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**Sex and age differences in the early identification and treatment of alcohol use: a population based study of patients with alcoholic cirrhosis**

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## ABSTRACT

**Aim:** To estimate sex differences in healthcare utilisation among harmful/hazardous drinkers in the period before alcoholic cirrhosis diagnosis, and estimate sex differences in the extent to which alcohol use and brief alcohol interventions were documented for these individuals compared with a control cohort.

**Design:** Retrospective study using linked UK general practice and hospital admissions data in England.

**Setting:** Three hundred and fifty-seven general practitioner (GP) practices in England.

**Participants:** A total of 2,479 individuals with alcoholic cirrhosis (mean age at diagnosis=56years) of whom 67% were men; and 24,790 controls without the disease.

**Measurements:** Rates of primary care visits and hospital admissions prior to the diagnosis of alcoholic cirrhosis for men and women, and the proportion of men and women with alcohol consumption and/or alcohol brief intervention documented in their medical record.

### Findings

Compared with the general population, patients with alcoholic cirrhosis used primary and secondary health-care services more frequently in the years leading up to their diagnosis. In the years prior to diagnosis, men used primary and secondary healthcare services more than did women (P for sex interaction  $P < 0.0001$ ). Men were more likely than women to have their alcohol use recorded [odds ratio (OR)men=1.96, 95% confidence interval (CI)=1.7–2.3; women=1.63, 95% CI=1.4–1.8, P for sex interaction  $P < 0.0017$ ]. By contrast, alcohol interventions were recorded more commonly among women (OR men=4.3, 95% CI=3.7–4.9; women=5.8, 95% CI=4.7–6.9, P for sex interaction=0.07), although less common with increasing age (P for age interaction=0.009).

### Conclusions

In the UK, prior to alcoholic cirrhosis diagnosis, excess healthcare utilisation is higher in men than women and men are more likely than women to have their alcohol use recorded. However, women appear to be more likely than men to receive alcohol brief interventions.

## **BACKGROUND**

Alcohol-use disorders are largely preventable, yet they remain widespread in Europe and North America (1). Among the various disorders, alcoholic liver cirrhosis in particular has seen a substantial increase in recent times(2). In the UK, alcoholic liver related deaths have increased 3-fold over the last three decades, hospitalisations have increased by over 100% between 2003 and 2010 and the number of new incident cases have increased by over 50% from 24.6 in 1998 to 38.4 per 100,000 person years in 2009 (3–6). Similarly, reports from Finland also suggest up to a 50% increase in rates from alcohol related liver deaths between 1998 and 2008(7).

Both internationally and in the UK, healthcare professionals are increasingly tasked with the responsibility of helping harmful or hazardous drinkers cut down on their alcohol consumption before they get to the point of developing chronic disorders such as cirrhosis (8–11). This can be achieved through screening for alcohol use using validated questionnaires, after which healthcare professionals can deliver brief interventions to those at higher risk(11–13). Previous research on brief interventions suggests that well designed alcohol brief interventions(ABI), which can be easily administered during patient consultations in primary care, are effective in reducing risky alcohol use and its related harms (13–17). Recognising this potential effectiveness, efforts to promote the implementation of screening and brief alcohol interventions in healthcare settings are now widespread in several healthcare systems(15,18).

Previous studies, however, suggest that certain subgroups of the population are less likely to make contact with health services and may therefore have fewer opportunities to receive opportunistic brief advice. For example, in the UK general population men have been shown to be less likely than women to utilise healthcare services(19,20). Such differences could have important implications for population strategies aimed at reducing alcohol related harm, particularly if these differences are apparent in populations that are at the highest risk of developing alcohol-related disorders. Despite this, little attention has been given to understanding healthcare utilisation patterns of high risk patient groups who develop alcohol use disorders, and there is a paucity of data on how often alcohol use is asked about and how often brief interventions are administered in such patient groups.

The occurrence of alcoholic cirrhosis is generally believed to require around 10 to 20 years of “heavy” drinking to become established(21–24). We therefore chose to examine opportunities for alcohol use identification and intervention in this particularly high-risk population as they represent a group of patients whose disease is entirely attributable to alcohol(25) and where most harm might be avoided through early identification. The aim of the study was twofold:

- 1) To estimate sex differences in primary and secondary care use among patients in the UK who later develop alcohol related cirrhosis in comparison to the general population.
- 2) To estimate sex differences in the extent to which alcohol use and brief alcohol interventions were documented for these individuals in comparison to the general population.

## **METHODS**

We used linked primary and secondary care data obtained from the Clinical Practice Research Datalink (CPRD) and Hospital Episodes Statistics (HES) for the period between 1997 and 2011.

CPRD contains electronic primary healthcare records of over 10 million patients from general practitioner (GP) practices in the UK. Information captured within the database includes details on all patient consultations with primary care, including clinical diagnoses, interventions offered, specialist referrals and lifestyle information such as alcohol use(26). Most of this information is electronically coded using a hierarchical Read coding system which is based on the International Classification of Diseases 10<sup>th</sup> revision (ICD10).

The HES database contains information on all admissions to the state-funded National Health Service (NHS) hospitals in England, including admission diagnoses coded using ICD 10. At the time of this study, 357 English GP practices that contribute to CPRD had given consent for their patients' primary care records to be linked to corresponding HES database records. The linkage between CPRD and HES was undertaken by a trusted third party using patient's NHS number, date of birth and gender prior to release for research.

### **Patient selection**

We had access to data from all 357 CPRD practices in England with HES-linked data between April 1997 and August 2011. We identified and selected all adult (>18 years) patients from these practices with a Read code in CPRD or ICD 10 code in HES for a definite diagnosis of alcoholic cirrhosis. Our code lists were adapted and updated from our previous validated definition(27). We excluded patients who had a history of any condition for which the differential diagnosis could have been alcoholic cirrhosis (e.g. cirrhosis or oesophageal varices of unspecified aetiology), as this may have introduced potential misclassification of the diagnosis date. Further exclusions were patients with less than a year of continuous medical data available prior to their diagnosis or patients with invalid diagnosis dates.

From the remaining CPRD-HES linked patients without a history of cirrhosis or oesophageal varices, we selected 10 control patients for each case frequency matched by age (+/- 5 years) and general practice.

A date of diagnosis, defined as the date for the first record of alcoholic cirrhosis, was assigned to cases. Controls were assigned a “pseudo-diagnosis” date which was a randomly generated date between 1 year after the start of the linked dataset (1997) up to the date they left the practice or died.

#### Observation period

Patients entered the study cohort on the latest of the following dates (i) the start of the linked dataset (1st April 1997), (ii) the date a patient registered with a GP practice, or (iii) the date when the practice attained an acceptable level of data recording. The study ended at the date of diagnosis for cases or pseudo-diagnosis date for controls.

#### **Study variables**

##### Primary and secondary care usage

For each patient we retrieved information on all direct contacts with primary care and admissions to secondary care during the study period. Each event was assigned to the year in which it occurred, counting back from the diagnosis/pseudo-diagnosis date (that is consultations and hospital admissions were coded as occurring in the 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup>...10<sup>th</sup> year before diagnosis of cirrhosis). If a patient had more than one consultation within a day (whether during the day, or during out-of-hours), we counted only one consultation for that day. Primary care consultations recorded as occurring during the same period as a patient was hospitalized were excluded to avoid double counting of healthcare contacts.

##### Alcohol related outcomes

All alcohol related records within patient files were assessed to identify patients with documented alcohol use or brief alcohol intervention. Overall, we identified four types of alcohol records:

1. Data on actual alcohol consumption i.e. number of alcohol units consumed by a patient per week
2. Read codes reflecting level of drinking such as codes for drinking within the recommended limits e.g. never, or moderate drinker or those reflecting excessive drinking e.g. hazardous or harmful drinker

3. Read codes reflecting the administration of a screening test such as the Alcohol Use Disorders Identification Test (AUDIT)
4. Read codes reflecting alcohol related advice or counselling, information leaflet or referral to alcohol treatment services

Patients with records relating to points 1, 2, or 3 were classified to have had a documented alcohol use enquiry and assigned to one of three drinking categories: “never drinkers”, “moderate drinkers” or “harmful/hazardous drinkers” using the highest alcohol consumption record available. Where it was not possible to assign a drinking status (usually for patients with a record of a screening test in the absence of any unit or other consumption category), an ‘unclear’ consumption status was assigned. Patients with records relating to point 4 were classed as having received an alcohol intervention and assigned to a category denoting the type of intervention received: alcohol brief intervention, referral or both. All other patients who had no alcohol use or intervention/referral records were labelled as ‘no data available’.

#### Exposure variables

Information on sex and age, were extracted from patients’ CPRD records. Age was calculated as age at diagnosis of cirrhosis (or at pseudo-diagnosis for controls) and categorised into five age bands of 18-44, 45-54, 55-64, 65-74, and  $\geq 75$  years.

#### **Statistical analyses**

Rates of healthcare service utilization were calculated for men and women for the entire study period, and for each year (yearly) leading up to diagnosis. For each group, excesses in healthcare use were calculated as the absolute difference in rates between cases and the corresponding control population; and rate ratios with 95% Confidence Intervals (95% CI) were estimated using Poisson regression. We tested for interaction between sex and primary care consulting rates by fitting an interaction term in a Poisson regression model and conducting a likelihood ratio test (LRT) at a significance level of  $p < 0.05$ . A similar model was fitted using hospital admission rates.

To examine alcohol use and intervention recording, we calculated the proportion of patients with both records. We examined proportions by age and sex and tested for interactions using



interaction terms and likelihood ratio tests in logistic regression models. Logistic regression was used to calculate the odds (95% CI) of both outcomes in people with alcoholic cirrhosis compared to controls for men and women separately. Age and consulting rate were then included in the regression models as potential confounding variables (based on theoretical plausibility) to obtain adjusted ORs.

Where possible, regression models were refitted applying the generalized estimating equation (GEE) approach with exchangeable correlation structure to test for heterogeneity with GP practices.

Due to the small number of patients contributing data more than 10 years before diagnosis, yearly consultation rates were only estimated for the 10 year period prior to diagnosis/pseudo-diagnosis. All analyses were conducted using the statistical software Stata v12.0 (StataCorp,Texas).

## RESULTS

The study population consisted of 2,479 people with alcoholic cirrhosis and 24,790 controls identified from 357 GP practices in England (Table 1). On average 83 patients (range 11-330 patients) were identified from each GP practice. The median observation period for patients with alcoholic cirrhosis was 5.7 years before diagnosis, whilst that of the control population was 4.6 years. The average age at diagnosis of cirrhosis for cases was 55.6 years and 67% of cases were men.

### General practice consultations before diagnosis

Compared to the control population, patients with alcoholic cirrhosis visited primary care more frequently (overall consultation rate per-person-year, cases: 9.1, controls: 5.9; IRR 1.52, (95% CI:1.51-1.53)), at an average excess of 3.0 consultations per-person-year (Figure 1a and Table 2). Greater excesses were found among men with an overall average excess of 4 consultations per-person-year, compared with 2.7 excess consultations for women (LRT *p* value for sex interaction: <0.001). Modest changes in the number of excess consultations were observed between 10 and 5 years prior to diagnosis with a more rapid rate of change observed from 4 years to 1 year prior to diagnosis, especially for men (figure 1a).

### Hospital admissions before diagnosis

The overall rate of admission was twice as high for patients with alcohol cirrhosis than for their controls (admission rate per 10-person-years, cases: 5.5, controls: 2.2; IRR 2.49, (95% CI:2.42-2.54))(Figure 1b and Table 3). The greatest excesses were again found amongst men with an average excess of 3.7 hospital admissions per 10-person years during the entire study period compared with 2.7 excess admissions for women (LRT *p* value for interaction between sex and admission rate: <0.001). As with primary care consultations, we found a gradual increase in admission rates as time prior to diagnosis decreased, with excesses higher in men than women in all years (Table 3).

### Alcohol use records

Alcohol consumption records (including records of being a non-drinker) were available for 2,088 (84.2%) cases and 16,752 (67.6%) controls and substantially more cases (60.0%, n=1,507) than controls (9.5%) had a record of harmful or hazardous drinking (Table 4). On

average, the time between a patient's first record of hazardous or harmful drinking and their diagnosis of alcoholic cirrhosis was 4.2 years (IQR:1.9-7.5 years).

Compared to the control population, men with alcoholic cirrhosis were more likely to have had a record of their alcohol use in the 10 years prior to diagnosis than women (85% compared to 82%,  $p$  value < 0.001)(Table 5). After adjusting for the effect of age and consulting rate, the odds of having an alcohol consumption record remained higher for men [OR 1.96 (95% CI:1.7-2.3),  $p$  value <0.001] than women [OR 1.63(95% CI:1.4-1.8),  $p$  <0.001] (Table 5).

### **Alcohol use interventions**

Electronically coded recording of an offer of an intervention was found for 22.8% (n=565) of cases and 4.7% (n=1,151) of controls. Both men and women were less likely to have records of interventions with increasing age, but the lowest proportions were found among women aged 65 years and above (Table 6). After adjusting for age and differences in consulting rate, women with alcoholic cirrhosis [Adjusted OR 5.8(95% CI:4.8-7.0),  $p$  < 0.001] were more likely than men [Adjusted OR 4.3(95% CI:3.7-4.9),  $p$  <0.001] to have an intervention record when compared to the control population (Table 5).

No substantial difference in point estimates were seen when regression models were refitted using the GEE approach.

## **DISCUSSION**

These results have shown that men with alcoholic cirrhosis have a greater excess use of both primary and secondary healthcare during the years leading up to their diagnosis than women and are more likely to have their alcohol use recorded. By contrast, women were more likely to be offered an ABI or referral, even after controlling for age and consulting rate. Interestingly, although the offer of brief alcohol interventions was generally low, those diagnosed with cirrhosis at an older age were less likely than the younger age groups to have received an offer of an intervention prior to the diagnosis of their disease.

### **Strengths and limitations**

This is the first longitudinal study to describe primary and secondary healthcare use (a proxy for intervention opportunities) among an important group of hazardous/harmful drinkers compared with a representative general population control group. The use of the linkage between primary and secondary care data has enabled the identification of a fully representative population of patients with alcoholic cirrhosis as it has been previously reported that using either primary care or secondary care data alone significantly underestimates the number of patients with this condition(28). We minimised the confounding effect of age and general practice on consulting rates by frequency matching cases with controls by these variables. We have also taken into account the differential contribution time of patients by calculating rates using the person time approach. This methodology allows us to be confident that increases in consultation or admission rates in the years closer to diagnosis are not as a result of more patients contributing data within those years.

Certain limitations should however be considered in the interpretation of our findings. With regard to recording of alcohol use or of intervention, it is possible that doctors have had discussions about alcohol use with patients and/or delivered interventions but have not made a specific record of this within the coded data system. Hence we may have underestimated the true proportion of patients who were asked about their alcohol use or offered interventions in this study. However, we believe that the magnitude of the differences identified between men and women and across age groups is unlikely to be explained by this potential bias alone, as it seems unlikely that there would be differential recording among

cirrhosis patients based on sex and age. We were unable to adjust our findings for some variables (e.g. socioeconomic status, and ethnicity) that may have a confounding effect on sex differences in health service utilisation, and this was because these measures were not available within the dataset for the study population we have defined. Additionally, although we attempted to account for any clustering effects within GP practices in our analysis, we had no information of other factors within practices which may affect the extent of intervention delivery or referral e.g. the availability of specialist treatment centres in the community where a practice is located, practitioners' willingness to discuss alcohol use or practitioners' views on the threshold of drinking which constitutes a problem. We therefore cannot rule out the possibility that some of our findings may be potentially influenced by residual or unmeasured confounding. Given that it is not possible to know the extent to which these unmeasured factors may have biased our findings and that no other observational study has explored such outcomes for patients with alcoholic cirrhosis to date, future studies may wish to consider approaches that can determine the magnitude of the potential impact of such confounders.

### **Comparison with previous studies**

Only two cross sectional studies have previously reported healthcare use of patients with alcohol problems and their findings are broadly consistent with our results in that they highlight patients with alcohol problems are often in contact with healthcare services(23,29). While the absence of control groups and small sample sizes may make the generalizability of these studies difficult, our use of an extremely large representative database affords us the opportunity to provide more generalizable estimates. Far less data are available on sex comparisons of healthcare utilisation in patients with alcohol problems with most studies examining sex differences in the use of health care services being reported on the general population(19,20,30–32) or in patients with specific symptoms such as pain (33,34). In line with most of these studies (19,20,30–32,35), we found higher absolute consultation rates in women compared to men. However, in relative terms when we examined men and women with alcoholic cirrhosis in comparison to general population, the increase in health service use associated with the disease was more dramatic in men than women. In terms of alcohol use recording and intervention delivery, consistent with our results, a number of studies have reported that the implementation of brief alcohol interventions within healthcare settings is generally slow in the UK as well as internationally (36–39).

## Implications

We believe the present study suggests that there are several opportunities, particularly in men, for the earlier identification and treatment of harmful/hazardous alcohol use. That a high proportion of people had an alcohol use record is encouraging and may reflect improvements over time in the extent to which GPs in the UK inquire about alcohol consumption during healthcare visits. However our results on interventions generate some concern. If true, the low rate of intervention we have identified cannot be explained by low access to healthcare services. This finding is also not entirely explained by a low drinking problem identification rate, because at least two-thirds (60.7%) of cases had had at least one problem drinking record on average four years prior to alcoholic cirrhosis diagnosis. The most plausible alternative explanations are that there may be a failure to record treatment of alcohol problems in primary care, that appropriate treatment services are not consistently available or that treatment of alcohol problems might truly be suboptimal.

As documented in other studies, the reasons why the delivery of brief alcohol interventions may be suboptimal include lack of time, lack of workplace support, poor financial reimbursement and feelings of inadequacy by healthcare staff(37,40–42); and we believe these factors also apply in the UK. To combat some of these shortfalls, it may be important to continuously educate healthcare professionals, who are committed to addiction reduction, on the public health damage of risky drinking and the effectiveness of brief alcohol interventions(43–45). Additionally, government support through policies e.g. incentivisation via pay for performance initiatives, work place programmes and management efforts may also help to improve brief alcohol intervention activity (37,45,46).

Another aspect of our results for which there are important implications is our finding that women, especially those of younger ages, were more likely than men to receive brief alcohol interventions. These findings need further exploration. However, if replicated in future, it would imply that strategies to treat alcohol problems on a population level may be undermined as men make up a significant proportion of the population of people with alcohol use disorders and are more likely to drink alcohol in excess of women (47,48).

## Conclusions

The findings of our study show a higher excess of healthcare use in men than women prior to alcoholic cirrhosis. While a high proportion of patients were asked about their alcohol use during these healthcare visits, few patients had records of interventions and men were less likely to receive interventions than women. We acknowledge that recording biases may partly explain the low absolute rates of intervention identified in this study. However, the identification of high risk patients relies heavily on doctors having access to both current and past records of patients' alcohol use, hence recording biases in and of themselves represents a key aspect of ABI delivery which needs to be addressed if the treatment of alcohol problems is to be improved. Given the potential effectiveness of ABI to reduce risky drinking behaviour and the need to reduce alcohol problems at a population level, these findings should encourage healthcare professionals to use ABI more often and policy makers to direct more effort towards integrating ABI into clinical practice.

## TABLES

**Table 1: Baseline demographics of cases of alcoholic cirrhosis and controls matched by age and GP practice**

	<b>Cases 2,479)</b>	<b>(n= Controls = 24,790)</b>	<b>(n</b>
<b>Age at diagnosis(years)<sup>a</sup></b>			
Mean(SD)	55.6 (11.7)	55.4 (12.4)	
Age group (n, %)			
18-44	419(16.9)	5,027(20.3)	
45-54	750(30.3)	6,772 (27.3)	
55-64	753(30.4)	7,222 (29.1)	
65-74	403 (16.3)	4,027 (16.2)	
≥ 75	154(6.2)	1,742 (7.0)	
<b>Observation time(years)</b>			
Median(IQR)	5.7 (3.0 – 9.2)	4.6(2.4 – 7.9)	
<b>Sex (n, %)<sup>a</sup></b>			
Male	1,660(67.0)	12,453 (50.2)	
Female	819 (33.0)	12,337 (49.8)	

<sup>a</sup>Chi squared tests p value < 0.001. SD= standard deviation; GP= general practitioner; IQR = Interquartile range.



**Table 2: Overall and yearly primary care consultation rates and rate ratios of cases of alcoholic cirrhosis and controls**

	Males Rate per person-years				Females Rate per person-years				Overall Rate per person-years			
	Cases	Controls	Excess	IRR(95% CI)	Cases	Controls	Excess	IRR(95% CI)	Cases	Controls	Excess	IRR(95% CI)
<b>Overall study period</b>	8.8	4.8	<b>4.0</b>	1.80(1.78-1.81)	9.7	7.0	<b>2.7</b>	1.36(1.35-1.38)	9.1	5.9	<b>3.0</b>	1.51(1.50-1.52)
<b>Time to diagnosis(yrs.)</b>												
<b>1</b>	14.4	5.9	8.5	2.43 (2.39- 2.46)	15.5	8.2	7.3	1.88(1.85-1.92)	14.8	7.1	7.7	2.09(2.07-2.11)
<b>2</b>	10.9	5.8	5.1	1.89 (1.86-1.92)	11.5	7.9	3.6	1.45(1.42-1.48)	11.1	6.8	4.3	1.62(1.60-1.64)
<b>3</b>	9.5	5.2	4.3	1.81(1.78-1.85)	9.8	7.4	2.4	1.31(1.27-1.34)	9.6	6.4	3.2	1.51(1.49-1.53)
<b>4</b>	8.2	4.8	3.4	1.70(1.66-1.74)	8.7	7.1	1.6	1.20(1.17-1.24)	8.4	6.0	2.4	1.39(1.37-1.41)
<b>5</b>	7.5	4.6	2.9	1.64 (1.60-1.68)	8.2	6.9	1.3	1.20(1.16-1.24)	7.8	5.7	2.1	1.36(1.33-1.38)
<b>6</b>	6.9	4.2	2.7	1.64 (1.58-1.68)	7.5	6.4	1.1	1.15(1.11-1.20)	7.0	5.3	1.7	1.33(1.29-1.36)
<b>7</b>	6.1	3.8	2.3	1.61 (1.56-1.66)	7.5	6.1	1.4	1.22(1.18-1.28)	6.5	4.9	1.6	1.32(1.29-1.36)
<b>8</b>	5.4	3.6	1.8	1.51 (1.45-1.57)	7.1	5.8	1.3	1.21(1.17-1.27)	6.0	4.7	1.3	1.27(1.24-1.31)
<b>9</b>	4.9	3.4	1.5	1.43 (1.36-1.49)	6.7	5.4	1.3	1.23(1.18-1.30)	5.5	4.4	1.1	1.25(1.20-1.29)
<b>10</b>	4.9	3.3	1.6	1.52 (1.44-1.59)	6.4	5.4	1.0	1.19(1.12-1.26)	5.4	4.3	1.1	1.25(1.21-1.30)

Likelihood ratio test p value for the interaction between sex and consultation rates, with adjustment for age: <0.0001. CI= confidence interval; IRR=Incidence rate ratio.

**Table 3: Overall and yearly admission rates and rate ratios of cases of alcoholic cirrhosis and controls**

	Males Rate per 10 person-years				Females Rate per 10 person-years				Overall Rate per 10 person-years			
	Cases	Controls	Excess	IRR(95% CI)	Cases	Controls	Excess	IRR(95% CI)	Cases	Controls	Excess	IRR(95% CI)
<b>Overall study period</b>	5.8	2.1	<b>3.7</b>	2.82(2.73-2.90)	5.0	2.4	<b>2.6</b>	2.09(2.01-2.19)	5.5	2.2	<b>3.3</b>	2.49(2.42-2.54)
<b>Time to diagnosis(yrs.)</b>												
<b>1</b>	13.5	2.9	<b>10.6</b>	4.64(4.40-4.89)	12.2	3.3	<b>8.9</b>	3.73(3.48-3.99)	13.1	3.1	<b>10</b>	4.23(4.06-4.41)
<b>2</b>	7.1	2.4	<b>4.7</b>	2.92(2.72-3.13)	6.2	2.7	<b>3.5</b>	2.32(2.11-2.56)	6.8	2.6	<b>4.2</b>	2.67(2.53-2.83)
<b>3</b>	6.1	2.1	<b>4</b>	2.89(2.67-3.14)	4.4	2.4	<b>2</b>	1.86(1.65-2.10)	5.5	2.2	<b>3.3</b>	2.47(2.32-2.64)
<b>4</b>	5.1	1.9	<b>3.2</b>	2.63(2.39-2.89)	3.7	2.2	<b>1.5</b>	1.73(1.50-1.99)	4.7	2.1	<b>2.6</b>	2.27(2.10-2.45)
<b>5</b>	3.5	1.9	<b>1.6</b>	1.88(1.67-2.11)	3.3	2.2	<b>1.1</b>	1.52(1.29-1.79)	3.5	2.0	<b>1.5</b>	1.71(1.56-1.88)
<b>6</b>	2.8	1.6	<b>1.2</b>	1.77(1.53-2.04)	2.4	2.0	<b>0.4</b>	1.17(0.95-1.44)	2.7	1.8	<b>0.9</b>	1.47(1.31-1.65)
<b>7</b>	2.8	1.2	<b>1.6</b>	2.28(1.95-2.69)	2.1	1.9	<b>0.2</b>	1.09(0.86-1.38)	2.6	1.6	<b>1</b>	1.63(1.44-1.86)
<b>8</b>	2.4	1.3	<b>1.1</b>	1.82(1.50-2.19)	2.3	1.9	<b>0.4</b>	1.26(0.98-1.61)	2.3	1.6	<b>0.7</b>	1.49(1.29-1.73)
<b>9</b>	1.8	1.6	<b>0.2</b>	1.19(0.94-1.49)	1.9	1.8	<b>0.1</b>	1.08(0.80-1.46)	1.9	1.7	<b>0.2</b>	1.12(0.93-1.34)
<b>10</b>	2.3	1.3	<b>1</b>	1.76(1.37-2.24)	3.1	1.8	<b>1.3</b>	1.69(1.29-2.22)	2.6	1.6	<b>1</b>	1.64(1.36-1.96)

Likelihood ratio test p value for the interaction between sex and admission rates with adjustment for age: <0.0001. CI = confidence interval; IRR= Incidence rate ratio.

**Table 4: Proportion of patients with records of alcohol use and brief alcohol interventions.**

	Cases (n, %)	Controls (n, %)
<b>Alcohol use status <sup>a</sup></b>		
Data available	2,088(84.2 )	16,752( 67.6)
Never	48(1.9)	2,347(9.5)
moderate	377(15.2)	11,374(45.9)
Hazardous/harmful <sup>b</sup>	1,507( 60.7)	2,344(9.5)
unclear	156( 6.3)	687(2.8)
Data unavailable	391(15.8)	8,038(32.4)
<b>Intervention (n, %)<sup>1</sup></b>		
Definitely offered an intervention	565(22.8)	1,151(4.7)
Offered brief alcohol intervention	520(20.9)	1,142(4.6)
Offered Referral	28(1.1)	7(<0.1)
Offered Both	17(0.7)	2(<0.1)
Data unavailable	1,914(77.2)	23,639(95.3)

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<sup>a</sup>  $\chi^2$  tests p value < 0.001. <sup>b</sup> Cases: hazardous drinkers n= 345(13.8%), harmful drinkers n=1162(46.9%). Controls: hazardous drinkers n=1674(6.8%), harmful drinkers n=670(2.7%).

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**Table 5: Proportion of patients with alcohol use records and brief alcohol interventions stratified by sex and age and OR and 95% CIs**

	Males			Females		
	Cases n=1,660	Controls n=12,453	OR(95% CI)	Cases n= 819	Controls n=12,337	OR(95% CI)
<b>Alcohol use records<sup>a,b</sup></b>	1,414(85.2)	8,103(65.1)	1.96(1.7-2.3) <sup>e</sup>	674(82.3)	8,649(70.1)	1.63(1.4-1.8) <sup>e</sup>
<b>Alcohol intervention<sup>c,d</sup></b>	385(23.2)	642(5.2)	4.3(3.7-4.9) <sup>e</sup>	180(22.0)	509(4.1)	5.8(4.7-6.9) <sup>e</sup>
18-44 years	57(20.8)	86(3.3)	7.6(5.3-11.1)	45(31.0)	84(3.4)	12.6(8.2-19.4)
45-54 years	110(22.4)	170(4.9)	5.6(4.3-7.4)	65(25.2)	144(4.4)	7.3(5.2-10.3)
55-64 years	135(26.2)	239(6.4)	5.2(4.1-6.6)	45(18.9)	147(4.2)	5.3(3.7-7.7)
65-74 years	68(24.1)	114(5.9)	5.3(3.8-7.5)	21(16.15)	91(4.4)	4.2(2.5-7.1)
≥ 75 years	15(14.2)	33(4.6)	3.4(1.8-6.5)	4(8.3)	43(4.2)	2.1(0.7-6.1)

<sup>a</sup>no significant age interaction for alcohol records, hence results are not stratified for age; <sup>b</sup>likelihood ratio test p value for interaction between sex and alcohol records =0.0017; <sup>c</sup>likelihood ratio test p value for interaction between age and interventions = 0.0009  
<sup>d</sup>likelihood ratio test p value for interaction between sex and interventions = 0.07. <sup>e</sup>OR adjusted for age and consulting rate CI= confidence interval; OR= odds ratio.

## Figures

Figure 1a: Yearly primary care consultation rates per person-year prior to alcoholic cirrhosis diagnosis

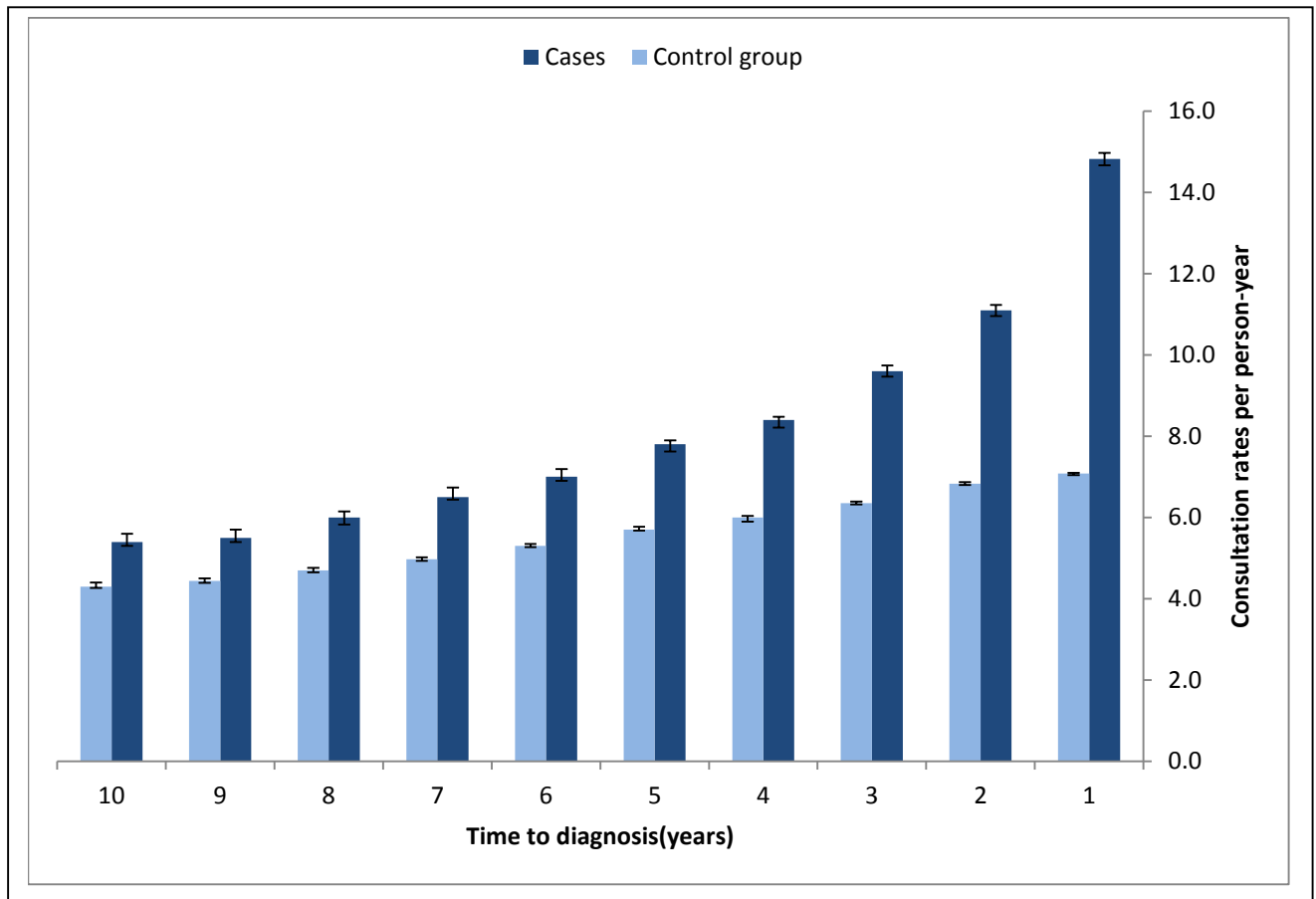
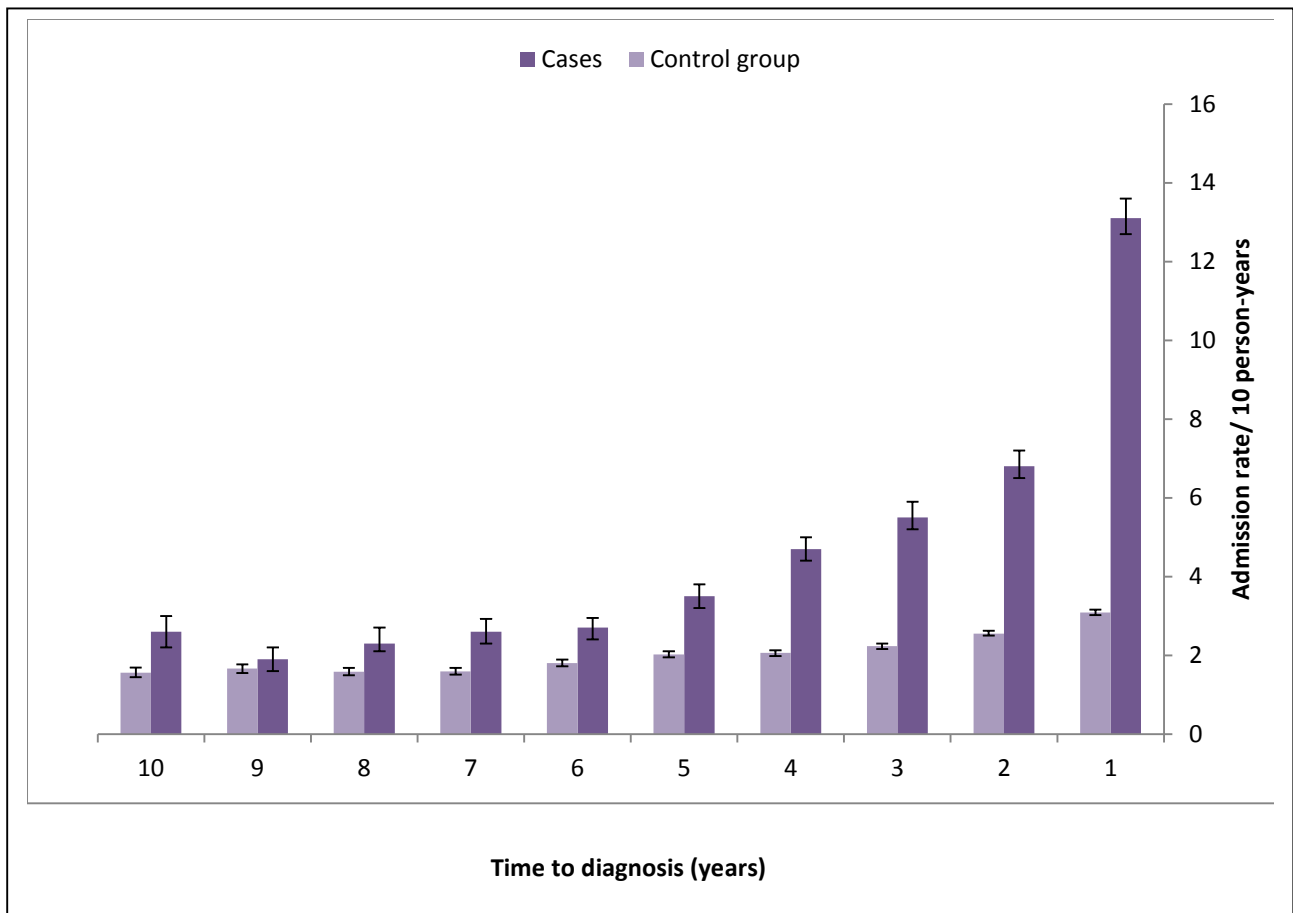


Figure 1b: Yearly hospital admission rates per 10 person-years prior to alcoholic cirrhosis diagnosis.



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**Declaration of transparency:** HEO and KMF affirm that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

**Data sharing:** no additional data available



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