A Comprehensive Risk Prediction Model for Cirrhosis Decompensation Using a Large National Claims Database

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Conflict of Interest Statement
Dr. VanWagner serves as an advisor for Numares, Novo-Nordisk and Gerson Lehrman Group, receives grant support from W.L. Gore & Associates and provides expert witness services outside the submitted work.

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Data sharing statement

The data used in the findings of this study were made available by UnitedHealth Group. Restrictions apply to the availability of these data, which were used under license for this study. With publication, data may only be made available to other investigators for other similar retrospective analyses after approval of a proposal and with a signed data access agreement as applicable on an individualized basis upon reasonable inquiry to the corresponding author, contingent upon involvement and permission of the data provider. Data include deidentified participant data, data dictionary, and statistical analysis plan by way of a prescribed, universally agreed upon method of secure communication.

Author Contributions

Concept and design: Ladner, Manski
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Drafting of the manuscript: Vitello, Hussein, Crippa, Manski, Ladner
Critical revision of the manuscript for important intellectual content: all authors
Statistical analysis: Crippa, Manski, Ladner
Obtained funding: Ladner, Manski
Administrative, technical, or material support: Banea, Dentici
Supervision: Ladner, Manski

Abbreviations:

AIDS: acquired immunodeficiency syndrome
ALD: alcohol associated liver disease
Alcohol+: alcohol associated liver disease plus another cirrhosis etiology
Alcohol+HCV: alcohol associated liver disease and hepatitis C virus associated liver disease
CHF: congestive heart failure
CKD: chronic kidney disease
COM: commercial insurance
COPD: chronic obstructive pulmonary disease
CVA: cerebrovascular accident
DM: diabetes mellitus

HBV: hepatitis B associated cirrhosis
HCV: hepatitis C virus associated cirrhosis
HCV+: hepatitis C virus associated cirrhosis plus another cirrhosis etiology
HD: hemodialysis
HE: hepatic encephalopathy
HPS: hepatopulmonary syndrome
HRS: hepatorenal syndrome
MA: Medicare Advantage
MASLD: metabolic dysfunction-associated steatotic liver disease
MetALD: metabolic dysfunction-associated steatotic liver disease with increased alcohol intake
MI: myocardial infarction
Other: one other cirrhosis etiology not otherwise specified
Other 2+: two or more other cirrhosis etiologies not otherwise specified
PAD: peripheral arterial disease
PUD: peptic ulcer disease
SBP: spontaneous bacterial peritonitis
SD: standard deviation
VB: variceal bleeding

Manuscript word count 3,183/3,500

ABSTRACT

Background: Care for patients with cirrhosis is chronic and complex. There are no tools available to stratify decompensation risk in a general cirrhosis population. The primary aim was to develop a model for decompensation risk that can be used as a clinical decision support tool.

Methods: A large, national, insurance, claims database was used to conduct a retrospective cohort study of patients with baseline compensated cirrhosis between 2012 and 2022. ICD-9, -10, and CPT codes were used to identify demographics, cirrhosis etiology, and laboratory values. Multivariable logistic regression was used to predict 6- and 12-month decompensation risk. The model was internally temporally cross-validated.

Findings: 188,526 patients were included. Among other etiologies, 47.1% had metabolic dysfunction-associated liver disease (MASLD), 12.2% had MASLD with increased alcohol intake (MetALD), 8.3% had biliary cirrhosis, and 2.1% had alcohol-associated liver disease (ALD). 9,841 (5.2%) and 18,907 (11.3%) decompensated by 6 and 12 months respectively. The model had excellent calibration, with an average deviance between observed and predicted of 0.0063. The 12-month decompensation risk was highest for those with ALD (OR 1.9 95% CI 1.6-2.3) and MetALD (OR 1.3 95% CI 1.1-1.5), and lowest for those with biliary cirrhosis (OR 0.5 95% CI 0.4-0.6). The presence of hepatocellular carcinoma (OR 1.9 95% CI 1.6-2.2) or chronic kidney disease requiring dialysis (OR 1.4 95% CI 1.1-1.7) conferred substantial increases in risk.

Interpretation: The model accurately predicts 6- and 12-month decompensation using clinicodemographic factors available to clinicians at baseline. The associated risk calculator may be used by clinicians to identify patients in need of escalated or deescalated care, including transplant. Future work will investigate identification of patients that benefit most from specialist referral and transplant listing.

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INTRODUCTION

An estimated 2 to 7 million adults in the United States are affected by cirrhosis.[1–4] This prevalence is projected to increase significantly over the next decade, particularly due to metabolic dysfunction-associated steatotic liver disease (MASLD) and MASLD with increased alcohol intake (MetALD).[1,5–7] As the average survival for compensated patients is 12 years, patients with cirrhosis require chronic, complex, and longitudinal care. This care involves specialty consultation, hepatocellular carcinoma (HCC) surveillance, and prevention and management of decompensation.(REF) Decompensation is associated with increased morbidity and mortality and is extremely resource intensive and costly, often requiring procedures or hospitalizations.[11]

Despite the severity of decompensation, there is a lack of comprehensive and validated understanding as to how cirrhosis etiologies and clinical factors influence risk. Prior studies have investigated subpopulations such as those within the Veterans Administration Health System (VHS), which phenotypically are unique with higher rates of chronic disease, lower socioeconomic status and older age compared to the general US population(REF), or patients listed for transplant, which is a highly biased sample and represents only 2% of all patients with cirrhosis (REF).[12,13] To our knowledge, no study has examined a generalizable, national population of patients with cirrhosis. As such, there are also no tools available for the stratification of decompensation risk, which could ultimately be used for the selection of patients for specialty care, preventative services, and transplant.

Given the need for a more comprehensive understanding of decompensation risk, the primary aim of this study is to investigate the association of demographic and clinical factors with decompensation. The secondary aim was to create a clinical decision-support tool to ascertain the risk of decompensation. The outcomes of interest were 6- and 12-month

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Abraldes JG, Caraceni P, Ghabril M, Garcia-Tsao G. Update in the Treatment of the Complications of Cirrhosis. Clin Gastroenterol Hepatol. 2023;21(8):2100-2109. doi:10.1016/j.cgh.2023.03.019

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Ginès, Pere et al.
The Lancet, Volume 398, Issue 10308, 1359 - 1376

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Kanwal F, Hernaez R, Liu Y, et al. Factors Associated With Access to and Receipt of Liver Transplantation in Veterans With End-stage Liver Disease. JAMA Intern Med. 2021;181(7):949–959. doi:10.1001/jamainternmed.2021.2051

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decompensation in baseline compensated patients with cirrhosis and the factors associated with decompensation.

METHODS

Study Design

A retrospective, longitudinal cohort study of claims data from a large national insurer in the United States between July 1, 2011, and July 1, 2024 was conducted. The study follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline for cohort studies and the transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD) statement (Supplemental Table 1 and 2).[14,15] The PROBAST tool was also used to minimize prediction model bias (Supplemental Table 3). The Northwestern University Institutional Review Board deemed this study exempt from review and waived the need for patient informed consent. The database included de-identified medical and pharmacy claims data for enrollees with various plan types. 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.

Study Participants

Patients with baseline compensated cirrhosis enrolled under any insurance plan type and at least 6 months of follow up were included in the analysis (Figure 1). The date of identification of cirrhosis was taken to be the index date and beginning of observation. The end of observation was defined as the time of decompensation, transplant, disenrollment from the database, or the end of the 6- or 12-month follow-up periods. To allow for adequate baseline and follow up periods, only patients identified with cirrhosis between January 1, 2012 and December 30, 2022 were selected.

Patients with cirrhosis were identified as having at least one claim under any plan 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, K74.5) in any position on the claim (Figure 1).[16–21] Cirrhosis

etiologies were defined by at least one claim specifying an ICD-9 or -10 code for: alcohol-associated (ALD), metabolic dysfunction-associated steatotic liver disease (MASLD, previously non-alcoholic steatohepatitis/NASH), hepatitis B virus (HBV), hepatitis C virus (HCV), biliary cirrhosis (e.g., primary sclerosing cholangitis, primary biliary cirrhosis), cardiac cirrhosis, genetic cirrhosis, and autoimmune hepatitis. Patients were categorized by mutually exclusive cirrhosis etiologies. Patients with ALD, HCV, or multiple etiologies were categorized using a hierarchical algorithm as shown in Supplemental Figure 1. Of note, MASLD/NASH did not have a dedicated ICD code prior to October 1, 2015. For data prior to October 1, 2015, MASLD/NASH was identified using a previously published algorithm (patients without specific cirrhosis etiology plus obesity, dyslipidemia, diabetes, and/or hypertension).[18,22] Validated ICD-9/-10 codes were used to define comorbidities, and quantify the Charlson Comorbidity Index.[23,24]

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Medical and Pharmacy Claims

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

Pharmacy claims were submitted by pharmacies at the time of dispensing, accounting 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.

Identifying Decompensation

Patients with 6- and 12-months of follow up were analyzed for the presence of any one event indicating cirrhosis decompensation in these timeframes. To avoid misidentifying patients who were decompensated at baseline as compensated, due to lag in charting codes in medical records, decompensation within the first 90 days of cirrhosis identification were considered to have occurred at baseline.[25] Decompensation was considered to be a claim listing a previously published, or where possible validated, ICD-9, ICD-10, or CPT code indicating ascites, hepatic encephalopathy (HE), variceal bleeding (VB), hepatorenal syndrome (HRS), spontaneous bacterial peritonitis (SBP), or hepatopulmonary syndrome (HPS). Etiology of decompensation was not considered to be mutually exclusive.

Statistical Analysis

Descriptive statistics were generated for baseline demographics including age, sex, insurance plan type, cirrhosis etiology, comorbidities, laboratory values. Rates were reported for decompensation and its etiology. Categorical variables are reported as the percentage of the cohort with associated number of patients. Continuous variables are reported as mean (standard deviation [SD]) or median (interquartile range [IQR]). A multivariable logistic regression model was created to predict the individualized risk of cirrhosis decompensation within 6- and 12-months of cirrhosis identification.

The model was created by selecting covariates based on clinical and literature reported relevance. Covariates used included baseline demographics as categorical variables and laboratory values as continuous. Those with missing laboratory values were excluded from the model. A sensitivity analysis was conducted comparing model performance with and without laboratory values (Supplementary Figures 4a and 4b). A 20-year-old male patient with MASLD, no comorbid conditions, and normal laboratory values was considered the reference. The model

was internally temporally cross validated by using patients identified from 2012 to 2019 as a training cohort and those identified from 2020 to 2022 as the validation cohort. Model validation was assessed by reporting model calibration (risk estimates) and model discrimination (receiver-operating characteristic). A sensitivity analysis was conducted by performing the validation procedure with interaction terms as detailed in the Supplemental Material.

The final model was then estimated using the entire cohort. This final output was reported in forest plots as odds ratios (ORs) with associated 95% confidence intervals (95% CI) for categorical variables as well as estimated decompensation risks. Calibration of the model was evaluated by comparing observed and predicted probabilities of decompensation across percentiles. The influence of continuous variables was displayed as changes in estimated risk using marginal effects plots. Descriptive tables were generated to show demographic information for patients at low risk of 12-month decompensation (<5th and 20th percentile) and high risk (>80th and 95th percentile). Significant predictors of decompensation as well as those of clinical interest were selected to create risk tables based on cirrhosis etiology, comorbid conditions, and laboratory values. A sensitivity analysis was conducted to confirm similar model performance. These predictors were then used to create a parsimonious version of the model. This version of the model was converted into a risk calculator and made available online to be used as a clinical decision support tool. P-values were calculated using Fisher's exact test and Welch's t-tests. A p-value of less than 0.05 was considered statistically significant. Statistical analyses were performed using Stata 18.5, College Station, Texas.

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RESULTS

Demographics

The cohort included 189,518 patients with baseline compensated cirrhosis (Figure 1), mean follow up time 4.2 (SD: 2.6) years, with a mean age of 63.3 and of which 49.3 % were female. Most patients were enrolled in Medicare Advantage (MA) plans (59.7%, N=113,078),

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and the mean Charlson Comorbidity Index (CCI) was 5.9 (3.2). Among the components of the CCI conditions, 39.9% (N=75,643) had uncomplicated diabetes mellitus (DM), 30.1% (N=56,956) chronic obstructive pulmonary disease (COPD), 20.0% (N=37,837) peripheral arterial disease (PAD), and 19.8% (N=37,432) complicated DM among others (Table 1). Cirrhosis etiologies were MASLD for 46.8% (N=88,673), HCV for 11.9% (N=22,544), MetALD for 5.3% (N=9,974), biliary disease for 5.8% (N=11,290), ALD for 3.5% (N=6,537) and Other for 2.1% (N=3,922) (Table 1). The median platelet count was 182,000 (52,000-312,000) per µL, sodium of 140 (136-144) mEq/L, creatinine 0.80 (0.52-1.26) mg/dL, albumin of 2.13 (1.07-3.19) g/dL, international normalized ratio (INR) of 1.1 (0.9-1.3), and bilirubin 0.7 (0-1.4) mg/dL. The median (IQR) Model for End Stage Liver Disease 3.0 (MELD) was 11 (6-16) (Supplemental Table 2b).

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Decompensation

In the cohort, 212,716 patients had at least 6 months of follow-up and 189,518 had at least 12 months of follow-up. Among the cohort, 10,759 (5.1%) decompensated by 6 months and 20,684 (10.9%) by 12 months (Table 2). Patients that decompensated within 12 months most frequently had ALD (27.8%; N=1,826), MetALD (18.5%; n=1846), or MASLD (10.8%; N= 9,587). Ascites (43.1%, N=8,918), variceal bleeding (VB) (35.5%, N=7,347), and hepatic encephalopathy (HE) (24.3%, N=5,021) were the most frequent decompensating events for the 12-month cohort.

When compared to patients at lowest risk for 12-month decompensation (<5th percentile), those is the highest risk group (>95th percentile) were older (54 years vs 65 years old), more likely to be male (32.6% vs 65.1%), more enrolled in MA plans (38.3% vs 70.0%), and had a higher CCI (4.1 vs 6.5) (Table 1). Almost all investigated comorbidities were universally more frequent for those with the highest decompensation risk compared to the

lowest. Patients with the lowest decompensation compared to highest risk, had biliary cirrhosis more frequently (38.1% vs 0.01%, p<0.05), ALD least frequently (0% vs 61.3%) (Table 1).

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Model for Decompensation Risk

The 6-month model demonstrated that, after adjusting for covariates, patients with ALD (OR 3.2 95% CI ***) and MetALD (OR 1.7 95% CI ***) had the highest odds of decompensation at 6 months. Patients with biliary (OR 0.5 95% CI ***) and viral etiologies (HBV OR 0.7 95% ***; HC OR 0.8 95% CI ***) had lower odds of decompensation. Comorbid conditions generally increased decompensation risk, with the greatest contributors being severe renal disease (OR 1.35 95% CI ***) and congestive heart failure (CHF) (OR 1.3 95% CI ***) (Figure 2a). A similar trend in risk factors is observed for the 12-month model (Figure 2b). Additionally, increasing age was associated with increasing risk, reaching a plateau at age 65 (Figure 3a). Similarly, laboratory findings were associated with decompensation risk, particularly baseline hyponatremia, thrombocytopenia, and hypoalbuminemia as well as higher baseline creatinine, international normalized ratio (INR), and total bilirubin (Figures 3b-g).

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Calibration was evaluated by comparing observed and predicted probabilities of decompensation across percentiles and the average deviance between these values was 0.0063, indicating close agreement between model predictions and observed outcomes (Figure 4; Supplemental Tables 4a and 4b). The sensitivity analysis revealed that, irrespective of the inclusion of interaction terms, model calibration and discrimination were similar (Supplemental Fig 1, 3, and 4; Supplemental Tables 4a and 4b; Supplemental Figures 4a and 4b). Upon conducting the sensitivity analysis of the parsimonious model, performance was found to be similar to that of the full model.

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Tables 3a-3c show examples of estimated 12-month decompensation risks for patients across the MELD score tertile distribution within the cohort (MELD 9, 16 21) using or model. The 12-month risk for patients with no comorbid conditions and a MELD of 9, was 24.9% for MASLD, 15.2% for ALD, 7.2% for MetALD, 5.8% for HCV, 4.9% for HBV and 6.7% for biliary cirrhosis (Table 3a). Comorbidities were associated with differences in risk consistent with the corresponding ORs. For example, patients with a MELD of 9, ALD, and AIDS had a 12-month decompensation risk of 28.3% (Table 3a). Comorbidities were associated with higher decompensation risk across etiologies, so that patients with biliary cirrhosis, a MELD of 9 and AIDS still were at comparatively lower risk (8.3%) (Table 1. Increasing MELD increased all risks, which was also proportional (Tables 1a-1c). For example a patient with ALD, a MELD of 21 and severe renal disease had a 12-month risk of 50.0%, while the same risk for a patient with biliary cirrhosis was less than half of this at 22.0% (Table 1c).

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DISCUSSION

Cirrhosis remains significant and increasing in its clinical impact in the United States.[1–4] Despite this, its natural history is poorly understood.[26] We found that 5.2% of patients decompensate by 6 months and 10.9% decompensate by 12 months after the diagnosis of cirrhosis. Cirrhosis etiology, comorbid conditions, and laboratory findings influenced these decompensation risks. Furthermore, models based on these factors resulted in accurate risk estimates. Importantly, patients with MASLD, MetALD, and ALD were at increased risk, particularly those with severe renal disease and CHF. While increasing MELD was associated with increased risk, many patients with low MELD scores had over a 30% risk to decompensate within 12 months. These findings deemphasize the utility of MELD to diagnose decompensation.[27,28] It also emphasizes the need for early decompensation risk assessment, as patients with increased decompensation risk will benefit from targeted use of specialist (which

exist in limited numbers) for optimization of care, as well as escalation or de-escalation of care.[29–33]

While many studies have examined the natural history of cirrhosis, few have done so in a general and generalizable cirrhosis population. Among these is a notable systematic review by D'Amico et al. published in 2006.[34] The authors analyzed decompensation for patients with baseline compensated cirrhosis in two prospective cohorts. While the annual rate of decompensation over 10 years of follow-up was 5% to 7%, the rates within the first 6 and 12 months were approximately 9% and 13.6%, respectively. Our findings show that patients decompensate at a rate of 5.2% within 6 months and 11.3% within 12 months higher as would be expected. First, the cohort described by D'Amico et al is a European cohort from the 1980's and the risk factors for decompensation were not analyzed. The disease epidemiology has changed significantly since then, and so have available medications (e.g., hcv treatment – ref). Most importantly, however, the D'Amico cohort was followed by specialists (gastroenterologists, hepatologists), while this is a natural cohort of patients with cirrhosis – many of which do not receive specialty care. It has been shown that specialty care does improve outcomes for patients with cirrhosis.[29,33,35]. Unfortunately, not enough specialists exist to support the 2-5M adult patients with cirrhosis. Hence, identifying those at highest risk is particularly important to prioritize patients who will benefit from specialty care and will likely progress to the highly morbid and lethal state of decompensation.[29]

A recent systematic review identified 16 studies describing the development of models for the prediction of liver decompensation.[36] Intentioned to find clinically useful models, the review highlights significant concerns or limitations in 14 of the 16 studies identified. These limitations commonly included strict cohort definitions, small cohort sizes, and unmet statistical reporting standards.[37–43] Unfortunately, the model that was deemed most clinically ready for implementation (the ANTICIPATE-LRE model) predicted the occurrence of decompensation or

development of HCC, limiting specific clinical utility towards decompensation and ignores these two entities as distinct in pathophysiology, prognosis and management. To improve upon these limitations, we focused on predicting hepatic decompensation among all patients with cirrhosis in a large, national cohort (Figure 1). We further used available tools to comprehensively report methods and findings (Supplementary Tables 1a-1c).

To this end we included over 160,000 patients with baseline compensated cirrhosis inclusive of a variety of etiologies based on updated nomenclature definitions.[44] The validated model had excellent calibration, with risk estimates within 0.5% of the observed frequency on average (Figure 2). Among all patients, those in the lowest 5th percentile had a less than 3% risk of decompensation at 12 months. Conversely those in the highest 5th percentile had a risk of over 29%. Contrasting these subgroups showed that high risk patients tended to be older (66 versus 52), male (56% versus 37%), insured under an MA plan (69% versus 31%), and have a higher CCI (7.4 versus 3.6) (Tables 1a and 1b). This analysis also revealed that etiology significantly influenced risk. Patients with MASLD, MetALD, ALD, HCC, and severe renal disease were at high risk for decompensation, while those with biliary cirrhosis and HCV were at lower risk (Figures 3a and 3b). In some instances, the difference in risk based on etiology alone was substantial. For example, patients with ALD had a 14.5% risk of decompensation within 12 months, whereas those with biliary cirrhosis only had a 4.6% risk (Table 3a). However, the combination of cirrhosis etiology, comorbid conditions, and laboratory findings offered the deepest insight into anticipated hepatic dysfunction (Supplemental Figure 3).

The model demonstrated that laboratory values significantly influence the risk of decompensation. As anticipated, laboratory findings suggestive of more severe liver dysfunction, such as hyponatremia, thrombocytopenia, and hypoalbuminemia all conferred an increase in risk (Figures 4b-g). In isolation, this finding generally aligns with the increasing degree of liver dysfunction for patients with higher MELD scores.[45,46] However, our model shows that sole reliance on MELD as a surrogate indicator for liver dysfunction may provide clinicians

with false reassurance. We estimated decompensation risks for patients in our cohort with MELDs of 9, 16, and 21 corresponding to estimated 90-day mortalities of 0.6%, 6.7%, and 24.8% respectively.[47] For patients with ALD and a MELD of 9, the minimum risk of decompensation was 14%, which increased to nearly 19% if severe renal disease was also present (Table 3a). For patients with a MELD of 16, risks were even higher, with 26% of patients with MASLD and 32% of patients with MetALD predicted to decompensate within 12 months. These risks are especially significant given that a MELD of less than 20 is generally held to be "low" and unlikely to result in waitlisting or transplantation.[48,49]

Clinically applicable risk stratification for hepatic decompensation holds the potential to change clinical practice. Because of the clinical utility of this model and its potential use, we created a risk calculator that is available for clinicians to use to assess individualized risk of decompensation (https://gil-peled.github.io/UHG/index.html). Future work will include the use of the risk calculator to determine which patients benefit most from, referral for subspecialty consultation, institution preventative measures such as statins or beta-blockers, and listing for transplant.

LIMITATIONS

This study should be interpreted in the context of its limitations. The analyses focus on patients within the United States enrolled with one, large national insurer. Hence, the results may differ from patients who are uninsured. However, it allows comparison of outcomes in a population with financially equitable care. Also, the retrospective nature of the study necessitates reliance upon the accuracy of ICD-9, -10 and CPT codes for the diagnosis of cirrhosis. However, by only using codes that have been validated in the literature to capture patients with cirrhosis we are able to optimize the validity of the results, enhaching its reproducibility.[16–18,21,22,50] Lastly, it is not possible to collect information on patients after they disenroll. For this reason, only patients with adequate follow-up time were included in the risk

prediction model. However, by restricting the cohort to patietns with adequate follow-up offers precise, time-bound risk estimates at 6 and 12 months, which may enchance its utility for informed clinical decision-making.

CONCLUSIONS

Cirrhosis remains significant and increasing in its clinical impact in the United States. Despite this, its natural history is poorly understood. We constructed a temporally validated model for 6- and 12-month decompensation risk prediction for patients with baseline compensated cirrhosis. Patients most likely to decompensate were those with MASLD, MetALD, ALD, severe renal disease or HCC, and laboratory findings suggestive of greater hepatic dysfunction. Those with biliary cirrhosis and HCV were at lower risk. The associated risk calculator may be used by clinicians to aid in shared decision-making. Future work will aim to maximize benefit of the calculator in clinical management.

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STROBE Statement

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Abstract	"A large, national, insurance, claims database was used to conduct a retrospective cohort study of patients with baseline compensated cirrhosis between 2012 and 2022."
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3	"Multivariable logistic regression was used to predict 6- and 12-month decompensation risk." "The model had excellent calibration in derivation and validation sets, with predicted risks within 0.8% of true risk, on average"
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5	"Decompensation is costly, increasing morbidity and mortality..." "there is a lack in understanding as to how cirrhosis etiologies and clinical factors influence risk"
Objectives	3	State specific objectives, including any prespecified hypotheses	5	"The primary aim of this study was to investigate the effects of demographic and clinical factors on decompensation. The secondary aim was to create a clinical decision-support tool to assess the risk of decompensation."
Methods				
Study design	4	Present key elements of study design early in the paper	6	"A retrospective, longitudinal cohort study"

Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6	"Claims data from a large national insurer in the United States between July 1st, 2011, and July 1st, 2024... patients identified between January 1st, 2012, and December 30th, 2022 were selected."
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	6	"Patients with baseline compensated cirrhosis enrolled under any insurance plan type and at least 6 months of follow up were included…"
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	N/A	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8	"Covariates used included baseline demographics as categorical variables and laboratory values as continuous… decompensation was considered to be a claim listing a validated ICD-9, ICD-10, or CPT code indicating ascites, hepatic encephalopathy (HE), variceal bleeding (VB), hepatorenal syndrome (HRS), spontaneous bacterial peritonitis (SBP), or hepatopulmonary syndrome (HPS)."
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6	"Medical claims… included ICD-9 and ICD-10 codes, CPT codes… when available, linked laboratory results… Pharmacy claims contain data on

				outpatient prescriptions including drug names, dosages…"
Bias	9	Describe any efforts to address potential sources of bias	8	"The model was internally temporally cross validated... A sensitivity analysis was conducted by performing the validation procedure with interaction terms…"
Study size	10	Explain how the study size was arrived at	6	"Patients with baseline compensated cirrhosis enrolled under any insurance plan type and at least 6 months of follow up were included in the analysis"

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8	"Covariates used included baseline demographics as categorical variables and laboratory values as continuous"
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8	"Multivariable logistic regression was used… adjusting for demographics, comorbidities, labs, and cirrhosis etiology."
		(*b*) Describe any methods used to examine subgroups and interactions	6	"A sensitivity analysis was conducted… with interaction terms as detailed in the Supplemental Material."
		(*c*) Explain how missing data were addressed	8	**"**Those with missing laboratory values were excluded from the model. A sensitivity analysis was conducted comparing model performance with and without laboratory values (Supplementary Figures 4a and 4b)."
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	6	"End of observation was defined as the time of decompensation, transplant, disenrollment… or end of follow-up."
		(e) Describe any sensitivity analyses	9	"A sensitivity analysis was conducted… performance was found to be similar… final model was parsimonious."
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10	"188,526 patients with 6 months of follow-up, 167,684 had 12 months…"

		(b) Give reasons for non-participation at each stage	6	**“**Patients with baseline compensated cirrhosis enrolled under any insurance plan type and at least 6 months of follow up were included in the analysis (Figure 1).” **“**The end of observation was defined as the time of decompensation, transplant, disenrollment from the database, or the end of the 6- or 12-month follow-up periods.”
		(c) Consider use of a flow diagram	6	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9	“Mean age… Charlson index… etiologies… labs and comorbidities”
		(b) Indicate number of participants with missing data for each variable of interest	Supplemental Table 2b	-
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	9	“Mean follow-up time was 4.2 (2.6) years.”
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	10	“9,841 (5.2%) decompensated by 6 months; 18,907 (11.3%) by 12 months.”
		Case-control study—Report numbers in each exposure category, or summary measures of exposure		
		Cross-sectional study—Report numbers of outcome events or summary measures		
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10	“Model demonstrated… OR 1.9 for ALD… OR 0.5 for biliary… adjusted for covariates.”

	(*b*) Report category boundaries when continuous variables were categorized	11	"Tables 3a–3c show tertiles of MELD score… patients at <5th, >95th percentiles of decompensation risk."
	(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	12	"Patients with MELD of 21 and ALD had 12-month risk of 50.0%... contrasted to 22.0% for biliary."

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9	"Marginal effects plots… interaction terms… parsimonious model tested."
Discussion				
Key results	18	Summarise key results with reference to study objectives	12	"5.2% of patients decompensate by 6 months and 11.3% decompensate by 12 months after the identification of cirrhosis." "models based on these factors resulted in accurate risk estimates"
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13	"This study should be interpreted in the context of its limitations…"
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15	"We constructed a temporally validated model for 6- and 12-month decompensation risk prediction for patients with baseline compensated cirrhosis. Patients most likely to decompensate were those with MASLD, MetALD, ALD, ~~CKD on HD~~Severe renal disease or HCC, and laboratory findings suggestive of greater hepatic dysfunction. Those with biliary cirrhosis and HCV were at lower risk."
Generalisability	21	Discuss the generalisability (external validity) of the study results	15	"The associated risk calculator may be used by clinicians to aid in shared decision-making."
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	2	"The R01DK131164 supported…"

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

TRIPOD Checklist

Section/Topic	Item		Checklist Item	Page
Title and abstract				
Title	1	D;V	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract	2	D;V	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	3
Introduction				
Background and objectives	3a	D;V	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	5
	3b	D;V	Specify the objectives, including whether the study describes the development or validation of the model or both.	5
Methods				
Source of data	4a	D;V	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	6
	4b	D;V	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	6
Participants	5a	D;V	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	6,7
	5b	D;V	Describe eligibility criteria for participants.	6
	5c	D;V	Give details of treatments received, if relevant.	NA
Outcome	6a	D;V	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	8
	6b	D;V	Report any actions to blind assessment of the outcome to be predicted.	7
Predictors	7a	D;V	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.	8
	7b	D;V	Report any actions to blind assessment of predictors for the outcome and other predictors.	8
Sample size	8	D;V	Explain how the study size was arrived at.	6
Missing data	9	D;V	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	8
Statistical analysis methods	10a	D	Describe how predictors were handled in the analyses.	9
	10b	D	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	9
	10c	V	For validation, describe how the predictions were calculated.	8,9
	10d	D;V	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	9
	10e	V	Describe any model updating (e.g., recalibration) arising from the validation, if done.	9
Risk groups	11	D;V	Provide details on how risk groups were created, if done.	9
Development vs. validation	12	V	For validation, identify any differences from the development data in setting, eligibility criteria, outcome, and predictors.	8
Results				
Participants	13a	D;V	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	9
	13b	D;V	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	9
	13c	V	For validation, show a comparison with the development data of the distribution of important variables (demographics, predictors and outcome).	10
Model development	14a	D	Specify the number of participants and outcome events in each analysis.	10
	14b	D	If done, report the unadjusted association between each candidate predictor and outcome.	10,11
Model specification	15a	D	Present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	NA
	15b	D	Explain how to the use the prediction model.	9
Model performance	16	D;V	Report performance measures (with CIs) for the prediction model.	10
Model-updating	17	V	If done, report the results from any model updating (i.e., model specification, model performance).	10
Discussion				
Limitations	18	D;V	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	13

Interpretation	19a	V	For validation, discuss the results with reference to performance in the development data, and any other validation data.	10
	19b	D;V	Give an overall interpretation of the results, considering objectives, limitations, results from similar studies, and other relevant evidence.	15
Implications	20	D;V	Discuss the potential clinical use of the model and implications for future research.	15
Other information				
Supplementary information	21	D;V	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	10
Funding	22	D;V	Give the source of funding and the role of the funders for the present study.	2

*Items relevant only to the development of a prediction model are denoted by D, items relating solely to a validation of a prediction model are denoted by V, and items relating to both are denoted D;V. We recommend using the TRIPOD Checklist in conjunction with the TRIPOD Explanation and Elaboration document.

Supplemental Table Legends

Supplemental Table 1: Summary of PROBAST Risk of Bias Assessment tool.

Supplemental Tables 2a and 2b: Baseline demographics showing all etiology definitions for patients included in the 12-month decompensation risk model. Abbreviations: AIDS: acquired immunodeficiency syndrome; ALD: alcohol associated liver disease; Alcohol+: alcohol associated liver disease plus another cirrhosis etiology; Alcohol+HCV: alcohol associated liver disease and hepatitis C virus associated liver disease; CHF: congestive heart failure; CKD: chronic kidney disease; COM: commercial insurance; COPD: chronic obstructive pulmonary disease; CVA: cerebrovascular accident; DM: diabetes mellitus; HBV: hepatitis B associated cirrhosis; HCV: hepatitis C virus associated cirrhosis; HCV+: hepatitis C virus associated cirrhosis plus another cirrhosis etiology; HD: hemodialysis; HE: hepatic encephalopathy; HPS: hepatopulmonary syndrome; HRS: hepatorenal syndrome; MA: Medicare Advantage; MASLD: metabolic dysfunction-associated steatotic liver disease; MetALD: metabolic dysfunction-associated steatotic liver disease with increased alcohol intake; MI: myocardial infarction; Other: one other cirrhosis etiology not otherwise specified; Other 2+: two or more other cirrhosis etiologies not otherwise specified; PAD: peripheral arterial disease; PUD: peptic ulcer disease; SBP: spontaneous bacterial peritonitis; SD: standard deviation; VB: variceal bleeding

Supplemental Tables 3a and 3b: Baseline demographics showing all etiology definitions for patients excluded due to having 6-12 months of follow up. Abbreviations: AIDS: acquired immunodeficiency syndrome; ALD: alcohol associated liver disease; Alcohol+: alcohol associated liver disease plus another cirrhosis etiology; Alcohol+HCV: alcohol associated liver disease and hepatitis C virus associated liver disease; CHF: congestive heart failure; CKD: chronic kidney disease; COM: commercial insurance; COPD: chronic obstructive pulmonary disease; CVA: cerebrovascular accident; DM: diabetes mellitus; HBV: hepatitis B associated cirrhosis; HCV: hepatitis C virus associated cirrhosis; HCV+: hepatitis C virus associated cirrhosis plus another cirrhosis etiology; HD: hemodialysis; HE: hepatic encephalopathy; HPS: hepatopulmonary syndrome; HRS: hepatorenal syndrome; MA: Medicare Advantage; MASLD: metabolic dysfunction-associated steatotic liver disease; MetALD: metabolic dysfunction-associated steatotic liver disease with increased alcohol intake; MI: myocardial infarction; Other: one other cirrhosis etiology not otherwise specified; Other 2+: two or more other cirrhosis etiologies not otherwise specified; PAD: peripheral arterial disease; PUD: peptic ulcer disease; SBP: spontaneous bacterial peritonitis; SD: standard deviation; VB: variceal bleeding

Supplemental Tables 4a and 4b: Baseline demographics showing all etiology definitions for patients excluded for having less than 6 months of follow up. Abbreviations: AIDS: acquired immunodeficiency syndrome; ALD: alcohol associated liver disease; Alcohol+: alcohol associated liver disease plus another cirrhosis etiology; Alcohol+HCV: alcohol associated liver disease and hepatitis C virus associated liver disease; CHF: congestive heart failure; CKD: chronic kidney disease; COM: commercial insurance; COPD: chronic obstructive pulmonary disease; CVA: cerebrovascular accident; DM: diabetes mellitus; HBV: hepatitis B associated cirrhosis; HCV: hepatitis C virus associated cirrhosis; HCV+: hepatitis C virus associated cirrhosis plus another cirrhosis etiology; HD: hemodialysis; HE: hepatic encephalopathy; HPS: hepatopulmonary syndrome; HRS: hepatorenal syndrome; MA: Medicare Advantage; MASLD: metabolic dysfunction-associated steatotic liver disease; MetALD: metabolic dysfunction-associated steatotic liver disease with increased alcohol intake; MI: myocardial infarction; Other: one other cirrhosis etiology not otherwise specified; Other 2+: two or more other cirrhosis etiologies not otherwise specified; PAD: peripheral arterial disease; PUD: peptic ulcer disease; SBP: spontaneous bacterial peritonitis; SD: standard deviation; VB: variceal bleeding

Supplemental Tables 5a and 5b: Model calibration tables for the 6- and 12-month risk prediction models. Abbreviations: MELD: model for end-stage liver disease 3.0; ALD: alcohol associated liver disease; Alcohol+: alcohol associated liver disease plus another cirrhosis etiology; Alcohol+HCV: alcohol associated liver disease and hepatitis C virus associated liver disease; HBV: hepatitis B associated cirrhosis; HCV: hepatitis C virus associated cirrhosis; HCV+: hepatitis C virus associated cirrhosis plus another cirrhosis etiology; MASLD: metabolic dysfunction-associated steatotic liver disease; MetALD: metabolic dysfunction-associated steatotic liver disease with increased alcohol intake; MI: myocardial infarction; Other: one other cirrhosis etiology not otherwise specified; Other 2+: two or more other cirrhosis etiologies not otherwise specified

Supplemental Tables

Table 1: PROBAST Risk of Bias Assessment

Domain	Item	Question	Response
Participants	1.1	Were appropriate data sources used?	Yes
	1.2	Were inclusion/exclusion criteria appropriate?	Yes
	Domain-level Risk of Bias Judgment		Low risk of bias
Predictors	2.1	Were predictors defined and assessed in a similar way for all participants?	Yes
	2.2	Were predictor assessments made without knowledge of outcome?	No
	2.3	Are all predictors available at the time the model is intended to be used?	Yes
	Domain-level Risk of Bias Judgment		Low risk of bias

Outcome	3.1	Was the outcome determined appropriately?	Yes
	3.2	Was a pre-specified or standard outcome definition used?	Yes
	3.3	Were predictors excluded from the outcome definition?	Yes
	3.4	Was the outcome defined and determined in a similar way for all participants?	Yes
	3.5	Was the outcome assessed without knowledge of predictors?	No
	3.6	Was the time interval between predictor assessment and outcome appropriate?	Yes
	Domain-level Risk of Bias Judgment		Low risk of bias
Analysis	4.1	Were there a reasonable number of participants with the outcome?	Yes
	4.2	Were continuous and categorical predictors handled appropriately?	Yes
	4.3	Were all enrolled participants included in the analysis?	Yes
	4.4	Were missing data handled appropriately?	No

	4.5	Was selection of predictors based on univariable analysis avoided?	Yes
	4.6	Were complexities in the data (e.g., censoring, competing risks, sampling of control participants) accounted for	Yes
	4.7	Were relevant model performance measures evaluated appropriately?	Yes
	4.8	Were model overfitting and optimism in model performance accounted for?	Yes
	4.9	Do predictors and their assigned weights in the final model correspond to the results from the reported multivariable analysis?	Yes
	Domain-level Risk of Bias Judgment		Low risk of bias
Overall Assessment	Overall Judgement about Risk of Bias		Low risk of bias

Supplemental Tables 2a and 2b: Baseline Demographics

Supplemental Table 2a

	Total	MASLD	METALD	ALD	HBV	HCV	Biliary	Other	Alcohol +	HCV +	Alcohol + HCV	Other 2+
Total N (% of row)	167684 (100%)	79031 (47.13%)	20508 (12.23%)	3573 (2.13%)	3294 (1.96%)	23706 (14.14%)	13935 (8.31%)	14270 (8.51%)	1112 (0.66%)	2258 (1.35%)	4360 (2.6%)	1637 (0.98%)
Age; mean (SD)	63.22 (12.46)	65.48 (12.12)	63.16 (11.31)	56.08 (13.2)	59.62 (13.3)	62.45 (8.92)	61.69 (14.01)	57.72 (16.02)	60.75 (12.33)	61.29 (11.41)	61.31 (8.61)	58.99 (14.96)
18-64; N (% of column)	78946 (47.08%)	31176 (39.45%)	9815 (47.86%)	2404 (67.28%)	1833 (55.65%)	13157 (55.5%)	6848 (49.14%)	8257 (57.86%)	642 (57.73%)	1310 (58.02%)	2588 (59.36%)	916 (55.96%)
65-69; N (% of column)	37814 (22.55%)	17264 (21.84%)	4834 (23.57%)	696 (19.48%)	671 (20.37%)	6453 (27.22%)	2806 (20.14%)	2955 (20.71%)	203 (18.26%)	444 (19.66%)	1194 (27.39%)	294 (17.96%)
70-74; N (% of column)	23554 (14.05%)	12993 (16.44%)	2943 (14.35%)	285 (7.98%)	413 (12.54%)	2450 (10.33%)	1915 (13.74%)	1501 (10.52%)	145 (13.04%)	274 (12.13%)	423 (9.7%)	212 (12.95%)
75-79; N (% of column)	14725 (8.78%)	8976 (11.36%)	1720 (8.39%)	120 (3.36%)	223 (6.77%)	1045 (4.41%)	1315 (9.44%)	877 (6.15%)	75 (6.74%)	131 (5.8%)	107 (2.45%)	136 (8.31%)
80+; N (% of column)	12645 (7.54%)	8622 (10.91%)	1196 (5.83%)	68 (1.9%)	154 (4.68%)	601 (2.54%)	1051 (7.54%)	680 (4.77%)	47 (4.23%)	99 (4.38%)	48 (1.1%)	79 (4.83%)
Male	85150 (50.78%)	36615 (46.33%)	14546 (70.93%)	2261 (63.28%)	2189 (66.45%)	14870 (62.73%)	2437 (17.49%)	6604 (46.28%)	679 (61.06%)	1330 (58.9%)	3294 (75.55%)	325 (19.85%)
Years of follow up after index mean	4.15 (2.63)	3.99 (2.51)	3.85 (2.45)	3.9 (2.56)	4.56 (2.85)	4.64 (2.82)	4.53 (2.8)	4.25 (2.75)	4.06 (2.63)	4.66 (2.86)	4.03 (2.51)	4.32 (2.66)
Insurance Plan Type												
COM; N (% of column)	57975 (34.57%)	23298 (29.48%)	6583 (32.1%)	1804 (50.49%)	1614 (49%)	8079 (34.08%)	6251 (44.86%)	6805 (47.69%)	516 (46.4%)	1008 (44.64%)	1163 (26.67%)	854 (52.17%)
MA; N (% of column)	98071 (58.49%)	49597 (62.76%)	12549 (61.19%)	1664 (46.57%)	1512 (45.9%)	14057 (59.3%)	6701 (48.09%)	6741 (47.24%)	505 (45.41%)	1078 (47.74%)	2988 (68.53%)	679 (41.48%)
Both; N (% of column)	11638 (6.94%)	6136 (7.76%)	1376 (6.71%)	105 (2.94%)	168 (5.1%)	1570 (6.62%)	983 (7.05%)	724 (5.07%)	91 (8.18%)	172 (7.62%)	209 (4.79%)	104 (6.35%)
Comorbidities												
Charlson; mean (SD)	5.77 (3.12)	6.66 (3.18)	5.77 (3.01)	3.45 (2.11)	4.83 (3.02)	5.13 (2.66)	4.52 (2.67)	4.27 (2.66)	5.51 (3.22)	5.43 (3.01)	5.33 (2.79)	4.41 (2.79)
Prior MI; N (% of column)	10226 (6.1%)	6200 (7.85%)	1550 (7.56%)	35 (0.98%)	108 (3.28%)	1083 (4.57%)	435 (3.12%)	251 (1.76%)	73 (6.56%)	121 (5.36%)	317 (7.27%)	53 (3.24%)
CHF; N (% of column)	25419 (15.16%)	15728 (19.9%)	3776 (18.41%)	160 (4.48%)	267 (8.11%)	2462 (10.39%)	1036 (7.43%)	824 (5.77%)	178 (16.01%)	295 (13.06%)	571 (13.1%)	122 (7.45%)
PAD; N (% of column)	38505 (22.96%)	22800 (28.85%)	5609 (27.35%)	202 (5.65%)	503 (15.27%)	4229 (17.84%)	1837 (13.18%)	1239 (8.68%)	290 (26.08%)	497 (22.01%)	1051 (24.11%)	248 (15.15%)
CVA; N (% of column)	19212 (11.46%)	11240 (14.22%)	2906 (14.17%)	94 (2.63%)	244 (7.41%)	1930 (8.14%)	1135 (8.14%)	540 (3.78%)	159 (14.3%)	278 (12.31%)	537 (12.32%)	149 (9.1%)
Dementia; N (% of column)	5285 (3.15%)	3043 (3.85%)	1088 (5.31%)	68 (1.9%)	54 (1.64%)	352 (1.48%)	243 (1.74%)	151 (1.06%)	41 (3.69%)	46 (2.04%)	168 (3.85%)	31 (1.89%)
COPD; N (% of column)	47844 (28.53%)	25815 (32.66%)	6836 (33.33%)	517 (14.47%)	572 (17.36%)	6015 (25.37%)	2811 (20.17%)	2223 (15.58%)	375 (33.72%)	704 (31.18%)	1608 (36.88%)	368 (22.48%)
Rheumatic Disease; N (% of colum	10227 (6.1%)	5342 (6.76%)	798 (3.89%)	62 (1.74%)	139 (4.22%)	1013 (4.27%)	1486 (10.66%)	666 (4.67%)	98 (8.81%)	188 (8.33%)	178 (4.08%)	257 (15.7%)
PUD; N (% of column)	4377 (2.61%)	2345 (2.97%)	672 (3.28%)	51 (1.43%)	81 (2.46%)	456 (1.92%)	273 (1.96%)	213 (1.49%)	47 (4.23%)	83 (3.68%)	115 (2.64%)	41 (2.5%)
Uncomplicated DA; N (% of column	65485 (39.05%)	43141 (54.59%)	7146 (34.84%)	0 (0%)	988 (29.99%)	7142 (30.13%)	3046 (21.86%)	1343 (9.41%)	337 (30.31%)	781 (34.59%)	1222 (28.03%)	339 (20.71%)
Complicated DA; N (% of column)	31430 (18.74%)	21645 (27.39%)	3434 (16.74%)	0 (0%)	409 (12.42%)	3033 (12.79%)	1176 (8.44%)	544 (3.81%)	144 (12.95%)	303 (13.42%)	629 (14.43%)	113 (6.9%)
Hemiplegia; N (% of column)	2158 (1.29%)	1158 (1.47%)	362 (1.77%)	17 (0.48%)	33 (1%)	258 (1.09%)	124 (0.89%)	69 (0.48%)	13 (1.17%)	27 (1.2%)	87 (2%)	10 (0.61%)
Malignancy; N (% of column)	21104 (12.59%)	11543 (14.61%)	2242 (10.93%)	185 (5.18%)	514 (15.6%)	2748 (11.59%)	1255 (9.01%)	1373 (9.62%)	168 (15.11%)	394 (17.45%)	533 (12.22%)	149 (9.1%)
Metastasis; N (% of column)	3152 (1.88%)	1979 (2.5%)	304 (1.48%)	32 (0.9%)	50 (1.52%)	304 (1.28%)	127 (0.91%)	222 (1.56%)	23 (2.07%)	34 (1.51%)	63 (1.44%)	14 (0.86%)
AIDS; N (% of column)	95 (0.06%)	26 (0.03%)	7 (0.03%)	2 (0.06%)	4 (0.12%)	32 (0.13%)	3 (0.02%)	4 (0.03%)	3 (0.27%)	5 (0.22%)	6 (0.14%)	3 (0.18%)
CKD; N (% of column)	23451 (13.99%)	14757 (18.67%)	2956 (14.41%)	70 (1.96%)	379 (11.51%)	2417 (10.2%)	1154 (8.28%)	639 (4.48%)	151 (13.58%)	259 (11.47%)	516 (11.83%)	153 (9.35%)
CKD on HD; N (% of column)	4392 (2.62%)	2576 (3.26%)	550 (2.68%)	15 (0.42%)	90 (2.73%)	566 (2.39%)	178 (1.28%)	147 (1.03%)	38 (3.42%)	87 (3.85%)	125 (2.87%)	20 (1.22%)

Supplemental Table 2b

	Total	MASLD	METALD	ALD	HBV	HCV	Biliary	Other	Alcohol +	HCV +	Alcohol + HCV	Other 2+
Total N (% of row)	167684 (100%)	79031 (47.13%)	20508 (12.23%)	3573 (2.13%)	3294 (1.96%)	23706 (14.14%)	13935 (8.31%)	14270 (8.51%)	1112 (0.66%)	2258 (1.35%)	4360 (2.6%)	1637 (0.98%)
Platelet; observations (% of column)	54157 (32.3%)	25354 (32.08%)	6273 (30.59%)	834 (23.34%)	1262 (38.31%)	8377 (35.34%)	4525 (32.47%)	3946 (27.65%)	422 (37.95%)	948 (41.98%)	1518 (34.82%)	698 (42.64%)
Platelet; median (IQR)	190000 (119000)	188000 (119000)	190000 (120000)	171000 (122750)	181000 (97750)	168000 (101000)	252000 (101000)	181000 (118000)	218000 (116750)	190000 (103250)	171000 (105000)	241500 (98000)
Sodium; observations (% of column)	61184 (36.49%)	29516 (37.35%)	7135 (34.79%)	914 (25.58%)	1393 (42.29%)	9026 (38.07%)	5055 (36.28%)	4255 (29.82%)	463 (41.64%)	1025 (45.39%)	1658 (38.03%)	744 (45.45%)
Sodium; median (IQR)	140 (4)	140 (4)	139 (4)	140 (3)	140 (3)	140 (3)	140 (4)	140 (3)	139 (4)	140 (3)	139 (4)	140 (4)
Creatinine; observations (% of column)	62949 (37.54%)	30355 (38.41%)	7342 (35.8%)	941 (26.34%)	1436 (43.59%)	9296 (39.21%)	5201 (37.32%)	4384 (30.72%)	478 (42.99%)	1054 (46.68%)	1702 (39.04%)	760 (46.43%)
Creatinine; median (IQR)	0.87 (0.32)	0.88 (0.35)	0.88 (0.33)	0.81 (0.27)	0.91 (0.32)	0.88 (0.29)	0.8 (0.26)	0.82 (0.28)	0.86 (0.28)	0.9 (0.3)	0.88 (0.3)	0.8 (0.27)
Albumin; observations (% of column)	62696 (37.39%)	29782 (37.68%)	7102 (34.63%)	937 (26.22%)	1442 (43.78%)	9196 (38.79%)	5655 (40.58%)	4523 (31.7%)	487 (43.79%)	1070 (47.39%)	1676 (38.44%)	826 (50.46%)
Albumin; median (IQR)	4.2 (0.5)	4.2 (0.5)	4.2 (0.6)	4.2 (0.7)	4.3 (0.5)	4.2 (0.5)	4.2 (0.4)	4.2 (0.7)	4.2 (0.6)	4.2 (0.6)	4.1 (0.6)	4.2 (0.4)
INR; observations (% of column)	22151 (13.21%)	9659 (12.22%)	2165 (10.56%)	395 (11.06%)	522 (15.85%)	4151 (17.51%)	1621 (11.63%)	1969 (13.8%)	205 (18.44%)	462 (20.46%)	697 (15.99%)	305 (18.63%)
INR; median (IQR)	1.1 (0.1)	1.1 (0.1)	1.1 (0.2)	1.1 (0.2)	1 (0.1)	1.1 (0.1)	1 (0)	1.1 (0.1)	1 (0.1)	1 (0.1)	1.1 (0.2)	1 (0.1)
Bilirubin; observations (% of column)	61038 (36.4%)	28745 (36.37%)	6868 (33.49%)	906 (25.36%)	1421 (43.14%)	9197 (38.8%)	5445 (39.07%)	4425 (31.01%)	481 (43.26%)	1059 (46.9%)	1684 (38.62%)	807 (49.3%)
Bilirubin; median (IQR)	0.6 (0.5)	0.6 (0.5)	0.6 (0.6)	0.7 (0.8)	0.6 (0.4)	0.6 (0.5)	0.5 (0.3)	0.6 (0.6)	0.6 (0.6)	0.6 (0.4)	0.6 (0.5)	0.5 (0.3)
MELD; observations (% of column)	14278 (8.51%)	6030 (7.63%)	1386 (6.76%)	271 (7.58%)	388 (11.78%)	2778 (11.72%)	1013 (7.27%)	1312 (9.19%)	134 (12.05%)	316 (13.99%)	457 (10.48%)	193 (11.79%)
MELD; median (IQR)	11 (4)	11 (4)	11 (5)	11 (5)	10 (2)	10 (3)	10 (2)	11 (4)	10 (6)	10 (3)	11 (4)	10 (4)
AST; observations (% of column)	62085 (37.02%)	29402 (37.2%)	7011 (34.19%)	924 (25.86%)	1454 (44.14%)	9129 (38.51%)	5622 (40.34%)	4491 (31.47%)	490 (44.06%)	1065 (47.17%)	1670 (38.3%)	827 (50.52%)
AST; median (IQR)	30 (26)	29 (23)	31 (31)	31 (31)	27 (17)	31 (36)	27 (20)	31 (28)	32 (32)	30 (29)	38 (50)	30 (24)
ALT; observations (% of column)	62868 (37.49%)	29648 (37.51%)	7049 (34.37%)	928 (25.97%)	1469 (44.6%)	9453 (39.88%)	5651 (40.55%)	4530 (31.74%)	492 (44.24%)	1087 (48.14%)	1732 (39.72%)	829 (50.64%)
ALT; median (IQR)	27 (28)	26 (25)	26 (26)	25 (23)	27 (22)	30 (43)	26 (26)	27 (30)	30 (36.25)	29 (35)	34 (49)	30 (31)
AST/ALT ratio; observations (% of colu	61740 (36.82%)	29228 (36.98%)	6964 (33.96%)	920 (25.75%)	1447 (43.93%)	9085 (38.32%)	5598 (40.17%)	4466 (31.3%)	485 (43.62%)	1060 (46.94%)	1665 (38.19%)	822 (50.21%)
AST/ALT ratio; median (IQR)	1.12 (0.58)	1.12 (0.56)	1.23 (0.7)	1.33 (0.75)	1.04 (0.48)	1.1 (0.54)	1.05 (0.51)	1.14 (0.63)	1.12 (0.64)	1.06 (0.55)	1.15 (0.62)	1.04 (0.56)
FIB-4; observations (% of column)	50835 (30.32%)	23590 (29.85%)	5850 (28.53%)	781 (21.86%)	1225 (37.19%)	7942 (33.5%)	4314 (30.96%)	3685 (25.82%)	403 (36.24%)	908 (40.21%)	1453 (33.33%)	684 (41.78%)
FIB-4; median (IQR)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Supplemental Tables 3a and 3b: Baseline Demographics of Patients with 6-12 Months of Follow-up

Supplemental Table 3a

	Total	MASLD	METALD	ALD	HBV	HCV	Biliary	Other	Alcohol +	HCV +	Alcohol + HCV	Other 2+
Total N (% of row)	20842 (100%)	9408 (45.14%)	2899 (13.91%)	651 (3.12%)	352 (1.69%)	2908 (13.95%)	1499 (7.19%)	1946 (9.34%)	110 (0.53%)	257 (1.23%)	612 (2.94%)	200 (0.96%)
Age; mean (SD)	62.22 (13.34)	65.31 (13.15)	61.4 (11.99)	55.28 (13.08)	56.98 (14.11)	61.52 (9.38)	60.43 (15.02)	56.21 (16.25)	58.3 (12.25)	60.21 (11.51)	59.6 (9.44)	55.24 (14.95)
18-64; N (% of column)	11287 (54.16%)	4116 (43.75%)	1672 (57.68%)	482 (74.04%)	232 (65.91%)	1836 (63.14%)	873 (58.24%)	1279 (65.72%)	80 (72.73%)	157 (61.09%)	421 (68.79%)	139 (69.5%)
65-69; N (% of column)	3804 (18.25%)	1721 (18.29%)	519 (17.9%)	94 (14.44%)	62 (17.61%)	632 (21.73%)	226 (15.08%)	324 (16.65%)	9 (8.18%)	55 (21.4%)	133 (21.73%)	29 (14.5%)
70-74; N (% of column)	2315 (11.11%)	1298 (13.8%)	330 (11.38%)	38 (5.84%)	18 (5.11%)	247 (8.49%)	136 (9.07%)	157 (8.07%)	11 (10%)	26 (10.12%)	42 (6.86%)	12 (6%)
75-79; N (% of column)	1541 (7.39%)	927 (9.85%)	200 (6.9%)	20 (3.07%)	22 (6.25%)	111 (3.82%)	124 (8.27%)	97 (4.98%)	8 (7.27%)	9 (3.5%)	9 (1.47%)	14 (7%)
80+; N (% of column)	1895 (9.09%)	1346 (14.31%)	178 (6.14%)	17 (2.61%)	18 (5.11%)	82 (2.82%)	140 (9.34%)	89 (4.57%)	2 (1.82%)	10 (3.89%)	7 (1.14%)	6 (3%)
Male	11480 (55.08%)	4718 (50.15%)	2111 (72.82%)	421 (64.67%)	248 (70.45%)	1900 (65.34%)	301 (20.08%)	1012 (52%)	72 (65.45%)	162 (63.04%)	487 (79.58%)	48 (24%)
Years of follow up after index mean	0.74 (0.14)	0.74 (0.14)	0.74 (0.14)	0.75 (0.15)	0.74 (0.14)	0.74 (0.14)	0.75 (0.14)	0.75 (0.15)	0.74 (0.13)	0.74 (0.14)	0.73 (0.15)	0.75 (0.14)
Insurance Plan Type												
COM; N (% of column)	10856 (52.09%)	4194 (44.58%)	1445 (49.84%)	421 (64.67%)	244 (69.32%)	1675 (57.6%)	935 (62.37%)	1270 (65.26%)	66 (60%)	144 (56.03%)	303 (49.51%)	159 (79.5%)
MA; N (% of column)	9536 (45.75%)	4929 (52.39%)	1384 (47.74%)	227 (34.87%)	103 (29.26%)	1196 (41.13%)	543 (36.22%)	663 (34.07%)	40 (36.36%)	107 (41.63%)	303 (49.51%)	41 (20.5%)
Both; N (% of column)	450 (2.16%)	285 (3.03%)	70 (2.41%)	3 (0.46%)	5 (1.42%)	37 (1.27%)	21 (1.4%)	13 (0.67%)	4 (3.64%)	6 (2.33%)	6 (0.98%)	0 (0%)
Comorbidities												
Charlson; mean (SD)	5.67 (3.51)	6.78 (3.66)	5.44 (3.24)	3.37 (2.23)	4.65 (3.4)	4.98 (2.95)	4.38 (3.06)	4.02 (2.82)	5.09 (3.3)	5.32 (3.63)	5.21 (3.14)	3.94 (2.86)
Prior MI; N (% of column)	1420 (6.81%)	881 (9.36%)	215 (7.42%)	5 (0.77%)	21 (5.97%)	124 (4.26%)	60 (4%)	35 (1.8%)	7 (6.36%)	15 (5.84%)	53 (8.66%)	4 (2%)
CHF; N (% of column)	3735 (17.92%)	2341 (24.88%)	558 (19.25%)	28 (4.3%)	32 (9.09%)	348 (11.97%)	138 (9.21%)	123 (6.32%)	22 (20%)	31 (12.06%)	103 (16.83%)	11 (5.5%)
PAD; N (% of column)	4906 (23.54%)	2963 (31.49%)	758 (26.15%)	32 (4.92%)	54 (15.34%)	481 (16.54%)	201 (13.41%)	161 (8.27%)	26 (23.64%)	57 (22.18%)	148 (24.18%)	25 (12.5%)
CVA; N (% of column)	2384 (11.44%)	1405 (14.93%)	409 (14.11%)	19 (2.92%)	22 (6.25%)	216 (7.43%)	124 (8.27%)	68 (3.49%)	10 (9.09%)	29 (11.28%)	63 (10.29%)	19 (9.5%)
Dementia; N (% of column)	895 (4.29%)	534 (5.68%)	183 (6.31%)	12 (1.84%)	6 (1.7%)	51 (1.75%)	44 (2.94%)	31 (1.59%)	3 (2.73%)	6 (2.33%)	23 (3.76%)	2 (1%)
COPD; N (% of column)	5949 (28.54%)	3194 (33.95%)	963 (33.22%)	92 (14.13%)	61 (17.33%)	720 (24.76%)	294 (19.61%)	247 (12.69%)	40 (36.36%)	72 (28.02%)	225 (36.76%)	41 (20.5%)
Rheumatic Disease; N (% of column)	1156 (5.55%)	585 (6.22%)	103 (3.55%)	10 (1.54%)	13 (3.69%)	120 (4.13%)	170 (11.34%)	74 (3.8%)	9 (8.18%)	21 (8.17%)	21 (3.43%)	30 (15%)
PUD; N (% of column)	473 (2.27%)	262 (2.78%)	85 (2.93%)	7 (1.08%)	5 (1.42%)	50 (1.72%)	25 (1.67%)	21 (1.08%)	1 (0.91%)	5 (1.95%)	9 (1.47%)	3 (1.5%)
Uncomplicated DA; N (% of column)	7763 (37.25%)	5074 (53.93%)	957 (33.01%)	0 (0%)	100 (28.41%)	829 (28.51%)	336 (22.41%)	149 (7.66%)	39 (35.45%)	87 (33.85%)	151 (24.67%)	41 (20.5%)
Complicated DA; N (% of column)	3708 (17.79%)	2531 (26.9%)	428 (14.76%)	0 (0%)	43 (12.22%)	353 (12.14%)	133 (8.87%)	84 (4.32%)	18 (16.36%)	39 (15.18%)	64 (10.46%)	15 (7.5%)
Hemiplegia; N (% of column)	305 (1.46%)	186 (1.98%)	44 (1.52%)	4 (0.61%)	3 (0.85%)	35 (1.2%)	16 (1.07%)	6 (0.31%)	0 (0%)	3 (1.17%)	8 (1.31%)	0 (0%)
Malignancy; N (% of column)	3295 (15.81%)	1764 (18.75%)	360 (12.42%)	55 (8.45%)	69 (19.6%)	461 (15.85%)	143 (9.54%)	243 (12.49%)	13 (11.82%)	52 (20.23%)	113 (18.46%)	22 (11%)
Metastasis; N (% of column)	850 (4.08%)	516 (5.48%)	80 (2.76%)	14 (2.15%)	14 (3.98%)	87 (2.99%)	37 (2.47%)	60 (3.08%)	2 (1.82%)	11 (4.28%)	24 (3.92%)	5 (2.5%)
AIDS; N (% of column)	8 (0.04%)	3 (0.03%)	0 (0%)	0 (0%)	2 (0.57%)	1 (0.03%)	1 (0.07%)	0 (0%)	0 (0%)	0 (0%)	1 (0.16%)	0 (0%)
CKD; N (% of column)	3031 (14.54%)	1950 (20.73%)	388 (13.38%)	8 (1.23%)	42 (11.93%)	297 (10.21%)	126 (8.41%)	97 (4.98%)	19 (17.27%)	40 (15.56%)	50 (8.17%)	14 (7%)
CKD on HD; N (% of column)	721 (3.46%)	421 (4.47%)	85 (2.93%)	5 (0.77%)	17 (4.83%)	95 (3.27%)	28 (1.87%)	30 (1.54%)	6 (5.45%)	11 (4.28%)	22 (3.59%)	1 (0.5%)

Supplemental Table 3b

	Total	MASLD	METALD	ALD	HBV	HCV	Biliary	Other	Alcohol +	HCV +	Alcohol + HCV	Other 2+
Total N (% of row)	20842 (100%)	9408 (45.14%)	2899 (13.91%)	651 (3.12%)	352 (1.69%)	2908 (13.95%)	1499 (7.19%)	1946 (9.34%)	110 (0.53%)	257 (1.23%)	612 (2.94%)	200 (0.96%)
Platelet; observations (% of column)	6231 (29.9%)	2730 (29.02%)	809 (27.91%)	151 (23.2%)	129 (36.65%)	965 (33.18%)	509 (33.96%)	529 (27.18%)	46 (41.82%)	112 (43.58%)	168 (27.45%)	83 (41.5%)
Platelet; median (IQR)	183000 (125000)	185000 (125000)	181000 (135000)	162000 (128500)	175000 (112000)	157000 (1e+05)	247000 (107000)	174000 (137000)	175500 (140000)	175500 (110500)	153500 (121500)	241000 (109000)
Sodium; observations (% of column)	7080 (33.97%)	3251 (34.56%)	921 (31.77%)	167 (25.65%)	141 (40.06%)	1037 (35.66%)	544 (36.29%)	578 (29.7%)	45 (40.91%)	121 (47.08%)	186 (30.39%)	89 (44.5%)
Sodium; median (IQR)	140 (3)	140 (4)	139 (4)	140 (4)	140 (2)	140 (3)	140 (3)	140 (3)	140 (4)	140 (4)	139 (4)	140 (4)
Creatinine; observations (% of column)	7300 (35.03%)	3357 (35.68%)	950 (32.77%)	177 (27.19%)	145 (41.19%)	1060 (36.45%)	563 (37.56%)	595 (30.58%)	47 (42.73%)	124 (48.25%)	189 (30.88%)	93 (46.5%)
Creatinine; median (IQR)	0.87 (0.35)	0.9 (0.4)	0.86 (0.36)	0.79 (0.27)	0.92 (0.34)	0.88 (0.33)	0.8 (0.27)	0.81 (0.28)	0.87 (0.41)	0.88 (0.33)	0.85 (0.3)	0.78 (0.28)
Albumin; observations (% of column)	7210 (34.59%)	3256 (34.61%)	913 (31.49%)	163 (25.04%)	139 (39.49%)	1065 (36.62%)	607 (40.49%)	604 (31.04%)	47 (42.73%)	127 (49.42%)	190 (31.05%)	99 (49.5%)
Albumin; median (IQR)	4.1 (0.7)	4 (0.7)	4 (0.8)	4.1 (0.8)	4.3 (0.55)	4.1 (0.6)	4.2 (0.5)	4.1 (0.6)	4.2 (0.7)	4.2 (0.7)	4 (0.8)	4.2 (0.55)
INR; observations (% of column)	2537 (12.17%)	1026 (10.91%)	273 (9.42%)	60 (9.22%)	53 (15.06%)	483 (16.61%)	181 (12.07%)	254 (13.05%)	22 (20%)	55 (21.4%)	93 (15.2%)	37 (18.5%)
INR; median (IQR)	1.1 (0.2)	1.1 (0.2)	1.1 (0.3)	1.1 (0.29)	1.1 (0.2)	1.1 (0.1)	1 (0.1)	1.1 (0.2)	1.1 (0.17)	1.1 (0.1)	1.1 (0.2)	1 (0.1)
Bilirubin; observations (% of column)	7004 (33.61%)	3128 (33.25%)	883 (30.46%)	160 (24.58%)	137 (38.92%)	1057 (36.35%)	592 (39.49%)	584 (30.01%)	45 (40.91%)	129 (50.19%)	191 (31.21%)	98 (49%)
Bilirubin; median (IQR)	0.6 (0.6)	0.6 (0.5)	0.7 (0.7)	0.85 (1.02)	0.7 (0.5)	0.6 (0.5)	0.5 (0.4)	0.7 (0.7)	0.7 (1.1)	0.6 (0.5)	0.7 (0.6)	0.6 (0.2)
MELD; observations (% of column)	1613 (7.74%)	629 (6.69%)	159 (5.48%)	41 (6.3%)	40 (11.36%)	322 (11.07%)	114 (7.61%)	171 (8.79%)	13 (11.82%)	34 (13.23%)	65 (10.62%)	25 (12.5%)
MELD; median (IQR)	11 (5)	11 (5)	13 (8)	13 (9)	10.5 (4)	11 (4)	10 (3.75)	11 (4)	12 (6)	10.5 (5.25)	11 (4)	11 (4)
AST; observations (% of column)	7129 (34.2%)	3181 (33.81%)	903 (31.15%)	170 (26.11%)	141 (40.06%)	1057 (36.35%)	614 (40.96%)	599 (30.78%)	48 (43.64%)	129 (50.19%)	186 (30.39%)	101 (50.5%)
AST; median (IQR)	31 (30)	30 (24)	34 (37.5)	34 (48.75)	27 (18)	37 (44)	28 (24.75)	33 (31)	42.5 (67.75)	36 (37)	51 (63)	33 (34)
ALT; observations (% of column)	7236 (34.72%)	3217 (34.19%)	910 (31.39%)	170 (26.11%)	143 (40.62%)	1095 (37.65%)	618 (41.23%)	605 (31.09%)	49 (44.55%)	132 (51.36%)	195 (31.86%)	102 (51%)
ALT; median (IQR)	28 (29)	26 (25)	27 (26)	27 (22)	27 (24)	34 (46.5)	28 (29)	29 (31)	32 (45)	32.5 (34)	43 (51.5)	32 (35)
AST/ALT ratio; observations (% of column)	7086 (34%)	3157 (33.56%)	898 (30.98%)	169 (25.96%)	141 (40.06%)	1052 (36.18%)	611 (40.76%)	594 (30.52%)	48 (43.64%)	129 (50.19%)	186 (30.39%)	101 (50.5%)
AST/ALT ratio; median (IQR)	1.16 (0.67)	1.16 (0.68)	1.33 (0.89)	1.46 (0.75)	1.06 (0.55)	1.12 (0.57)	1.05 (0.54)	1.14 (0.66)	1.16 (0.92)	1.06 (0.58)	1.25 (0.7)	1.05 (0.57)
FIB-4; observations (% of column)	5807 (27.86%)	2499 (26.56%)	755 (26.04%)	141 (21.66%)	124 (35.23%)	925 (31.81%)	482 (32.15%)	488 (25.08%)	41 (37.27%)	111 (43.19%)	161 (26.31%)	80 (40%)
FIB-4; median (IQR)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Supplemental Tables 4a and 4b: Baseline Demographics of Patients with <6 months of Follow-up

Supplemental Table 4a

	Total	MASLD	METALD	ALD	HBV	HCV	Biliary	Other	Alcohol +	HCV +	Alcohol + HCV	Other 2+
Total N (% of row)	23651 (100%)	11078 (46.84%)	3666 (15.5%)	810 (3.42%)	441 (1.86%)	2801 (11.84%)	1418 (6%)	2131 (9.01%)	172 (0.73%)	258 (1.09%)	713 (3.01%)	163 (0.69%)
Age; mean (SD)	62.4 (14.21)	66.33 (13.85)	61.28 (12.76)	53.26 (13.79)	56.72 (14.06)	61.14 (9.45)	58.24 (15.66)	55.26 (17.09)	57.6 (14.97)	59.02 (11.42)	59.98 (9.81)	53.34 (14.14)
18-64; N (% of column)	12410 (52.47%)	4507 (40.68%)	2080 (56.74%)	613 (75.68%)	300 (68.03%)	1742 (62.19%)	881 (62.13%)	1417 (66.49%)	111 (64.53%)	178 (68.99%)	465 (65.22%)	116 (71.17%)
65-69; N (% of column)	4335 (18.33%)	1998 (18.04%)	666 (18.17%)	109 (13.46%)	70 (15.87%)	651 (23.24%)	230 (16.22%)	349 (16.38%)	27 (15.7%)	49 (18.99%)	158 (22.16%)	28 (17.18%)
70-74; N (% of column)	2409 (10.19%)	1349 (12.18%)	386 (10.53%)	47 (5.8%)	33 (7.48%)	237 (8.46%)	111 (7.83%)	146 (6.85%)	10 (5.81%)	14 (5.43%)	66 (9.26%)	10 (6.13%)
75-79; N (% of column)	1788 (7.56%)	1175 (10.61%)	261 (7.12%)	25 (3.09%)	15 (3.4%)	100 (3.57%)	91 (6.42%)	80 (3.75%)	13 (7.56%)	7 (2.71%)	14 (1.96%)	7 (4.29%)
80+; N (% of column)	2709 (11.45%)	2049 (18.5%)	273 (7.45%)	16 (1.98%)	23 (5.22%)	71 (2.53%)	105 (7.4%)	139 (6.52%)	11 (6.4%)	10 (3.88%)	10 (1.4%)	2 (1.23%)
Male	13354 (56.46%)	5723 (51.66%)	2673 (72.91%)	542 (66.91%)	310 (70.29%)	1831 (65.37%)	290 (20.45%)	1124 (52.75%)	107 (62.21%)	162 (62.79%)	556 (77.98%)	36 (22.09%)
Years of follow up after index mean	0.24 (0.14)	0.24 (0.14)	0.23 (0.14)	0.23 (0.14)	0.24 (0.14)	0.25 (0.14)	0.24 (0.14)	0.23 (0.14)	0.25 (0.14)	0.24 (0.14)	0.23 (0.13)	0.23 (0.14)
Insurance Plan Type												
COM; N (% of column)	12386 (52.37%)	4767 (43.03%)	1937 (52.84%)	550 (67.9%)	306 (69.39%)	1659 (59.23%)	974 (68.69%)	1404 (65.88%)	114 (66.28%)	174 (67.44%)	369 (51.75%)	132 (80.98%)
MA; N (% of column)	10784 (45.6%)	6012 (54.27%)	1647 (44.93%)	256 (31.6%)	133 (30.16%)	1116 (39.84%)	418 (29.48%)	705 (33.08%)	54 (31.4%)	77 (29.84%)	338 (47.41%)	28 (17.18%)
Both; N (% of column)	481 (2.03%)	299 (2.7%)	82 (2.24%)	4 (0.49%)	2 (0.45%)	26 (0.93%)	26 (1.83%)	22 (1.03%)	4 (2.33%)	7 (2.71%)	6 (0.84%)	3 (1.84%)
Comorbidities												
Charlson; mean (SD)	6.02 (3.97)	7.29 (4.13)	5.75 (3.75)	3.42 (2.79)	4.73 (3.72)	5.05 (3.23)	4.19 (3.19)	4.07 (3.1)	5.56 (4.05)	5.01 (3.3)	5.46 (3.38)	3.93 (3.4)
Prior MI; N (% of column)	2228 (9.42%)	1429 (12.9%)	365 (9.96%)	12 (1.48%)	16 (3.63%)	174 (6.21%)	55 (3.88%)	72 (3.38%)	18 (10.47%)	17 (6.59%)	64 (8.98%)	6 (3.68%)
CHF; N (% of column)	5341 (22.58%)	3435 (31.01%)	847 (23.1%)	51 (6.3%)	55 (12.47%)	393 (14.03%)	136 (9.59%)	200 (9.39%)	46 (26.74%)	31 (12.02%)	135 (18.93%)	12 (7.36%)
PAD; N (% of column)	6533 (27.62%)	4113 (37.13%)	1074 (29.3%)	43 (5.31%)	71 (16.1%)	519 (18.53%)	176 (12.41%)	220 (10.32%)	49 (28.49%)	54 (20.93%)	191 (26.79%)	23 (14.11%)
CVA; N (% of column)	3297 (13.94%)	1989 (17.95%)	593 (16.18%)	36 (4.44%)	38 (8.62%)	267 (9.53%)	119 (8.39%)	102 (4.79%)	32 (18.6%)	25 (9.69%)	83 (11.64%)	13 (7.98%)
Dementia; N (% of column)	1459 (6.17%)	941 (8.49%)	275 (7.5%)	20 (2.47%)	14 (3.17%)	70 (2.5%)	47 (3.31%)	36 (1.69%)	6 (3.49%)	11 (4.26%)	37 (5.19%)	2 (1.23%)
COPD; N (% of column)	7659 (32.38%)	4197 (37.89%)	1335 (36.42%)	124 (15.31%)	82 (18.59%)	795 (28.38%)	309 (21.79%)	372 (17.46%)	58 (33.72%)	72 (27.91%)	280 (39.27%)	35 (21.47%)
Rheumatic Disease; N (% of column)	1340 (5.67%)	718 (6.48%)	151 (4.12%)	7 (0.86%)	16 (3.63%)	111 (3.96%)	166 (11.71%)	90 (4.22%)	14 (8.14%)	16 (6.2%)	30 (4.21%)	21 (12.88%)
PUD; N (% of column)	638 (2.7%)	335 (3.02%)	125 (3.41%)	14 (1.73%)	9 (2.04%)	49 (1.75%)	41 (2.89%)	27 (1.27%)	16 (9.3%)	9 (3.49%)	9 (1.26%)	4 (2.45%)
Uncomplicated DA; N (% of column)	8895 (37.61%)	5940 (53.62%)	1216 (33.17%)	0 (0%)	119 (26.98%)	784 (27.99%)	307 (21.65%)	172 (8.07%)	47 (27.33%)	81 (31.4%)	192 (26.93%)	37 (22.7%)
Complicated DA; N (% of column)	4439 (18.77%)	3128 (28.24%)	562 (15.33%)	0 (0%)	56 (12.7%)	349 (12.46%)	113 (7.97%)	74 (3.47%)	20 (11.63%)	28 (10.85%)	95 (13.32%)	14 (8.59%)
Hemiplegia; N (% of column)	499 (2.11%)	283 (2.55%)	94 (2.56%)	6 (0.74%)	4 (0.91%)	44 (1.57%)	12 (0.85%)	21 (0.99%)	3 (1.74%)	7 (2.71%)	24 (3.37%)	1 (0.61%)
Malignancy; N (% of column)	4343 (18.36%)	2502 (22.59%)	568 (15.49%)	78 (9.63%)	96 (21.77%)	448 (15.99%)	153 (10.79%)	288 (13.51%)	27 (15.7%)	49 (18.99%)	116 (16.27%)	18 (11.04%)
Metastasis; N (% of column)	1605 (6.79%)	1013 (9.14%)	197 (5.37%)	38 (4.69%)	26 (5.9%)	126 (4.5%)	44 (3.1%)	101 (4.74%)	10 (5.81%)	12 (4.65%)	33 (4.63%)	5 (3.07%)
AIDS; N (% of column)	7 (0.03%)	2 (0.02%)	0 (0%)	0 (0%)	1 (0.23%)	1 (0.04%)	0 (0%)	1 (0.05%)	0 (0%)	0 (0%)	2 (0.28%)	0 (0%)
CKD; N (% of column)	4082 (17.26%)	2695 (24.33%)	579 (15.79%)	22 (2.72%)	58 (13.15%)	314 (11.21%)	132 (9.31%)	127 (5.96%)	27 (15.7%)	32 (12.4%)	86 (12.06%)	10 (6.13%)
CKD on HD; N (% of column)	1051 (4.44%)	676 (6.1%)	136 (3.71%)	8 (0.99%)	20 (4.54%)	116 (4.14%)	24 (1.69%)	32 (1.5%)	9 (5.23%)	9 (3.49%)	19 (2.66%)	2 (1.23%)

Supplemental Table 4b

	Total	MASLD	METALD	ALD	HBV	HCV	Biliary	Other	Alcohol +	HCV +	Alcohol + HCV	Other 2+
Total N (% of row)	23651 (100%)	11078 (46.84%)	3666 (15.5%)	810 (3.42%)	441 (1.86%)	2801 (11.84%)	1418 (6%)	2131 (9.01%)	172 (0.73%)	258 (1.09%)	713 (3.01%)	163 (0.69%)
Platelet; observations (% of column)	6198 (26.21%)	2870 (25.91%)	858 (23.4%)	130 (16.05%)	155 (35.15%)	884 (31.56%)	437 (30.82%)	472 (22.15%)	46 (26.74%)	101 (39.15%)	183 (25.67%)	62 (38.04%)
Platelet; median (IQR)	191500 (131000)	191000 (130000)	193000 (127750)	164500 (150000)	190000 (104000)	160500 (109000)	263000 (110000)	183000 (137250)	227500 (114500)	191000 (113000)	190000 (125000)	250500 (90000)
Sodium; observations (% of column)	7087 (29.96%)	3376 (30.47%)	1034 (28.21%)	143 (17.65%)	174 (39.46%)	976 (34.84%)	411 (28.99%)	506 (23.74%)	41 (23.84%)	107 (41.47%)	197 (27.63%)	63 (38.65%)
Sodium; median (IQR)	139 (4)	139 (4)	139 (5)	139 (5)	140 (3)	140 (3)	140 (3)	140 (4)	139 (4)	139 (3)	139 (4)	139 (4)
Creatinine; observations (% of column)	7299 (30.86%)	3476 (31.38%)	1069 (29.16%)	146 (18.02%)	176 (39.91%)	998 (35.63%)	489 (34.49%)	522 (24.5%)	45 (26.16%)	109 (42.25%)	205 (28.75%)	64 (39.26%)
Creatinine; median (IQR)	0.88 (0.37)	0.92 (0.44)	0.87 (0.35)	0.78 (0.29)	0.92 (0.28)	0.88 (0.3)	0.79 (0.26)	0.82 (0.31)	0.81 (0.27)	0.9 (0.36)	0.85 (0.31)	0.8 (0.3)
Albumin; observations (% of column)	7125 (30.13%)	3330 (30.06%)	1004 (27.39%)	154 (19.01%)	174 (39.46%)	993 (35.45%)	532 (37.52%)	514 (24.12%)	49 (28.49%)	107 (41.47%)	200 (28.05%)	68 (41.72%)
Albumin; median (IQR)	4.1 (0.7)	4 (0.8)	4.1 (0.7)	4.1 (0.8)	4.35 (0.6)	4.1 (0.7)	4.2 (0.43)	4.1 (0.7)	4.2 (1)	4.2 (0.45)	4.1 (0.8)	4.1 (0.53)
INR; observations (% of column)	2417 (10.22%)	992 (8.95%)	312 (8.51%)	58 (7.16%)	62 (14.06%)	441 (15.74%)	154 (10.86%)	210 (9.85%)	13 (7.56%)	47 (18.22%)	97 (13.6%)	31 (19.02%)
INR; median (IQR)	1.1 (0.2)	1.1 (0.21)	1.1 (0.3)	1.1 (0.28)	1.1 (0.1)	1.1 (0.17)	1 (0)	1.1 (0.2)	1 (0.1)	1 (0.1)	1.1 (0.2)	1 (0)
Bilirubin; observations (% of column)	6884 (29.11%)	3189 (28.79%)	960 (26.19%)	150 (18.52%)	172 (39%)	998 (35.63%)	498 (35.12%)	500 (23.46%)	47 (27.33%)	112 (43.41%)	193 (27.07%)	65 (39.88%)
Bilirubin; median (IQR)	0.6 (0.6)	0.6 (0.6)	0.7 (0.8)	1 (1.3)	0.6 (0.4)	0.7 (0.6)	0.5 (0.3)	0.6 (0.7)	0.6 (0.85)	0.6 (0.4)	0.6 (0.7)	0.5 (0.3)
MELD; observations (% of column)	1626 (6.87%)	649 (5.86%)	203 (5.54%)	43 (5.31%)	46 (10.43%)	325 (11.6%)	93 (6.56%)	147 (6.9%)	6 (3.49%)	33 (12.79%)	62 (8.7%)	19 (11.66%)
MELD; median (IQR)	11 (5)	11 (7)	12 (9)	13 (6.5)	10 (2)	11 (3)	10 (4)	11 (5)	11 (8)	11 (3)	12 (6)	11 (6.5)
AST; observations (% of column)	7069 (29.89%)	3283 (29.64%)	1001 (27.3%)	155 (19.14%)	178 (40.36%)	995 (35.52%)	533 (37.59%)	506 (23.74%)	47 (27.33%)	107 (41.47%)	197 (27.63%)	67 (41.1%)
AST; median (IQR)	33 (36)	31 (30)	37 (49)	45 (79.5)	27.5 (23.75)	40 (51)	29 (27)	33 (32)	32 (35)	34 (39)	41 (68)	30 (27)
ALT; observations (% of column)	7161 (30.28%)	3313 (29.91%)	1006 (27.44%)	155 (19.14%)	179 (40.59%)	1019 (36.38%)	535 (37.73%)	522 (24.5%)	47 (27.33%)	116 (44.96%)	202 (28.33%)	67 (41.1%)
ALT; median (IQR)	29 (34)	28 (28)	29 (33)	36 (38.5)	28 (27)	36 (56)	30 (36)	30 (32)	28 (23.5)	34.5 (51.75)	39.5 (54.5)	33 (36.5)
AST/ALT ratio; observations (% of column)	7033 (29.74%)	3264 (29.46%)	996 (27.17%)	155 (19.14%)	178 (40.36%)	988 (35.27%)	530 (37.38%)	505 (23.7%)	46 (26.74%)	107 (41.47%)	197 (27.63%)	67 (41.1%)
AST/ALT ratio; median (IQR)	1.15 (0.71)	1.17 (0.71)	1.3 (0.91)	1.45 (1.19)	1 (0.47)	1.11 (0.61)	0.99 (0.47)	1.12 (0.72)	1.12 (0.7)	1.03 (0.54)	1.18 (0.79)	0.95 (0.53)
FIB-4; observations (% of column)	5721 (24.19%)	2614 (23.6%)	800 (21.82%)	124 (15.31%)	147 (33.33%)	837 (29.88%)	413 (29.13%)	425 (19.94%)	40 (23.26%)	96 (37.21%)	165 (23.14%)	60 (36.81%)
FIB-4; median (IQR)	0 (0)	0 (0)	0 (0)	0 (0.01)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Supplemental Tables 5a and 5b: Model Calibration for 6- and 12-month Decompensation Prediction

Supplemental Table 5a

		Groups	Patients	Observed	Predicted Probability	Predicted Probability, interactions model
1	Age	<47	4518	0.04	0.036	0.037
2		47-65	22905	0.055	0.052	0.052
3		>65	37138	0.057	0.056	0.056
4	Sex	M	32403	0.056	0.056	0.056
5		F	32158	0.054	0.05	0.051
6	Etiology	MASLD	34108	0.055	0.054	0.054
7		HCV	5767	0.048	0.048	0.049
8		ALD	1452	0.074	0.085	0.085
9		METALD	8989	0.072	0.065	0.063
10		Biliary	4907	0.024	0.023	0.025
11		HBV	1019	0.031	0.027	0.027
12		Alcohol +	432	0.062	0.041	0.041
13		HCV +	556	0.045	0.038	0.038
14		Alcohol + HCV	1482	0.061	0.066	0.067
15		Other 2+	613	0.018	0.021	0.021
16		Other	5236	0.064	0.056	0.056
17	MELD score	Low (<15)	4776	0.051	0.049	0.049
18		Medium (15-25)	653	0.107	0.114	0.117
19		High (>25)	62	0.097	0.128	0.133
20		Missing MELD	59070	0.055	0.052	0.053
21	Charleson Comorbidities Index	Mild (1-2)	6050	0.034	0.039	0.04
22		Moderate (3-4)	16025	0.044	0.046	0.046
23		Severe (5 or more)	42486	0.062	0.057	0.057
24	Predicted Risk	First quartile	16141	0.025	0.024	0.024
25		Second quartile	16140	0.043	0.045	0.044
26		Third quartile	16140	0.06	0.055	0.056
27		Fourth quartile	16140	0.091	0.088	0.088

Supplemental Table 5b

		Groups	Patients	Observed	Predicted Probability	Predicted Probability, interactions model
1	Age	<47	3825	0.088	0.079	0.079
2		47-65	20003	0.119	0.113	0.113
3		>65	33401	0.12	0.121	0.121
4	Sex	M	28474	0.119	0.12	0.12
5		F	28755	0.116	0.11	0.111
6	Etiology	MASLD	30370	0.12	0.118	0.119
7		HCV	5118	0.095	0.101	0.102
8		ALD	1196	0.17	0.187	0.187
9		METALD	7864	0.148	0.142	0.139
10		Biliary	4416	0.06	0.053	0.055
11		HBV	915	0.071	0.074	0.075
12		Alcohol +	384	0.086	0.086	0.09
13		HCV +	500	0.068	0.079	0.08
14		Alcohol + HCV	1288	0.122	0.138	0.14
15		Other 2+	549	0.064	0.055	0.056
16		Other	4629	0.136	0.122	0.124
17	MELD score	Low (<15)	4358	0.113	0.107	0.109
18		Medium (15-25)	556	0.203	0.217	0.221
19		High (>25)	54	0.185	0.233	0.231
20		Missing MELD	52261	0.117	0.115	0.115
21	Charleson Comorbidities	Mild (1-2)	5132	0.074	0.086	0.087
22		Moderate (3-4)	14206	0.093	0.104	0.103
23		Severe (5 or more)	37891	0.133	0.123	0.124
24	Predicted Risk	First quartile	14308	0.058	0.055	0.054
25		Second quartile	14307	0.097	0.1	0.099
26		Third quartile	14307	0.13	0.122	0.125
27		Fourth quartile	14307	0.187	0.183	0.183

Supplemental Figure Legends

Supplemental Figure 1: Diagram depicting the method of classifying cirrhosis etiology for individuals within the cohort. Abbreviations: ALD: alcohol associated liver disease; Alcohol+: alcohol associated liver disease plus another cirrhosis etiology; Alcohol+HCV: alcohol associated liver disease and hepatitis C virus associated liver disease; HBV: hepatitis B associated cirrhosis; HCV: hepatitis C virus associated cirrhosis; HCV+: hepatitis C virus associated cirrhosis plus another cirrhosis etiology; MASLD: metabolic dysfunction-associated steatotic liver disease; MetALD: metabolic dysfunction-associated steatotic liver disease with increased alcohol intake; MI: myocardial infarction; Other: one other cirrhosis etiology not otherwise specified; Other 2+: two or more other cirrhosis etiologies not otherwise specified

Supplemental Figure 2: Model calibration table showing model performance with and without interaction terms between cirrhosis etiologies and comorbidities.

Supplemental Figures 3a-3d: Plot demonstrating the prediction of risk based on MELD, platelets, AST to ALT ratio, and FIB-4 models compared to our model. Darker dots indicate patients that classified as high risk whereas lighter dots represent patients classified as having lower risk. Abbreviations: MELD: model for end stage liver disease 3.0; AST: aspartate transaminase; ALT: alanine transaminase; FIB-4: index for liver fibrosis 4

Supplemental Figures 4a and 4b: Receiver-operating curves showing 6- and 12-month decompensation prediction model discrimination

Supplemental Figures

Supplemental Figure 1: Cirrhosis Etiology Classification Diagram

Supplemental Figure 2: Model Calibration with and without Interaction Terms

Supplemental Figures 3a-3d: Net Reclassification Plot

Supplemental Figures 4a and 4b: Receive-Operating Curves for 6- and 12-month Decompensation Prediction Models

Commented [PBM25]: whare are these? and how do we write about thise?