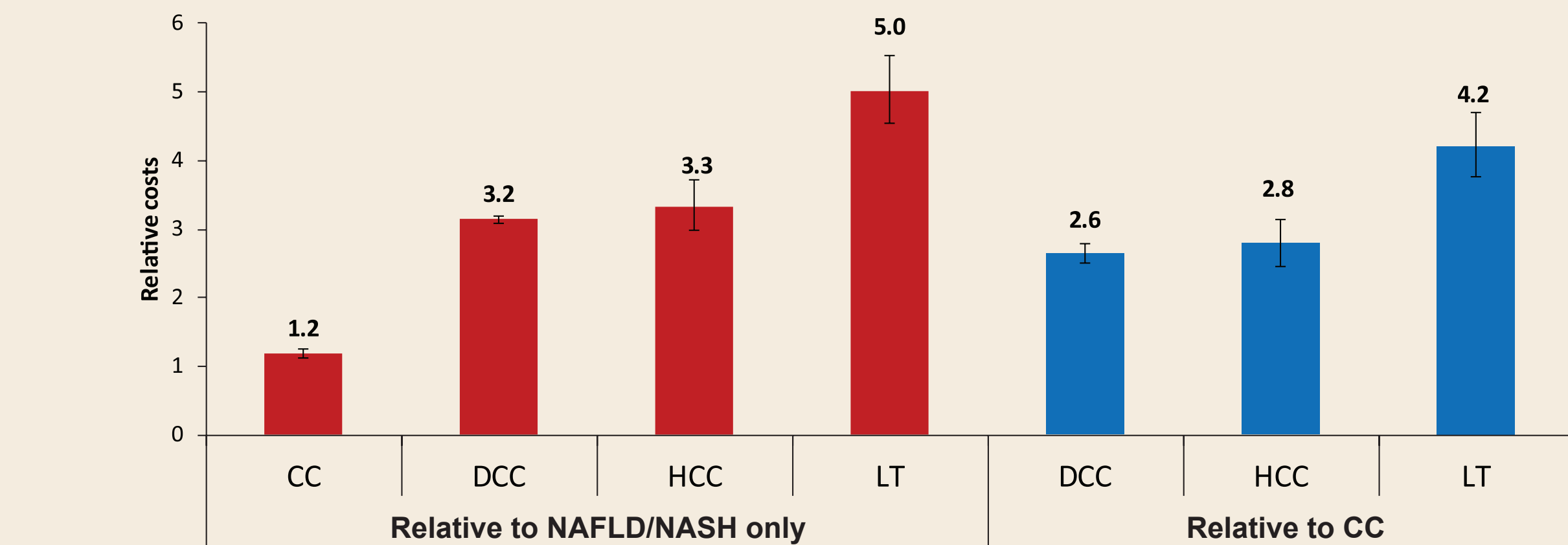
Figure 3. Components Percentages of Annual All-cause Healthcare Costs for NAFLD/NASH Patients by Severity of Liver Disease



Note: CC, compensated cirrhosis; DCC, decompensated cirrhosis; HCC, hepatocellular carcinoma; LT, liver transplant; NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis.

- Components of healthcare services contributing to total annual all-cause costs varied by severity of liver disease, with inpatient services as a key driver for the increased healthcare costs in patients with advanced liver disease.
- The largest cost component was associated with inpatient care provided to patients with DCC or LT at 52.3% of total all-cause costs among DCC patients and 64.7% for LT patients.

Figure 4. Impact of Liver Disease Severity Progression on Costs for NAFLD/NASH Patients GLM model for relative costs adjusted for patients demographics and comorbidities



All comparisons to NAFLD/NASH or CC statistically significant at p<0.001. Cox regression model adjusted for patient age, race, gender, and the comorbidities of cardiovascular disease, renal impairment, diabetes, hyperlipidemia, obesity, smoking, hyperlipidemia, and hypertension.

- After adjustment for patient demographics and comorbid health conditions, progression to advanced liver disease was associated with significantly higher costs (p<0.001).
- Specifically, patients diagnosed with CC, DCC, HCC, or LT incurred costs that were 1.2, 3.2, 3.3, and 5.0 times higher, respectively, than NAFLD/NASH only patients. There was similar pattern of significantly higher costs in patients diagnosed with DCC, HCC, or LT compared with CC.

Conclusions

- This study of Medicare NAFLD/NASH patients found:
 - In patients with advanced liver disease (CC/DCC/HCC/LT) due to NASH, at least 58% had all three of the metabolic comorbidities of diabetes mellitus and hypertension and hyperlipidemia.
 - The vast majority (93%) of patients with cirrhosis due to NASH were first identified as DCC patients.
 - HCRU and healthcare costs significantly increased in patients with more advanced stages of liver disease: CC patients had mean annual total costs of \$26,538, DCC patients had mean annual total costs exceeding \$74,000, those with HCC were over \$68,000, and mean annual total costs for LT patients totaled \$129,276, with inpatient services as a major driver of increased costs.
 - After adjustment for patient demographics and comorbidities, patients diagnosed with CC, DCC, HCC, or LT incurred costs that were 1.2, 3.2, 3.3, and 5.0 times higher, respectively, than NAFLD/NASH only patients and DCC patients had 2.6 times higher costs than CC patients.
 - Halting or reversing fibrosis due to NASH to prevent progression to CC and ESLD may decrease HCRU and associated costs.

Limitations

- NAFLD/NASH patient group may include F0-F3 patients as well as undiagnosed F4 (CC) patients due to under coding and lack of ICD code for F0-F3.
- Results are limited to the US Medicare population.
- As with any claims database, these data were subject to data coding limitations, data entry error, and misclassification of NAFLD/NASH.
- Results characterized all-cause costs rather than liver-specific costs.

Disclosures

- Study funded by Gilead Sciences, Inc.