Research article

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Cirrhosis epidemiology in Denmark 1998–2022, and 2030 forecast

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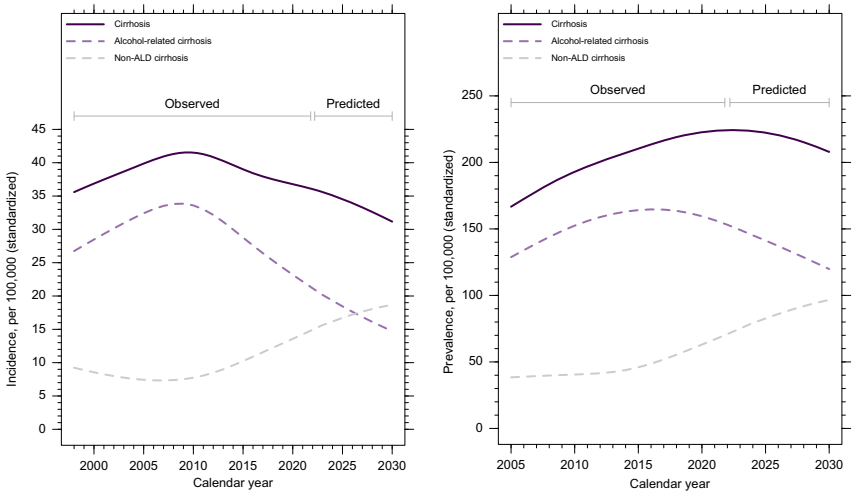
Graphical abstract

Cirrhosis epidemiology in Denmark 1998–2022 and 2030 forecast

- Included: 30,747 patients with ALD cirrhosis and 9,548 with non-ALD cirrhosis
- Median age at cirrhosis diagnosis increased from 56 to 66 years between 1998 and 2022
- ALD cirrhosis proportion declined from 80%-58% in 1998-2022
- Overall cirrhosis prevalence will peak in 2024
- Non-ALD cirrhosis will outnumber ALD cirrhosis from 2027
- Survival improved for patients with elective presentation but not for those with acute presentation



Highlights:

- Median age at cirrhosis diagnosis in Denmark increased from 56 years in 1998 to 66 years in 2022.
- The ALD cirrhosis proportion declined from around 80% in 1998–2014 to 58% in 2022.
- The overall prevalence of cirrhosis will have peaked in 2024, and unspecified cirrhosis will outnumber ALD cirrhosis from 2027.
- Survival has improved for patients with elective presentation but not for patients with acute presentation.

Impact and implications:

Alcohol-related liver (ALD) cirrhosis poses a substantial and growing burden on hospitals worldwide. Information about the current and imminent epidemiology of cirrhosis is important for our understanding of the public health, for researchers designing trials of interventions, and for planning of future assignments of healthcare systems. In the current study, we used Danish nationwide healthcare registries to study past, current, and future trends in the epidemiology of cirrhosis. Our results forecast a change in cirrhosis epidemiology and thereby a change in hepatology practice in Denmark. We expect that patients with ALD cirrhosis will be outnumbered by increasingly older patients who present in the outpatient clinic with cirrhosis from MASLD and a higher burden of comorbidities.

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Cirrhosis epidemiology in Denmark 1998–2022, and 2030 forecast

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Background & Aims: The incidence of cirrhosis resulting from alcohol-related liver disease (ALD) is decreasing in Denmark, whereas the incidence of obesity is increasing, driving an increase in metabolic dysfunction-associated steatotic liver disease (MASLD). We aimed to perform an up-to-date study of the epidemiology of cirrhosis in Denmark, including etiologies, and a forecast through to 2030.

Methods: We identified all patients diagnosed with cirrhosis between 1998 and 2022, categorized into ALD and non-ALD cirrhosis, in nationwide Danish healthcare registries. Cirrhosis prevalence and incidence were computed. We used an age–period–cohort model to visualize impacts of age, calendar year, and birthyear on etiology-specific cirrhosis incidence rates (alcohol or non-alcohol, interpreted as mainly the result of MASLD), with predicted incidence rates for 2023–2030. The Kaplan-Meier function was used for survival probabilities.

Results: We included 30,747 (76%) patients with ALD cirrhosis and 9,548 (24%) with non-ALD cirrhosis. Patients with non-ALD cirrhosis were older and had more comorbidities compared with patients with ALD cirrhosis; median age at diagnosis was 66 *vs.* 59 years, increasing in both groups overall, from 56 years in 1998 to 66 years in 2022. The ALD cirrhosis proportion was stable at around 80% from 1998 to the end of 2014, and gradually declined to 58% in 2022. Overall cirrhosis prevalence will have peaked in 2024, and non-ALD cirrhosis will outnumber ALD cirrhosis from 2027. Thus, mortality among patients with cirrhosis is declining owing to fewer deaths the first year after cirrhosis diagnosis.

Conclusions: We forecast a change in cirrhosis epidemiology affecting hepatology practice in Denmark: patients will be older, fewer will have ALD, more will have MASLD, and their longer life expectancy and comorbidities will be more burdensome for healthcare systems.

Introduction

Liver cirrhosis represents the end stage of chronic liver disease and causes substantial morbidity and mortality worldwide.[1] In many high-income countries, hazardous alcohol consumption is the dominant cause of cirrhosis. This is the case in Denmark, where, from 1996 to 2006, alcohol was the cause of cirrhosis in 79% of patients.[2] Alcohol-related liver disease (ALD), particularly cirrhosis due to ALD (ALD cirrhosis), is a sizable burden on hospitals, and has been increasing in the USA,[3,4] UK,[5] and Germany,[5] but decreasing in Denmark, at least until the end of 2018.[6] According to the Global Burden of Disease study, ALD cirrhosis caused 371,964 deaths and 11.2 million disability-adjusted life years (DALYs) to be lost worldwide in 2019.[7,8]

Metabolic dysfunction-associated steatotic liver disease (MASLD, previously non-alcoholic liver disease [NAFLD]) and metabolic dysfunction-associated steatohepatitis (MASH, previously non-alcoholic steatohepatitis [NASH]) represent another cirrhosis etiology with increasing incidence worldwide because of the markedly increasing prevalence of obesity. A recent review reported a prevalence of MASLD of 32% in the Middle East, 24% in the USA, and 23% in Europe.[8] Another study described predicted increases in the prevalence of MASLD from 2016 to 2030 in China, Japan, the USA, and five European countries, with the largest increase in China.[9] In the USA, MASLD cirrhosis has become the leading indication for liver transplantation, after HCV cirrhosis.[10] The proportion of MASLD in Denmark is also expected to rise with the increasing prevalence of obesity.[11,12]

Information about the current and imminent epidemiology of cirrhosis is important for our understanding of public health, for researchers designing trials of interventions, and for future planning for healthcare systems. Given this background, we used Danish nationwide healthcare registries to study past, current, and future trends in the epidemiology of cirrhosis. This gives us a unique possibility to follow the shift in cirrhosis etiology and to forecast future trends.

Patients and methods

Denmark has tax-funded public healthcare, and no private hospital manages patients with liver disease. All Danish citizens

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have a general practitioner, and workup for liver disease requires a referral from the general practitioner to a public hospital or presentation to the emergency department. This means that the obligatory hospital-derived health registries have complete and nationwide information on the epidemiology of diagnosed cirrhosis cases.

We used the Danish National Patient Registry to identify all patients with ALD cirrhosis and non-ALD cirrhosis from 1998 to 2022. This registry records data from all hospital contacts. Established in 1977, it recorded only inpatient hospitalizations until 1994, but from 1995 it has recorded all hospital contacts, whether inpatient, outpatient, or emergency department visits.[13] The data, interlinked via each citizen's unique personal identifier, include death, demographic information (*e.g.* age, sex, and residence), one primary diagnosis code, up to 20 secondary diagnosis codes, the type of hospital contact (inpatient, outpatient, or emergency department), and whether the hospital contact was acute or elective. Since 1994, diagnosis codes were coded according to the 10th version of the *International Classification of Diseases* (*ICD-10*).

In this study, the patient's 'diagnosis date' was the earliest date on which they received a diagnosis code for cirrhosis (K70.3, K70.4, or K74.6). These diagnosis codes are given by the treating physician and recorded in the National Patient Registry when the patient is discharged from a hospital admission or at the end of an outpatient program. We included patients with cirrhosis in our cohort at the beginning of their admission or outpatient program because we assumed, based on our clinical experience, that the diagnosis was usually made shortly after admission. No patients were included on the basis of their referral diagnosis.

Next, we categorized patients as having ALD cirrhosis or non-ALD cirrhosis. Patients with ALD cirrhosis had a diagnosis code for ALD cirrhosis (K70.3 or K70.4) on the diagnosis date, or they had the diagnosis code K74.6 on the diagnosis date plus a diagnosis code indicative of harmful alcohol consumption any time before or on the date of cirrhosis diagnosis. The codes for hazardous alcohol consumption were those identified as 'wholly alcohol-attributable conditions' by Public Health England (Table 2 in[14]). Patients with a diagnosis code for non-ALD cirrhosis (K74.6) and no diagnosis code indicative of hazardous alcohol consumption were used in this study as a proxy for patients with MASLD cirrhosis (see Discussion for further detail).

We recorded whether the patient's hospital contact on the diagnosis date was acute or elective: 'acute presentation' was defined by presentation through the emergency department or as an acute in- or outpatient hospital contact. All other presentations were defined as 'elective presentation'. Acute presentation is a proxy for having more severe cirrhosis and a higher mortality.[15]

Our analyses included all patients whose diagnosis date was between 1 January 1998 and 31 December 2022, and who were aged between 20 and 95 years on that date. Diagnoses were available from 1995, and we used the data from 1995 to 1997 to ensure that patients diagnosed in 1998 or later were truly newly diagnosed and did not have a diagnosis code for cirrhosis before 1998.

We extracted diagnoses of selected comorbidities and plausible causes of non-ALD cirrhosis from the National Patient Registry: chronic viral hepatitis (ICD-10: B18*), diabetes (ICD-10: E10*–E14*), and ischemic heart disease (IHD) (ICD-10: I20*–I25*).

Statistical analyses

Incidence of cirrhosis

We computed the incidence rate of cirrhosis in a year as the number of patients diagnosed with cirrhosis in that year divided by the number of Danish citizens aged 20–95 years on 1 January of that year. The overall incidence rate for the 1998–2022 period was computed as the ratio of the sum of annual numerators divided by the sum of annual denominators. Similarly, the incidence rates for subsets by type of cirrhosis (ALD cirrhosis or non-ALD cirrhosis) and by sex were computed by restricting the numerator and denominator accordingly. We used direct standardization to adjust annual incidence rates for changes in the age distribution of the Danish population. The standard population was the Danish population on 1 January 2023. The demographic data are freely downloadable from Statistics Denmark (www.statistikbanken.dk).

We used an age–period–cohort model to estimate the effects of age, calendar year (period), and birth year (cohort) on the incidence rate of cirrhosis. We used the age–period–cohort model function 'apcspline' in Stata.[16] First, we tweaked the model to forecast the incidence rates for 2018–2022 using data from 1998–2017. The tweaking entailed that we increased the degrees of freedom (*i.e.* flexibility) of the spline functions modeling the effects of age, period, and cohort, as well as the 'damping' (*i.e.* attenuation of effects) over calendar time.[16] We compared the fit of the resulting models to observed data visually, aiming to find the simplest model the forecasts of which fit acceptably to the observed incidence rates (the 'final age–period–cohort model').

We used the final age–period–cohort model to visualize the impacts of age, calendar year, and birth year on the incidence rate of cirrhosis, and then used it to model the annual incidence rates from 1998 to 2022 with predicted annual incidence rates for 2023–2030, all standardized to the age distribution of the Danish population on 1 January 2023. For the predictions, we obtained the demographic projections downloadable from Statistics Denmark (www.statistikbanken.dk). The Danish population aged 20–95 years grew from 4.0 million in 1995 (median age 44 years) to 4.5 million in 2021 (median age 50 years) and will grow to a predicted 4.7 million in 2030 (median age 51 years). Confidence intervals were estimated by summing the stratum-specific lower and upper bounds of predicted numbers of patients. Strata were defined by age and calendar year, and the bounds were computed from the standard error of the predicted number of patients.[16]

Burden of cirrhosis

We used an age–period–cohort model for the prevalence of cirrhosis. This model used the same degrees of freedom as the final age–period–cohort model for incidence, and the only differences between the two models were: (1) the prevalence model was based on prevalence counts for cirrhosis from 2005, not 1998, because prevalence counts are generally underestimated in the first years after a registry is established; and (2) the prevalence model used the number of Danish citizens who were alive and diagnosed with cirrhosis on 1 January 2005

(and, subsequently, 2006, 2007, and so on), rather than the number of citizens who were diagnosed during the year 2005.

We used the Kaplan-Meier function to compute the 1-, 3-, and 5-year survival probabilities from the cirrhosis diagnosis date by calendar year of diagnosis date. In supplementary landmark analyses, we computed survival probabilities by year of cirrhosis diagnosis conditional on having survived to the 1-year landmark, (*i.e.* for the subset of patients who were still alive 1 year after cirrhosis diagnosis). We conducted similar analyses from the 3- and 5-year landmarks.

We computed the prevalence of chronic viral hepatitis, diabetes, and ischemic heart disease (IHD) at the time of cirrhosis diagnosis. By our definition, patients with cirrhosis had prevalent comorbidity if they had received a diagnosis code for chronic viral hepatitis between 3 years before and 30 days after the cirrhosis diagnosis date.

Ethics

The study was approved in 2019 by the Danish Health Data Authority of and by the Danish Data Protection Agency (Journal number 1-16-02-338-19). All research was conducted in accordance with both the Declarations of Helsinki and Istanbul. According to Danish law, approval from the Danish Committee on Health Research Ethics was not necessary. Given that this is a register-based study, written consent was not required.

Results

We included 40,295 patients diagnosed with cirrhosis between 1998 and 2022 at age 20–95 years. Of these, 30,747 (76%) had ALD cirrhosis and 9,548 (24%) had non-ALD cirrhosis. During the study period, the proportion with ALD cirrhosis decreased: It was stable at around 80% from 1998 until the end of 2014 and then declined gradually to 58% in 2022 (Fig. S1). Men accounted for 26,630 (66%) of the 40,295 patients (66% of patients with ALD cirrhosis and 56% of patients with non-ALD cirrhosis). The median age at diagnosis was 60 years, and patients with ALD cirrhosis were younger at diagnosis compared with those with non-ALD cirrhosis (median age: 59 *vs.* 66 years, respectively) (Table 1). The median age at diagnosis increased gradually for both groups during the study period; overall, it increased from 56 in 1998 to 66 years in 2022 (Fig. S2). The proportion of patients with acute presentation was 61% overall, but fell considerably after 2010, to 71% in 1998, 70% in 2010, 48% in 2018, and 41% in 2022.

The standardized incidence rate of cirrhosis from 1998 to 2022 was 39.2 per 100,000 person-years (ALD cirrhosis, 29.4; non-ALD cirrhosis, 9.8). It was 53.3 per 100,000 for men and 26.0 per 100,000 for women. The annual adjusted incidence rate was 36.5 per 100,000 in 1998, peaking at 43.3 per 100,000 in 2009 before falling to 33.9 per 100,000 in 2022 (Table 1 and Fig. 1).

Forecast to the end of 2030

The age–period–cohort model provided accurate forecasts for 2018–2022 based on data for 1998–2017 (Figs. S3 and S4). With the final age–period–cohort model, we visualized the effects of patient age, birth cohort, and calendar year on the standardized incidence rate of ALD cirrhosis (Fig. S5). The overall incidence rate of cirrhosis peaked in 2009 (41.5 per 100,000, 95% CI 40.4–42.7) and will continue its subsequent decline to the end of 2030 (31.2 per 100,000, 95% CI 28.2–34.4) (Fig. 1). This is the result of a marked decrease in the incidence of ALD cirrhosis, which is partially compensated for by an increase in the incidence of non-ALD cirrhosis. In 2027, the incidence of non-ALD cirrhosis (17.7 per 100,000, 95% CI

Table 1. Characteristics of Danish patients diagnosed with cirrhosis in 1998, 2009 (the year of peak cirrhosis incidence), and 2022, and overall from 1998 to 2022.

	Year			
Characteristic	**1998**	**2009**	**2022**	**1998–2022**
Incidence, n				
Alcohol-related	1,059	1,481	897	30,747
Non-ALD	318	295	658	9,548
Overall	1,377	1,776	1,555	40,295
Male sex, %				
Alcohol-related	68	69	72	69
Non-ALD	59	55	60	56
Overall	66	67	67	66
Median age at diagnosis (IQR), years				
Alcohol-related	54 (47–62)	58 (52–65)	62 (55–70)	59 (52–66)
Non-ALD	62 (51–73)	64 (55–73)	69 (61–76)	66 (57–75)
Overall	56 (48–64)	59 (52–66)	66 (57–73)	60 (53–68)
Incidence rate per 100,000 PY, crude				
Alcohol-related	26.2	35.6	19.6	29.0
Non-ALD	7.9	7.1	14.4	9.0
Overall	34.1	42.7	34.0	38.0
Incidence rate per 100,000 PY, adjusted				
Alcohol-related	27.4	35.4	19.5	29.4
Non-ALD	9.1	7.8	14.4	9.8
Overall	36.5	43.3	33.9	39.2
1-year survival (95% CI), %				
Alcohol-related	69 (66–72)	66 (64–69)	73 (70–75)*	67 (66–68)
Non-ALD	63 (57–68)	69 (63–74)	73 (69–76)*	70 (69–71)
Overall	67 (65–70)	67 (64–69)	73 (71–75)*	68 (67–68)

*Survival probabilities are for the year 2021, not 2022, because patients diagnosed in 2022 could not be followed for a full year. ALD, alcohol-related liver disease; PY, person-years.

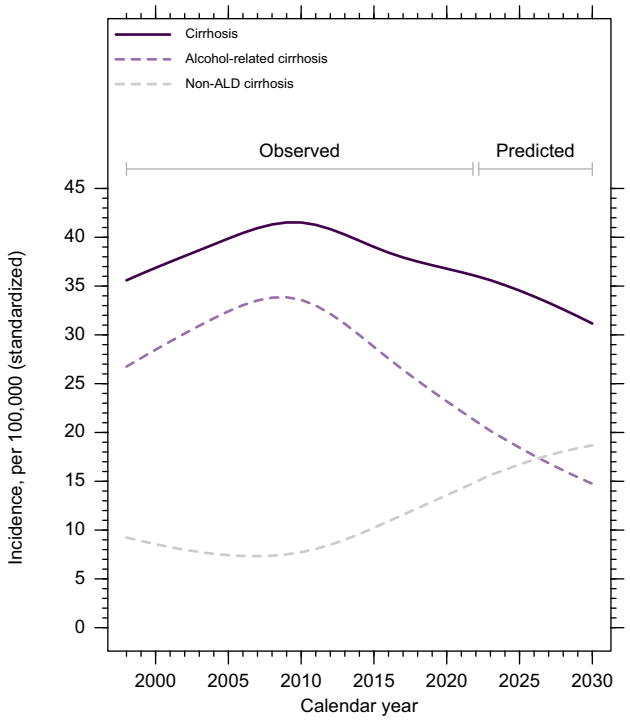

Fig. 1. Standardized incidence rate of cirrhosis in the Danish population aged 20–95 years from 1998 to 2022 with forecasted incidence rates for 2023 to 2030. ALD, alcohol-related liver disease.

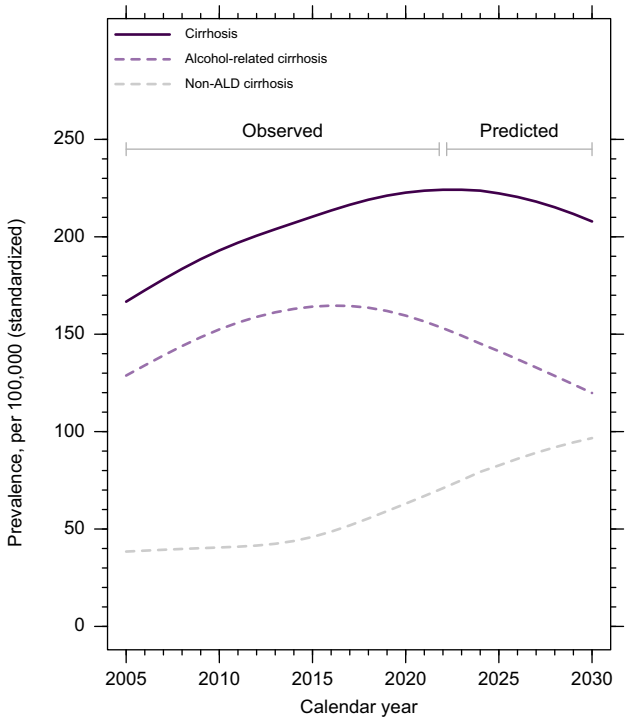

Fig. 2. Standardized prevalence of cirrhosis in the Danish population aged 20–95 years from 1998 to 2022 with forecasted incidence rates for 2023 to 2030. ALD, alcohol-related liver disease.

15.4–20.3) will surpass the incidence of ALD cirrhosis (16.9 per 100,000, 95% CI 15.2–18.6). By 2030, the incidence rates will be 18.7 per 100,000 (95% CI 15.7–22.2) and 14.7 per 100,000 (95% CI 13.1–16.7), respectively.

Burden of cirrhosis

Based on the final age–period–cohort model, the prevalence of cirrhosis peaked in 2023 (224 per 100,000 population, 95% CI 220–229) and, by 2030, will have fallen to 208 per 100,000 (95% CI 198–219), similar to its level in 2014 (207 per 100,000 population, 95% CI 204–210) (Fig. 2). The prevalence patterns are very different for ALD cirrhosis and non-ALD cirrhosis: the prevalence of ALD cirrhosis peaked in 2016 (165 per 100,000 population, 95% CI 162–167), whereas that of non-ALD cirrhosis continues to increase, and will reach 97 per 100,000 population (95% CI 88–106) in 2030 (Fig. 2).

The survival of patients with cirrhosis has improved since 2010 after a slight deterioration between 1995 and 2010; 1-year survival was 62% in 2010 and 73% in 2021 (Fig. S6). This pattern was seen for both sexes (Fig. S7) and both cirrhosis etiologies (Fig. 3). Survival was worse for patients with acute presentation than for patients with elective presentation, and the improvement in survival since 2010 appeared to be restricted to patients with elective presentation (Fig. S8). The landmark analyses showed that there was no discernible improvement in survival for patients who had survived to the 1-year landmark or to the 3- or 5-year landmarks (Fig. S9).

Comorbidities were more prevalent among patients with cirrhosis in 2022 than they were in 1998 and more prevalent among patients with non-ALD cirrhosis. Specifically, the prevalence of diabetes among those with non-ALD cirrhosis was 10% in 1998 and 19% in 2022, after peaking at 28% in 2018, whereas for patients with ALD cirrhosis, it was 9% in 1998 and 11% in 2022 after peaking at 15% in 2013. The prevalence of IHD was stable and, in 2022, reached 7% among patients with non-ALD cirrhosis and 4% among patients with ALD cirrhosis. Chronic viral hepatitis among patients with non-ALD cirrhosis had fallen to 7% in 2022 after peaking at 23% in 2012, whereas it was 5% in 2012 and 2% in 2022 among patients with ALD cirrhosis (Fig. 4).

Discussion

This nationwide study provides insights into the current and future burden of ALD cirrhosis and non-ALD cirrhosis in Denmark. Overall, the incidence of cirrhosis has been decreasing since 2009, driven by a steep decline in the incidence of ALD cirrhosis, whereas the incidence of non-ALD cirrhosis has increased continuously, albeit not so much as to increase the overall incidence. The increased incidence of non-ALD cirrhosis over the past decades is taken to largely reflect MASLD. The burden of ALD cirrhosis has been decreasing since 2009 for both sexes, and the predicted incidence rate in 2030 is half of what it was at its peak 20 years earlier. Given that patients live longer, the prevalence of ALD cirrhosis peaks later and declines more slowly than its incidence. Specifically, we found improved 1-year survival probability, but no signs of improved survival from 1 year after the cirrhosis diagnosis. The improvement in survival was limited to patients who presented with cirrhosis as elective patients, whereas we found no improvement in survival for patients with acute presentation.

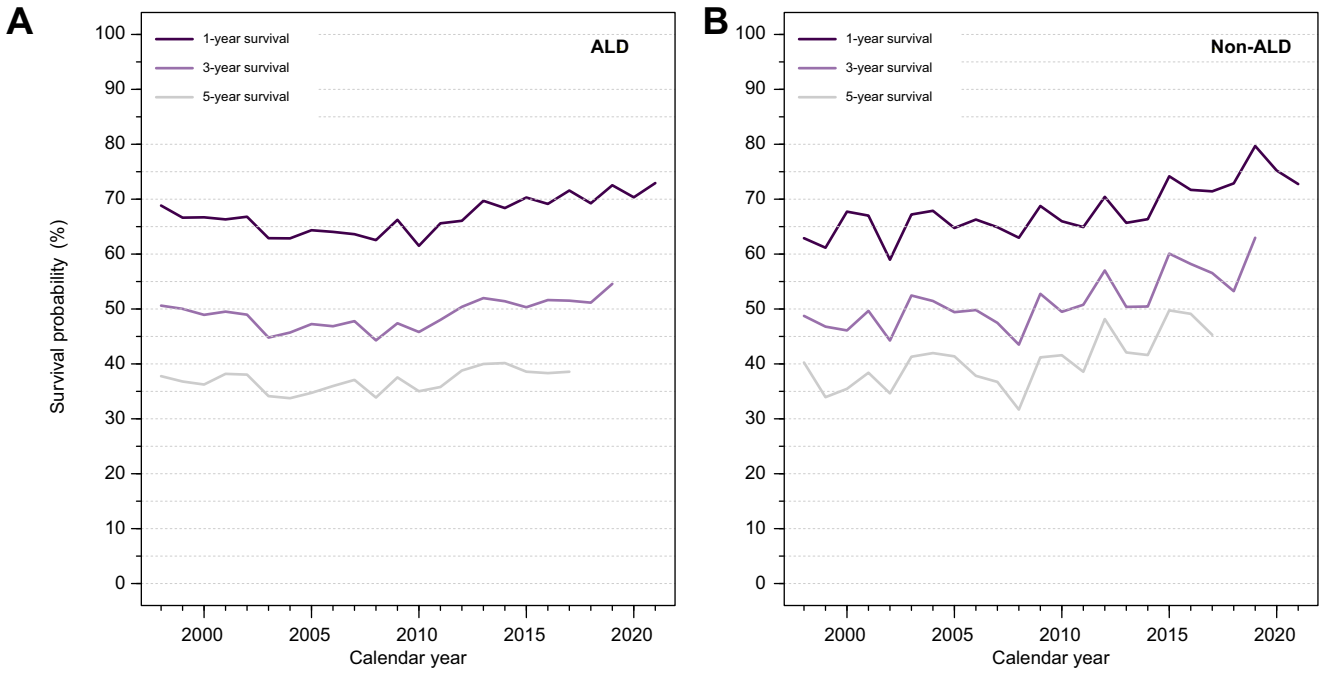

Fig. 3. Survival probabilities for Danish patients with cirrhosis diagnosed from 1998 to 2021. (A) Survival for patients with alcohol-related cirrhosis. (B) Survival for patients with non-ALD cirrhosis. For each year, the curves show the 1-, 3-, and 5-year survival probabilities of patients diagnosed with cirrhosis in that year. The total number of patients with ALD cirrhosis was 30,747, and the total number of patients with non-ALD cirrhosis was 9,548. ALD, alcohol-related liver disease.

A paramount strength of our study is the historical organization of the Danish public healthcare system and its obligatory diagnosis registration. The validity of our results is highly dependent on the validity of these cirrhosis diagnosis codes, which have been validated repeatedly by us and others by means of paper records and collateral registries, showing positive predictive values of 85–100 % and completeness exceeding 90%.[17–19] There is no reason to believe that the coding validity has changed during the study period.

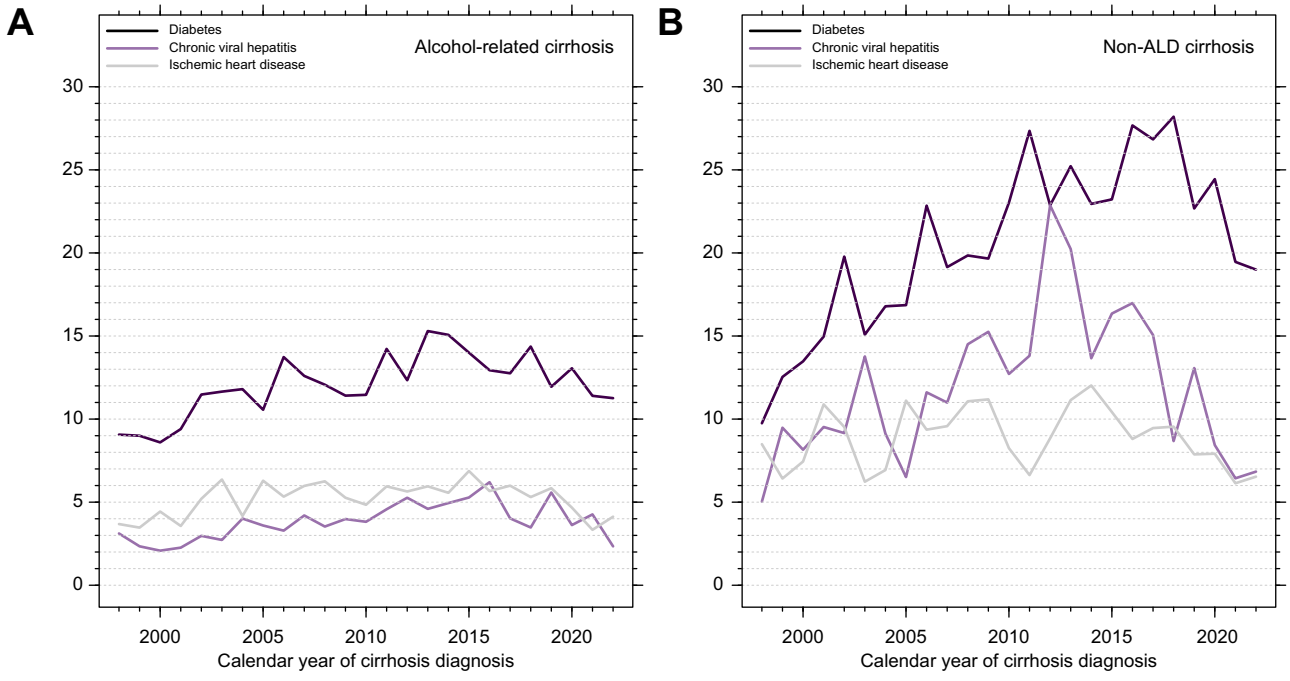

Fig. 4. Prevalence of comorbidities for Danish patients diagnosed with cirrhosis from 1998 to 2022. (A) Comorbidity among patients with ALD cirrhosis. (B) Comorbidity among patients with non-ALD cirrhosis. ALD, alcohol-related liver disease.

A limitation of our study is that we could not account for the diagnoses represented as 'non-ALD cirrhosis'. We argue that most of these patients have MASLD cirrhosis, which does not have a specific diagnosis code for cirrhosis related to MASLD in the *ICD-10*.[20,21] First, the prevalence of chronic viral hepatitis in the Danish general population is low, and decreasing for HCV, especially after the introduction of HCV treatment. The prevalence of HCV in the adult population in Denmark fell from 0.38% in 2007 to 0.21% in 2016, whereas that of HBV increased slightly from 0.24% in 2007 to 0.29% in 2016.[22–24] Second, we demonstrated that patients with chronic viral hepatitis constituted a diminishing minority of our patients with non-ALD cirrhosis, from 24% in 2012 to 7% in 2022. Third, autoimmune hepatitis (AIH), primary biliary cholangitis, and primary sclerosing cholangitis are many-fold rarer than MASLD among patients with chronic liver disease; the incidence of AIH (the most prevalent of the three) in Denmark was 1.68 per 100.000 persons compared with the estimated European incidence of MASLD of ∼35–50 per 1000 persons.[25,26] However, we do not have data on these specific diagnoses, which is a limitation of our study. Fourth, the prevalence of diabetes and IHD was ∼1.5-fold higher among our patients with non-ALD cirrhosis than among our patients with ALD cirrhosis. Fifth, the declining prevalence of diabetes among our patients with non-ALD cirrhosis or ALD cirrhosis is explained by a shift in the organization of diabetes management in Denmark: From 2017, the responsibility for managing patients with uncomplicated type 2 diabetes mellitus moved from a collaboration between primary and secondary healthcare to primary care alone. In the general Danish population, the prevalence of type 2 diabetes mellitus quadrupled to 6.8% between 1996 and 2023, and continues to rise.[27] Concordantly, the prevalence of adult obesity tripled from 6.1% in 1987 to 18.4% in 2021.[12] The prevalence of MASLD in (Western) Europe has been estimated to be ∼25%,[26,28] corresponding to more than 1 million cases in Denmark. There are no studies to date on the incidence of MASLD in Denmark, but, given that the incidence of MASLD is tightly linked to the incidence of both type 2 diabetes mellitus and obesity, an increased incidence of MASLD appears inevitable.

A new nomenclature was introduced during late 2023 with the new category 'metabolic and alcohol-related liver disease' (MetALD) reflecting that the cirrhosis etiology in some patients is a combination of metabolism- and alcohol-related factors.[29] Our study included patients with MetALD cirrhosis, but we cannot know whether they are categorized as ALD cirrhosis or non-ALD cirrhosis. The explanation is that neither MASLD nor MetALD has a diagnosis code in *ICD-10*. This is a limitation of the World Health Organization (WHO) classification system for diagnoses, which inevitably lacks behind the clinical reality, including the new nomenclature for steatotic liver diseases. Fortunately, the international hepatology societies are working with the WHO toward an up-to-date classification of diagnoses.

Another potential limitation lies in the age–period–cohort model for predictions of cirrhosis incidence and prevalence. This model is a strong tool for projecting trends, but cannot predict future changes in alcohol habits reflecting cultural or societal norms or trends. It performed well in predicting cirrhosis incidence between 2018 and 2022 compared with the true incidence in those years, but there is no guarantee that it automatically performs as well in forecasting future trends until the end of 2030.

Finally, we could have included more patients with cirrhosis by expanding the definition of cirrhosis to include diagnosis codes for cirrhosis complications. It is a limitation of our study that we did not have the data to try out alternative cirrhosis definitions in sensitivity analyses, but a broader definition always comes at the cost of including some patients who do in fact not have cirrhosis. We acknowledge that our definition of cirrhosis is narrower than the consensus-based definition recommended by Shearer *et al.*,[30] but we believe that our conclusions would have been the same if we had used the broader consensus definition.

The decreasing incidence of ALD cirrhosis is in contrast to other European and Nordic countries.[6] The per capita alcohol consumption has decreased gradually in Denmark from 10.0 L in 1995 to 7.8 L in 2020 with no dramatic change after 2010. As suggested in our previous study,[6] we believe that the decrease after 2010 is a birth cohort effect, reflecting a change in cultural and generational norms regarding alcohol consumption. Data from the Danish National Health Surveys show that the average annual consumption of pure alcohol decreased by 22.4% from 1994 to 2018. Furthermore, high-risk alcohol consumption (>252/168 g alcohol per week for men/women) decreased from 10.6% to 6.9% from 2010 to 2017. The decrease was most pronounced in persons younger than 44 years of age.[31]

A recent Swedish nationwide register-based study reported a linear increase (47%) in the incidence of ALD cirrhosis between 2005 and 2019, with the highest incidence rates in the 60–69-year age group, but with no information about the changes within individual age groups.[32] Thus, it appears that the time-trends in ALD incidence differ between Denmark and Sweden, but the reasons for that disparity are unclear.

We were surprised that survival has improved for patients with elective presentation but not for patients with acute presentation. Mortality after variceal bleeding has decreased in Denmark,[33] and we speculate that the time-trends in survival for patients with acute *vs.* elective presentation (Fig. S8) have more to do with changing referral patterns and patient characteristics than with changing treatment of cirrhosis and its complications. Unfortunately, the data we have are not sufficiently detailed to allow us to determine the reasons for the improved survival, or to determine whether the improved survival results from reduced cirrhosis-related mortality.

In conclusion, we describe a decrease in the incidence of cirrhosis in Denmark since 2010 driven by a marked decrease in the incidence of ALD cirrhosis, whereas the incidence of non-ALD cirrhosis, taken to reflect MASLD, increased steadily. We forecast that these trends will continue to the end of 2030, causing profound changes in cirrhosis

epidemiology and affecting future hepatology practice in Denmark. Previously, we have treated mostly younger patients with ALD cirrhosis presenting acutely before the age of 60 years; today and in the future, we expect increasingly old patients who present to the outpatient clinic with cirrhosis from MASLD and a higher burden of comorbidities. Thus, we foresee a need for closer collaboration between general practitioners, hepatologists, and endocrinologists to ensure timely diagnosis and treatment of future patients with cirrhosis and their comorbidities.

Affiliations

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Abbreviations

AIH, autoimmune hepatitis; ALD, alcohol-related liver disease; DALY, disability-adjusted life years; IHD, ischemic heart disease; MASH, metabolic dysfunction-associated steatohepatitis; MASLD, metabolic dysfunction-associated steatotic liver disease; MetALD, metabolic and alcohol-related liver disease; NAFLD, non-alcoholic liver disease; NASH, non-alcoholic steatohepatitis; PY, person-years; WHO, World Health Organization.

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Conflicts of interest

The authors declare no conflicts of interest.

Please refer to the accompanying ICMJE disclosure forms for further details.

Authors' contributions

Study conception and design: PJ, LSK, FK, GA, HV. Data collection: PJ. Analysis and interpretation of results: PJ, LSK, FK, GA, HV. Draft manuscript preparation: LSK, PJ. All authors reviewed the results and approved the final version of the manuscript.

Data availability statement

According to Danish law, we cannot share the data. Interested researchers may apply for data from the Danish healthcare registries via https://sundhedsdatastyrelsen.dk/da/forskerservice.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhepr.2025.101353.

References

Author names in bold designate shared co-first authorship

[1] **Asrani SK**, **Devarbhavi H**, Eaton J, et al. Burden of liver diseases in the world. J Hepatol 2019;70:151–171.

[2] Fialla AD, De Muckadell OBS, Touborg Lassen A. Incidence, etiology and mortality of cirrhosis: a population-based cohort study. Scand J Gastroenterol 2012;47:702–709.

[3] Julien J, Ayer T, Bethea ED, et al. Projected prevalence and mortality associated with alcohol-related liver disease in the USA, 2019–40: a modelling study. Lancet Public Health 2020;5:e316–e323.

[4] Tapper EB, Parikh ND. Mortality due to cirrhosis and liver cancer in the United States, 1999–2016: observational study. BMJ 2018;362:k2817.

[5] Williams R, Aspinall R, Bellis M, et al. Addressing liver disease in the UK: a blueprint for attaining excellence in health care and reducing premature mortality from lifestyle issues of excess consumption of alcohol, obesity, and viral hepatitis. Lancet 2014;384:1953–1997.

[6] Kraglund F, Deleuran T, Askgaard G, et al. Decreasing incidence of alcohol-related liver disease in Denmark: a 25-year nationwide study. Clin Epidemiol 2021;13:1–11.

[7] Shield KD, Rylett M, Rehm J. Public health successes and missed opportunities - trends in alcohol consumption and attributable mortality in the WHO European region, 1990–2014. Geneva: WHO; 2016.

[8] Jepsen P, Younossi ZM. The global burden of cirrhosis: a review of disability-adjusted life-years lost and unmet needs. J Hepatol 2021;75(Suppl. 1):S3–S13.

[9] Estes C, Anstee QM, Arias-Loste MT, et al. Modeling NAFLD disease burden in China, France, Germany, Italy, Japan, Spain, United Kingdom, and United States for the period 2016–2030. J Hepatol 2018;69:896–904.

[10] Younossi Z, Anstee QM, Marietti M, et al. Global burden of NAFLD and NASH: trends, predictions, risk factors and prevention. Nat Rev Gastroenterol Hepatol 2018;15:11–20.

[11] Thomsen BL, Ekstrøm CT, Sørensen TIA. Development of the obesity epidemic in Denmark: cohort, time and age effects among boys born 1930-1975. Int J Obes Relat Metab Disord 1999;23:693–701.

[12] Schramm S, Sørensen TIA, Davidsen M, et al. Changes in adult obesity prevalence in Denmark, 1987–2021: age–period–cohort analysis of nationally representative data. Eur J Public Health 2023;33:463.

[13] Lynge E, Sandegaard JL, Rebolj M. The Danish national patient register. Scand J Public Health 2011;39:30–33.

[14] Public Health England. Alcohol-attributable fractions for England: an update. London: Public Health England; 2020.

[15] Ratib S, Fleming KM, Crooks CJ, et al. 1 and 5 year survival estimates for people with cirrhosis of the liver in England, 1998-2009: a large population study. J Hepatol 2014;60:282–289.

[16] Sasieni PD. Age-period-Cohort models in Stata. Stata J 2012;12:45–60.

[17] Vestberg K, Thulstrup AM, Sørensen HT, et al. Data quality of administratively collected hospital discharge data for liver cirrhosis epidemiology. J Med Syst 1997;21:11–20.

[18] Thygesen SK, Christiansen CF, Christensen S, et al. The predictive value of ICD-10 diagnostic coding used to assess Charlson comorbidity index conditions in the population-based Danish National Registry of Patients. BMC Med Res Methodol 2011;11:83.

[19] Jepsen P, Vilstrup H, Sørensen HT. Alcoholic cirrhosis in Denmark – population-based incidence, prevalence, and hospitalization rates between 1988 and 2005: a descriptive cohort study. BMC Gastroenterol 2008;8:3.

[20] Hagström H, Adams LA, Allen AM, et al. Administrative coding in electronic health care record-based research of NAFLD: an expert panel consensus statement. Hepatology 2021;74:474–482.

[21] Hagström H, Adams LA, Allen AM, et al. The future of International Classification of Diseases coding in steatotic liver disease: an expert panel Delphi consensus statement. Hepatol Commun 2024;8:e0386.

[22] Christensen PB, Debrabant B, Cowan S, et al. Hepatitis C time trends in reported cases and estimates of the hidden population born before 1965, Denmark and Sweden, 1990 to 2020. Euro Surveill 2022;27:2200243.

[23] Nielsen S, Hansen JF, Hay G, et al. Hepatitis C prevalence in Denmark in 2016—an updated estimate using multiple national registers. PLoS ONE 2020;15:e0238203.

[24] Bollerup S, Wessman M, Hansen JF, et al. Increasing prevalence of chronic hepatitis B virus infection and low linkage to care in Denmark on 31 December 2016 - an update based on nationwide registers. Infect Dis 2023;55:17–26.

[25] Jepsen P, Grønbæk L, Vilstrup H. Worldwide incidence of autoimmune liver disease. Dig Dis 2015;33(Suppl. 2):2–12.

[26] Younossi ZM, Golabi P, Paik JM, et al. The global epidemiology of nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH): a systematic review. Hepatology 2023;77:1335–1347.

[27] Diabetestal.nu. Prevalence of type 2 diabetes in Denmark 2015–2023. https://www.diabetestal.nu/resultshare?id=788. [Accessed 18 February 2025].

[28] Younossi ZM, Koenig AB, Abdelatif D, et al. Global epidemiology of nonalcoholic fatty liver disease—meta-analytic assessment of prevalence, incidence, and outcomes. Hepatology 2016;64:73–84.
[29] Rinella ME, Lazarus JV, Ratziu V, et al. A multisociety Delphi consensus statement on new fatty liver disease nomenclature. Hepatology 2023;78:1966–1986.
[30] Shearer JE, Gonzalez JJ, Min T, et al. Systematic review: development of a consensus code set to identify cirrhosis in electronic health records. Aliment Pharmacol Ther 2022;55:645–657.
[31] The Danish National Health Survey. www.danskernessundhed.dk. [Accessed 18 February 2025].
[32] Nasr P, von Seth E, Mayerhofer R, et al. Incidence, prevalence and mortality of chronic liver diseases in Sweden between 2005 and 2019. Eur J Epidemiol 2023;77:S82.
[33] Hobolth L, Krag A, Bendtsen F. The recent reduction in mortality from bleeding oesophageal varices is primarily observed from Days 1 to 5. Liver Int 2010;30:455–462.

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