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Association between smoking status and inpatient outcomes of acute cholangitis in the United States: a propensity matched analysis

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Abstract

Background Acute cholangitis (AC) is an infection of the biliary tract superimposed on stasis. This study aimed to investigate the effects of smoking on inpatient outcomes of AC.

Methods We identified primary AC hospitalizations using the National Inpatient Sample database (2017-2020). Using a 1:1 matching method, we created a matched comparison cohort of AC patients who were non-smokers, based on demographics, hospital characteristics and comorbidities.

Results We matched 3960 smoker patients with 3960 non-smoker patients within the AC population. Non-smokers were older than smokers (70 vs. 59 years, P<0.001). Smokers had a stronger association with bile duct calculi (74.37% vs. 69.29%, P<0.001) and other bile duct disorders (clots, parasites, extrinsic compression and other rare disorders) (6.82% vs. 5.05%, P=0.011). No significant difference in inpatient mortality, median length of stay (LOS), or median inpatient cost (MIC) was found between the matched cohorts (P>0.05). However, smoking was associated with higher odds of complications, including sepsis without shock (0.88% vs. 0.51%, P=0.042), sepsis with shock (1.26% vs. 0.51%, P<0.001), biliary pancreatitis (6.57% vs. 4.42%, P<0.001) and myocardial infarction (6.19% vs. 3.54%, P<0.001), as well as a greater need for inpatient endoscopic retrograde cholangiopancreatography (ERCP) (72.85% vs. 63.76%, P<0.001) and early ERCP (50.76% vs. 42.32%, P<0.001) compared to non-smokers.

Conclusions This study found no difference in mortality, LOS, or MIC in acute cholangitis-related hospitalizations associated with smoking. However, smoking was associated with a higher risk of complications and a greater need for ERCP and early ERCP.

Keywords Acute cholangitis, smoking, national inpatient sample, inpatient outcomes

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Conflict of Interest: None

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Introduction

Acute cholangitis (AC) is an infection that is superimposed on biliary tract stasis [1]. It is a relatively uncommon disease, with fewer than 200,000 cases per year in the United States (US) [2]. AC has been associated with high morbidity and mortality, with mortality rates widely ranging from 2-65% [3].

Smoking is known to have an impact on the inpatient outcomes of various medical conditions, including infections [4,5]. It affects innate as well as humoral immune systems, and has been shown to disrupt immunological homeostasis through various mechanisms, including its effects on nuclear factor-κB (NF-κB) and MAPK signaling pathways, as well as histone modification. This can result in either an exaggerated immunological response, leading to autoimmunity, or a weakened immune response that increases susceptibility

to infections [6]. Smoking also has been identified as a risk factor for hepatobiliary diseases, including gallstone disease and possibly AC, yet it is unclear what effects smoking has on inpatient outcomes of AC [7-9].

Smoking remains a significant public health issue in the US, despite the fact that smoking rates have been declining in the US in recent years. According to the Centers for Disease Control, 12.5% of adults were current smokers in the US in 2020 [10]. Therefore, it is important to investigate the effects of smoking on inpatient outcomes of AC, as smoking is a major cause of preventable deaths in the US. We analyzed the National Inpatient Sample (NIS), the largest inpatient database in the US, to compare AC-related inpatient outcomes between smokers and non-smokers.

Materials and methods

Data source and study population

The NIS is the largest publicly available all-payer inpatient database in the US. Developed as a stratified probability sample, it includes hospitalizations from non-federal hospitals across 48 states and the District of Columbia [11]. We queried the NIS database from 2017-2020 using codes from the International Classification of Diseases, 10th revision, Clinical Modification (ICD-10-CM) to identify adult patients (≥18 years of age) hospitalized with a primary diagnosis of AC (Supplementary Table 1). The sample population was then stratified based on current smoking status. We excluded hospitalizations for patients under 18 years of age and those with incomplete data. Detailed information on the sampling methods used by the NIS can be found at https://www.hcup-us.ahrq.gov.

Outcomes of interest

The primary outcomes of interest involved comparing inpatient mortality, median length of stay (LOS), and median inpatient cost (MIC) between smokers and non-smokers presenting with AC. Secondary outcomes included comparing patient and hospital characteristics, comorbidities, risk factors for AC development, complications such as sepsis without shock, sepsis with shock, biliary pancreatitis, liver abscess, portal vein thrombosis, acute kidney injury, blood transfusion, pulmonary embolism and myocardial infarction, as well as the need for endoscopic retrograde cholangiopancreatography (ERCP) and early ERCP between the 2 cohort groups.

Statistical analysis

Statistical analysis was conducted using STATA version 17.0 software (StataCorp LLC, College Station, TX, USA). We performed propensity-matched analysis to minimize the effects of imbalances in patient and hospital characteristics and comorbidities between the 2 cohorts [12,13]. Each hospitalization was assigned a propensity score using a multivariate logistic regression model that incorporated patient and hospital characteristics and comorbidities shown in Tables 1 and 2. Propensity scores were matched between the 2 cohorts using 1:1 matching within 0.1 standard deviation of the calculated propensity scores. The balance of covariates between the cohorts was analyzed and visualized using 2-way plots, as shown in Fig. 1 and 2. We used the chi-square test for categorical variables and the Wilcoxon rank-sum (Mann-Whitney) test for continuous variables, given the nonparametric nature of the NIS database. Categorical variables were reported as frequency (N) and percentage (%), while continuous variables were reported as median with interquartile range (IQR). A P-value ≤0.05 was considered statistically significant, and all P-values were two-sided. The study was exempt from institutional review board approval and patient consent as the NIS databases are publicly available and contain de-identified patient information.

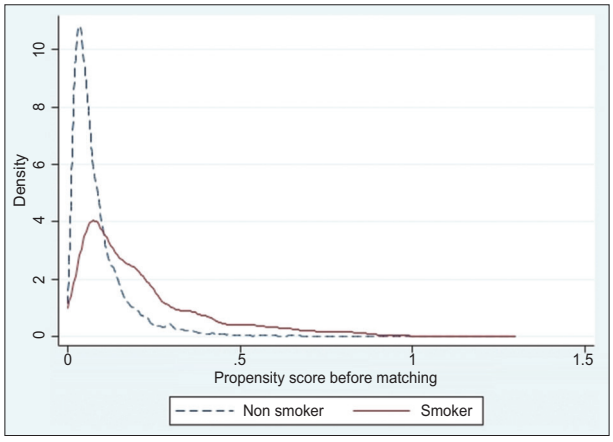

Figure 1 Covariate balance before propensity matching in the present study

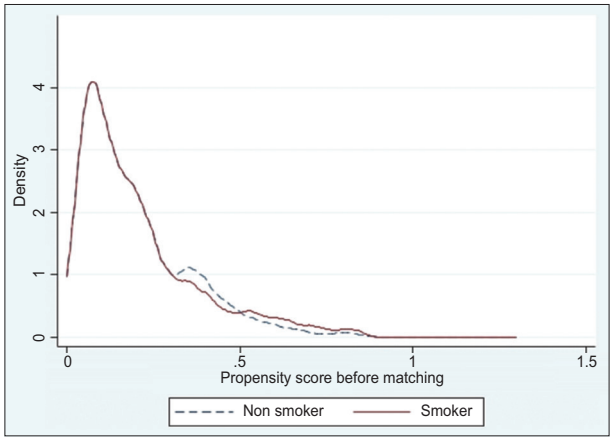

Figure 2 Covariate balance after propensity matching in the present study

Results

Between 2017 and 2020, we identified 43,725 patients who met our inclusion criteria. Prior to matching, 4345 (11.03%) patients were active smokers, while the rest were non-smokers. Using 1:1 matching, we paired 3960 hospitalizations from the smoker cohort (cases) with an equal number from the non-smoker cohort (controls). Propensity scores were generated using hospital-level variables (Table 1) and comorbidities (Table 2), and covariate balance was assessed with two-way plots (Fig. 1, before matching, and Fig. 2, after matching).

No significant differences in major comorbidities were observed between the matched cohorts (P>0.05). Most patients were white, hospitalized on weekdays and treated in large teaching hospitals (Table 1). The most prevalent risk factors for AC were bile duct calculi, bile duct stricture or stenosis, cholelithiasis, other bile duct disorders and bile duct malignancy (Table 3). Smokers showed a stronger association

Table 1 Biodemographic and hospital characteristics of acute cholangitis-related hospitalizations in the United States in 2017-2020 stratified by smoking status

Patient and hospital characteristics	Acute cholangitis					
	Unmatched cohorts			Propensity matched cohorts		
	Non-smoker	Smoker	P-value	Non-smoker	Smoker	P-value
Number of hospitalizations (n)	39,380	4,345		3,960	3,960	
Median age, years (IQR)	70 (57-81)	59 (47-69)	<0.001	60 (41-72)	60 (48-69)	0.397
Sex						
Male	18,290 (46.44%)	2,210 (50.86%)	<0.001	2,009 (50.73%)	1,975 (49.87%)	0.440
Female	21,090 (53.56%)	2,135 (49.14%)		1,951 (49.27%)	1,985 (50.13%)	
Race						
White	27,010 (70.91%)	3,190 (75.32%)	<0.001	2,980 (75.25%)	2,990 (75.51%)	0.980
Black	2,635 (6.92%)	450 (10.63%)		425 (10.73%)	420 (10.61%)	
Hispanic	4,890 (12.84%)	355 (8.38%)		325 (8.21%)	330 (8.33%)	
Asian or Pacific Islander	2,100 (5.51%)	85 (2.01%)		85 (2.15%)	85 (2.15%)	
Others	1,455 (3.82%)	155 (3.66%)		145 (3.66%)	135 (3.41%)	
Median household income national quartile for patient ZIP code						
$1-$43,999	8,930 (23.03%)	1,465 (34.35%)	<0.001	1,385 (34.97%)	1,360 (34.34%)	0.880
$44,000-$55,999	10,675 (27.53%)	1,260 (29.54%)		1,130 (28.54%)	1,140 (28.79%)	
$56,000-$73,999	10,150 (26.18%)	875 (20.52%)		841 (21.24%)	835 (21.09%)	
$74,000 or more	9,015 (23.25%)	665 (15.59%)		604 (15.25%)	625 (15.78%)	
Insurance type						
Medicare	23,965 (62.48%)	1,930 (46.06%)	<0.001	1,740 (43.94%)	1,840 (46.46%)	0.100
Medicaid	3,655 (9.53%)	875 (20.88%)		840 (21.21%)	805 (20.33%)	
Private including HMO	9,815 (25.59%)	1,150 (27.45%)		1,165 (29.42%)	1,090 (27.53%)	
Others	920 (2.40%)	235 (5.61%)		215 (5.43%)	225 (5.68%)	
Elixhauser Comorbidity Index (ECI)						
0	2,970 (7.54%)	400 (9.21%)	<0.001	330 (8.33%)	360 (9.09%)	0.480
1	5,810 (14.75%)	710 (16.34%)		690 (17.42%)	655 (16.54%)	
2	11,430 (29.02%)	1,255 (28.88%)		1,105 (27.90%)	1,125 (28.41%)	
≥ 3	19,170 (48.68%)	1,980 (45.57%)		1,835 (46.34%)	1,820 (45.96%)	
Size of hospital						
Small	6,685 (16.98%)	815 (18.76%)	0.003	845 (21.34%)	770 (19.44%)	0.004
Medium	10,120 (25.70%)	1,145 (26.35%)		946 (23.89%)	1,065 (26.89%)	
Large	22,575 (57.33%)	2,385 (54.89%)		2,169 (54.77%)	2,125 (53.66%)	
Hospital teaching status						
Non-Teaching Hospital	8,360 (21.23%)	995 (22.90%)	0.011	815 (20.58%)	875 (22.10%)	0.100
Teaching Hospital	31,020 (78.77%)	3,350 (77.10%)		3,145 (79.42%)	3,085 (77.90%)	
Region of hospital						
Northeast	9,260 (23.51%)	790 (18.18%)	<0.001	705 (17.80%)	735 (18.56%)	0.021
Midwest	9,090 (23.08%)	1,105 (25.43%)		1,050 (26.52%)	985 (24.87%)	
South	12,360 (31.39%)	1,650 (37.97%)		1,415 (35.73%)	1,520 (38.38%)	
West	8,670 (22.02%)	800 (18.41%)		790 (19.95%)	720 (18.18%)	

IQR, interquartile range

Table 2 Elixhauser comorbidities among the patients hospitalized with acute cholangitis in 2017-2020 in the United States stratified by smoking status

Elixhauser comorbidities	Acute cholangitis					
	Unmatched cohorts			Propensity matched cohorts		
	Non-smoker	Smoker	P-value	Non-smoker	Smoker	P-value
	N=39,380	N=4,345		N=3,960	N=3,960	
Congestive heart failure	4,660 (11.83%)	240 (5.52%)	<0.001	245 (6.19%)	225 (5.68%)	0.340
Cardiac arrhythmias	8,335 (21.17%)	510 (11.74%)	<0.001	480 (12.12%)	475 (11.99%)	0.860
Valvular disease	1,940 (4.93%)	155 (3.57%)	<0.001	145 (3.66%)	135 (3.41%)	0.540
Pulmonary circulation disorders	945 (2.40%)	45 (1.04%)	<0.001	40 (1.01%)	45 (1.14%)	0.590
Peripheral vascular disorders	2,105 (5.35%)	245 (5.64%)	0.420	195 (4.92%)	235 (5.93%)	0.047
Hypertension, uncomplicated	17,100 (43.42%)	1,970 (45.34%)	0.016	1,779 (44.92%)	1,800 (45.45%)	0.640
Hypertension, complicated	160 (0.41%)	15 (0.35%)	0.550	10 (0.25%)	15 (0.38%)	0.320
Paralysis	2,185 (5.55%)	250 (5.75%)	0.580	235 (5.93%)	230 (5.81%)	0.810
Other neurological disorders	5,565 (14.13%)	1,240 (28.54%)	<0.001	1,045 (26.39%)	1,110 (28.03%)	0.100
Chronic pulmonary disease	5,730 (14.55%)	590 (13.58%)	0.084	555 (14.02%)	540 (13.64%)	0.630
Diabetes, uncomplicated	4,975 (12.63%)	455 (10.47%)	<0.001	470 (11.87%)	430 (10.86%)	0.160
Diabetes, complicated	7,040 (17.88%)	455 (10.47%)	<0.001	470 (11.87%)	400 (10.10%)	0.012
Hypothyroidism	5,985 (15.20%)	415 (9.55%)	<0.001	405 (10.23%)	390 (9.85%)	0.570
Renal failure	6,485 (16.47%)	700 (16.11%)	0.550	680 (17.17%)	625 (15.78%)	0.096
Liver disease	1,070 (2.72%)	130 (2.99%)	0.290	95 (2.40%)	105 (2.65%)	0.470
Peptic ulcer disease excluding bleeding	60 (0.15%)	25 (0.58%)	<0.001	15 (0.38%)	25 (0.63%)	0.110
AIDS/HIV	330 (0.84%)	35 (0.81%)	0.820	45 (1.14%)	30 (0.76%)	0.082
Lymphoma	2,085 (5.29%)	225 (5.18%)	0.750	195 (4.92%)	205 (5.18%)	0.610
Metastatic cancer	3,990 (10.13%)	310 (7.13%)	<0.001	285 (7.20%)	285 (7.20%)	>0.99
Solid tumor without metastasis	1,250 (3.17%)	140 (3.22%)	0.860	110 (2.78%)	135 (3.41%)	0.100
Rheumatoid arthritis/collagen vascular diseases	4,040 (10.26%)	370 (8.52%)	<0.001	315 (7.95%)	335 (8.46%)	0.410
Coagulopathy	6,220 (15.79%)	725 (16.69%)	0.130	685 (17.30%)	675 (17.05%)	0.770
Obesity	3,220 (8.18%)	395 (9.09%)	0.038	290 (7.32%)	345 (8.71%)	0.023
Weight loss	13,360 (33.93%)	1,490 (34.29%)	0.630	1,270 (32.07%)	1,380 (34.85%)	0.009
Fluid and electrolyte disorders	185 (0.47%)	5 (0.12%)	<0.001	5 (0.13%)	5 (0.13%)	>0.99
Blood loss anemia	1,675 (4.25%)	135 (3.11%)	<0.001	175 (4.42%)	120 (3.03%)	0.001
Deficiency anemia	1,020 (2.59%)	485 (11.16%)	<0.001	390 (9.85%)	400 (10.10%)	0.710
Alcohol abuse	700 (1.78%)	485 (11.16%)	<0.001	375 (9.47%)	415 (10.48%)	0.130
Drug abuse	215 (0.55%)	80 (1.84%)	<0.001	70 (1.77%)	65 (1.64%)	0.660
Psychoses	4,480 (11.38%)	615 (14.15%)	<0.001	631 (15.93%)	565 (14.27%)	0.038
Depression	7,815 (19.85%)	485 (11.16%)	<0.001	470 (11.87%)	460 (11.62%)	0.730

with bile duct calculi (74.37% vs. 69.29%, P<0.001) and other bile duct disorders, including clots, parasites and extrinsic compression (6.82% vs. 5.05%, P=0.011).

After propensity matching, a higher proportion of smokers died, but the difference was not statistically significant-although it nearly reaching significance (1.01% vs. 0.63%, P=0.063). No significant difference in LOS or MIC was found between the 2 cohorts (P>0.05). Smoking was associated with a higher risk of complications, including sepsis without shock (0.88% vs. 0.51%, P=0.042), sepsis with shock (1.26% vs. 0.51%, P<0.001),

Table 3 Risk factors for acute cholangitis among acute cholangitis-related hospitalizations in the United States in 2017-2020 stratified by smoking status

Risk factors	Acute cholangitis		
	Propensity matched cohorts		
	Non-smoker	Smoker	P-value
Bile duct calculi	2,744 (69.29%)	2,945 (74.37%)	<0.001
Bile duct stricture or stenosis	305 (7.70%)	320 (8.08%)	0.530
Cholelithiasis	350 (8.84%)	290 (7.32%)	0.063
Other bile duct disorders (including clots, parasites, extrinsic compression)	200 (5.05%)	270 (6.82%)	0.011
Bile duct malignancy	90 (2.27%)	60 (1.52%)	0.093
Gall bladder malignancy	0 (0.00%)	0 (0.00%)	
Ampullary malignancy	5 (0.13%)	0 (0.00%)	
Duodenal malignancy	10 (0.25%)	15 (0.38%)	0.320
Biliary cyst	5 (0.13%)	5 (0.13%)	>0.99
Bile duct injury (including iatrogenic)	0 (0.00%)	0 (0.00%)	

Table 4 Primary and secondary outcomes of acute cholangitis related hospitalizations in the United States in 2017-2020 stratified by smoking status

Outcomes	Acute cholangitis					
	Unmatched cohorts			Propensity matched cohorts		
	Non-smoker	Smoker	P-value	Non-smoker	Smoker	P-value
No. of hospitalizations	39,380	4,345		3,960	3,960	
Inpatient mortality	335 (0.85%)	40 (0.92%)	0.640	25 (0.63%)	40 (1.01%)	0.063
Median LOS, days (IQR)	3 (2-5)	3 (2-5)	0.215	3 (2-5)	3 (2-5)	0.350
Median MIC, USD (IQR)	41,955 (25,876-66,565)	40,240 (25,448-63,456)	<0.003	39,986 (24,508-64,257)	40,090 (25,648-61,974)	0.510
Sepsis without shock	285 (0.72%)	45 (1.04%)	0.024	20 (0.51%)	35 (0.88%)	0.042
Sepsis with shock	455 (1.16%)	50 (1.15%)	0.980	20 (0.51%)	50 (1.26%)	<0.001
Biliary pancreatitis	2,390 (6.07%)	295 (6.79%)	0.061	175 (4.42%)	260 (6.57%)	<0.001
Liver abscess	320 (0.81%)	45 (1.04%)	0.130	55 (1.39%)	40 (1.01%)	0.120
Portal vein thrombosis	535 (1.36%)	70 (1.61%)	0.180	50 (1.26%)	60 (1.52%)	0.340
Acute kidney injury	6,265 (15.91%)	525 (12.08%)	<0.001	475 (11.99%)	485 (12.25%)	0.730
Blood transfusion	805 (2.04%)	75 (1.73%)	0.160	80 (2.02%)	70 (1.77%)	0.410
Pulmonary embolism	120 (0.37%)	10 (0.28%)	0.410	15 (0.45%)	10 (0.31%)	0.350
Myocardial infarction	2,015 (5.12%)	260 (5.98%)	0.015	140 (3.54%)	245 (6.19%)	<0.001
ERCP	26,880 (68.26%)	3,180 (73.19%)	<0.001	2,525 (63.76%)	2,885 (72.85%)	<0.001
Early ERCP	17,700 (44.95%)	2,185 (50.29%)	<0.001	1,676 (42.32%)	2,010 (50.76%)	<0.001

LOS, median length of stay; MIC, median inpatient cost; IQR, interquartile range; ERCP, endoscopic retrograde cholangiopancreatography

biliary pancreatitis (6.57% vs. 4.42%, P<0.001), and myocardial infarction (6.19% vs. 3.54%, P<0.001). Additionally, smokers had a higher need for inpatient ERCP (72.85% vs. 63.76%, P<0.001) and early ERCP (50.76% vs. 42.32%, P<0.001) compared to non-smokers (Table 4).

Discussion

Smoking affects both innate and humoral immunity. It mediates its impact on immunity through several mechanisms, including the regulation of NF-κB and MAPK

pathways, as well as histone modification. This can result in either an unregulated and abnormally exacerbated immune response, potentially leading to autoimmunity, or a weakened immune response, which can cause infections [6]. Previous studies have demonstrated that smoking is associated with longer hospital stays, greater morbidity and higher inpatient mortality compared to non-smokers [5,14,15]. Moreover, research has shown a connection between smoking status and autoimmune diseases [16,17]. Smoking may elevate the risk of developing gallbladder disease, through an unknown mechanism, and it also increases the risk of diabetes and reduces plasma high-density lipoproteins, both of which are potential risk factors for gallbladder disease development. A higher risk of gallbladder disease may heighten the risk of developing AC in smokers. Although smoking has been linked to gallbladder disease, and may increase the risk of AC, its effects on inpatient outcomes related to AC remain largely unknown. Therefore, we conducted a retrospective study on hospitalizations related to acute cholangitis in the United States between 2017 and 2020 to better understand the relationship between smoking status and inpatient outcomes for acute cholangitis.

Prior to matching, the non-smoker AC cohort had a significantly larger number of patients compared to the smoker AC cohort. The non-smoker AC patients were generally older (67±0.08 vs. 56±0.27 years), resulting in a higher proportion of patients with an Elixhauser Comorbidity Index of 3 or greater. The smoker AC cohort contained more males than females, which could be attributed to sex-related differences in smoking prevalence within the US [18,19].

In the matched cohorts, the most prevalent risk factor for AC was bile duct calculi, bile duct stricture/stenosis, cholelithiasis, and other bile duct disorders (including clots, parasites, and exogenous compression). Consistently with previous studies, bile duct calculi were identified as the most common cause of AC, followed by biliary stricture and malignancy [3]. Bile duct calculi and other bile duct disorders were more frequently observed in AC patients who were smokers compared to non-smokers.

The AC patients who were smokers had a higher proportion of in-hospital deaths; however, the difference was not statistically significant, though it nearly reached significance (1.01% vs. 0.63%, P=0.063). No statistically significant differences were observed in the LOS or morbidity between the two cohorts (P>0.05). Nevertheless, smoking in AC patients was associated with a greater need for inpatient ERCP (72.85% vs. 63.76%, P<0.001) and early ERCP (50.76% vs. 42.32%, P<0.001), and higher odds of developing complications, including sepsis without shock (0.88% vs. 0.51%, P=0.042), sepsis with shock (1.26% vs. 0.51%, P<0.001), biliary pancreatitis (6.57% vs. 4.42%, P < 0.001) and myocardial infarction (6.19% vs. 3.54%, P<0.001) compared to non-smokers. In the past, smoking has been identified as a predictor of the need for urgent endoscopic intervention [20]. The greater need for ERCP and early ERCP, as well as the higher odds of complications, probably indicate more severe disease in smokers.

This study, based on the NIS database, has several strengths and limitations. One significant strength is the large sample size, which enhances the generalizability of the findings to a broader patient population. Furthermore, the NIS database provides a wealth of information on patient demographics, diagnoses and procedures, enabling researchers to analyze a wide range of variables.

However, there are some limitations to consider. The retrospective nature of the study may have introduced selection bias and limited the ability to establish causal relationships. The NIS database relies on administrative codes for diagnoses and procedures, which can lead to potential inaccuracies and misclassification [21]. As the NIS is based on discharge records, there may be a lack of granularity in the data, such as detailed clinical information, laboratory results or longitudinal follow up [22]. Lastly, unmeasured confounders may impact the validity of the study's conclusions [23]. Despite these limitations, the study offers valuable insights into the subject matter, which can be further explored and validated through additional research.

In conclusion, our study demonstrated that smoking did not result in greater mortality, LOS or MIC among patients hospitalized with acute cholangitis. However, it was associated with a higher risk of complications, such as sepsis, biliary pancreatitis and myocardial infarction, as well as the need for inpatient ERCP and early ERCP. These findings emphasize the importance of further research to better understand the relationship between smoking and inpatient outcomes of acute cholangitis.

Summary Box

What is already known:

- Acute cholangitis (AC) arises from stasis and infection within the biliary tract
- Smoking has been linked to gallstone formation and might be indirectly associated with the development of AC
- Smoking has been found to be related to poorer inpatient outcomes in sepsis

What the new findings are:

- Smoking was not linked to increased inpatient mortality in patients with AC
- Smoking was not found to be associated with a higher median length of stay or median inpatient cost
- In AC patients, smoking was correlated with a greater need for endoscopic retrograde cholangiopancreatography (ERCP) and early ERCP, as well as a higher risk of complications such as sepsis, biliary pancreatitis, and myocardial infarction

References

1. Boey JH, Way LW. Acute cholangitis. *Ann Surg* 1980;**191**:264-270.
2. Ahmed M. Acute cholangitis - an update. *World J Gastrointest Pathophysiol* 2018;**9**:1-7.
3. Kimura Y, Takada T, Kawarada Y, et al. Definitions, pathophysiology, and epidemiology of acute cholangitis and cholecystitis: Tokyo Guidelines. *J Hepatobiliary Pancreat Surg* 2007;**14**:15-26.
4. Zhang N, Liu Y, Yang C, et al. Association between smoking and risk of death in patients with sepsis: A systematic review and meta-analysis. *Tob Induc Dis* 2022;**20**:65.
5. Alroumi F, Abdul Azim A, Kergo R, Lei Y, Dargin J. The impact of smoking on patient outcomes in severe sepsis and septic shock. *J Intensive Care* 2018;**6**:42.
6. Qiu F, Liang CL, Liu H, et al. Impacts of cigarette smoking on immune responsiveness: Up and down or upside down? *Oncotarget* 2017;**8**:268-284.
7. Yeom DH, Oh HJ, Son YW, Kim TH. What are the risk factors for acute suppurative cholangitis caused by common bile duct stones? *Gut Liver* 2010;**4**:363-367.
8. Logan RF, Skelly MM. Smoking and hepato-biliary disease. *Eur J Gastroenterol Hepatol* 2000;**12**:863-867.
9. Degirmenci B, Albayrak R, Haktanir A, Acar M, Yucel A. Acute effect of smoking on gallbladder emptying and refilling in chronic smokers and nonsmokers: a sonographic study. *World J Gastroenterol* 2006;**12**:5540-5543.
10. Centers for Disease Control and Prevention. Current cigarette smoking among adults in the United States. Available from: https://www.cdc.gov/tobacco/data_statistics/fact_sheets/adult_data/cig_smoking/index.htm [Accessed 9 July 2023].
11. HCUP-US NIS Overview. Available from: https://www.hcup-us.ahrq.gov/nisoverview.jsp [Accessed 9 July 2023].
12. Yang JY, Webster-Clark M, Lund JL, Sandler RS, Dellon ES, Stürmer T. Propensity score methods to control for confounding in observational cohort studies: a statistical primer and application to endoscopy research. *Gastrointest Endosc* 2019;**90**:360-369.
13. Austin PC. An introduction to propensity score methods for reducing the effects of confounding in observational studies. *Multivariate Behav Res* 2011;**46**:399-424.
14. Adrish M, Chilimuri S, Mantri N, et al. Association of smoking status with outcomes in hospitalised patients with COVID-19. *BMJ Open Respir Res* 2020;**7**:e000716.
15. Hall TS, Ørn S, Zannad F, et al. The association of smoking with hospitalization and mortality differs according to sex in patients with heart failure following myocardial infarction. *J Womens Health (Larchmt)* 2022;**31**:310-320.
16. Lee J, Taneja V, Vassallo R. Cigarette smoking and inflammation: cellular and molecular mechanisms. *J Dent Res* 2012;**91**:142-149.
17. Perricone C, Versini M, Ben-Ami D, et al. Smoke and autoimmunity: The fire behind the disease. *Autoimmun Rev* 2016;**15**:354-374.
18. Peters SA, Huxley RR, Woodward M. Do smoking habits differ between women and men in contemporary Western populations? Evidence from half a million people in the UK Biobank study. *BMJ Open* 2014;**4**:e005663.
19. Kaduri P, Voci S, Zawertailo L, Chaiton M, McKenzie K, Selby P. Real-world effectiveness of varenicline versus nicotine replacement therapy in patients with and without psychiatric disorders. *J Addict Med* 2015;**9**:169-176.
20. Pang YY, Chun YA. Predictors for emergency biliary decompression in acute cholangitis. *Eur J Gastroenterol Hepatol* 2006;**18**:727-731.
21. O'Malley KJ, Cook KF, Price MD, Wildes KR, Hurdle JF, Ashton CM. Measuring diagnoses: ICD code accuracy. *Health Serv Res* 2005;**40**:1620-1639.
22. Khera R, Krumholz HM. With great power comes great responsibility: big data research from the National Inpatient Sample. *Circ Cardiovasc Qual Outcomes* 2017;**10**:e003846.
23. Ananth CV, Schisterman EF. Hidden biases in observational epidemiology: the case of unmeasured confounding. *BJOG* 2018;**125**:644-646.

Supplementary material

Supplementary Table 1 List of ICD-10 codes used in the present study

Diagnosis	ICD-10 codes
Acute cholangitis	K83.0, K80.30, K80.31, K80.32, K80.33, K80.36, K80.37.
Smoking	F17.210, F17.200, F17.201, F17.203, F17.208, F17.209, F17.210, F17.211, F17.213, F17.218, F17.219, F17.220, F17.221, F17.223, F17.228, F17.229, F17.290, F17.291, F17.293, F17.298, F17.299.
Bile duct calculi	K80.3, K80.30, K80.31, K80.32, K80.33, K80.34, K80.35, K80.36, K80.37, K80.40, K80.41, K80.42, K80.43, K80.44, K80.45, K80.46, K80.47, K80.50, K80.51.
Bile duct stricture or stenosis	K83.1, Q44.3.
Cholelithiasis	K80.00, K80.01, K80.10, K80.11, K80.12, K80.13, K80.18, K80.19, K80.20, K80.21, K80.60, K80.61, K80.62, K80.63, K80.64, K80.65, K80.66, K80.67, K80.70, K80.71.
Other bile duct disorders (including clots, parasites, extrinsic compression)	K83.8, K83.9
Bile duct malignancy	C24.9, C24.8, C24.0, C22.1.
Gall bladder malignancy	C23
Ampullary malignancy	C24.1
Duodenal malignancy	C17.0, C7A.010, D13.2, D3A.010.
Biliary cyst	K83.5
Bile duct injury (including iatrogenic)	S36.13XS
ARDS	J80
Mechanical ventilation	Z99.11
DIC	D65
Sepsis without shock	R65.20
Sepsis with shock	R65.21
Acute kidney injury	N17.0, N17.1, N17.2, N17.8, N17.9.
Blood transfusion	30230H1, 30230N1, 30233N1, 30240H1, 30240N1, 30243H1, 30243N1.
Pulmonary embolis	I26.09, I26.01, I26.90, I26.99, Z86.711.
Bowel ischemia	K55.011, K55.012, K55.019, K55.031, K55.032, K55.039, K55.051, K55.052, K55.059.
Myocardial infarction	I21.0, I21.01, I21.02, I21.09, I21.1, I21.11, I21.19, I21.21, I21.3, I21.4,I21.29, I22.0, I22.1, I22.2, I22.8, I22.9, I25.2, I23.0, I23.1, I23.2, I23.3, I23.4, I23.5, I23.6, I23.8.
Congestive heart failure	I09.81, I11.0, I13.0, I13.2, I50.1, I50.20, I50.21, I50.22, I50.23, I50.30, I50.31, I50.32, I50.33, I50.40, I50.41, I50.42, I50.43, I50.810, I50.811, I50.812, I50.813, I50.814, I50.82, I50.83, I50.84, I50.89, I50.9, I51.81, I97.130, I97.131, O29.121, O29.122, O29.123, O29.129, R57.0, Z95.811, Z95.812.
Valvular disease	M32.11, A18.84, A32.82, A39.51, A52.03, B33.21, B37.6, I01.1, I01.8, I01.9, I02.0, I05.0, I05.1, I05.2, I05.8, I05.9, I06.0, I06.1, I06.2, I06.8, I06.9, I07.0, I07.1, I07.2, I07.8, I07.9, I08.0, I08.1, I08.2, I08.3, I08.8, I08.9, I09.1, I09.89, I33.0, I33.9, I34.0, I34.1, I34.2, I34.8, I34.81, I34.89, I34.9, I35.0, I35.1, I35.2, I35.8, I35.9, I36.0, I36.1, I36.2, I36.8, I36.9, I37.0, I37.1, I37.2, I37.8, I37.9, I38.0, I39, Q22.0, Q22.1, Q22.2, Q22.3, Q22.4, Q22.5, Q22.6, Q22.8, Q22.9, Q23.0, Q23.1, Q23.2, Q23.3, Q23.4, Q23.8, Q23.9, T82.01XA, T82.01XD, T82.01XS, T82.02XA, T82.02XD, T82.02XS, T82.03XA, T82.03XD, T82.03XS, T82.09XA, T82.09XD, T82.09XS, T82.221A, T82.221D, T82.221S, T82.222A, T82.222D, T82.222S, T82.223A, T82.223D, T82.223S, T82.228A, T82.228D, T82.228S, T82.6XXA, T82.6XXD, T82.6XXS, Z95.2, Z95.3, Z95.4.
Cardiac arrhythmias	T82.1, Z45.0, Z95.0, I44.1, I44.2, I44.3, I45.6, I45.9, I47, I48, I49, R00.0, R00.1, R00.8
Pulmonary circulation disorders	I27.0, I27.1, I27.2, I27.2, I27.2, I27.2, I27.2, I27.2, I27.2, I27.81, I27.82, I27.83, I27.89, I27.9, I28.0, I28.1, I28.8, I28.9

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Supplementary Table 1 (*Continued*)

Diagnosis	ICD-10 codes
Peripheral vascular disorders	A52.00, A52.01, A52.02, A52.09, I70.0, I70.1, I70.201, I70.202, I70.203, I70.208, I70.209, I70.211, I70.212, I70.213, I70.218, I70.219, I70.221, I70.222, I70.223, I70.228, I70.229, I70.231, I70.232, I70.233, I70.234, I70.235, I70.238, I70.239, I70.241, I70.242, I70.243, I70.244, I70.245, I70.248, I70.249, I70.25, I70.261, I70.262, I70.263, I70.268, I70.269, I70.291, I70.292, I70.293, I70.298, I70.299, I70.301, I70.302, I70.303, I70.308, I70.309, I70.311, I70.312, I70.313, I70.318, I70.319, I70.321, I70.322, I70.323, I70.328, I70.329, I70.331, I70.332, I70.333, I70.334, I70.335, I70.338, I70.339, I70.341, I70.342, I70.343, I70.344, I70.345, I70.348, I70.349, I70.35, I70.361, I70.362, I70.363, I70.368, I70.369, I70.391, I70.392, I70.393, I70.398, I70.399, I70.401, I70.402, I70.403, I70.408, I70.409, I70.411, I70.412, I70.413, I70.418, I70.419, I70.421, I70.422, I70.423, I70.428, I70.429, I70.431, I70.432, I70.433, I70.434, I70.435, I70.438, I70.439, I70.441, I70.442, I70.443, I70.444, I70.445, I70.448, I70.449, I70.450, I70.461, I70.462, I70.463, I70.468, I70.469, I70.491, I70.492, I70.493, I70.498, I70.499, I70.501, I70.502, I70.503, I70.508, I70.509, I70.511, I70.512, I70.513, I70.518, I70.519, I70.521, I70.522, I70.523, I70.528, I70.529, I70.531, I70.532, I70.533, I70.534, I70.535, I70.538, I70.539, I70.541, I70.542, I70.543, I70.544, I70.545, I70.548, I70.549, I70.550, I70.561, I70.562, I70.563, I70.568, I70.569, I70.591, I70.592, I70.593, I70.598, I70.599, I70.601, I70.602, I70.603, I70.608, I70.609, I70.611, I70.612, I70.613, I70.618, I70.619, I70.621, I70.622, I70.623, I70.628, I70.629, I70.631, I70.632, I70.633, I70.634, I70.635, I70.638, I70.639, I70.641, I70.642, I70.643, I70.644, I70.645, I70.648, I70.649, I70.650, I70.661, I70.662, I70.663, I70.668, I70.669, I70.691, I70.692, I70.693, I70.698, I70.699, I70.701, I70.702, I70.703, I70.708, I70.709, I70.711, I70.712, I70.713, I70.718, I70.719, I70.721, I70.722, I70.723, I70.728, I70.729, I70.731, I70.732, I70.733, I70.734, I70.735, I70.738, I70.739, I70.741, I70.742, I70.743, I70.744, I70.745, I70.748, I70.749, I70.75, I70.761, I70.762, I70.763, I70.768, I70.769, I70.91, I70.92, I70.93, I70.98, I70.99, I71.701, I71.702, I71.703, I71.708, I71.709, I71.711, I71.712, I71.713, I71.718, I71.719, I71.721, I71.722, I71.723, I71.728, I71.729, I71.731, I71.732, I71.733, I71.734, I71.735, I71.738, I71.739, I71.741, I71.742, I71.743, I71.744, I71.745, I71.748, I71.749, I71.75, I71.761, I71.762, I71.763, I71.768, I71.769, I71.91, I71.92, I71.93, I71.98, I71.99, I72.0, I72.90, I72.91, I72.92, I71.0, I71.1, I71.010, I71.011, I71.012, I71.019, I71.2, I71.3, I71.1, I71.2, I71.3, I71.4, I71.5, I71.6, I71.8, I71.9, I72.0, I72.1, I72.2, I72.3, I72.4, I72.5, I72.6, I72.8, I72.9, I73.01, I73.1, I73.81, I73.89, I73.9, I74.01, I74.09, I74.10, I74.11, I74.19, I74.2, I74.3, I74.4, I74.5, I74.8, I74.9, I75.011, I75.012, I75.013, I75.019, I75.021, I75.022, I75.023, I75.029, I75.81, I75.89, I77.0, I77.1, I77.2, I77.3, I77.4, I77.5, I77.6, I77.70, I77.71, I77.72, I77.73, I77.74, I77.75, I77.76, I77.77, I77.79, I77.810, I77.811, I77.812, I77.819, I77.82, I77.89, I77.9, I78.0, I78.1, I78.8, I78.9, I79.0, I79.1, I79.8, K55.1, Z95.820, Z95.828.
Hypertension, uncomplicated	I10, I16.0, I16.9, O10.011, O10.012, O10.013, O10.019, O10.02, O10.03.
Hypertension, complicated	I11.0, I13.0, I13.2, H35.031, H35.032, H35.033, H35.039, I11.9, I12.0, I12.9, I13.10, I13.11, I15.0, I15.1, I15.2, I15.8, I15.9, I16.1, I67.4, O10.111, O10.112, O10.113, O10.119, O10.2, O10.3, O10.211, O10.212, O10.213, O10.219, O10.2, O10.3, O10.411, O10.412, O10.413, O10.419, O10.42, O10.43, O10.911, O10.912, O10.913, O10.919, O10.92, O10.93, O11.1, O11.2, O11.3, O11.4, O11.5, O11.9, O16.1, O16.2, O16.3, O16.4, O16.5, O16.9
Paralysis	G04.1, G80.0, G80.1, G80.2, G80.8, G80.9, G81.00, G81.01, G81.02, G81.03, G81.04, G81.10, G81.11, G81.12, G81.13, G81.14, G81.90, G81.91, G81.92, G81.93, G81.94, G82.20, G82.21, G82.22, G82.50, G82.51, G82.52, G82.53, G82.54, G83.0, G83.10, G83.11, G83.12, G83.13, G83.20, G83.21, G83.22, G83.23, G83.24, G83.4, G83.5, G83.81, G83.82, G83.83, G83.84, G83.89, G83.9, I69.031, I69.032, I69.033, I69.034, I69.039, I69.041, I69.042, I69.043, I69.044, I69.049, I69.051, I69.052, I69.053, I69.054, I69.059, I69.061, I69.062, I69.063, I69.064, I69.065, I69.069, I69.131, I69.132, I69.133, I69.134, I69.139, I69.141, I69.142, I69.143, I69.144, I69.149, I69.151, I69.152, I69.153, I69.154, I69.159, I69.161, I69.162, I69.163, I69.164, I69.165, I69.169, I69.231, I69.232, I69.233, I69.234, I69.239, I69.241, I69.242, I69.243, I69.244, I69.249, I69.251, I69.252, I69.253, I69.254, I69.259, I69.261, I69.262, I69.263, I69.264, I69.265, I69.269, I69.331, I69.332, I69.333, I69.334, I69.339, I69.341, I69.342, I69.343, I69.344, I69.349, I69.351, I69.352, I69.353, I69.354, I69.359, I69.361, I69.362, I69.363, I69.364, I69.365, I69.369, I69.831, I69.832, I69.833, I69.834, I69.839, I69.841, I69.842, I69.843, I69.844, I69.849, I69.851, I69.852, I69.853, I69.854, I69.859, I69.861, I69.862, I69.863, I69.864, I69.865, I69.869, I69.931, I69.932, I69.933, I69.934, I69.939, I69.941, I69.942, I69.943, I69.944, I69.949, I69.951, I69.952, I69.953, I69.954, I69.959, I69.961, I69.962, I69.963, I69.964, I69.965, I69.969, R53.2.

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Supplementary Table 1 (*Continued*)

Diagnosis	ICD-10 codes
Other neurological disorders	K76.82, E75.00, E75.01, E75.02, E75.09, E75.10, E75.11, E75.19, E75.23, E75.25, E75.26, E75.29, E75.4, F05., F84.2, G35, G36.0, G36.8, G36.9, G37.0, G37.1, G37.2, G37.3, G37.4, G37.5, G37.8, G37.9, G47.411, G47.419, G47.421, G47.429, G89.0, G91.0, G91.1, G91.2, G91.3, G91.4, G91.8, G91.9, G93.0, G93.40, G93.41, G93.49, G93.5, G93.6, G93.7, G93.81, G93.82, G93.89, G93.9, G94., O99.350, O99.351, O99.352, O99.353, O99.354, O99.355, P91.60, P91.61, P91.62, P91.63.
Diabetes, uncomplicated	E08.00, E08.01, E08.10, E08.11, E08.9, E09.00, E09.01, E09.10, E09.11, E09.9, E10.10, E10.11, E11.9, E11.00, E11.01, E11.10, E11.11, E11.9, E13.00, E13.01, E13.10, E13.11, E13.9, O24.011, O24.012, O24.013, O24.019, O24.02, O24.03, O24.111, O24.112, O24.113, O24.119, O24.12, O24.13, O24.311, O24.312, O24.313, O24.319, O24.32, O24.33, O24.410, O24.414, O24.415, O24.419, O24.420, O24.424, O24.425, O24.429, O24.430, O24.434, O24.435, O24.439, O24.811, O24.812, O24.813, O24.819, O24.82, O24.83, O24.911, O24.912, O24.913, O24.919, O24.92, O24.93.
Diabetes, complicated	E08.21, E08.22, E08.29, E08.311, E08.319, E08.321, E08.3211, E08.3212, E08.3213, E08.3219, E08.329, E08.3291, E08.3292, E08.3293, E08.3299, E08.331, E08.3311, E08.3312, E08.3313, E08.3319, E08.339, E08.3391, E08.3392, E08.3393, E08.3399, E08.341, E08.3411, E08.3412, E08.3413, E08.3419, E08.349, E08.3491, E08.3492, E08.3493, E08.3499, E08.351, E08.3511, E08.3512, E08.3513, E08.3519, E08.3521, E08.3522, E08.3523, E08.3529, E08.3531, E08.3532, E08.3533, E08.3539, E08.3541, E08.3542, E08.3543, E08.3549, E08.3551, E08.3552, E08.3553, E08.3559, E08.359, E08.3591, E08.3592, E08.3593, E08.3599, E08.36, E08.37X1, E08.37X2, E08.37X3, E08.37X9, E08.39, E08.40, E08.41, E08.42, E08.43, E08.44, E08.49, E08.51, E08.52, E08.59, E08.610, E08.618, E08.620, E08.621, E08.622, E08.628, E08.630, E08.638, E08.641, E08.649, E08.65, E08.69, E08.8, E09.21, E09.22, E09.29, E09.311, E09.319, E09.321, E09.3211, E09.3212, E09.3213, E09.3219, E09.329, E09.3291, E09.3292, E09.3293, E09.3299, E09.331, E09.3311, E09.3312, E09.3313, E09.3319, E09.339, E09.3391, E09.3392, E09.3393, E09.3399, E09.341, E09.3411, E09.3412, E09.3413, E09.3419, E09.349, E09.3491, E09.3492, E09.3493, E09.3499, E09.351, E09.3511, E09.3512, E09.3513, E09.3519, E09.3521, E09.3522, E09.3523, E09.3529, E09.3531, E09.3532, E09.3533, E09.3539, E09.3541, E09.3542, E09.3543, E09.3549, E09.3551, E09.3552, E09.3553, E09.3559, E09.359, E09.3591, E09.3592, E09.3593, E09.3599, E09.36, E09.37X1, E09.37X2, E09.37X3, E09.37X9, E09.39, E09.40, E09.41, E09.42, E09.43, E09.44, E09.49, E09.51, E09.52, E09.59, E09.610, E09.618, E09.620, E09.621, E09.622, E09.628, E09.630, E09.638, E09.641, E09.649, E09.65, E09.69, E09.8, E10.21, E10.22, E10.29, E10.311, E10.319, E10.321, E10.3211, E10.3212, E10.3213, E10.3219, E13.321, E13.3211, E13.3212, E13.3213, E13.3219, E13.329, E13.3291, E13.3292, E13.3293, E13.3299, E13.31, E13.311, E13.312, E13.313, E13.319, E13.39, E13.391, E13.392, E13.393, E13.399, E13.41, E13.411, E13.412, E13.413, E13.419, E13.49, E13.491, E13.492, E13.493, E13.499, E13.51, E13.511, E13.512, E13.513, E13.519, E13.521, E13.522, E13.523, E13.529, E13.531, E13.532, E13.533, E13.539, E13.541, E13.542, E13.543, E13.549, E13.551, E13.552, E13.553, E13.559, E13.59, E13.591, E13.592, E13.593, E13.599, E13.6, E13.37X1, E13.37X2, E13.37X3, E13.37X9, E13.39, E13.40, E13.41, E13.42, E13.43, E13.44, E13.49, E13.51, E13.52, E13.59, E13.610, E13.618, E13.620, E13.621, E13.622, E13.628, E13.630, E13.638, E13.641, E13.649, E13.65, E13.69, E13.8.
Hypothyroidism	E00.0, E00.1, E00.2, E00.9, E01.0, E01.1, E01.2, E01.8, E02., E03.0, E03.1, E03.2, E03.3, E03.4, E03.5, E03.8, E03.9, E89.0
Renal failure	N18.3, N18.30, N18.31, N18.32, N18.9, N19, I13.2, I12.0, I13.11, N18.4, N18.5, N18.6, Z49.01, Z49.02, Z49.31, Z49.32, Z91.15, Z94.0, Z99.2
Liver disease	K70.10, K70.11, A51.45, A52.74, B18.0, B18.1, B18.2, B18.8, B18.9, B19.10, B19.20, B19.9, B25.1, B58.1, K70.0, K70.2, K70.30, K70.31, K70.9, K71.3, K71.4, K71.50, K71.51, K71.6, K71.7, K71.8, K73.0, K73.1, K73.2, K73.8, K73.9, K74.0, K74.00, K74.01, K74.02, K74.1, K74.2, K74.3, K74.4, K74.5, K74.60, K74.69, K75.1, K75.2, K75.3, K75.4, K75.81, K75.89, K75.9, K76.0, K76.1, K76.2, K76.3, K76.4, K76.8.1, K76.8.2, K76.8.9, K76.9, K77, B19.0, B19.11, B19.21, I85.00, I85.01, I85.10, I85.11, I86.4, K70.40, K70.41, K72.10, K72.11, K72.90, K72.91, K76.5, K76.6, K76.7, K91.82, Z94.4.
Peptic ulcer disease excluding bleeding	K25.0, K25.1, K25.2, K25.3, K25.4, K25.5, K25.6, K25.7, K25.9, K26.0, K26.1, K26.2, K26.3, K26.4, K26.5, K26.6, K26.7, K26.9, K27.0, K27.1, K27.2, K27.3, K27.4, K27.5, K27.6, K27.7, K27.9, K28.0, K28.1, K28.2, K28.3, K28.4, K28.5, K28.6, K28.7, K28.9.
AIDS/HIV	B20, O98.711, O98.712, O98.713, O98.719, O98.72, O98.73, Z21.

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Supplementary Table 1 (*Continued*)

Diagnosis	ICD-10 codes
Lymphoma	C81.00, C81.01, C81.02, C81.03, C81.04, C81.05, C81.06, C81.07, C81.08, C81.09, C81.10, C81.11, C81.12, C81.13, C81.14, C81.15, C81.16, C81.17, C81.18, C81.19, C81.20, C81.21, C81.22, C81.23, C81.24, C81.25, C81.26, C81.27, C81.28, C81.29, C81.30, C81.31, C81.32, C81.33, C81.34, C81.35, C81.36, C81.37, C81.38, C81.39, C81.40, C81.41, C81.42, C81.43, C81.44, C81.45, C81.46, C81.47, C81.48, C81.49, C81.70, C81.71, C81.72, C81.73, C81.74, C81.75, C81.76, C81.77, C81.78, C81.79, C81.90, C81.91, C81.92, C81.93, C81.94, C81.95, C81.96, C81.97, C81.98, C81.99, C82.00, C82.01, C82.02, C82.03, C82.04, C82.05, C82.06, C82.07, C82.08, C82.09, C82.10, C82.11, C82.12, C82.13, C82.14, C82.15, C82.16, C82.17, C82.18, C82.19, C82.20, C82.21, C82.22, C82.23, C82.24, C82.25, C82.26, C82.27, C82.28, C82.29, C82.30, C82.31, C82.32, C82.33, C82.34, C82.35, C82.36, C82.37, C82.38, C82.39, C82.40, C82.41, C82.42, C82.43, C82.44, C82.45, C82.46, C82.47, C82.48, C82.49, C82.50, C82.51, C82.52, C82.53, C82.54, C82.55, C82.56, C82.57, C82.58, C82.59, C82.60, C82.61, C82.62, C82.63, C82.64, C82.65, C82.66, C82.67, C82.68, C82.69, C82.80, C82.81, C82.82, C82.83, C82.84, C82.85, C82.86, C82.87, C82.88, C82.89, C82.90, C82.91, C82.92, C82.93, C82.94, C82.95, C82.96, C82.97, C82.98, C82.99, C83.00, C83.01, C83.02, C83.03, C83.04, C83.05, C83.06, C83.07, C83.08, C83.09, C83.10, C83.11, C83.12, C83.13, C83.14, C83.15, C83.16, C83.17, C83.18, C83.19, C83.30, C83.31, C83.32, C83.33, C83.34, C83.35, C83.36, C83.37, C83.38, C83.39, C83.50, C83.51.
Metastatic cancer	C77.0, C77.1, C77.2, C77.3, C77.4, C77.5, C77.8, C77.9, C78.00, C78.01, C78.02, C78.1, C78.2, C78.30, C78.39, C78.4, C78.5, C78.6, C78.7, C78.80, C78.89, C79.00, C79.01, C79.02, C79.10, C79.11, C79.19, C79.2, C79.31, C79.32, C79.40, C79.49, C79.51, C79.52, C79.60, C79.61, C79.62, C79.63, C79.70, C79.71, C79.72, C79.81, C79.82, C79.89, C79.9, C7.B00, C7.B01, C7.B02, C7.B03, C7.B04, C7.B09, C7.B1, C7.B8, C80.0.
Solid tumor without metastasis	D00.00, D00.01, D00.02, D00.03, D00.04, D00.05, D00.06, D00.07, D00.08, D00.1, D00.2, D01.0, D01.1, D01.2, D01.3, D01.40, D01.49, D01.5, D01.7, D01.9, D02.0, D02.1, D02.2, D02.20, D02.21, D02.22, D02.3, D02.4, D03.0, D03.1, D03.11, D03.111, D03.112, D03.2, D03.21, D03.22, D03.20, D03.21, D03.22, D03.30, D03.39, D03.4, D03.51, D03.52, D03.59, D03.60, D03.61, D03.62, D03.70, D03.71, D03.72, D03.8, D03.9, D04.0, D04.1, D04.11, D04.12, D04.2, D04.21, D04.22, D04.30, D04.31, D04.32, D04.30, D04.39, D04.4, D04.5, D04.60, D04.61, D04.62, D04.70, D04.71, D04.72, D04.8, D04.9, D05.00, D05.01, D05.02, D05.10, D05.11, D05.12, D05.80, D05.81, D05.82, D05.90, D05.91, D05.92, D06.0, D06.1, D06.7, D06.9, D07.0, D07.1, D07.2, D07.30, D07.39, D07.4, D07.5, D07.60, D07.61, D07.69, D09.0, D09.10, D09.19, D09.20, D09.21, D09.22, D09.3, D09.8, D09.9, C00.0, C00.1, C00.2, C00.3, C00.4, C00.5, C00.6, C00.8, C00.9, C01.0, C02.0, C02.1, C02.2, C02.3, C02.4, C02.8, C02.9, C03.0, C03.1, C03.9, C04.0, C04.1, C04.8, C04.9, C05.0, C05.1, C05.2, C05.8, C05.9, C06.0, C06.1, C06.2, C06.8, C06.9, C07.0, C07.1, C07.2, C07.8, C07.9, C08.0, C08.1, C08.9, C09.0, C09.1, C09.8, C09.9, C10.0, C10.1, C10.2, C10.3, C10.4, C10.8, C10.9, C11.0, C11.1, C11.2, C11.3, C11.8, C11.9, C12, C13.0, C13.1, C13.2, C13.8, C13.9, C14.0, C14.2, C14.8, C15.3, C15.4, C15.5, C15.8, C15.9, C16.0, C16.1, C16.2, C16.3, C16.4, C16.5, C16.6, C16.8, C16.9, C17.0, C17.1, C17.2, C17.3, C17.8, C17.9, C18.0, C18.1, C18.2, C18.3, C18.4, C18.5, C18.6, C18.7, C18.8, C18.9, C19, C20, C21.0, C21.1, C21.2, C21.8, C22.0, C22.1, C22.2, C22.3, C22.4, C22.7, C22.8, C22.9, C23, C24.0, C24.1, C24.8, C24.9, C25.0, C25.1, C25.2, C25.3, C25.4, C25.7, C25.8, C25.9, C30, C31.0, C31.1, C31.2, C31.3, C31.8, C31.9, C32.0, C32.1, C32.2, C32.3, C32.8, C32.9, C33, C34.00, C34.01, C34.02, C34.10, C34.11, C34.12, C34.2, C34.30, C34.31, C34.32, C34.80, C34.81, C34.82, C34.90, C34.91, C34.92, C41, C43.0, C43.10, C43.11, C43.12, C43.2, C43.21, C43.22, C43.30, C43.31, C43.39, C43.4, C43.51, C43.52, C43.59, C43.60, C43.61, C43.62, C43.70, C43.71, C43.72, C43.8, C43.9, C44.00, C44.09, C44.101, C44.102, C44.1021, C44.1022, C44.109, C44.1091, C44.1092, C44.131, C44.1321, C44.1322, C44.1391, C44.1392, C44.191, C44.192, C7A.093, C7A.094, C7A.095, C7A.096, C7A.098, C7A.1, C7A.8, D46.9, E31.21, E31.22, E31.23.

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Supplementary Table 1 (*Continued*)

Diagnosis	ICD-10 codes
Rheumatoid arthritis/collagen vascular diseases	A18.01, A18.02, A39.84, A54.41, A54.42, L40.50, L40.51, L40.54, L40.59, L90.0, L94.0, L94.1, L94.3, M05.00, M05.011, M05.012, M05.019, M05.021, M05.022, M05.029, M05.031, M05.032, M05.039, M05.041, M05.042, M05.049, M05.051, M05.052, M05.059, M05.061, M05.062, M05.069, M05.071, M05.072, M05.079, M05.09, M05.10, M05.111, M05.112, M05.119, M05.121, M05.122, M05.129, M05.131, M05.132, M05.139, M05.141, M05.142, M05.149, M05.151, M05.152, M05.159, M05.161, M05.162, M05.169, M05.171, M05.172, M05.179, M05.19, M05.20, M05.211, M05.212, M05.219, M05.221, M05.222, M05.229, M05.231, M05.232, M05.239, M05.241, M05.242, M05.249, M05.251, M05.252, M05.259, M05.261, M05.262, M05.269, M05.271, M05.272, M05.279, M05.29, M05.30, M05.311, M05.312, M05.319, M05.321, M05.322, M05.329, M05.331, M05.332, M05.339, M05.341, M05.342, M05.349, M05.351, M05.352, M05.359, M05.361, M05.362, M05.369, M05.371, M05.372, M05.379, M05.39, M05.40, M05.411, M05.412, M05.419, M05.421, M05.422, M05.429, M05.431, M05.432, M05.439, M05.441, M05.442, M05.449, M05.451, M05.452, M05.459, M05.461, M05.462, M05.469, M05.471, M05.472, M05.479, M05.49, M05.50, M05.511, M05.512, M05.519, M05.521, M05.522, M05.529, M05.531, M05.532, M05.539, M05.541, M05.542, M05.549, M05.551, M05.552, M05.559, M05.561, M05.562, M05.569, M05.571, M05.572, M05.59, M05.60, M05.611, M05.612, M05.619, M05.621, M05.622, M05.629, M05.631, M05.632, M05.639, M05.641, M05.642, M05.649, M05.651, M05.652, M05.659, M05.661, M05.662, M05.669, M05.671, M05.672, M05.679, M05.69, M05.70, M05.711, M05.712, M05.719, M05.721, M05.722, M05.729, M05.731, M05.732, M05.739, M05.741, M05.742, M05.749, M05.751, M05.752, M05.759, M05.761, M05.762, M05.769.
Coagulopathy	D61.09, D61.1, D61.2, D61.3, D61.810, D61.811, D61.818, D61.82, D61.89, D61.9, D65, D66, D67, D68.0, D68.00, D68.01, D68.020, D68.021, D68.022, D68.023, D68.029, D68.03, D68.04, D68.09, D68.1, D68.2, D68.311, D68.312, D68.318, D68.32, D68.4, D68.8, D68.9, D69.1, D69.3, D69.41, D69.42, D69.49, D69.51, D69.59, D69.6, D69.8, D69.9, D75.82, D75.821, D75.822, D75.828, D75.829, D75.84, O99.111, O99.112, O99.113, O99.119, O99.12, O99.13.
Obesity	E66.01, E66.09, E66.1, E66.2, E66.8, E66.9, O99.210, O99.211, O99.212, O99.213, O99.214, O99.215, R93.9, Z68.30, Z68.31, Z68.32, Z68.33, Z68.34, Z68.35, Z68.36, Z68.37, Z68.38, Z68.39, Z68.41, Z68.42, Z68.43, Z68.44, Z68.45, Z68.54.
Weight loss	E40, E41, E42, E43, E44.0, E44.1, E45, E46, E64., O25.10, O25.11, O25.12, O25.13, O25.2, O25.3, R63.4, R64.
Blood loss anemia	D50.0
Deficiency anemia	D50.1, D50.8, D50.9, D51.0, D51.1, D51.2, D51.3, D51.8, D51.9, D52.0, D52.1, D52.8, D52.9, D53.0, D53.1, D53.2, D53.8, D53.9, D63.0, D63.1, D63.8, D64.9, O99.011, O99.012, O99.013, O99.019.
Alcohol abuse	F10.10, F10.11, F10.120, F10.121, F10.129, F10.130, F10.131, F10.132, F10.139, F10.4, F10.150, F10.151, F10.159, F10.180, F10.181, F10.182, F10.188, F10.9, F10.20, F10.21, F10.220, F10.221, F10.229, F10.230, F10.231, F10.232, F10.239, F10.4, F10.250, F10.251, F10.259, F10.26, F10.27, F10.280, F10.281, F10.282, F10.288, F10.9, F10.94, F10.950, F10.951, F10.959, F10.96, F10.97, F10.980, G62.1, I42.6, K29.20, K29.21, K70.10, K70.11, O99.310, O99.311, O99.312, O99.313, O99.314, O99.315.

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Supplementary Table 1 (*Continued*)

Diagnosis	ICD-10 codes
Drug abuse	F11.10, F11.11, F11.120, F11.121, F11.122, F11.129, F11.3, F11.4, F11.50, F11.51, F11.59, F11.81, F11.82, F11.88, F11.9, F12.0, F12.1, F12.20, F12.21, F12.22, F12.29, F12.3, F12.4, F12.50, F12.51, F12.59, F12.81, F12.82, F12.88, F12.9, F13.10, F13.11, F13.120, F12.121, F12.122, F12.129, F12.13, F12.150, F12.151, F12.159, F12.180, F12.188, F12.19, F12.20, F12.21, F12.220, F12.221, F12.222, F12.229, F12.23, F12.250, F12.251, F12.259, F12.280, F12.288, F12.29, F13.10, F13.11, F13.120, F13.121, F13.129, F13.130, F13.131, F13.132, F13.139, F13.14, F13.150, F13.151, F13.159, F13.180, F13.181, F13.182, F13.188, F13.19, F13.20, F13.21, F13.220, F13.221, F13.229, F13.230, F13.231, F13.232, F13.239, F13.24, F13.250, F13.251, F13.259, F13.26, F13.27, F13.280, F13.281, F13.282, F13.288, F13.29, F14.10, F14.11, F14.120, F14.121, F14.122, F14.129, F14.13, F14.14, F14.150, F14.151, F14.159, F14.180, F14.181, F14.182, F14.188, F14.19, F14.20, F14.21, F14.220, F14.221, F14.222, F14.229, F14.23, F14.24, F14.250, F14.251, F14.259, F14.280, F14.281, F14.282, F14.288, F14.29, F15.10, F15.11, F15.120, F15.121, F15.122, F15.129, F15.13, F15.14, F15.150, F15.151, F15.159, F15.180, F15.181, F15.182, F15.188, F15.19, F15.20, F15.21, F15.220, F15.221, F15.222, F15.229, F15.23, F15.24, F15.250, F15.251, F15.259, F15.280, F15.281, F15.282, F15.288, F15.29, F16.10, F16.11, F16.120, F16.121, F16.122, F16.129, F16.14, F16.150, F16.151, F16.159, F16.180, F16.183, F16.188, F16.19, F16.20, F16.21, F16.220, F16.221, F16.222, F16.229, F16.24, F16.250, F16.251, F16.259, F16.280, F16.283, F16.288, F16.29, F18.10, F18.11, F18.120, F18.121, F18.129, F18.14, F18.150, F18.151, F18.159, F18.17, F18.180, F18.188, F18.19, F18.20, F18.21, F18.220, F18.221, F18.229, F18.24, F18.250, F18.251, F18.259, F18.27, F18.280, F18.288, F18.29, F19.10, F19.11, F19.120, F19.121, F19.122, F19.129, F19.130, F19.131, F19.132, F19.139, F19.14, F19.150, F19.151, F19.159, F19.16, F19.17, F19.180, F19.181, F19.182, F19.188, F19.19, F19.20, F19.21, F19.220, F19.221, F19.222, F19.229, F19.230, F19.231, F19.232, F19.239, F19.24, F19.250, F19.251, F19.259, F19.26, F19.27, F19.280, F19.281, F19.282, F19.288, F19.29, O99.320, O99.321, O99.322, O99.323, O99.324, O99.325, Z72.0, Z71.5.
Psychoses	F11.150, F11.151, F11.159, F11.250, F11.251, F11.259, F12.150, F12.151, F12.159, F12.250, F12.251, F12.259, F13.150, F13.151, F13.159, F13.250, F13.251, F13.259, F14.150, F14.151, F14.159, F14.250, F14.251, F14.259, F15.150, F15.151, F15.159, F15.250, F15.251, F15.259, F16.150, F16.151, F16.159, F16.250, F16.251, F16.259, F18.150, F18.151, F18.159, F18.250, F18.251, F18.259, F19.150, F19.151, F19.159, F19.250, F19.251, F19.259, F06.0, F06.1, F06.2, F06.30, F06.33, F11.950, F11.951, F11.959, F12.950, F12.951, F12.959, F13.950, F13.951, F13.959, F14.950, F14.951, F14.959, F15.950, F15.951, F15.959, F16.950, F16.951, F16.959, F18.950, F18.951, F18.959, F19.950, F19.951, F19.959, F20.0, F20.1, F20.2, F20.3, F20.5, F20.81, F20.89, F20.9, F21, F22, F23, F24, F25.0, F25.1, F25.8, F25.9, F28, F29, F30.10, F30.11, F30.12, F30.13, F30.2, F30.3, F30.4, F30.8, F30.9, F31.0, F31.10, F31.11, F31.12, F31.13, F31.2, F31.30, F31.31, F31.32, F31.4, F31.5, F31.60, F31.61, F31.62, F31.63, F31.64, F31.70, F31.71, F31.72, F31.73, F31.74, F31.75, F31.76, F31.77, F31.78, F31.81, F31.89, F31.9, F32.4, F32.5, F33.40, F33.41, F33.42, F34.0, F34.8, F34.81, F34.89, F34.9, F39, F48.89, F84.3.
Depression	F06.31, F06.32, F06.34, F32.0, F32.1, F32.2, F32.3, F32.8, F32.81, F32.89, F32.9, F32.A, F33.0, F33.1, F33.2, F33.3, F33.8, F33.9, F34.1.