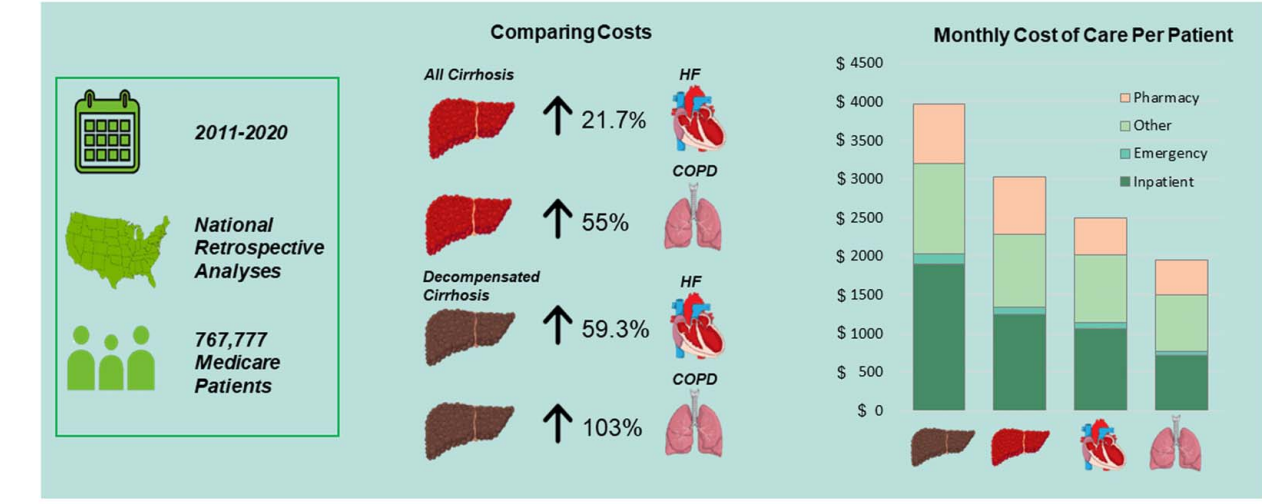
Comparing the cost of cirrhosis to other common chronic diseases: A longitudinal study in a large national insurance database

VISUAL ABSTRACT



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Comparing the cost of cirrhosis to other common chronic diseases: A longitudinal study in a large national insurance database

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Abstract

Background and Aims: Cirrhosis prevalence is increasing, yet costs associated with its chronic, complex care are poorly understood. The aim was to characterize the costs of care for patients with cirrhosis and compare them to other chronic diseases such as heart failure (HF) and chronic obstructive pulmonary disease (COPD), for which the public health burden is better recognized.

Approach and Results: Patients enrolled in Medicare Advantage plans from a large national insurer between 2011 and 2020 with cirrhosis, HF, and COPD

Abbreviations: COPD, chronic obstructive pulmonary disease; CPT, current procedure terminology; ETOH, alcohol-associated cirrhosis; HCPCS, Healthcare Common Procedure Coding System; HF, heart failure; HMO, health maintenance organization; HRRP, Hospital Readmission Reduction Program; ICD, International Classification of Diseases; MA, Medicare advantage; MASH, Metabolic dysfunction-associated steatohepatitis; MetALD, metabolic dysfunction-associated steatotic liver disease with increased alcohol intake; NIS, National inpatient sample; NUTORC, Northwestern University Transplant Outcomes Collaborative; STROBE, Strengthening the Reporting of Observational Studies in Epidemiology; VHA, Veterans health administration.

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were identified by ICD-9/-10 codes. Costs (USD) of care were calculated per patient-month and included inpatient medical, emergency medical, pharmacy, and other costs. In all, 93,308 patients with cirrhosis, 355,520 patients with HF, and 318,949 patients with COPD were analyzed. Patients with cirrhosis, HF, and COPD had a mean (SD) age of 69.6 (9.5), 75.9 (9.7), and 72.9 (9.8) years, respectively. The most frequent etiologies were metabolic dysfunction–associated steatohepatitis (37.7%) and alcohol-associated cirrhosis (22.1%). The total monthly cost of care for patients with cirrhosis, HF, and COPD was $3032.00, $2491.60, and $1955.60 respectively. The cost for patients with cirrhosis exceeded that for HF by $540.40 (21.7% higher) and COPD by $1076.30 (55.0% higher). The monthly cost of care for decompensated cirrhosis was $3969.30, which was 59.3% ($1477.70) higher than for HF and 103.0% ($1,955.60) higher than for COPD.

Conclusions: The cost of care for cirrhosis is high, significantly higher than HF and COPD. Interventions directed at optimizing care to prevent progression to cirrhosis and decompensation are likely to alleviate this public health burden.

Keywords: chronic obstructive pulmonary disease, decompensated, health policy, health sector, heart failure

INTRODUCTION

Chronic liver disease affects an estimated 112.8 million adults in the United States. It is further estimated that 2–7 million adults are affected by cirrhosis.[1–4] Importantly, the prevalence of chronic liver disease and cirrhosis are projected to increase significantly over the next decade, particularly due to metabolic dysfunction–associated steatotic liver disease (previously NAFLD) and metabolic dysfunction–associated steatotic liver disease with increased alcohol intake.[5–7] Cirrhosis often requires complex multidisciplinary care for extended periods of time, as the average survival for compensated patients is 12 years and decreases when patients decompensate.[1,8–10] Care involves specialty consultation, HCC surveillance, and often procedures or hospitalizations to manage complications.[5,11–13]

Based on expenditure data from 2016, the national cost of cirrhosis-related care was estimated to be $32.5 billion.[14] Despite this significant financial burden, cirrhosis does not garner the same attention for public health interventions as other chronic diseases, such as heart failure (HF) and chronic obstructive pulmonary disease (COPD).[15,16] In fact, little is known about the total cost per cirrhosis patient. Studies have largely focused on the cost per hospitalization, with estimates ranging from $8596 to $74,730.[17,18] Importantly, this does not account for outpatient and medication costs, which are significant components of cirrhosis care.[19,20] A recent study reported monthly costs per patient within Veterans Health Administration (VHA) to be $3358. However, it remains unclear if costs outside of a federal system, such as the VHA, are comparable.[21] Thus, the financial burden of the continuum of cirrhosis care outside of the VHA remains poorly understood. In large part, this is due to the scarcity of cirrhosis cohorts available for analyses. By contrast, the costs of other chronic diseases of comparable complexity, such as HF and COPD, have been better studied. As a result, HF and COPD have garnered national attention and incorporation into policy. Specifically, efforts such as the Hospital Readmission Reduction Program (HRRP), which reduced 30-day rehospitalization rates for HF and COPD, have not focused on cirrhosis—likely because the associated costs are not considered notable.[15,22] This study aimed to use a longitudinal administrative claims database from a large national insurer to assess the health care costs for patients with cirrhosis from 2011 to 2020. To frame the costs in a more familiar context, we compared them with HF and COPD.

METHODS

Study design

A retrospective, longitudinal cohort study was conducted between January 1, 2011, and December 31, 2020, by using claims data from the UnitedHealth Group (UHG), a large national insurer in the United States. The study

follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline for cohort studies.[23] The Northwestern University Institutional Review Board deemed this study exempt from review and waived the need for patient-informed consent. The database included deidentified medical and pharmacy claims data for enrollees. Available data included claims for all medical services and prescription medications that were submitted to the insurer for payment, patient diagnoses, and, when available, linked laboratory results. For this study, all enrollees were defined and reported as patients.

Study participants

Patients enrolled in non-health maintenance organization (HMO), Medicare Advantage (MA) plans between January 1, 2011, and December 31, 2020, were included in the analysis. Because provider fees under HMO plans/capitated contracts are not available in large insurer data sets, this study focused on patients covered under non-HMO plans (ie, non-capitated claims). Previously validated and published codes were used. Patients diagnosed with cirrhosis were defined as those with at least 1 claim specifying a validated cirrhosis code from the International Classification of Diseases, 9th Revision (ICD-9) or 10th Revision (ICD-10) (571.2, 571.5, 571.6, K70.30, K70.31, K74.0, K74.60, K74.69, K74.3, K74.4, and K74.5), in any position on the claim (Supplemental Figure S1, http://links.lww.com/HEP/J672).[24–29] Cirrhosis etiologies were defined by at least 1 claim specifying an ICD-9 or -10 code for: alcohol-associated (ETOH), metabolic dysfunction–associated steatohepatitis (MASH, previously NASH), HBV, HCV, biliary cirrhosis (eg, primary sclerosing cholangitis and primary biliary cirrhosis), cardiac cirrhosis, genetic cirrhosis (eg, hereditary hemochromatosis), and autoimmune hepatitis. Patients were included in the HCV cohort even if they had multiple etiologies, any one of which was HCV. Other etiologies were analyzed separately unless otherwise specified. Of note, MASH/NASH did not have a dedicated ICD code before October 1, 2015. For data before October 1, 2015, MASH/NASH was identified using a previously published algorithm (patients without specific cirrhosis etiology plus obesity, dyslipidemia, diabetes, and/or hypertension).[26,30] Patients were categorized into 5 mutually exclusive groups by etiology: MASH, ETOH (which includes alcohol-associated liver disease and metabolic dysfunction–associated steatotic liver disease with increased alcohol intake), HCV, biliary (primary biliary cirrhosis and primary sclerosing cholangitis), and “Other” (eg, hemochromatosis). Validated ICD-9/-10 codes were used to define comorbidities, and quantify the Charlson Comorbidity Index.[31,32]

Patients with HF and COPD

To provide a tangible comparison, costs associated with cirrhosis were compared with costs associated with HF and COPD. Patients with HF and COPD were identified by ICD-9/-10 codes as previously published.[33–37] A sample of these patients was included in the cohort as detailed in Supplemental Figure S1, http://links.lww.com/HEP/J672, and the Supplemental Appendix, http://links.lww.com/HEP/J672.

Medical and pharmacy claims

Medical claims from all covered visits and service types, including specialty, preventive, emergency, inpatient, and office-based services, were collected. Medical claims including ICD-9 and ICD-10 codes, procedure codes, Healthcare Common Procedure Coding System (HCPCS), Current Procedural Terminology (CPT) codes and modifiers, Diagnosis-related Group codes, place of service codes, provider specialty codes, revenue codes, deidentified provider and patient codes, charges, and detailed paid amounts were analyzed.

Pharmacy claims accounted for all covered prescribed medications. Pharmacy claims contain data on outpatient prescriptions including drug names, dosages, number of days supplied, deidentified prescriber or patient codes, and detailed paid amounts. A 15% rebate was accounted for nongeneric medications with in-class competition.[38]

Calculating cost

Analyses were performed at the patient-month level. Costs are reported per patient-month unless otherwise specified. For patients with cirrhosis, the index date was the earliest listed date of service on a claim with a diagnosis of cirrhosis or cirrhosis decompensation. For patients with HF and COPD, the index date was the earliest listed date of service on a claim for the appropriate corresponding diagnosis. Diagnoses on claims were defined and identified by validated inclusion ICD codes.[31,32,35,39,40] If the index code for a patient with cirrhosis indicated decompensation, the patient was considered to be decompensated at the time of inclusion.[26,30–32] To most closely represent the epidemiological reality, cirrhosis, HF, and COPD were not considered mutually exclusive. All months of coverage for all included patients under non-HMO MA plans, including and following the index month until the end of observation, were analyzed. The end of observation was defined as disenrollment, transplant, or the end of the cohort study period (December 31, 2020). In the case of a patient receiving a transplant, the entire month of transplantation was censored.

TABLE 1 Demographics of cirrhosis, HF, and COPD cohorts at inclusion

Demographics	Total cirrhosis (n = 93,308)	Always compensated (n = 30,766)	Ever decompensated (n = 62,542)	HF (n = 355,520)	HF: compensated (n = 299,246)	HF: decompensated (n = 56,274)	COPD (n = 318,949)	COPD: non-exacerbated (n = 296,105)	COPD: exacerbated (n = 22,844)
Age; mean (SD)	69.59 (9.51)	68.94 (8.95)	69.91 (9.76)	75.91 (9.70)	75.78 (9.72)	76.62 (9.59)	72.87 (9.84)	72.92 (9.86)	72.22 (9.45)
18–64 y; N (%)	22,326 (23.93)	7147 (23.23)	15,179 (24.27)	37,690 (10.60)	32,066 (10.72)	5624 (9.99)	50,760 (15.91)	46,639 (15.75)	4121 (18.04)
65–69 y; N (%)	25,214 (27.02)	9701 (31.53)	15,513 (24.80)	51,956 (14.61)	44,679 (14.93)	7277 (12.93)	65,687 (20.59)	61,028 (20.61)	4659 (20.39)
70–74 y; N (%)	18,571 (19.90)	6424 (20.88)	12,147 (19.42)	60,870 (17.12)	52,033 (17.39)	8837 (15.70)	62,495 (19.59)	57,855 (19.54)	4640 (20.31)
75–79 y; N (%)	12,761 (13.68)	3760 (12.22)	9001 (14.39)	61,035 (17.17)	51,503 (17.21)	9532 (16.94)	52,566 (16.48)	48,712 (16.45)	3854 (16.87)
80 or more years; N (%)	14,435 (15.47)	3734 (12.14)	10,701 (17.11)	143,967 (40.49)	118,963 (39.75)	25,004 (44.43)	87,438 (27.41)	81,868 (27.65)	5570 (24.38)
Female; N (%)	44,754 (47.96)	16,229 (52.75)	28,525 (45.61)	192,040 (54.02)	162,624 (54.34)	29,416 (52.27)	175,935 (55.16)	162,763 (54.97)	13,172 (57.66)
Follow-up months; mean (SD)	29.49 (24.83)	29.52 (24.25)	29.48 (25.12)	29.60 (24.75)	29.02 (24.58)	32.65 (25.41)	34.04 (27.13)	33.32 (26.77)	43.39 (29.84)
Charlson Comorbidity Index; mean (SD)	8.88 (4.47)	6.25 (3.77)	10.17 (4.21)	7.73 (3.73)	7.48 (3.70)	9.06 (3.60)	6.63 (3.99)	6.55 (3.98)	7.68 (4.04)
Comorbidities									
Prior myocardial infarction; N (%)	20,921 (22.42)	3898 (12.67)	17,023 (27.22)	121,913 (34.29)	93,648 (31.29)	28,265 (50.23)	76,139 (23.87)	68,038 (22.98)	8101 (35.46)
CHF; N (%)	43,541 (46.66)	8089 (26.29)	35,452 (56.69)	355,416 (99.97)	299,143 (99.97)	56,273 (100.00)	148,420 (46.53)	132,650 (44.80)	15,770 (69.03)
PVD; N (%)	46,839 (50.20)	12,046 (39.15)	34,793 (55.63)	225,002 (63.29)	183,917 (61.46)	41,085 (73.01)	174,150 (54.60)	159,610 (53.90)	14,540 (63.65)
CVD; N (%)	36,133 (38.72)	8459 (27.49)	27,674 (44.25)	178,766 (50.28)	146,882 (49.08)	31,884 (56.66)	134,999 (42.33)	123,988 (41.87)	11,011 (48.20)
Dementia; N (%)	15,065 (16.15)	2984 (9.70)	12,081 (19.32)	97,097 (27.31)	81,838 (27.35)	15,259 (27.12)	64,087 (20.09)	59,207 (20.00)	4880 (21.36)
COPD; N (%)	52,855 (56.65)	14,660 (47.65)	38,195 (61.07)	221,948 (62.43)	178,618 (59.69)	43,330 (77.00)	318,949 (100.00)	296,105 (100.00)	22,844 (100.00)
Rheumatological disease; N (%)	10,446 (11.20)	3384 (11.00)	7062 (11.29)	38,636 (10.87)	31,944 (10.67)	6692 (11.89)	34,851 (10.93)	31,947 (10.79)	2904 (12.71)
PUD; N (%)	14,135 (15.15)	2142 (6.96)	11,993 (19.18)	30,993 (8.72)	24,796 (8.29)	6197 (11.01)	25,571 (8.02)	23,160 (7.82)	2411 (10.55)
Mild liver disease; N (%)	93,304 (100.00)	30,766 (100.00)	62,538 (99.99)	70,406 (19.80)	57,651 (19.27)	12,755 (22.67)	66,966 (21.00)	61,509 (20.77)	5457 (23.89)

Diabetes; N (%)	53,795 (57.65)	15,507 (50.40)	38,288 (61.22)	204,989 (57.66)	168,187 (56.20)	36,802 (65.40)	155,181 (48.65)	142,622 (48.17)	12,559 (54.98)
Diabetes with end organ failure; N (%)	37,903 (40.62)	9985 (32.45)	27,918 (44.64)	142,789 (40.16)	113,459 (37.91)	29,330 (52.12)	97,202 (30.48)	89,243 (30.14)	7959 (34.84)
Hemiplegia; N (%)	5774 (6.19)	1163 (3.78)	4611 (7.37)	30,925 (8.70)	25,906 (8.66)	5019 (8.92)	21,187 (6.64)	19,569 (6.61)	1618 (7.08)
Moderate or severe ESRD; N (%)	43,370 (46.48)	8992 (29.23)	34,378 (54.97)	195,572 (55.01)	152,822 (51.07)	42,750 (75.97)	127,817 (40.07)	117,044 (39.53)	10,773 (47.16)
Lymphoma; N (%)	31,042 (33.27)	7812 (25.39)	23,230 (37.14)	96,463 (27.13)	80,225 (26.81)	16,238 (28.86)	89,615 (28.10)	82,429 (27.84)	7186 (31.46)
Moderate-severe liver disease; N (%)	41,909 (44.91)	6139 (19.95)	35,770 (57.19)	10,542 (2.97)	7981 (2.67)	2561 (4.55)	7703 (2.42)	7073 (2.39)	630 (2.76)
Metastatic solid tumor; N (%)	10,438 (11.19)	1899 (6.17)	8539 (13.65)	27,284 (7.67)	23,064 (7.71)	4220 (7.50)	28,173 (8.83)	25,846 (8.73)	2327 (10.19)
AIDS; N (%)	1111 (1.19)	406 (1.32)	705 (1.13)	1444 (0.41)	1221 (0.41)	223 (0.40)	1536 (0.48)	1425 (0.48)	111 (0.49)
Etiology									
NASH; N (%)	35,161 (37.68)	12,270 (39.88)	22,891 (36.60)	—	—	—	—	—	—
ETOH; N (%)	20,654 (22.14)	4937 (16.05)	15,717 (25.13)	—	—	—	—	—	—
HCV; N (%)	20,174 (21.62)	7512 (24.42)	12,662 (20.25)	—	—	—	—	—	—
Other; N (%)	13,290 (14.24%)	3614 (11.75)	9676 (15.47)	—	—	—	—	—	—
Biliary disease; N (%)	4029 (4.32)	2433 (7.91)	1596 (2.55)	—	—	—	—	—	—
Complications of decompensation									
Ascites; N (%)	47,609 (51.02)	—	47,609 (76.12)	—	—	—	—	—	—
HE; N (%)	36,158 (38.75)	—	36,158 (57.81)	—	—	—	—	—	—
VB; N (%)	31,180 (33.42)	—	31,180 (49.85)	—	—	—	—	—	—
HRS; N (%)	4209 (4.51)	—	4209 (6.73)	—	—	—	—	—	—
SBP; N (%)	5359 (5.74)	—	5359 (8.57)	—	—	—	—	—	—
HPS; N (%)	334 (0.36)	—	334 (0.53)	—	—	—	—	—	—
HCC; N (%)	8167 (8.75)	—	6543 (10.46)	—	—	—	—	—	—
TIPS; N (%)	1038 (1.11)	—	1028 (1.64)	—	—	—	—	—	—

Note: Baseline demographics by cirrhosis (total, compensated, and decompensated), HF (total, compensated, and decompensated), and COPD (total, non-exacerbated, and exacerbated).
Abbreviations: CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CVD, cerebrovascular disease; ESRD, end-stage renal disease; ETOH, alcohol-associated cirrhosis; HF, heart failure; HPS, hepatopulmonary syndrome; HRS, hepatorenal syndrome; MASH, metabolic dysfunction–associated steatohepatitis; PUD, peptic ulcer disease; PVD, peripheral vascular disease; SBP, spontaneous bacterial peritonitis; VB, variceal bleeding.

Months of coverage were subcategorized into compensated and decompensated cirrhosis patient-months. The date of decompensation was defined as the date of service on the first claim under any plan that listed an ICD or CPT code for a decompensation event (ie, ascites, spontaneous bacterial peritonitis, HE, variceal bleeding, hepatorenal syndrome, or hepatopulmonary syndrome) (see the Supplemental Appendix, http://links.lww.com/HEP/J672).[25,28,41,42] Patients were considered to have decompensated cirrhosis starting from and including the month of the decompensation date until the end of observation. The total number of patient-months with compensated cirrhosis was calculated from the index month until the decompensation month. Inpatient costs were calculated by identifying claims between admission and discharge. The same method of categorizing months of coverage was applied to decompensated HF and exacerbated COPD. Decompensated HF and exacerbated COPD were defined as inpatient admissions with the corresponding condition as the primary diagnosis.

Statistical analysis

Cost was defined as the total amount paid by the insurer and patient, taking the health care sector cost perspective. These data were analyzed and reported over time using mean costs in a specific calendar month during the study period. Data reported per patient-year were estimated by multiplying patient-month data by 12. Following common practice, denied service lines were excluded from cost calculation. Average costs were adjusted for inflation to 2021 US dollars using the Bureau of Labor Statistics consumer price index to adjust for inflation between 2011 and 2020. Mean costs were reported with corresponding standard deviations ($\pm$SD). Comparisons between relevant subgroups were performed using unequal variance, 2-sided Student *t* tests. Contained in the Supplemental Appendix, http://links.lww.com/HEP/J672, is a discussion of the process of generating the patient data and the assumptions underlying the standard inference methods. To identify predictors of increased cost, a multivariable linear regression model of costs for patients with cirrhosis was performed. The outcome of interest was the cost per patient per month, which was modeled continuously. The reference group was non-female patients with ETOH. All statistical analyses were performed using Stata 14.1.

RESULTS

Demographics

The cohort included 93,308 patients with cirrhosis, with a mean age of 69.6 years and 48.0% were female (Supplemental Figure S1, http://links.lww.com/HEP/J672, Supplemental Figure S3, http://links.lww.com/HEP/J672). Cirrhosis etiologies were MASH for 37.7% (N = 35,161), ETOH for 22.1% (N = 20,654), HCV for 21.6% (N = 20,174), biliary disease for 4.3% (N = 4029), and Other for 14.2% (N = 13,290). Among the patients, 30,766 (33.0%) had compensated cirrhosis throughout the observation period. There were 62,542 (67.0%) patients who had decompensated cirrhosis at inclusion or became decompensated during observation. The mean Charlson Comorbidity Index was 8.9, and the mean follow-up time was 29.5 months. Compensated patients were more likely to have MASH (39.9% vs. 36.6%), HCV (24.4% vs. 20.3%), biliary (7.9% vs. 2.6%), and less likely to have ETOH (16.1% vs. 25.1%) compared to patients who ever decompensated. Among decompensation events, ascites (52.7%, N = 49,181), HE (40.0%, N = 37,295), and variceal bleeding (34.4%, N = 32,055) were most common. Among all patients with cirrhosis, 8167 (8.8%) had HCC. There were 1038 (1.1%) patients who underwent TIPS placement (Table 1). In comparison, 355,520 patients with HF, and 318,949 patients with COPD were included. Patients with HF and COPD were, on average, 6.3 and 3.3 years older, were more frequently female (54.0% and 55.2%), with lower Charlson Comorbidity Indices (7.7 and 6.6), and with longer follow-up times (29.6 and 34.0 mo), respectively (Table 1) (Supplemental Table S1, http://links.lww.com/HEP/J672, Supplemental Figure S4, http://links.lww.com/HEP/J672).

Costs

Costs are reported in patient-months and rounded to the nearest $0.10 unless otherwise specified. Total costs for cirrhosis were $3032.00 per patient-month overall, which includes $1250.70 (41.3%) for inpatient medical costs, $87.60 (2.9%) for emergency medical costs, $950.60 (31.4%) for other medical costs, and $743.10 (24.5%) for outpatient pharmacy costs. Total costs for patient-months pertaining to decompensated cirrhosis were $3969.30, while the total costs for patient-months pertaining to compensated cirrhosis were $1749.60 (a difference of $2219.70). For compensated patient-months versus decompensated patient-months, medical costs accounted for 59.8% and 80.5% of the total cost, respectively. Pharmacy costs accounted for the remainder of the total cost for each subgroup. The greatest contribution to medical costs was Other (neither emergency nor inpatient) (37.2%) for compensated patient-months and inpatient medical (48.0%) costs for decompensated patient-months, respectively (Table 2) (Supplemental Table S2, http://links.lww.com/HEP/J672, Supplemental Table S3, http://links.lww.com/HEP/J672, Supplemental Figure S4, http://links.lww.com/HEP/J672, Supplemental Figure S5, http://links.

TABLE 2 Costs of cirrhosis, HF, and COPD cohorts per patient-month

Costs	Total cirrhosis	Compensated patient-months	Decompensated patient-months	HF	HF: compensated patient-months	HF: decompensated patient-months	COPD	COPD: non-exacerbated patient-months	COPD: exacerbated patient-months
Total costs; mean (SD), % of total cost	3031.96 (8825.46), 100.00%	1749.64 (5103.86), 100.00%	3969.28 (10,663.03), 100.00%	2491.60 (7713.32), 100.00%	2257.61 (7193.61), 100.00%	4247.38 (10,683.29), 100.00%	1955.64 (6162.93), 100.00%	1875.68 (6056.08), 100.00%	3220.47 (7545.44), 100.00%
Medical costs; mean (SD), % of total cost	2288.88 (8237.97), 75.49%	1046.61 (3879.25), 59.82%	3196.92 (10,223.35), 80.54%	2024.34 (7498.82), 81.25%	1798.81 (6969.27), 79.68%	3716.60 (10,510.75), 87.50%	1497.50 (5901.62), 76.57%	1427.51 (5792.28), 76.11%	2604.65 (7331.57), 80.88%
Inpatient medical costs; mean (SD), % of total cost	1250.71 (7580.08), 41.25%	355.75 (3079.93), 20.33%	1904.88 (9566.04), 47.99%	1060.84 (6888.63), 42.58%	893.83 (6376.22), 39.59%	2313.98 (9832.35), 54.48%	713.86 (5329.28), 36.50%	659.11 (5220.99), 35.14%	1580.03 (6758.47), 49.06%
Emergency medical costs; mean (SD), % of total cost	87.55 (404.14), 2.89%	39.82 (236.79), 2.28%	122.45 (488.72), 3.08%	74.53 (353.11), 2.99%	66.99 (333.00), 2.97%	131.14 (473.90), 3.09%	58.45 (306.27), 2.99%	54.48 (295.16), 2.90%	121.26 (441.86), 3.77%
Other medical costs; mean (SD), % of total cost	950.62 (2821.84), 31.35%	651.03 (2174.72), 37.21%	1169.60 (3195.73), 29.47%	888.97 (2618.74), 35.68%	837.99 (2511.32), 37.12%	1271.48 (3290.43), 29.94%	725.18 (2189.93), 37.08%	713.92 (2179.85), 38.06%	903.36 (2336.41), 28.05%
Pharmacy costs; mean (SD), % of total cost	743.08 (3109.43), 24.51%	703.03 (3260.67), 40.18%	772.35 (2993.71), 19.46%	467.26 (1669.59), 18.75%	458.79 (1653.76), 20.32%	530.79 (1782.61), 12.50%	458.15 (1637.77), 23.43%	448.18 (1637.13), 23.89%	615.82 (1639.89), 19.12%

Note: The paneled table shows the total, medical, and pharmacy costs for patients with cirrhosis, HF, and COPD. Supplemental Table S1, http://links.lww.com/HEP/J672, also shows these same costs for compensated and decompensated cirrhosis patient-months, compensated and decompensated HF patient-months, and finally non-exacerbated and exacerbated COPD patient-months.
Abbreviations: COPD, chronic obstructive pulmonary disease; HF, heart failure.

TABLE 3 Costs of cirrhosis by etiology and decompensation event per patient-month

	Total cirrhosis	Compensated patient-months	Decompensated patient-months
Etiology			
HCV; mean (SD)	3352.68 (9282.67)	2249.79 (6845.82)	4351.07 (10938.42)
Other; mean (SD)	3215.78 (9559.23)	1560.82 (4304.69)	4210.76 (11512.61)
MASH; mean (SD)	3116.08 (8985.56)	1738.99 (4600.45)	4104.12 (11006.77)
ETOH; mean (SD)	2744.58 (8147.67)	1454.15 (4184.15)	3398.51 (9480.62)
Biliary disease; mean (SD)	1720.25 (5225.48)	1210.42 (3445.68)	2911.46 (7831.95)
Complications of cirrhosis			
SBP; mean (SD)	5266.06 (14,682.96)	—	5682.78 (15,415.83)
HRS; mean (SD)	4946.13 (12,821.75)	—	5631.07 (13,843.80)
TIPS; mean (SD)	4662.32 (11,015.16)	1485.07 (4554.62)	5123.90 (11,587.43)
HPS; mean (SD)	4494.59 (10,428.81)	—	4948.17 (11,053.28)
HE; mean (SD)	4246.66 (11,128.67)	—	4661.27 (11,895.96)
Ascites; mean (SD)	4020.89 (10,897.75)	—	4401.86 (11,637.70)
HCC; mean (SD)	3936.16 (9376.50)	2609.26 (6952.43)	4697.32 (10,442.02)
VB; mean (SD)	3695.95 (10,202.73)	—	3978.45 (10,788.09)

Note: Mean total cost for cirrhosis per patient-month by etiology and decompensating events and complications/interventions.
Abbreviations: ETOH, alcohol-associated cirrhosis; HPS, hepatopulmonary syndrome; HRS, hepatorenal syndrome; MASH, metabolic dysfunction–associated steatohepatitis; SBP, spontaneous bacterial peritonitis; VB, variceal bleeding.

lww.com/HEP/J672). By etiology, patients with HCV had the highest total cost ($3352.70). By complication, patients who were diagnosed with spontaneous bacterial peritonitis incurred the highest total cost ($5266.10) (Table 3).

For HF, the total cost was $2491.60 (medical: $2024.30 and pharmaceutical: $467.30), and for COPD, the total cost was $1955.60 (medical: $1497.50 and pharmaceutical: $458.20) per patient-month. Compared to patients with HF, patients with cirrhosis had 21.7% higher overall costs by $540.40 per patient-month, 13.1% higher medical costs by $264.50 per patient-month, and 59.0% higher pharmaceutical costs by $275.80 per patient-month. Compared to patients with COPD, patients with cirrhosis had 55.0% higher costs overall by $1076.30 per patient-month, with 52.8% higher medical costs by $791.40 per patient-month, and 62.2% higher pharmaceutical costs by $284.90 per patient-month. Across all patients with cirrhosis and HF, inpatient costs contributed the most toward total cost. Other costs contributed the most toward the total cost for COPD ($725.2, 37.1%); however, this was followed closely by inpatient costs ($713.9, 36.5%) (Table 2).

For patients with cirrhosis (stratified by compensated patient-months and decompensated patient-months), HF, and COPD, average monthly total (Figure 1A), medical (Figure 1B), inpatient (Figure 1C), and pharmaceutical (Figure 1D) costs were graphed by year. These graphs include patients only diagnosed in those same years. Total, medical (including inpatient), and pharmaceutical costs were highest for decompensated patient-months for every year between 2011 and 2020, followed by all patients with cirrhosis and compensated patient-months (Figures 1A–D). Medical costs were consistently lowest for COPD and compensated cirrhosis patient-months (Figures 1B, C). Costs generally increased from 2011 to 2020, with the total cost of cirrhosis, HF, and COPD rising by 29.9%, 25.2%, and 27.9%, respectively. Notably, decompensated patient-months had the greatest increase, rising by 35.4%. Pharmacy costs rose 78.0% for cirrhosis, 69.4% for HF, and 71.5% for COPD. Inpatient medical costs increased for all conditions from 2011 to 2012 and continued to rise for decompensated cirrhosis patient-months. Inpatient medical costs were relatively stable from 2012 to 2020 for other subgroups. Between 2011 and 2020, total costs for MASH and HCV were the highest, with biliary cirrhosis consistently being the least costly (Figure 2A). Notably, pharmaceutical costs for all patients with cirrhosis increased substantially from 2013 to 2015 (Figure 1D). A similar pattern is seen for HCV patient total and pharmaceutical costs (Figures 2A, B). After the year of diagnosis, costs decreased across all conditions (Figure 3). Over follow-up time, the cost for cirrhosis decreased by $897 (32.5%), compensated cirrhosis decreased by $670 (44.1%), and decompensated cirrhosis by $1067 (31.4%). While the costs for HF and COPD decreased by $412 (18.8%) and $298 (16.2%), respectively, cirrhosis was still the most costly condition after 8 years of follow-up (Figure 3).

Annualized costs for cirrhosis, HF, and COPD are shown in Figure 4. The percentage of patient-months contributing to these groups is shown, with more patient-months attributed to decompensated cirrhosis (57.8%) than compensated (42.2%). A small proportion of patient-months contributed to costs for decompensated HF (11.8%) and exacerbated COPD (6.0%). Similarly, there was a small proportion of patient-

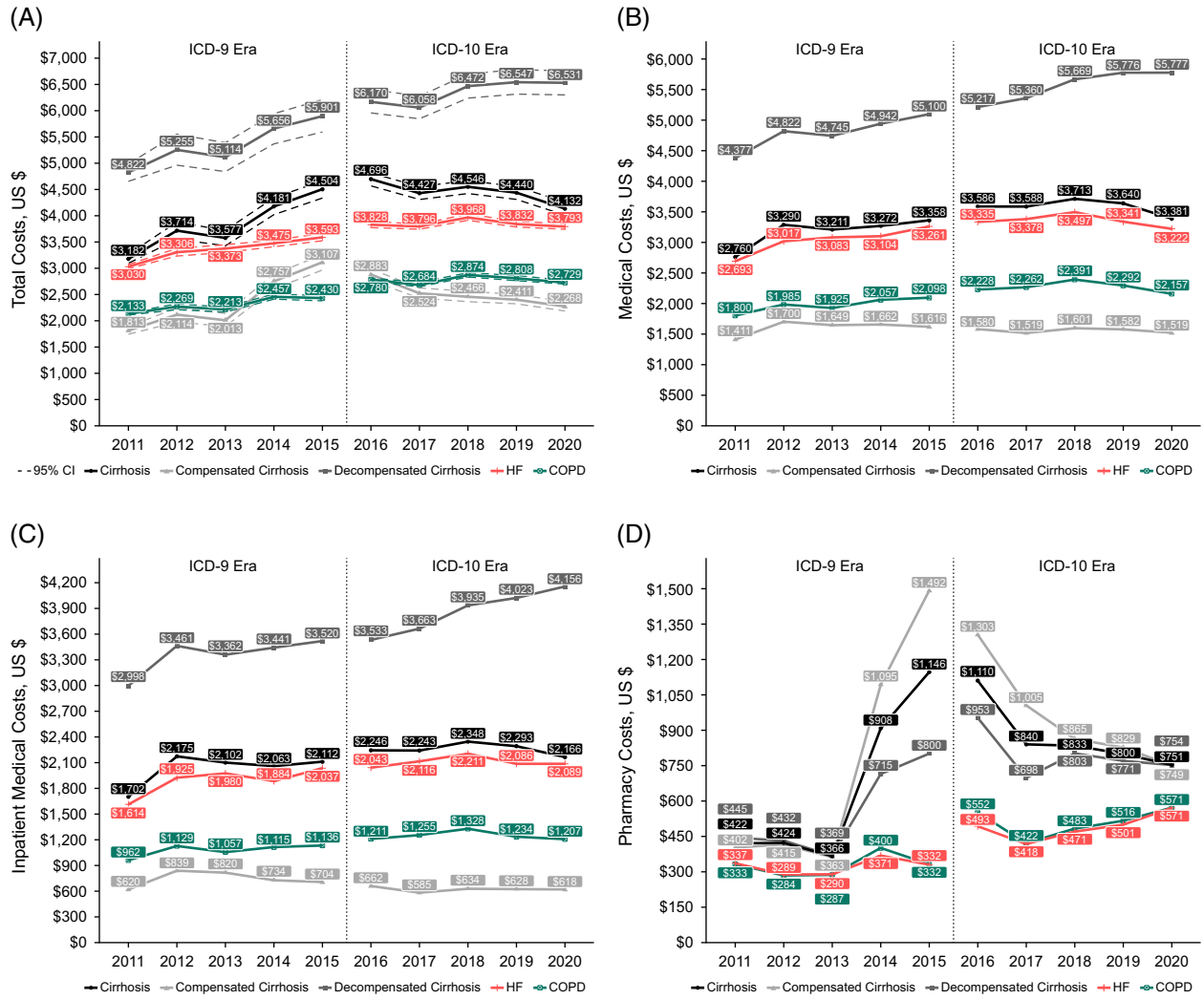


FIGURE 1 (A) Mean total cost per patient-month by year. (B) Mean medical cost per patient-month by year. (C) Mean inpatient medical cost per patient-month by year. (D) Mean pharmacy cost per patient-month by year. *Note*: (A–D) Cost per patient-month stratified by cirrhosis (total, compensated, and decompensated), HF, and COPD. Total costs per patient-month (A), medical costs (B), inpatient medical costs (C), and pharmacy costs (1D) are shown by year (diagnosed in that same year). Abbreviations: COPD, chronic obstructive pulmonary disease; HF, heart failure.

months pertaining to patients hospitalized for cirrhosis. The annualized cost for cirrhosis per patient was $36,384 (inpatient medical $15,009, emergency: $1051, and pharmaceutical: $8917). Compared to all patients with cirrhosis, the annualized cost was 42% lower for patients with compensated cirrhosis ($20,996) and 31% higher for patients with decompensated cirrhosis ($47,631). By comparison to patients with cirrhosis, annualized costs were 18% lower for patients with HF ($29,899 vs. $36,384) and 35% lower for patients with COPD ($23,469 vs. $36,384) (Figure 4). While patient-months pertaining to decompensated HF ($50,969) and exacerbated COPD ($38,646) were more costly than decompensated cirrhosis ($47,631), the costliest subgroup was patients with cirrhosis who were hospitalized ($63,992) (Figure 4).

Multivariable linear regression analysis

While peptic ulcer disease and uncomplicated diabetes were not associated with a significant difference in total cost, the presence of any other comorbidity did increase cost. While adjusting for other covariates, AIDS was associated with the greatest increase in total cost ($2282.80), followed by decompensation ($1609.50) (Figure 5A). Of note, comorbid HF was associated with a greater increase in cost ($888.50) than COPD ($255.30) (Figure 5A). Decompensation was associated with the greatest increase in medical cost ($1583.20), followed by the presence of a metastatic solid tumor ($1089.40) and HF ($791.90) (Figure 5B). For pharmacy costs, AIDS ($2110.3) and HCV were associated with the greatest increases ($663.80) (Figure 5C).

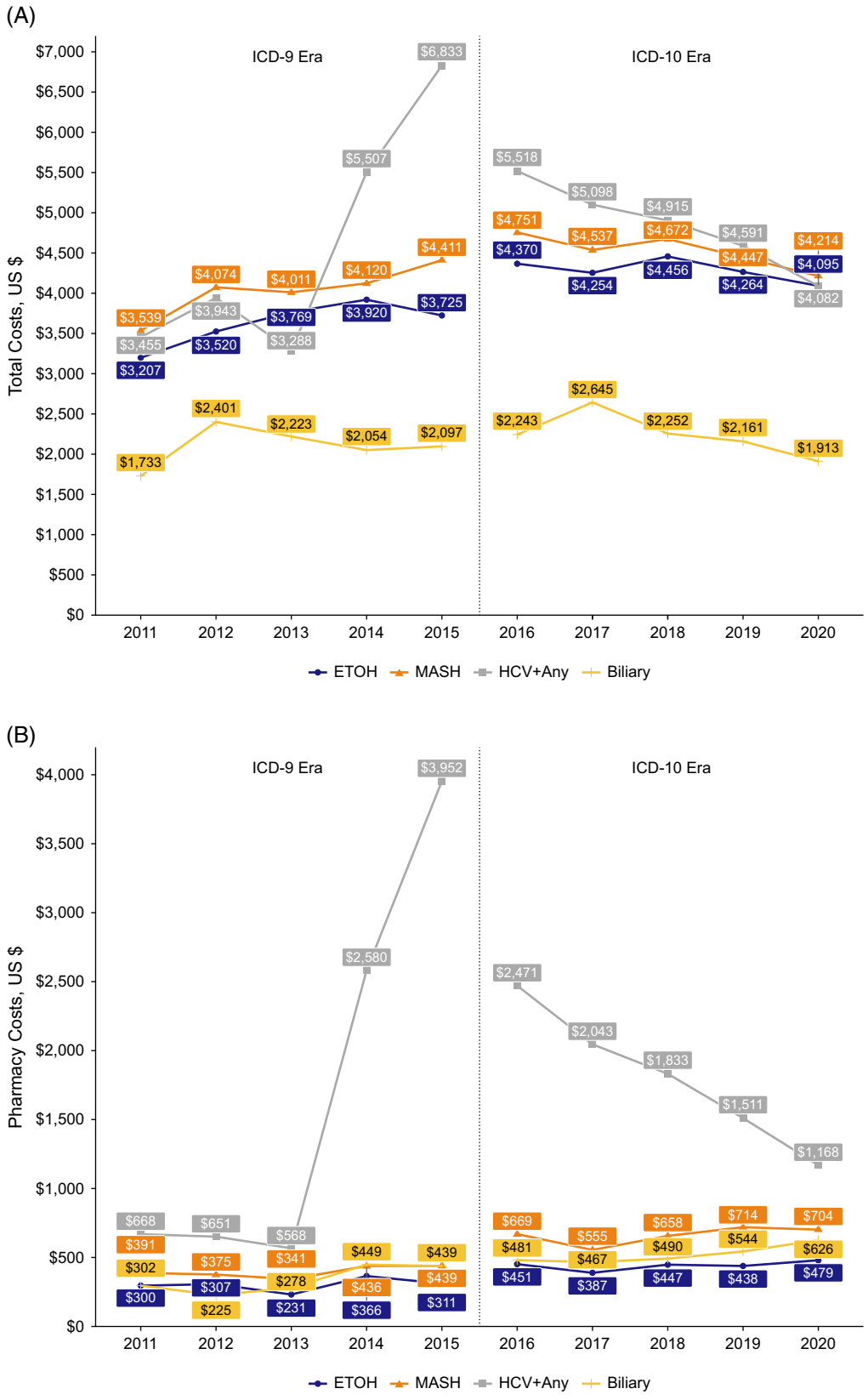


FIGURE 2 (A) Mean total cost per patient-month by cirrhosis etiology. (B) Mean pharmacy cost per patient-month by cirrhosis etiology. *Note*: (A, B) Mean total cost (A) and pharmacy cost (B) per patient-month by year (only for patients diagnosed in that same year). Abbreviations: ETOH, alcohol-associated cirrhosis; MASH, metabolic dysfunction–associated steatohepatitis

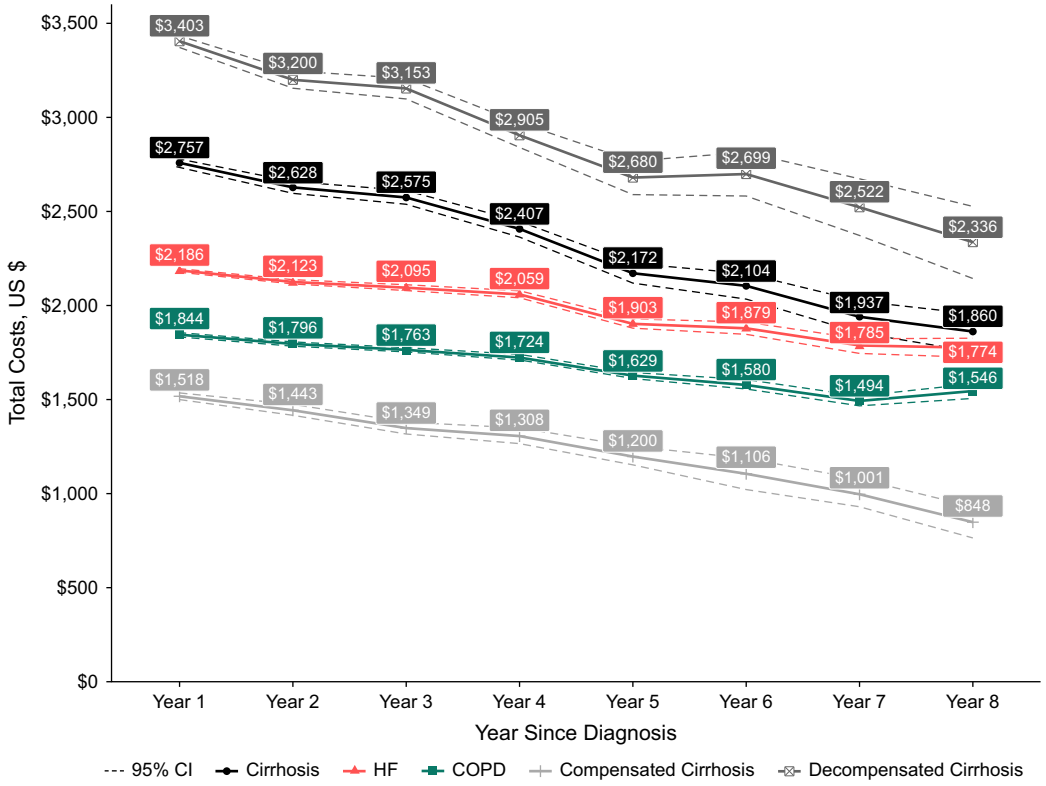


FIGURE 3 Total cost per month by follow-up time for patients with cirrhosis, HF, and COPD. *Note*: Cost per patient-month stratified by cirrhosis (total, compensated, and decompensated), HF, and COPD. Total costs are shown by number of years of follow-up. Abbreviations: COPD, chronic obstructive pulmonary disease; HF, heart failure.

DISCUSSION

The cost of care of non-HMO MA-covered patients with decompensated cirrhosis was $3969.3 per patient-month ($47,631 per patient-year), with compensated cirrhosis was $1749.6 per patient-month ($20,996 per patient-year), and for all patients with cirrhosis was $3032.00 per patient-month ($36,384 per patient-year) (Table 2, Figure 4). This is significantly higher than the per-patient cost of care for HF or COPD, surpassing them by 21.7% and 55.0%, respectively. As anticipated, decompensated cirrhosis patient-months had a high cost of care, exceeding HF by 45.5% and COPD by 85.3%. This study not only highlights the high costs associated with medical care ($27,467 per patient-year) for cirrhosis, but also the high cost associated with medications ($8917 per patient-year) (Figure 4). Of note, patients with cirrhosis had a higher Charlson comorbidity index than patients with HF or COPD (Table 1). The linear regression analysis demonstrated that a greater number of comorbid conditions were associated with increased costs (Figure 5). This highlights the need for more complex and specialized care for patients with cirrhosis.

Importantly, our study takes into account all aspects of care—inpatient, outpatient, and costs of pharmaceuticals.[43] Our findings also support recently published work by Kanwal and colleagues, which reported the adjusted cost of care for patients with cirrhosis within the VHA. This is of particular interest, as the VHA is a closed system that serves patients with a different demographic profile, pattern of disease, and access to specialized care than privately insured, non-VHA patients. Yet, the reported annual costs were very similar, namely $36,383.50 per patient-year in this study and $35,029 following the first year after cirrhosis diagnosis within the VHA.[21] The fact that both studies have reached similar findings, despite significant differences in the cirrhosis cohorts studied and the manner in which cost is computed, emphasizes the magnitude of costs associated with cirrhosis.

In characterizing the cost of cirrhosis, the costs of HF and COPD were characterized for comparison. To provide balanced comparisons for decompensated cirrhosis, costs were also calculated for decompensated HF and exacerbated COPD (Figure 4). The annualized costs for patients with decompensated HF ($50,969) and exacerbated COPD ($38,646) were high, with decompensated HF exceeding the costs for patients with decompensated cirrhosis ($47,631). This was likely due to decompensated HF and COPD exacerbations being defined and identified based on inpatient admissions, which contribute considerably toward total cost. To provide a more direct comparison, the annualized costs for patients hospitalized for cirrhosis were calculated. It was found that the cost for patients with cirrhosis who were hospitalized was

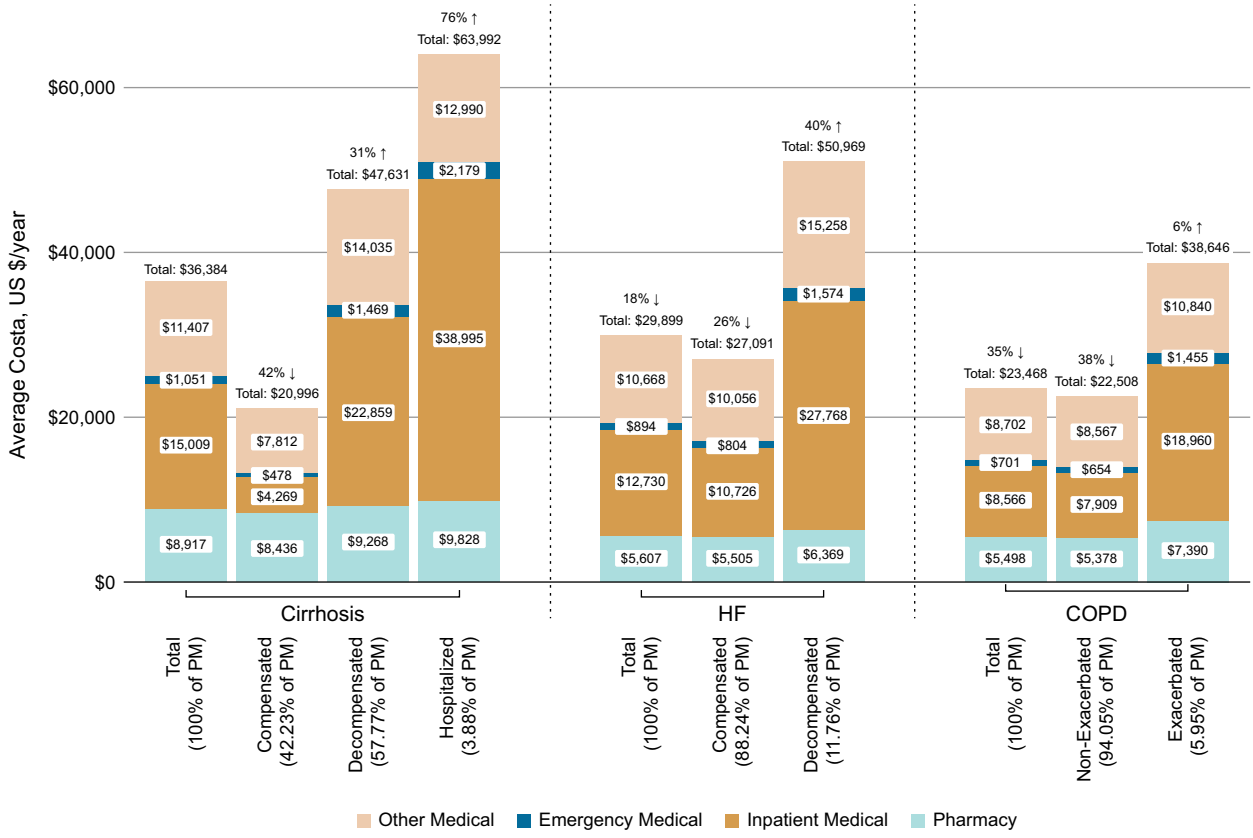


FIGURE 4 Annualized total costs and components of costs for cirrhosis, HF, and COPD. *Note*: Annualized costs per patient by pharmacy cost, inpatient medical cost, emergency cost, and other medical costs. Cirrhosis: total, compensated, decompensated, and hospitalized by patient-months (PM); heart failure: total, compensated, and decompensated; COPD: total, non-exacerbated, and exacerbated. Abbreviations: COPD, chronic obstructive pulmonary disease; HF, heart failure.

$63,992 per patient-year, even greater than decompensated HF or exacerbated COPD.

Decompensated patient-months accounted for over twice the cost compared to compensated patient-months ($3969.30 versus $1749.60). The greatest proportion of the total cost for decompensated patient-months stems from inpatient medical costs ($1904.90, 48.0%), representing longer, more medically complex hospitalizations for patients who are decompensated (Table 2) (Supplemental Table S2, http://links.lww.com/HEP/J672, Supplemental Table S3, http://links.lww.com/HEP/J672). These findings corroborate those of other studies focusing only on costs of hospitalization.[44–46] Using the National Inpatient Sample (NIS) cohort, annual costs for patients with compensated and decompensated cirrhosis were reported to be $2.80 billion and $4.57 billion, respectively.[44] Similarly, Gordon et al[45,46] found that patients with decompensated cirrhosis had more than a 3-fold increase in cost compared to those with mild disease. Hence, early diagnosis and optimal care early in the course of disease are likely to reduce associated costs. An example of improved disease management is bariatric surgery for patients with compensated MASH cirrhosis. This has shown to have an incremental cost-effectiveness ratio of $66,119 per quality-adjusted life-year by slowing the rate of progression to decompensated cirrhosis.[26,47]

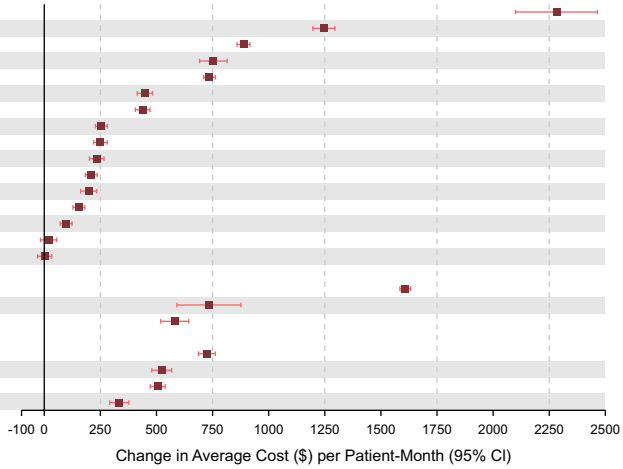
Pharmaceutical costs contribute significantly to the total cost (24.5%). In 2014, direct-acting antivirals were approved for the treatment of chronic HCV, which reduced likelihood of decompensation by 64% and development of HCC by 27%.[48] This appears to be represented by the increase in total and pharmaceutical costs for HCV starting in 2013 and peaking in 2015, which has since resolved (Figure 2B). Because decompensation is very costly, interventions, such as direct-acting antivirals that prevent disease progression may represent substantial cost-saving measures.[49,50] The 2-fold cost difference between compensated and decompensated cirrhosis should serve as an incentive to optimize care for patients with compensated cirrhosis, in particular, to prevent the progression of cirrhosis.

When examining costs by calendar year, some abrupt changes can be seen from 2015 to 2016 (Figures 1A–D). It is not possible to precisely determine, using these study data, the reason for the abrupt changes. However, starting in 2016, ICD-10 codes were available for identifying patients by diagnosis in this, and a number of other studies.[36,40] It is well reported that changes to ICD codes used for diagnosis result in

(A)

Total Cost

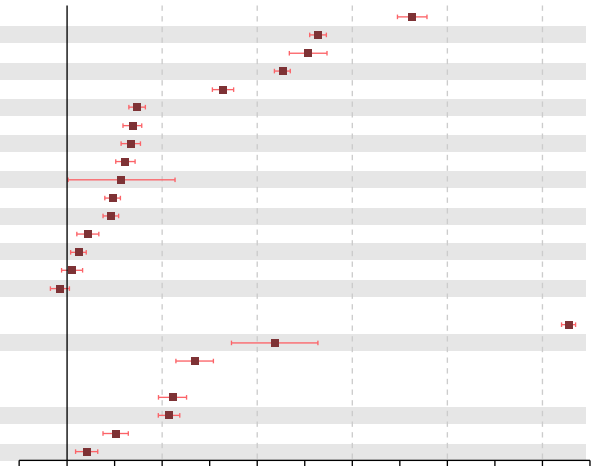
Covariate	β	N (Patient-Months)
Comorbidities (Reference: No Comorbidities)		
AIDS	$2282.75	29,711
Metastatic Solid Tumor	$1246.56	242,395
Congestive Heart Failure (CHF)	$888.50	1,138,337
Hemiplegia	$754.69	165,946
Moderate or Severe ESRD	$736.45	1,148,649
Prior Myocardial Infarction	$449.38	571,169
Complicated Diabetes	$438.96	1,006,965
Chronic Obstructive Pulmonary Disease (COPD)	$255.25	1,423,786
Lymphoma	$250.98	817,762
Dementia	$235.97	420,313
Cerebrovascular Disease (CVD)	$210.70	1,038,008
Rheumatological Disease	$198.94	317,797
Peripheral Vascular Disease (PVD)	$155.78	1,316,474
Moderate-Severe Liver Disease	$98.33	1,055,982
Peptic Ulcer Disease	$20.78	424,382
Uncomplicated Diabetes	$3.73	1,397,448
Complications/Interventions (Reference: No Complications/Interventions)		
Decompensated	$1609.50	1,348,237
TIPS	$735.14	32,063
HCC	$582.21	192,537
Etiologies (Reference: ETOH)		
HCV	$725.77	532,266
Other Etiologies	$524.74	370,714
MASH	$507.10	812,353
Biliary	$335.73	126,394



(B)

Medical Cost

Covariate	β	N (Patient-Months)
Comorbidities (Reference: No Comorbidities)		
Metastatic Solid Tumor	$1089.42	242,395
Congestive Heart Failure (CHF)	$791.89	1,138,337
Hemiplegia	$761.30	165,946
Moderate or Severe ESRD	$679.75	1,148,649
Prior Myocardial Infarction	$492.85	571,169
Cerebrovascular Disease (CVD)	$221.75	1,038,008
Lymphoma	$206.78	817,762
Complicated Diabetes	$201.62	1,006,965
Dementia	$184.24	420,313
AIDS	$172.43	29,711
Chronic Obstructive Pulmonary Disease (COPD)	$144.24	1,423,786
Peripheral Vascular Disease (PVD)	$139.69	1,316,474
Peptic Ulcer Disease	$65.84	424,382
Moderate-Severe Liver Disease	$36.23	1,055,982
Rheumatological Disease	$16.34	317,797
Uncomplicated Diabetes	$-22.46	1,397,448
Complications/Interventions (Reference: No Complications/Interventions)		
Decompensated	$1583.17	1,348,237
TIPS	$656.17	32,063
HCC	$404.09	192,537
Etiologies (Reference: ETOH)		
Other Etiologies	$334.22	370,714
MASH	$322.62	812,353
Biliary	$154.09	126,394
HCV	$61.94	532,266



(C)

Pharmacy Cost

Covariate	β	N (Patient-Months)
Comorbidities (Reference: No Comorbidities)		
AIDS	$2110.31	29,711
Complicated Diabetes	$237.34	1,006,965
Rheumatological Disease	$182.60	317,797
Metastatic Solid Tumor	$157.15	242,395
Chronic Obstructive Pulmonary Disease (COPD)	$111.00	1,423,786
Congestive Heart Failure (CHF)	$96.60	1,138,337
Moderate-Severe Liver Disease	$62.10	1,055,982
Moderate or Severe ESRD	$56.70	1,148,649
Dementia	$51.72	420,313
Lymphoma	$44.19	817,762
Uncomplicated Diabetes	$26.19	1,397,448
Peripheral Vascular Disease (PVD)	$16.08	1,316,474
Hemiplegia	$-6.61	165,946
Cerebrovascular Disease (CVD)	$-11.05	1,038,008
Prior Myocardial Infarction	$-43.46	571,169
Peptic Ulcer Disease	$-45.06	424,382
Complications/Interventions (Reference: No Complications/Interventions)		
HCC	$178.13	192,537
TIPS	$78.98	32,063
Decompensated	$26.33	1,348,237
Etiologies (Reference: ETOH)		
HCV	$663.83	532,266
Other Etiologies	$190.52	370,714
MASH	$184.49	812,353
Biliary	$181.63	126,394

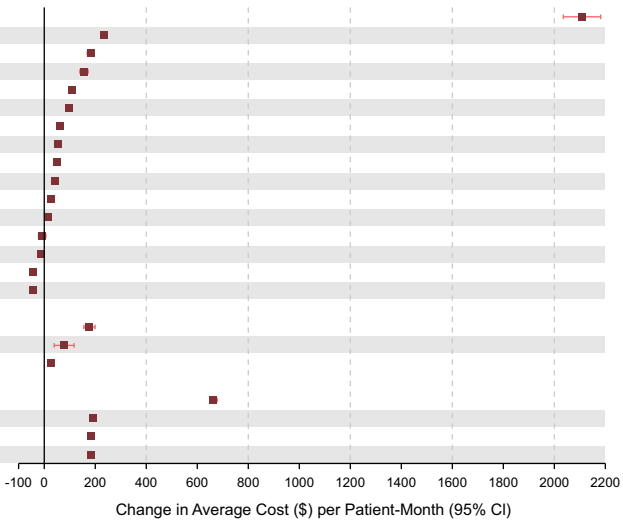


FIGURE 5 (A) Multivariable linear regression of the total cost of cirrhosis. (B) Multivariable linear regression of the medical cost of cirrhosis. (C) Multivariable linear regression of the pharmaceutical cost of cirrhosis. (A–C) The paneled figure shows 3 forest plots demonstrating the results of the multivariable linear regression analysis. They show the effects of included covariates on the total (A), medical (B), and pharmacy (C) costs. The average change in cost (β) per patient-month when adjusting for other covariates is shown for the corresponding covariates. The reference patient is one with ETOH and without any comorbidities or complications. Abbreviations: β, linear regression coefficient; COPD, chronic obstructive pulmonary disease; ETOH, alcohol-associated cirrhosis; HF, heart failure; ICD, International Classification of Diseases; MASH, metabolic dysfunction–associated steatohepatitis; N, number of patient-months; PM, patient-months.

changes to the cohort identified and the cost estimates.[39,51,52] Based on the literature, abrupt changes in cost across the years 2015 and 2016 are expected. This change in case mix is reflected as a discontinuity shown in Figures 1A–D and 2A, B. Except for decompensated cirrhosis, the cost after 2016 remained flat. This is in part due to the fact that in recent years (2016–2020), patients were hospitalized at a lower rate. This is likely due to policy changes that incentivize the reduction of hospitalization.[53,54] Also, our study captures actual payments rather than charges, and changes to the Centers for Medicare and Medicaid reimbursement formula have reduced reimbursement.[53,55,56]

In this study, we demonstrate the financial magnitude of cirrhosis care, especially for patients with decompensated cirrhosis. Our work, and that of others, also shows the growing burden of cirrhosis.[1] Yet, public health interventions to reduce costs and improve outcomes, such as the HRRP, have paid cirrhosis little attention.[15,22] Given that cirrhosis affects 2–7 million adults in the United States and is more costly than HF and COPD, the findings in this study emphasize the need to address cirrhosis from a public health perspective. Public health interventions to prevent diseases that lead to cirrhosis and to promote guideline-adherent care for those who have developed cirrhosis, such as cancer screening and annual specialty care, will be important in reducing the cost of cirrhosis.[57–60]

LIMITATIONS

There are a few limitations to this study. The analyses focus on non-HMO Medicare Advantage plan–enrolled patients by one, large, national insurer in the United States. Hence, the results may differ from those insured by other payors or with traditional Medicare fee-for-service coverage only. Also, the retrospective nature of the study necessitates reliance upon the accuracy of ICD-9, -10, and CPT codes for the diagnosis of cirrhosis. This can affect the identification of conditions such as MASH, which needed to be identified using the published algorithm of a nonspecific cirrhosis etiology plus obesity, dyslipidemia, diabetes, and/or hypertension. However, only codes and methods that have been validated in the literature to capture patients with cirrhosis were used, to optimize the validity of the results.[24–26,29,30,41]

Furthermore, the study examined the cost of all care received. Thus, the data and methods used do not allow us to differentiate which costs were specific only to the particular condition. Importantly, the cost of premature death due to cirrhosis based on the statistical value of life adjusted for ages 55–62, which is not part of these cost analyses, is estimated at $3.43 million per person.[61,62] These costs are important to consider also when calculating the cost of this chronic disease. Lastly, while the database used may include claims denied by the insurer, no denied services were included in the cost calculation. Their omission may result in an underestimation of cost.[63] This is an inherent limitation of claims data and is further discussed within the Supplemental Appendix, http://links.lww.com/HEP/J672.

CONCLUSIONS

The cost of care of non-HMO MA-covered patients with decompensated cirrhosis was $3969.3 per patient-month ($47,631 per patient-year), $1749.6 per patient-month for compensated cirrhosis ($20,996 per patient-year), and $3032.00 per patient-month for all patients with cirrhosis ($36,384 per patient-year) (Table 2, Figure 4). This is significantly higher than the per-patient cost of care for HF or COPD, surpassing them by 21.7% and 55.0%, respectively ($p < 0.001$). Of note, patients with cirrhosis had a higher Charlson comorbidity index than patients with HF or COPD (Table 1). The linear regression analysis demonstrated that a greater number of comorbid conditions were associated with increased costs. As anticipated, decompensated cirrhosis patient-months had a high cost of care, exceeding HF by 45.5% and COPD by 85.3%. This study highlights the high costs for cirrhosis associated with medical care ($27,467 per patient-year), and the high cost associated with medications ($8917 per patient-year) (Figure 4). Focusing public health interventions on the reduction of progression to cirrhosis and progression of cirrhosis to decompensation will not only significantly improve health outcomes but also significantly decrease the financial burden of cirrhosis.

DATA AVAILABILITY STATEMENT

The data is deposited in a secure database. The link to the repository is: https://prism.northwestern.edu/communities/ladnerlab-cost-paper-hepatology

AUTHOR CONTRIBUTIONS

Concept and design: Daniela P. Ladner and Charles F. Manski. Acquisition, analysis, or interpretation of data: Michael Gmeiner, Eleena Koep, Filip Obradović, Praneet Polineni, Bima J. Hasjim, Daniela P. Ladner, Dominic J. Vitello, and Aditya Jain. Drafting of the manuscript: Dominic J. Vitello, Bima J. Hasjim, Filip Obradović, Joy Obayemi, Daniela P. Ladner, Charles F. Manski, and Aditya Jain. Critical revision of the manuscript for important intellectual content: all authors. Statistical analysis: Filip Obradović, Charles F. Manski, Lihui Zhao, and Daniela P. Ladner. Obtained funding: Daniela P. Ladner and Charles F. Manski. Administrative, technical, or material support: Therese Banea and Julianna M. Doll. Supervision: Daniela P. Ladner and Charles F. Manski.

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CONFLICTS OF INTEREST

Andrés Duarte-Rojo received grants from Echosens. Laura Kulik consults for, advises, is on the speakers' bureau for, and is on the steering committee for AstraZeneca. She consults for, is on the speakers' bureau for, and is on the steering committee for Genentech. She advises Fujifilm. She received grants from Glycotest and HCC Target. Lisa B. VanWagner advises and consults for Gerson Lehrman Group and Slingshot Insights. She received grants from W.L. Gore & Associates and Madrigal. She serves as an expert witness. The remaining authors have no conflicts to report.

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REFERENCES

1. Ladner DP, Gmeiner M, Hasjim BJ, Mazumder N, Kang R, Parker E, et al. Increasing prevalence of cirrhosis among insured adults in the United States, 2012–2018. PLoS One. 2024;19:e0298887.
2. Beste LA, Leipertz SL, Green PK, Dominitz JA, Ross D, Ioannou GN. Trends in burden of cirrhosis and hepatocellular carcinoma by underlying liver disease in US Veterans, 2001–2013. Gastroenterology. 2015;149:1471–482.e5.
3. Moon AM, Singal AG, Tapper EB. Contemporary epidemiology of chronic liver disease and cirrhosis. Clin Gastroenterol Hepatol. 2020;18:2650–66.
4. Browning JD, Szczepaniak LS, Dobbins R, Nuremberg P, Horton JD, Cohen JC, et al. Prevalence of hepatic steatosis in an urban population in the United States: Impact of ethnicity. Hepatology. 2004;40:1387–95.
5. Younossi Z, Anstee QM, Marietti M, Hardy T, Henry L, Eslam M, et al. Global burden of NAFLD and NASH: Trends, predictions, risk factors and prevention. Nat Rev Gastroenterol Hepatol. 2018;15:11–20.
6. Estes C, Razavi H, Loomba R, Younossi Z, Sanyal AJ. Modeling the epidemic of nonalcoholic fatty liver disease demonstrates an exponential increase in burden of disease. Hepatology (Baltimore, Md). 2018;67:123–33.
7. Grant BF, Chou SP, Saha TD, Pickering RP, Kerridge BT, Ruan WJ, et al. Prevalence of 12-month alcohol use, high-risk drinking, and DSM-IV alcohol use disorder in the United States, 2001-2002 to 2012-2013: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. JAMA Psychiatry. 2017;74:911–23.
8. D'Amico G, Garcia-Tsao G, Pagliaro L. Natural history and prognostic indicators of survival in cirrhosis: A systematic review of 118 studies. J Hepatol. 2006;44:217–31.
9. Hasjim BJ, Mohammadi M, Balbale SN, Paukner M, Banea T, Shi H, et al. High hospitalization rates and risk factors among frail patients with cirrhosis: A 10-year population-based cohort study. Clin Gastroenterol Hepatol. 2024. doi:10.1016/j.cgh.2024.08.044
10. Hasjim BJ, Harris A, Balbale SN, Obayemi JE, Beestrum M, Polineni P, et al. Social disadvantage and disparities in chronic liver disease: A systematic review. Am J Gastroenterol. 2022:1–19. doi:10.14309/ajg.0000000000003171.
11. Younossi ZM, Blissett D, Blissett R, Henry L, Stepanova M, Younossi Y, et al. The economic and clinical burden of nonalcoholic fatty liver disease in the United States and Europe. Hepatology (Baltimore, Md). 2016;64:1577–86.
12. Kim D, Cholankeril G, Li AA, Kim W, Tighe SP, Hameed B, et al. Trends in hospitalizations for chronic liver disease-related liver failure in the United States, 2005-2014. Liver Int. 2019;39:1661–71.
13. Asrani SK, Hall L, Hagan M, Sharma S, Yeramaneni S, Trotter J, et al. Trends in chronic liver disease-related hospitalizations: A population-based study. Am J Gastroenterol. 2019;114:98–106.
14. Ma C, Qian AS, Nguyen NH, Stukalin I, Congly SE, Shaheen AA, et al. Trends in the economic burden of chronic liver diseases and cirrhosis in the United States: 1996–2016. Am J Gastroenterol. 2021;116:2060.

15. Desai NR, Ross JS, Kwon JY, Herrin J, Dharmarajan K, Bernheim SM, et al. Association between hospital penalty status under the hospital readmission reduction program and readmission rates for target and nontarget conditions. JAMA. 2016;316:2647–56.
16. Mohammadi M, Hasjim B, Balbale S, et al. Predicting the unpredictable: Disease trajectory and competing risks of patients with cirrhosis in the US. PLoS One. 2024.
17. Saleem S, Katragadda R, Weissman S, Bleibel W. Morbidity and mortality of infections in the cirrhotic patients: A US population-based study. Gastroenterol Hepatol Bed Bench. 2019;12:233–8.
18. Desai AP, Mohan P, Nokes B, Sheth D, Knapp S, Boustani M, et al. Increasing economic burden in hospitalized patients with cirrhosis: Analysis of a national database. Clin Transl Gastroenterol. 2019;10:e00062.
19. Neff GW, Duncan CW, Schiff ER. The current economic burden of cirrhosis. Gastroenterol Hepatol. 2011;7:661.
20. Hirode G, Vittinghoff E, Wong RJ. Increasing clinical and economic burden of nonalcoholic fatty liver disease among hospitalized adults in the United States. J Clin Gastroenterol. 2019;53:765–71.
21. Kanwal F, Nelson R, Liu Y, Kramer JR, Hernaez R, Cholankeril G, et al. Cost of care for patients with cirrhosis. Am J Gastroenterol. 2022;119:497–504.
22. Gupta A, Allen LA, Bhatt DL, Cox M, DeVore AD, Heidenreich PA, et al. Association of the hospital readmissions reduction program implementation with readmission and mortality outcomes in heart failure. JAMA Cardiol. 2018;3:44–53.
23. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: Guidelines for reporting observational studies. Epidemiology. 2007;18:800.
24. Goldberg DS, Lewis JD, Halpern SD, Weiner MG, Re VL. Validation of a coding algorithm to identify patients with hepatocellular carcinoma in an administrative database. Pharmacoepidemiol Drug Saf. 2013;22:103–7.
25. Shearer JE, Gonzalez JJ, Min T, Parker R, Jones R, Su GL, et al. Systematic review: Development of a consensus code set to identify cirrhosis in electronic health records. Aliment Pharmacol Therapeut. 2022;55:645–57.
26. Corey KE, Kartoun U, Zheng H, Shaw SY. Development and validation of an algorithm to identify nonalcoholic fatty liver disease in the electronic medical record. Dig Dis Sci. 2016;61:913–9.
27. Nehra MS, Ma Y, Clark C, Amarasingham R, Rockey DC, Singal AG. Use of administrative claims data for identifying patients with cirrhosis. J Clin Gastroenterol. 2013;47:e50–4.
28. Lapointe-Shaw L, Georgie F, Carlone D, Cerocchi O, Chung H, Dewit Y, et al. Identifying cirrhosis, decompensated cirrhosis and hepatocellular carcinoma in health administrative data: A validation study. PLoS One. 2018;13:e0201120.
29. Hayward KL, Johnson AL, Mckillen BJ, Burke NT, Bansal V, Horsfall LU, et al. ICD-10-AM codes for cirrhosis and related complications: Key performance considerations for population and healthcare studies. BMJ Open Gastroenterol. 2020;7:e000485.
30. Hagström H, Adams LA, Allen AM, Byrne CD, Chang Y, Grønbæk H, et al. Administrative coding in electronic health care record-based research of NAFLD: An expert panel consensus statement. Hepatology. 2021;74:474–82.
31. Quan H, Li B, Couris CM, Fushimi K, Graham P, Hider P, et al. Updating and validating the Charlson Comorbidity Index and score for risk adjustment in hospital discharge abstracts using data from 6 countries. Am J Epidemiol. 2011;173:676–82.
32. Quan H, Sundararajan V, Halfon P, Fong A, Burnand B, Luthi JC, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. Med Care. 2005;43:1130–9.
33. Dalal A. Direct costs of chronic obstructive pulmonary disease among managed care patients. COPD. 2010;5:341.
34. Mapel DW, Dutro MP, Marton JP, Woodruff K, Make B. Identifying and characterizing COPD patients in US managed care. A retrospective, cross-sectional analysis of administrative claims data. BMC Health Serv Res. 2011;11:43.
35. Stanford RH, Engel-Nitz NM, Bancroft T, Essoi B. The identification and cost of acute chronic obstructive pulmonary disease exacerbations in a United States population healthcare claims database. COPD: J Chron Obstruct Pulmon Dis. 2020;17:499–508.
36. Urbich M, Globe G, Pantiri K, Heisen M, Bennison C, Wirtz HS, et al. A systematic review of medical costs associated with heart failure in the USA (2014–2020). Pharmacoeconomics. 2020;38:1219–36.
37. Huang H, Turner M, Raju S, Reich J, Leatherman S, Armstrong K, et al. Identification of acute decompensated heart failure hospitalizations using administrative data. Am J Cardiol. 2017;119:1791–6.
38. Mansley EC, Carroll NV, Chen KS, Shah ND, Piech CT, Hay JW, et al. Good research practices for measuring drug costs in cost-effectiveness analyses: A managed care perspective: The ISPOR Drug Cost Task Force Report—Part III. Value Health. 2010;13:14–7.
39. Olchanski N, Vest AR, Cohen JT, Neumann PJ, DeNofrio D. Cost comparison across heart failure patients with reduced and preserved ejection fractions: Analyses of inpatient decompensated heart failure admissions. Int J Cardiol. 2018;261:103–8.
40. Lesyuk W, Kriza C, Kolominsky-Rabas P. Cost-of-illness studies in heart failure: A systematic review 2004–2016. BMC Cardiovasc Disord. 2018;18:74.
41. Tapper EB, Korovaichuk S, Baki J, Williams S, Nikirk S, Waljee AK, et al. Identifying patients with hepatic encephalopathy using administrative data in the ICD-10 era. Clin Gastroenterol Hepatol. 2021;19:604–6.e1.
42. Gonzalez JJ, Dziwis J, Patel YA, Tapper EB. Identifying ascites in patients with cirrhosis using administrative codes and diuretic use: A multicenter study. Dig Dis Sci. 2022;67:4695–701.
43. Asrani SK, Kouznetsova M, Ogola G, Taylor T, Masica A, Pope B, et al. Increasing health care burden of chronic liver disease compared with other chronic diseases, 2004–2013. Gastroenterology. 2018;155:719–729.e4.
44. Desai AP, Mohan P, Nokes B, Sheth D, Knapp S, Boustani M, et al. Increasing economic burden in hospitalized patients with cirrhosis: Analysis of a national database. Clin Transl Gastroenterol. 2019;10:e00062.
45. C. Gordon S, Fraysse J, Li S, Ozbay AB, Wong RJ. Disease severity is associated with higher healthcare utilization in nonalcoholic steatohepatitis medicare patients. Am J Gastroenterol. 2020;115:562–74.
46. Gordon SC, Pockros PJ, Terrault NA, Hoop RS, Buikema A, Nerenz D, et al. Impact of disease severity on healthcare costs in patients with chronic hepatitis C (CHC) virus infection. Hepatology. 2012;56:1651–60.
47. Klebanoff MJ, Corey KE, Samur S, Choi JG, Kaplan LM, Chhatwal J, et al. Cost-effectiveness analysis of bariatric surgery for patients with nonalcoholic steatohepatitis cirrhosis. JAMA Netw Open. 2019;2:e190047.
48. Ogawa E, Chien N, Kam L, Yeo YH, Ji F, Huang DQ, et al. Association of direct-acting antiviral therapy with liver and nonliver complications and long-term mortality in patients with chronic hepatitis C. JAMA Intern Med. 2023;183:97.
49. Kaplan DE, Serper M, Kaushik A, Durkin C, Raad A, El-Moustaid F, et al. Cost-effectiveness of direct-acting antivirals for chronic hepatitis C virus in the United States from a payer perspective. JMCP. 2022;28:1138–48.
50. Chahal HS, Marseille EA, Tice JA, Pearson SD, Ollendorf DA, Fox RK, et al. Cost-effectiveness of early treatment of hepatitis C virus genotype 1 by stage of liver fibrosis in a US treatment-naive population. JAMA Intern Med. 2016;176:65.

51. Goff DC Jr, Pandey DK, Chan FA, Ortiz C, Nichaman MZ. Congestive heart failure in the United States: Is there more than meets the I(CD Code)? The Corpus Christi Heart Project. Arch Intern Med. 2000;160:197–202.
52. Albert NM, Swindle JP, Buysman EK, Chang C. Lower hospitalization and healthcare costs with sacubitril/valsartan versus angiotensin-converting enzyme inhibitor or angiotensin-receptor blocker in a retrospective analysis of patients with heart failure. JAHA. 2019;8:e011089.
53. Ibrahim AM, Nuliyalu U, Lawton EJ, O'Neil S, Dimick JB, Gulseren B, et al. Evaluation of US hospital episode spending for acute inpatient conditions after the Patient Protection and Affordable Care Act. JAMA Netw Open. 2020;3:e2023926.
54. Pickens G, Karaca Z, Cutler E, Dworsky M, Eibner C, Moore B, et al. Changes in hospital inpatient utilization following health care reform. Health Serv Res. 2018;53:2446–69.
55. Rama A Policy Research Perspectives. American Medical Association. *Payment and Delivery in the U.S. Health Care System: Key Policy Issues*. Published 2022. Accessed March 19, 2024. https://www.ama-assn.org/system/files/2022-prp-payment-and-delivery.pdf
56. Congressional Budget Office. Budget and economic data. Accessed August 15, 2024. https://www.cbo.gov/data/budget-economic-data#3
57. Gupta A, Fonarow GC. The Hospital Readmissions Reduction Program—Learning from failure of a healthcare policy. Eur J Heart Fail. 2018;20:1169–74.
58. Leidner AJ, Chesson HW, Xu F, Ward JW, Spradling PR, Holmberg SD. Cost-effectiveness of hepatitis C treatment for patients in early stages of liver disease. Hepatology. 2015;61:1860–9.
59. Rinella ME, Neuschwander-Tetri BA, Siddiqui MS, Abdelmalek MF, Caldwell S, Barb D, et al. AASLD Practice Guidance on the clinical assessment and management of nonalcoholic fatty liver disease. Hepatology. 2023;77:1797.
60. Martin NK, Vickerman P, Miners A, Foster GR, Hutchinson SJ, Goldberg DJ, et al. Cost-effectiveness of hepatitis C virus antiviral treatment for injection drug user populations. Hepatology. 2012;55:49–57.
61. Aldy JE, Viscusi WK. Adjusting the value of a statistical life for age and cohort effects. Rev Econ Stat. 2008;90:573–81.
62. Ladner DP, Manski CF. Financial burden of cirrhosis is significantly reduced after liver transplantation. Liver Transpl. 2024;30:875.
63. Cutler DM, Ghosh K, Landrum MB. The value of medicaid during a recession: evidence from the COVID-19 pandemic. National Bureau of Economic Research; 2021. Accessed March 2, 2024. https://www.nber.org/system/files/working_papers/w29010/w29010.pdf

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