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Supporting Information

Supplementary methods and results

Appendix to: Bhasker V, Fong JR, Clark PJ, et al. Cause-specific mortality among Queensland people with cirrhosis, by cirrhosis aetiology and decompensation status, 2007–22: a retrospective cohort study. *Med J Aust* 2025; doi: 10.5694/mja2.70036.

Supplementary methods

We performed a retrospective cohort study of all hospitalised patients with cirrhosis in Queensland during 2007-2022. The manuscript has been reported in line with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) criteria for cohort studies.[1]

We analysed a population-based dataset from the Queensland Hospital Admitted Patient Data Collection (QHAPDC) and, using probabilistic data-linkage, assessed underlying cause of death (also referred to as cause of death) and associated (or contributing) cause of death using death registrations from the Queensland Registry of Births, Deaths, and Marriages. Underlying cause of death is the disease, injury, circumstances of the accident or violence that initiated the train of events leading directly to death, commonly referred to as the primary cause of death.

Selection of cases and index admission

We identified all hospital admissions with cirrhosis included in their disease coding using the International Classification of Diseases, tenth revision, Australian modification (ICD-10-AM).[2] Patients were eligible if admitted with cirrhosis at least once during 1 July 2007 and 31 December 2022, aged ≥18 years old, and residing in Queensland. We identified the first admission with cirrhosis, ascites, hepatic encephalopathy, variceal bleeding, primary liver cancer, hepatorenal syndrome, or hepatic failure for each individual included in the study during this period, referred to as the index admission (list of ICD-10-AM codes in **Table 1**). Patients were followed from index admission until date of death, liver transplant, or 31 December 2022, whichever came first. Based on QHAPDC and Death Registry data and using a hierarchical algorithm to define aetiology, patients were categorised as alcohol-related cirrhosis, metabolic dysfunction-associated steatotic liver disease (MASLD) or cryptogenic (referred to hereafter as MASLD), hepatitis C virus (HCV), hepatitis B virus (HBV), and 'other' causes.[3] The latter included a heterogeneous group of patients, each representing <3% of the data, namely: haemochromatosis, autoimmune hepatitis, primary biliary cholangitis, primary sclerosing cholangitis, Wilson's disease, alpha-1 antitrypsin deficiency, Budd-Chiari syndrome, inflammatory liver disease unspecified, and cystic fibrosis.

Measurements

Sociodemographic data were obtained from QHAPDC and causes and date of death from the Death Registry. Using a previously reported algorithm for identification of Indigenous status,[4] patients were identified as Indigenous if noted in at least one of their records within the study period. Sex, referred to as biological differences (chromosomal, hormonal, reproductive) at birth, was categorized as male/female. Place of residence at index admission was mapped according to population-level data categories for remoteness (Accessibility/Remoteness Index of Australia, ARIA) [5] and Socio-Economic Index for Areas (SEIFA) for relative socioeconomic disadvantage.[6] Comorbidity was measured using the Charlson Comorbidity Index (CCI)[7, 8] calculated based on medical conditions recorded in the index admission (except liver disease and hepatocellular carcinoma). Severity of liver disease was assessed by presence of cirrhosis decompensation (variceal bleeding, ascites or hepatic encephalopathy), hepatorenal syndrome, or hepatic failure at index admission. Patients were considered to have decompensated during follow-up after the index admission if they had at least one subsequent admission with an ICD-10-AM code for variceal bleeding, ascites or hepatic encephalopathy.

Outcomes

The primary outcome was death. The underlying cause of death was categorised as either: (1) Liver-related (including liver diseases, chronic hepatitis, and primary liver malignancies); (2) Extrahepatic cancers (including all cancers except for primary liver malignancies); (3) Cardiovascular disease-related (including major adverse cardiovascular events as coded using the Charlson Comorbidity Index algorithm)[7]; (4) Diabetes; (5) Diseases of

the respiratory system; (6) Infectious or parasitic diseases (excluding chronic hepatitis); (7) External causes of morbidity and mortality (accident, self-harm, suicide and homicide); or (8) Other causes (for ICD groupings with <2% prevalence). We examined the distribution of all causes of death, including underlying and associated cause of death. All causes of death were categorised according to the chapters of the ICD-10-AM book, and selected subgroups of interest were also described.

Table 1. ICD-10-AM codes used for identification of patients with cirrhosis and to assess severity of liver disease

ICD-10-AM code		PPV* (95% CI)	NPV* (95% CI)
Cirrhosis			
K70.3	Alcoholic cirrhosis of liver	0.97 (0.95-0.99)	0.35 (0.30-0.40)
K74.4	Secondary biliary cirrhosis	1.00	0.24 (0.21-0.28)
K74.5	Biliary cirrhosis, unspecified	0.67 (0.28-0.94)	0.23 (0.20-0.27)
K74.6	Other and unspecified cirrhosis of liver	0.96 (0.93-0.99)	0.33 (0.28-0.38)
K71.7	Toxic liver disease with fibrosis & cirrhosis of liver	NA	NA
Severity of liver disease			
Cirrhosis decompensation			
I85.0	Oesophageal varices with bleeding	1.00	0.58 (0.54-0.62)
I98.3	Oesophageal varices with bleeding in diseases classified elsewhere	1.00	0.60 (0.55-0.64)
R18	Ascites	0.97 (0.94-0.99)	0.76 (0.71-0.80)
G31.2	Degeneration of nervous system due to alcohol	0.37 (0.21-0.55)	0.74 (0.70-0.78)
G93.4	Encephalopathy, unspecified	0.71 (0.54-0.84)	0.77 (0.73-0.80)
G31.2, G93.4	Grouped hepatic encephalopathy	0.55 (0.43-0.67)	0.78 (0.74-0.81)
C22	Primary liver cancer	0.97 (0.92-1.00)	0.98 (0.96-0.99)
K72.9	Hepatic failure	NA	NA
K76.7	Hepatorenal syndrome	NA	NA

International Classification of Diseases 10th edition – Australian Modification (ICD-10-AM); Not available (NA); Non-alcoholic fatty liver disease (NAFLD); Non-alcoholic steatohepatitis (NASH); * Positive predictive values (PPV) and negative predictive values (NPV) were obtained from a study reported by Hayward et al.[9]

References

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3. Philip G, Djerboua M, Carlone D, Flemming JA. Validation of a hierarchical algorithm to define chronic liver disease and cirrhosis etiology in administrative healthcare data. *PLoS One*. 2020;15:e0229218.

4. Whop LJ, Diaz A, Baade P, et al. Using probabilistic record linkage methods to identify Australian Indigenous women on the Queensland Pap Smear Register: the National Indigenous Cervical Screening Project. *BMJ Open*. 2016;6:e009540.

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7. Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care*. 2005;43:1130-1139.

8. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40:373-383.

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Supplementary results

Table 2. Frequency of deaths for each underlying cause of death according to cirrhosis aetiology among 12,387 patients with cirrhosis who died during the follow-up period

Cause of death	Alcohol	MASLD	HCV	HBV
Compensated cirrhosis at index admission	**1637**	**1189**	**753**	**160**
Liver disease	523 (31.9%)	230 (19.3%)	331 (44.0%)	81 (50.6%)
Extrahepatic cancer	261 (15.9%)	266 (22.4%)	113 (15.0%)	30 (18.8%)
Cardiovascular disease	245 (15.0%)	205 (17.2%)	74 (9.8%)	18 (11.2%)
Type 2 diabetes	30 (1.8%)	63 (5.3%)	≤ 5	≤ 5
Respiratory disease	137 (8.4%)	92 (7.7%)	36 (4.8%)	≤ 5
Infections and parasitic diseases	47 (2.9%)	35 (2.9%)	12 (1.6%)	≤ 5
External causes	79 (4.8%)	29 (2.4%)	71 (9.4%)	≤ 5
Other causes	315 (19.2%)	269 (22.6%)	112 (14.9%)	18 (11.2%)
Decompensated cirrhosis at index admission	**3890**	**1473**	**1714**	**239**
Liver disease	2,538 (65.2%)	595 (40.4%)	1,158 (67.6%)	137 (57.3%)
Extrahepatic cancer	255 (6.6%)	241 (16.4%)	95 (5.5%)	16 (6.7%)
Cardiovascular disease	284 (7.3%)	179 (12.2%)	59 (3.4%)	14 (5.9%)
Type 2 diabetes	46 (1.2%)	71 (4.8%)	15 (0.9%)	6 (2.5%)
Respiratory disease	142 (3.7%)	67 (4.5%)	34 (2.0%)	11 (4.6%)
Infections and parasitic diseases	65 (1.7%)	29 (2.0%)	46 (2.7%)	12 (5.0%)
External causes	89 (2.3%)	23 (1.6%)	56 (3.3%)	≤ 5
Other causes	471 (12.1%)	268 (18.2%)	251 (14.6%)	41 (17.2%)
Age ≤ 60 years at index admission	**2454**	**330**	**1820**	**189**
Liver disease	1,503 (61.2%)	108 (32.7%)	1,114 (61.2%)	110 (58.2%)
Extrahepatic cancer	133 (5.4%)	82 (24.8%)	119 (6.5%)	15 (7.9%)
Cardiovascular disease	201 (8.2%)	26 (7.9%)	93 (5.1%)	16 (8.5%)
Type 2 diabetes	28 (1.1%)	15 (4.5%)	10 (0.5%)	≤ 5
Respiratory disease	95 (3.9%)	13 (3.9%)	49 (2.7%)	7 (3.7%)
Infections and parasitic diseases	50 (2.0%)	15 (4.5%)	47 (2.6%)	7 (3.7%)
External causes	99 (4.0%)	≤ 5	110 (6.0%)	≤ 5
Other causes	345 (14.1%)	66 (20.0%)	278 (15.3%)	29 (15.3%)

Cause of death	Alcohol	MASLD	HCV	HBV
Age > 60 years at index admission	**3073**	**2332**	**647**	**210**
Liver disease	1,558 (50.7%)	717 (30.7%)	375 (58.0%)	108 (51.4%)
Extrahepatic cancer	383 (12.5%)	425 (18.2%)	89 (13.8%)	31 (14.8%)
Cardiovascular disease	328 (10.7%)	358 (15.4%)	40 (6.2%)	16 (7.6%)
Type 2 diabetes	48 (1.6%)	119 (5.1%)	9 (1.4%)	6 (2.9%)
Respiratory disease	184 (6.0%)	146 (6.3%)	21 (3.2%)	9 (4.3%)
Infections and parasitic diseases	62 (2.0%)	49 (2.1%)	11 (1.7%)	9 (4.3%)
External causes	69 (2.2%)	47 (2.0%)	17 (2.6%)	≤ 5
Other causes	441 (14.4%)	471 (20.2%)	85 (13.1%)	30 (14.3%)
Absence of diabetes and cardiovascular disease at index admission	**3644**	**1026**	**1922**	**249**
Liver disease	2,168 (59.5%)	359 (35.0%)	1,211 (63.0%)	158 (63.5%)
Extrahepatic cancer	358 (9.8%)	277 (27.0%)	160 (8.3%)	30 (12.0%)
Cardiovascular disease	256 (7.0%)	85 (8.3%)	79 (4.1%)	14 (5.6%)
Type 2 diabetes	12 (0.3%)	16 (1.6%)	≤ 5	≤ 5
Respiratory disease	183 (5.0%)	69 (6.7%)	59 (3.1%)	9 (3.6%)
Infections and parasitic diseases	72 (2.0%)	25 (2.4%)	45 (2.3%)	9 (3.6%)
External causes	122 (3.3%)	20 (1.9%)	105 (5.5%)	≤ 5*
Other causes	473 (13.0%)	175 (17.1%)	259 (13.5%)	26 (10.4%)
Presence of diabetes and/or cardiovascular disease at index admission	**1883**	**1636**	**545**	**150**
Liver disease	893 (47.4%)	466 (28.5%)	278 (51.0%)	60 (40.0%)
Extrahepatic cancer	158 (8.4%)	230 (14.1%)	48 (8.8%)	16 (10.7%)
Cardiovascular disease	273 (14.5%)	299 (18.3%)	54 (9.9%)	18 (12.0%)
Type 2 diabetes	64 (3.4%)	118 (7.2%)	15 (2.8%)	8 (5.3%)
Respiratory disease	96 (5.1%)	90 (5.5%)	11 (2.0%)	7 (4.7%)
Infections and parasitic diseases	40 (2.1%)	39 (2.4%)	13 (2.4%)	7 (4.7%)
External causes	46 (2.4%)	32 (2.0%)	22 (4.0%)	≤ 5*
Other causes	313 (16.6%)	362 (22.1%)	104 (19.1%)	33 (22.0%)

Metabolic dysfunction-associated steatotic liver disease (MASLD); Chronic hepatitis C virus (HCV); Chronic hepatitis B virus (HBV)

* Exact number not reported to ensure privacy.

Table 3. Ten-year all-cause and cause-specific mortality in 16,735 patients who had their index admission between 2012 and 2022

	Liver disease		Extrahepatic cancer		Cardiovascular disease		All-cause mortality	
Cirrhosis aetiology	**Mortality (95% CI) ***	**Adjusted sHR (95% CI) †**	**Mortality (95% CI) ***	**Adjusted sHR (95% CI) †**	**Mortality (95% CI)***	**Adjusted sHR (95% CI) †**	**Mortality (95%CI) ***	**Adjusted OR (95% CI) ‡**
Alcohol	46.3% (44.0-48.7)	Reference	11.4% (9.9-13.1)	Reference	12.7% (10.9-14.9)	Reference	71.8% (69.9-73.7)	Reference
MASLD	27.4% (24.5-30-6)	**0.54 (0.49-0.61)**	18.8% (15.5-22.7)	1.18 (0.97-1.43)	15.2% (12.2-18.8)	0.96 (0.79-1.17)	69.1% (65.9-72.2)	**0.84 (0.79-0.90)**
HCV	42.8% (40.0-45.7)	**1.20 (1.11-1.31)**	7.7% (6.0-10.0)	0.91 (0.73-1.13)	4.9% (3.8-6.4)	**0.58 (0.44-0.75)**	59.8% (57.0-62.5)	1.04 (0.97-1.11)
HBV	40.6% (33.5-47.6)	0.99 (0.83-1.19)	10.5% (7.0-15.7)	0.90 (0.60-1.35)	8.9% (4.9-16.1)	0.72 (0.45-1.13)	62.5% (55.9-69.1)	**0.83 (0.72-0.95)**

Metabolic dysfunction-associated steatotic liver disease (MASLD); Chronic hepatitis C virus (HCV); Chronic hepatitis B virus (HBV); Subhazard ratio (sHR); Odds ratio (OR); Confidence interval (CI);

* Kaplan–Meier failure function according to cirrhosis aetiology, proportion and 95% CI are reported;

† Fine and Gray subhazard model included sex, Indigenous status, decompensation event and type 2 diabetes during the follow-up period, and age, socioeconomic status, remoteness of residence, Charlson comorbidity score and severity of liver disease at index admission;

‡ Cox regression model included sex, Indigenous status, decompensation event and type 2 diabetes during the follow-up period, and age, socioeconomic status, remoteness of residence, Charlson comorbidity score and severity of liver disease at index admission.

STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

Note: The page numbers in this checklist refer to the submitted manuscript, not to the published article or its Supporting Information file.

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3-4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	4
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-5
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	
Bias	9	Describe any efforts to address potential sources of bias	4
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4-5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, explain how loss to follow-up was addressed	
		(*e*) Describe any sensitivity analyses	
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	5 14
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	

Descriptive data		14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	
			(b) Indicate number of participants with missing data for each variable of interest	
			(c) Summarise follow-up time (eg, average and total amount)	
Outcome data		15*	Report numbers of outcome events or summary measures over time	6
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	6-7
			(*b*) Report category boundaries when continuous variables were categorized	
			(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17		Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6
Discussion				
Key results	18		Summarise key results with reference to study objectives	8
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	10
Interpretation	20		Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10
Generalisability	21		Discuss the generalisability (external validity) of the study results	10
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	Title page

*Give information separately for exposed and unexposed groups.

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 http://www.strobe-statement.org.