

**Title:**

Number of hospital contacts with alcohol problems predicts later risk of alcoholic liver cirrhosis

**Short title:**

Hospital contacts and later alcoholic liver cirrhosis

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Abbreviations: HR: Hazard ratios

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## Abstract

### Aims:

Alcoholic liver cirrhosis is usually preceded by years of heavy drinking. We investigated if risk of alcoholic liver cirrhosis increases as number of hospital contacts with alcohol problems goes up.

### Methods:

This was a supplementary analysis on a nationwide register-based cohort study. All patients in Denmark with an initial hospital contact with alcohol problems (alcohol intoxication, harmful alcohol use, or alcohol dependence) 1998-2002, free of liver disease, were followed for diagnosis of alcoholic liver cirrhosis. Number of subsequent hospital contacts with alcohol problems was estimated as a time-dependent variable for each patient.

### Results:

In all were 36,044 hospital patients with an initial hospital contact with alcohol problems included. These patients had 301,525 subsequent hospital contacts with alcohol problems. Risk of alcoholic liver cirrhosis increased ( $p < 0.0001$ ) with number of alcohol hospital contacts in both men and women up to nine contacts.

### Conclusions:

The number of prior hospital contacts with alcohol problems might provide clinicians with a helpful metric in deciding whether to offer preventive interventions for alcoholic liver cirrhosis.

Keywords: alcoholic liver disease, hospital contacts, prevention, epidemiology, cohort study

## Introduction

Alcoholic liver cirrhosis is a preventable disease responsible for around 0.5 million deaths globally per year [1]. This disease is usually preceded by a decade of heavy drinking [2]. Alcohol problems are common among hospital patients, and hospital contacts with alcohol problems could represent an opportunity for prevention of alcoholic liver cirrhosis if alcohol treatment and non-invasive assessment of liver disease were provided [3, 4]. Hospital patients with an initial hospital contact with alcohol problems had a high risk of 5-6% after 15 years for alcoholic liver cirrhosis that corresponds to an incidence more than 10 times greater than the general population [5].

Data from other settings suggests that some patients with alcohol problems will recover without any intervention [6]. The number of prior hospital contacts with alcohol problems might provide clinicians with a helpful metric in deciding whether to offer preventive interventions to decrease consumption and thus risk of liver cirrhosis. We test whether risk of alcoholic liver cirrhosis increases as number of hospital contacts with alcohol problems goes up. We investigated this in a nationwide study in Denmark.

## Methods

The study population was all patients in Denmark with an initial hospital contact with alcohol problems (alcohol intoxication, harmful alcohol use, or alcohol dependence) 1998-2002, free of liver cirrhosis and alcoholic liver disease at time of the diagnosis of the alcohol problem. The cohort was followed for the outcome of an incident diagnosis of alcoholic liver cirrhosis, death, or end of 2014, whatever occurred first. All data were derived from nationwide Danish registers on somatic and psychiatric hospital contacts and on death and migration to and from

Denmark. The unique personal identifier was used to link the data. A detailed description on data sources and the definition of the study cohort was described previously [5].

Cox regression models with time-dependent variables were estimated in Stata 14 with length of follow-up as the time dimension. The risk associated with number of subsequent hospital contacts with alcohol problems was estimated as a time-dependent variable for each patient. Analyses were adjusted for age. The proportional hazard assumption was tested graphically for each covariate and no violations were detected.

## Results

In all, 36,044 hospital patients with an initial hospital contact with alcohol problems were included (24,727 men, 11,317 women). The alcohol problem diagnosis of the initial contact was intoxication in 41%-42% of men and women of the included hospital patients, harmful use in 20%-21%, and dependence in 37%-39%. During follow-up, these patients had 301,525 subsequent hospital contacts with alcohol problems and 1966 were diagnosed with alcoholic liver cirrhosis. Of the included men, 13,924 (56%) had a second hospital contact with alcohol problems during follow-up, 10,382 (42%) a third, 7114 (29%) a fifth, and 4147 (17%) had ten or more during the follow-up, with similar percentages found for women.

Table 1 shows that risk of alcoholic liver cirrhosis increased ( $p < 0.0001$ ) with number of alcohol hospital contacts in both men and women up to nine contacts.

## Discussion

In this nationwide study, we found that risk of alcoholic liver cirrhosis increased with number of hospital contacts with alcohol problems up to nine contacts. No previous studies have assessed the number of hospital contacts with alcohol problems on later risk of alcoholic liver

cirrhosis. Several hospital contacts with alcohol problems reflect a longer period of heavy drinking than does a single hospital contact with alcohol problems. This is in line with a previous study finding a greater liver cirrhosis risk with increased duration of heavy drinking [7].

Consistent management of alcohol problems in hospital patients have been suggested as a prevention strategy for alcoholic liver cirrhosis [4]. Our results suggest that clinicians may take account of number of prior hospital contacts with alcohol problems in deciding where to invest resources to reduce risk.

Table 1. Hazard ratios (95% confidence interval) for alcoholic liver cirrhosis according to the number of hospital contacts with alcohol problems.

	Men (n = 24,727)		Women (n = 11,317)	
	No of cases	HR (95% CI)	No of cases	HR (95% CI)
Hospital contacts with alcohol problems				
After first contact	353	Reference	145	Reference
After a second contact	234	1.4 (1.2, 1.7)	89	1.4 (1.0, 2.0)
After three or four contacts	257	1.8 (1.5, 2.2)	99	1.9 (1.4,2.7)
After five to nine contacts	262	2.2 (1.8, 2.7)	111	2.5 (1.8, 3.4)
After 10 or more contacts	300	1.7 (1.7, 2.1)	116	1.7 (1.3,2.4)
Test for trend		<0.0001		<0.0001

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