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Population-Based Study of Alcohol-Related Liver Disease in England in 2001–2018: Influence of Socioeconomic Position

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INTRODUCTION: **England has seen an increase in deaths due to alcohol-related liver disease (ALD) since 2001. We studied the influence of socioeconomic position on the incidence of ALD and the mortality after ALD diagnosis in England in 2001–2018.**

METHODS: **This was an observational cohort study based on health records contained within the UK Clinical Practice Research Datalink covering primary care, secondary care, cause of death registration, and deprivation of neighborhood areas in 18.8 million residents. We estimated incidence rate and incidence rate ratios of ALD and hazard ratios of mortality.**

RESULTS: **ALD was diagnosed in 57,784 individuals with a median age of 54 years and of whom 43% had cirrhosis. The ALD incidence rate increased by 65% between 2001 and 2018 in England to reach 56.1 per 100,000 person-years in 2018. The ALD incidence was 3-fold higher in those from the most deprived quintile vs those from the least deprived quintile (incidence rate ratio 3.30, 95% confidence interval 3.21–3.38), with reducing inequality at older than at younger ages. For 55- to 74-year-olds, there was a notable increase in the incidence rate between 2001 and 2018, from 96.1 to 158 per 100,000 person-years in the most deprived quintile and from 32.5 to 70.0 in the least deprived quintile. After ALD diagnosis, the mortality risk was higher for patients from the most deprived quintile vs those from the least deprived quintile (hazard ratio 1.22, 95% confidence interval 1.18–1.27), and this ratio did not change during 2001–2018.**

DISCUSSION: **The increasing ALD incidence in England is a greater burden on individuals of low economic position compared with that on those of high socioeconomic position. This finding highlights ALD as a contributor to inequality in health.**

KEYWORDS: alcohol-related liver disease; epidemiology; England; deprivation; socioeconomic inequality

SUPPLEMENTARY MATERIAL accompanies this paper at http://links.lww.com/AJG/D185; http://links.lww.com/AJG/D186

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INTRODUCTION

Alcohol-related liver disease (ALD) results from chronic heavy drinking and is the most common cause of liver-related death in Europe (1). Today, ALD causes 100,000 deaths in Europe per year, and the number is projected to increase (2).

At the country level, the incidence of ALD typically follows the consumption of alcohol per capita (1), but England has broken this pattern since 2001: age-standardized deaths due to ALD have increased by more than 40% despite a reduction in alcohol consumption (3,4). One possible explanation is that drinking patterns and resulting trends in ALD incidence differ across socioeconomic or demographic gradients. For example, individuals of low socioeconomic position are more vulnerable to alcohol-related harm and may have seen the highest rise in ALD incidence. And according to age, drinking may have increased in individuals older than 45 years and decreased in those who are

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younger: among deaths caused by alcohol, deaths from ALD are much more frequent in decedents older than 45 years, while deaths from alcohol poisoning are more frequent in younger decedents (4).

Health inequalities are the systematic differences in health outcomes observed as a gradient across the population ranked by socioeconomic position such as neighborhood area–derived deprivation risk (5). Several governments, including the English, aim to reduce health inequalities because they are acknowledged as unfair and avoidable (6,7). Knowing how ALD incidence and mortality vary by socioeconomic position could be useful for prevention. For example, population-based interventions might need to be tailored to socioeconomic position such as minimum unit pricing that decreases alcohol consumption relatively more in groups of low socioeconomic position (8). In addition, inequality in mortality risk after ALD would support health care–based interventions aiming to improve the prognosis in groups of low socioeconomic position, such as those to increase early detection of ALD or increase the uptake of care for ALD in these patients (9,10).

Socioeconomic variation in ALD incidence and mortality has been studied mainly in Scandinavian countries, but the pattern may be unique in every country, and England has a higher economic inequality than the Scandinavian countries (11–14). In addition, time trends in socioeconomic variation of ALD according to age and sex have not been previously studied. We report a population-based study using data from primary and secondary care and from mortality statistics aiming to describe the socioeconomic variation in ALD incidence and in mortality after ALD diagnosis according to neighborhood area deprivation in England from 2001 to 2018.

METHODS

We used linked population-based electronic health care data in England to identify incident cases of ALD between 2001 and 2018. We calculated incidence rates of ALD stratified by the index of multiple deprivation quintile, age, sex, and calendar year. We then analyzed whether deprivation influenced all-cause mortality in patients diagnosed with ALD.

Data sources

Full descriptions of the databases used in this study have been published (15–17). In brief, the Clinical Practice Research Datalink (CPRD) is a not-for-profit research service in the UK government, which uses diagnostic codes collected in a proportion of general practices: CPRD-linked practices. For this study, primary care data from its GOLD and Aurum databases were linked with secondary care data from the Hospital Episodes Statistics data (18) and with cause of death registration data from the Office for National Statistics (17). The patient records in secondary care and cause of death registration are coded using a combination of the *International Classification of Diseases*, *10th Revision* codes for diagnoses and the Office of Population, Censuses and Surveys Classification of Surgical Operations and Procedures version 4 codes for any procedure. General practice data are coded with Read and SNOMED coding, which use standardized core sets of clinical health care terminology for electronic health records. The population providing data for this project was extracted from the May 2020 version of the datasets approved by the CPRD Independent Scientific Advisory Committee (ISAC) reference number: 19_239.

The at-risk population used as the denominators of the ALD incidence analysis and from which cases were drawn comprised registered adults (aged 18 years or older) at contributing CPRD general practices in England eligible for data linkage to Hospital Episodes Statistics, cause of death registration, and index of multiple deprivation for any period between January 1, 2001, and December 31, 2018. We excluded people with missing information on geographic region (n = 9,337) and with an indeterminate sex (n = 952). We used an open cohort design, with individuals entering the at-risk population on the latest of the following dates: the individual's 18-year birthday; 3 months after the individual's registration with their CPRD general practice; start of data collection date for the practice; and January 1, 2001 (16,19). The date of leaving the at-risk population was the earliest of the following: when the individual ended their registration with their CPRD practice, end of data collection date for the practice, date of individual's death as recorded in CPRD, or December 31, 2018. This follows the recommended approach by CPRD (19). Link to ISAC Protocol: https://www.cprd.com/protocol/stage-diagnosis-and-subsequent-health-care-provision-patients-alcoholic-liver-disease-and.

Alcohol-related liver disease

We identified patients with an incident diagnosis of ALD within primary care, secondary care, or the cause of death registry in 2001–2018. We excluded ALD diagnosed before 2001.

We defined ALD in primary and secondary care data as either (i) a diagnosis code specifying ALD or (ii) the combination of a diagnosis code for liver disease of unknown etiology preceded by a diagnosis code indicating alcohol use disorder. We defined ALD in the cause of death registry by (i) a diagnosis code specifying ALD or (ii) the combination of a diagnosis code for liver disease of unknown etiology and a diagnosis code indicating alcohol use disorder among the registered causes of death. The definition of alcohol-related cirrhosis that we used was similar to that of a prior study (20), but, in this study, we expanded the diagnostic codes to include non-cirrhotic ALD. The code lists we used to define ALD, cirrhosis, and decompensation are found in Supplementary Appendix A (see Supplementary Digital Content 1, http://links.lww.com/AJG/D185). For all patients, the earliest date of the diagnosis code for liver disease defined the date of ALD diagnosis. Patients with the combination of codes for liver disease of unknown etiology and alcohol use disorder accounted for 31% of the total cohort.

The severity of ALD at diagnosis was defined as either non-cirrhotic liver disease, cirrhosis, or decompensated cirrhosis based on diagnostic and procedure codes recorded before or within the first 3 months after the initial ALD diagnosis. Patients with ALD had cirrhosis if they had a diagnostic code for cirrhosis and decompensated cirrhosis if a procedure or diagnostic code indicated variceal bleeding or ascites (21). An exception to this definition was patients with a diagnostic code for a cancer (other than hepatocellular carcinoma) in the year before the diagnosis of ALD; in these patients, ascites did not count as having decompensated cirrhosis. Comorbidity was defined according to the Charlson comorbidity index score and calculated based on diagnosis codes, excluding codes for liver disease.

Socioeconomic position

The English Index of Multiple Deprivation 2015 is derived from 37 indicators grouped into 7 empirically weighted domains that are used to rank small geographical areas linked to postcodes from the least deprived to the most deprived (22). The geographical areas have a minimum of 1,000 people within it, a mean of 1,500 people, and a maximum of 3,000 people. The 7 domains and their weights are as follows: income deprivation (22.5%) based on government benefits; employment deprivation (22.5%) based on government benefits and allowances; health deprivation and disability (13.5%) based on a number of health measures; education, skills, and training deprivation (13.5%) based on participation and attainment; barriers to housing and services (9.3%) based on local amenities and rehousing rates; crime (9.3%) based on recorded crime levels; and living environment deprivation (9.3%) based on housing quality, air quality, and traffic accidents. Their indicators are listed and discussed in detail in the English Indices of Deprivation 2015 (22).

Statistical analysis

We computed the incidence rate of ALD as the number of incident cases divided by the total person-years at risk. This was performed overall and within strata defined by deprivation quintile, age group (18–34, 35–44, 45–54, 55–64, 65–74, 75–84, and 85 years or older), sex, and calendar year. In a supplemental analysis, and to facilitate comparison with other countries, we standardized the overall incidence rate of England in 2001 (first year of the study period) and in 2018 (last year of study period) to the European 2013 standard population (23).

As the measure of inequality in ALD incidence, we used Poisson regression to estimate the incidence rate ratio (IRR) of the ALD incidence rate in the least deprived quintile compared with the most deprived quintile while adjusting for age, sex, and calendar year. Evidence of statistical interaction between age in years and deprivation quintile on ALD incidence was assessed by fitting a model including an interaction term between age and deprivation and then using the likelihood ratio test to determine whether the model with the interaction term gave a statistically significantly better fit to the observed data (24). We used the same approach to assess the statistical interaction between deprivation quintile, sex, and calendar year.

Next, we used Cox regression to analyze the influence of deprivation on all-cause mortality after diagnosis of ALD, excluding those patients who died the same day they were diagnosed with ALD (n = 1,544). In the mortality analysis, we followed up patients from the date of ALD diagnosis until death date, as recorded in the cause of death registry, and we censored survivors when follow-up ended on May 30, 2020. The Cox regression was adjusted for age at diagnosis of ALD, sex, severity of the liver disease at diagnosis (non-cirrhotic, cirrhotic, or decompensated cirrhosis), Charlson comorbidity index (0, 1, and $\geq$2), and calendar year of ALD diagnosis. All analyses were calculated with Stata version 18.

Sensitivity analyses

First, we examined whether the IRR of ALD and the hazard ratio (HR) for mortality according to deprivation index were similar when stratified by English region. Second, we examined whether our results for ALD incidence and all-cause mortality after ALD diagnosis according to socioeconomic position changed when our definition of ALD was narrowed to ALD based on ALD codes exclusively, hence excluding those cases defined by the combination of an unspecific liver disease code and an alcohol code. Third, we examined whether results changed when liver-related mortality was used as the outcome instead of all-cause mortality. Liver-related mortality was defined as mentioning of liver disease as the underlying cause of death, with similar codes that we used to define ALD in ONS (see Supplementary Appendix A, Supplementary Digital Content 1, http://links.lww.com/AJG/D185). We used the same Cox regression model for this analysis of cause-specific mortality. Fourth, we included data on the latest recording of body mass index (BMI) in CPRD and included this variable in the analysis of overall mortality to examine whether the association between deprivation and all-cause mortality could be explained by differences in BMI.

Data availability

Electronic health records are, by definition, considered sensitive data in the UK by the Data Protection Act and cannot be shared through public deposition because of information governance restrictions in place to protect patient confidentiality. Access to data is available only once approval has been obtained through the individual constituent entities controlling access to the data. The primary care data can be requested through application to the Clinical Practice Research Datalink (https://www.cprd.com).

RESULTS

A total of 18,765,679 individuals contributed with person-years to the at-risk population (see Supplementary Table S1, Supplementary Digital Content 2, http://links.lww.com/AJG/D186). From 2001 to 2018, we observed 57,784 patients with an incident diagnosis of ALD (Table 1). The proportion of men was 69%, and this did not change during 2001–2018, whereas the median age at diagnosis increased slightly from 52.5 years in 2001 to 55.7 years in 2018 (see Supplementary Figure S1 and S2, Supplementary Digital Content 2, http://links.lww.com/AJG/D186). The proportion diagnosed with non-cirrhotic ALD increased during the study period from 52% in 2001 to 63% in 2018 (see Supplementary Figure S3, Supplementary Digital Content 2, http://links.lww.com/AJG/D186). In 1,544 (2.7%) patients, the date of death coincided with their date of ALD diagnosis. Supplemental Table S2 (see Supplementary Digital Content 2, http://links.lww.com/AJG/D186) summarizes characteristics of the included cases with ALD identified in the Aurum and GOLD databases.

Overall ALD incidence

The ALD incidence per 100,000 person-years increased during the study period from 33.8 (95% confidence interval [CI] 32.4–35.3) in 2001 to 56.1 (95% CI 54.4–57.9) in 2018. The overall ALD incidence rate was more than twice as high for men as it was for women 63.8 (95% CI 63.2–64.4) vs 28.0 (95% CI 27.6–28.4) per 100,000 person-years (Table 1). ALD incidence peaked for 55–64 years age group: increasing from 10.5 (95% CI 10.1–10.8) per 100,000 person-years for 18–34 years age group, to 83.4 (95% CI 82.0–84.7) for 55–64 years age group, and then declining to 15.4 (95% CI 14.2–16.7) for 85 years or older age group. The largest absolute increase in ALD incidence between 2001 and 2018 was observed for 55–74 years age group, and the smallest absolute increase was observed for 18–34 years age group (Figure 1), with the same trends observed for men and women according to age (see Supplementary Figure S4, Supplementary Digital Content 2, http://links.lww.com/AJG/D186).

Table 1. Incidence rate and incidence rate ratios according to socioeconomic position and demographic characteristics of individuals newly diagnosed with alcohol-related liver disease in England, 2001–2018

	n (%)	Person-years in 100,000	Incidence rate per 100,000 person-years (95% CI)	Adjusted incidence rate ratios (95% CI)
Overall	57,784 (100)	1,263	45.8 (43.9–46.1)	—
Index of multiple deprivation[a]				
1 (least deprived)	8,079 (14)	289	27.9 (27.3–28.5)	1 (reference)
2	8,991 (16)	265	34.0 (33.3–34.7)	1.25 (1.21–1.29)
3	10,203 (18)	251	40.7 (39.9–41.5)	1.53 (1.50–1.58)
4	12,962 (22)	243	53.4 (52.5–54.3)	2.13 (2.07–2.19)
5 (most deprived)	17,549 (30)	215	81.6 (80.4–82.8)	3.30 (3.21–3.38)
Sex				
Women	17,856 (31)	280	28.0 (27.6–28.4)	1 (reference)
Men	39,928 (69)	6,379	63.8 (63.2–64.4)	2.22 (2.18–2.26)
Age at diagnosis, y				
18–34	3,644 (6.3)	348	10.5 (10.1–10.8)	1 (reference)
35–44	9,922 (17)	239	41.5 (40.6–42.3)	4.55 (4.38–4.72)
45–54	16,032 (28)	221	72.3 (71.2–73.5)	8.28 (7.99–8.58)
55–64	15,312 (26)	184	83.4 (82.0–84.7)	9.97 (9.62–10.34)
65–74	9,187 (16)	139	65.7 (64.4–67.1)	8.04 (7.74–8.36)
75–84	3,096 (5.4)	92	33.8 (32.6–35.0)	4.23 (4.03–4.44)
≥85	591 (1.0)	38	15.4 (14.2–16.7)	1.95 (1.78–2.13)

Incidence rate ratios were mutually adjusted for socioeconomic position, sex, age, and calendar year.
CI, confidence interval.
[a]Index of multiple deprivation is an area-based measure of socioeconomic position.

ALD incidence by socioeconomic position

Newly diagnosed patients with ALD from the most deprived quintile were on average younger than those from the least deprived quintile (median age of 51 vs 57 years) (Table 2). The severity of ALD and comorbidity index score at ALD diagnosis were similar according to deprivation quintile.

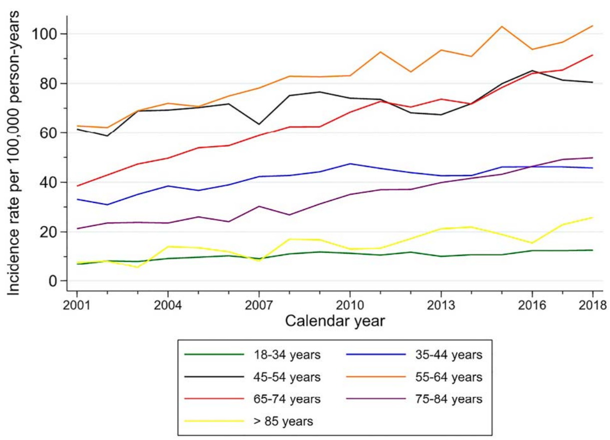

Figure 1. Incidence rate of alcohol-related liver disease (ALD) by age group according to calendar year in England 2001–2018. This figure shows that the incidence rate of ALD was highest in the age groups of 45–54, 55–64, and 65–74 years and that these age groups also had the most pronounced absolute increase in ALD incidence during 2001–2018.

Overall, there was a 3-fold higher incidence rate of ALD in individuals from the most deprived quintile compared with those from the least deprived quintile (IRR 3.30, 95% CI 3.21–3.38). Figure 2 shows that the most deprived experienced the highest increase in incidence rate from 2001 to 2018. The relative difference in ALD incidence between the most and least deprived, as measured by the IRR, declined during the study period, but the decline was due to a higher relative increase in ALD incidence among the least deprived compared with that among the most deprived.

Stratifying analyses by age groups showed that the highest absolute increase in ALD incidence during the study period was found in the most deprived of 55–74 years age group. For example, the incidence rate increased from 96.1 to 158 per 100,000 person-years in the most deprived quintile and from 32.5 to 70.0 in the least deprived quintile between 2001 and 2018 (Figure 3). The IRR of ALD incidence according to deprivation was largest for the youngest age group of 18–54 years and declined with increasing age.

There was evidence of statistical interaction between the IRR of ALD incidence according to deprivation quintile and age, calendar year, and sex, respectively (P for interaction tests $<$0.001), indicating that the influence of deprivation on the ALD incidence rate was different according to age, calendar year, and sex. Stratified analyses showed the decreasing IRR of ALD

Table 2. Characteristics according to socioeconomic position of newly diagnosed individuals with alcohol-related liver disease in England, 2001–2018 (n = 56,240)

		Index of multiple deprivation				
	Total	Least deprived	2	3	4	Most deprived
n	56,240[a]	7,884	8,783	9,944	12,601	17,028
Men (%)	38,831 (69)	5,327 (68)	6,006 (68)	6,781 (68)	8,846 (70)	11,871 (70)
Age, median (IQR)	54 (45–63)	57 (48–66)	56 (47–65)	55 (46–65)	53 (44–62)	51 (43–61)
Diabetes	15,575 (28)	2,215 (28)	2,453 (28)	2,806 (28)	3,497 (28)	4,604 (27)
Chronic viral hepatitis C	2,071 (3.7)	140 (1.8)	186 (2.1)	300 (3.0)	463 (3.7)	982 (5.8)
Severity of liver disease						
Non-cirrhotic	32,321 (57)	4,515 (57)	5,092 (58)	5,661 (57)	7,217 (57)	9,836 (58)
Cirrhosis	11,714 (21)	1,678 (21)	1,792 (20)	2,087 (21)	2,617 (21)	3,540 (21)
Decompensated cirrhosis	12,205 (22)	1,691 (22)	1,899 (22)	2,196 (22)	2,767 (22)	3,652 (21)
Charlson comorbidity index						
0	30,686 (55)	4,333 (55)	4,821 (55)	5,417 (54)	6,945 (55)	9,170 (54)
1	13,402 (24)	1,729 (22)	1,995 (23)	2,343 (24)	3,035 (24)	4,300 (25)
≥2	12,152 (22)	1,822 (23)	1,967 (22)	2,184 (22)	2,621 (21)	3,558 (21)

IQR, interquartile range.
[a]A total of 1,544 patients died the day they were diagnosed with alcohol-related liver disease, and they were not included in this table.

incidence from 2001 to 2018 was statistically significant for 18- to 54-year-old men and not for women, but otherwise, the IRR showed a similar pattern in men and women according to age and calendar year (see Supplementary Figure S5 and Supplementary Table S3, Supplementary Digital Content 2, http://links.lww.com/AJG/D186, which summarizes the IRR in individuals from the most deprived quintile compared with those from the least deprived quintile stratified by age, calendar year, and sex).

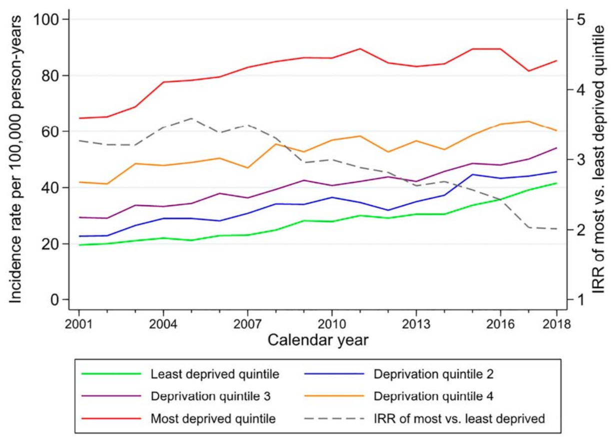

Figure 2. Incidence rate of alcohol-related liver disease (ALD) by deprivation quintile of neighborhood areas according to calendar year in England 2001–2018. This figure shows that the ALD incidence rate increased with increasing deprivation of the neighborhood area and that the most deprived experienced the highest absolute increase in incidence rate from 2001 to 2018. The relative difference in ALD incidence between the most and least deprived, as measured by the incidence rate ratio (IRR), declined during the study period, but the decline was due to a higher relative increase in ALD incidence among the least deprived compared with that among the most deprived.

Mortality after ALD diagnosis by socioeconomic position

During 302,889 person-years of follow-up, 27,134 patients with ALD died, yielding an overall mortality rate of 86.7 per 1,000 person-years. The overall mortality risk after 1, 5, and 10 years was 20% (95% CI 19%–20%), 55% (95% CI 55%–56%), and 81% (95% CI 80%–81%). Mortality risk was higher in patients from the most deprived quintile (adjusted HR of 1.22 vs patients from the least deprived quintile [1.18–1.27]) (Table 3). The unadjusted mortality rate was similar in the 3 calendar periods, 2001–2006, 2007–2012, and 2013–2018, but when we adjusted for confounders, the mortality rate had clearly declined during the study period. This decline, however, was seen in all deprivation quintiles, so the most deprived patients with ALD retained a 20% higher mortality rate throughout the study period (Table 3 and see Supplementary Table S4, Supplementary Digital Content 2, http://links.lww.com/AJG/D186).

Sensitivity analyses

First, the difference in incidence and mortality according to deprivation index did not vary appreciably by English region, although the magnitude of the IRR was lower in East of England and in London (see Supplementary Tables S4 and S5, Supplementary Digital Content 2, http://links.lww.com/AJG/D186). Second, when we restricted to codes implying ALD and not the combination of liver and alcohol codes, we included 36,133 individuals, but the IRR of ALD in the most deprived quintile vs the least deprived quintile was similar (IRR 3.40 vs 3.30 in our original analysis) (see Supplementary Table S5, Supplementary Digital Content 2, http://links.lww.com/AJG/D186). In addition, the gradient for all-cause mortality according to socioeconomic

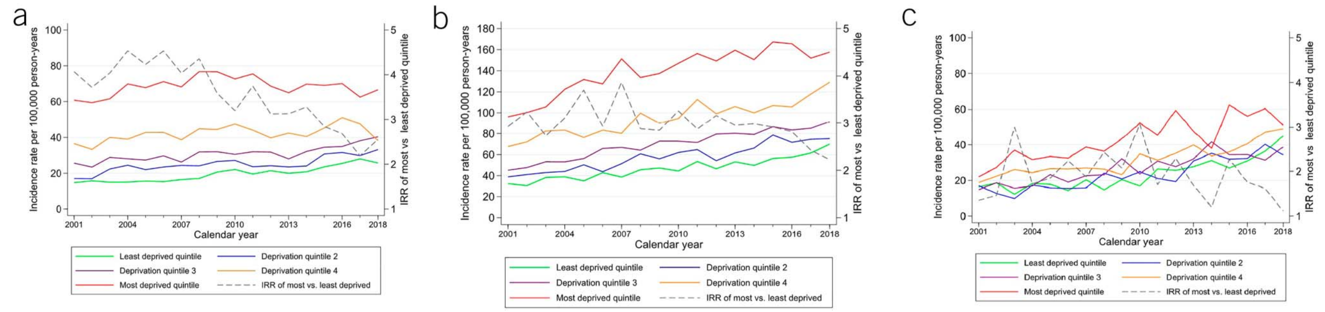

Figure 3. Incidence rate of alcohol-related liver disease (ALD) by deprivation quintile of neighborhood areas according to calendar year in England 2001–2018 and stratified by age group showing (**a**) 18–54 years, (**b**) 55–74 years, and (**c**) 75 years or older. This figure shows that the highest increase in ALD incidence during the study period was found in the most deprived of 55–74 years (**b**). The relative difference in ALD incidence between the most and least deprived, as measured by the incidence rate ratio (IRR), was largest for the youngest age group of 18–54 years (**a**), lower for the age group of 55–74 years (**b**) and nearly absent for those older than 75 years (**c**).

status was unchanged compared with our main analysis 1.22 (95% CI 1.16–1.28) (see Supplementary Table S6, Supplementary Digital Content 2, http://links.lww.com/AJG/D186). Third, there was no difference in the risk of liver-related mortality for patients from the most deprived quintile vs those from the least deprived quintile (adjusted HR 1.05, 95% CI 0.99–1.11) (see Supplementary Table S7, Supplementary Digital Content 2, http://links.lww.com/AJG/D186). Fourth, data on BMI were available in 69% of patients, and the median BMI was a little lower in those from the most deprived quintile compared with those from the least deprived quintile (see Supplementary Table S9, Supplementary Digital Content 2, http://links.lww.com/AJG/D186). Adjustment for BMI did not change the socioeconomic gradient in mortality compared with our main analysis (see Supplementary Table S10, Supplementary Digital Content 2, http://links.lww.com/AJG/D186).

DISCUSSION

This study showed that individuals from the most deprived quintile in England had a 3-fold higher incidence of ALD compared with individuals from the least deprived quintile. The overall ALD incidence increased by 65% from 2001 to 2018, mainly driven by increases across all deprivation quintiles in those aged 55–74 years. After ALD diagnosis, patients from the most deprived quintile had a higher mortality risk than those from the least deprived quintile, and this mortality gap did not change during the study period.

The striking increase of 65% in ALD incidence from 2001 to 2018 explains the 43% increase in deaths due to ALD observed in England from 2001 to 2019, as reported by the Office for National Statistics (4). In addition, the time trends for ALD incidence by age group that we report in this study also mirror the time trends for alcohol-specific deaths in the UK: Alcohol-specific deaths have decreased slightly or been unchanged for ages 30–54 years, increased substantially for ages 55–74 years, and increased slightly for ages 75 years or older during 2001–2019 in the UK (see Supplementary Figure S6, Supplementary Digital Content 2, http://links.lww.com/AJG/D186). However, some of the increase in ALD incidence from 2001 to 2018 is likely ascribed to earlier detection of ALD during the study period, as reflected by the increasing proportion diagnosed with non-cirrhotic ALD.

The 3-fold higher incidence in ALD between the least deprived and most deprived quintiles that we observed is similar to the socioeconomic patterns for alcohol-specific deaths in the UK and for variceal bleeding in England (4,25). Our finding of a larger inequality in ALD incidence for younger compared with that for older ages is in line with prior literature on inequality in alcohol-related outcomes (11,26,27). The influence of deprivation on mortality risk after ALD diagnosis in this study also replicates prior findings in patients with chronic liver disease (12,13). For example, patients with cirrhosis of low occupational skill level had increased mortality risk compared with those of higher skill level in a study from Sweden (12).

Strengths of this study include the ability to include an open cohort of 18.8 million individuals in hospital-linked CPRD practices that have been shown to be socioeconomically and sociodemographically representative of England (28). Validation studies of CPRD Aurum have found that more than 90% of diagnostic codes for chronic diseases are correct when compared with medical records (24,29). Our definition of ALD in the CPRD has not been validated, but it builds on the definition of alcohol-related cirrhosis that we used in a prior study (20). In this prior study, more than 75% of cases with cirrhosis in CPRD had evidence of the cirrhosis diagnosis in both primary and secondary health care records. A validation study based on HES data found a similar liver disease severity and mortality for patients coded with a primary code of ALD and a combination of a liver code and alcohol code, when compared with a manual review of patient records (30). The similar clinical characteristics of cases with ALD in the 2 data systems that we used, Aurum and GOLD (see Supplementary Table S2, Supplementary Digital Content 2, http://links.lww.com/AJG/D186), corroborate the validity of the included diagnosis codes. Finally, the IRR of ALD and the HR for mortality for the most deprived vs least deprived were similar when we restricted our definition of ALD to primary codes of ALD (see Supplementary Tables S5 and S6, Supplementary Digital Content 2, http://links.lww.com/AJG/D186).

It was a limitation of the study that socioeconomic position was inferred from the location and not at the individual level because area-level socioeconomic position may underestimate the true influence of socioeconomic position on health (31). Several factors such as regional and cultural differences in drinking habits and ethnic background influence the risk of ALD (32). For example, the lower difference in ALD incidence between the most and least deprived in the region of London compared

Table 3. HR of all-cause mortality according to socioeconomic position and adjusting variables of newly diagnosed individuals with alcohol-related liver disease in England, 2001–2018 (n = 56,240)

	No. of deaths	Person-years	Rate per 1,000 person years	Adjusted HR (95% CI)
Overall	27,134	312,880	86.7	—
Index of multiple deprivation				
1 (least deprived)	3,597	42,870	83.9	1 (reference)
2	4,149	48,571	85.4	1.07 (1.02–1.11)
3	4,796	54,577	87.9	1.10 (1.06–1.15)
4	6,131	70,121	87.4	1.16 (1.11–1.21)
5 (most deprived)	8,461	96,751	87.5	1.22 (1.18–1.27)
Severity of liver disease				
Non-cirrhotic	11,829	209,952	56.3	1 (reference)
Cirrhosis	6,858	54,856	125.0	1.89 (1.83–1.94)
Decompensated cirrhosis	8,447	48,014	175.7	2.64 (2.57–2.72)
Charlson comorbidity index				
0	11,708	164,636	71.1	1 (reference)
1	5,390	88,279	88.3	1.11 (1.08–1.14)
≥2	10,036	87,197	115.1	1.43 (1.39–1.48)
Sex				
Women	8,333	96,137	86.7	1 (reference)
Men	18,801	216,752	86.7	0.99 (0.97–1.02)
Age at diagnosis, yr				
18–34	973	29,223	33.3	1 (reference)
35–44	3,789	69,029	54.9	1.49 (1.39–1.60)
45–54	6,922	94,833	73.0	1.82 (1.70–1.95)
55–64	7,677	76,197	100.8	2.34 (2.19–2.51)
65–74	5,211	34,830	149.6	3.19 (2.98–3.42)
75–84	2,133	7,933	268.9	4.45 (4.48–5.24)
≥85	429	843	508.9	8.12 (7.23–9.12)
Calendar period				
2001–2006	10,390	118,674	87.55	1 (reference)
2007–2012	10,529	123,636	85.16	0.83 (0.81–0.85)
2013–2018	6,215	70,580	88.06	0.61 (0.59–0.63)

The Cox regression analysis was adjusted for severity of liver disease at diagnosis, Charlson comorbidity index, sex, age at diagnosis, and calendar period of diagnosis.
CI, confidence interval; HR, hazard ratio.

with that in other regions of England may reflect a higher proportion of nondrinking immigrants from Asian or Muslim countries that live in deprived areas (32). Another limitation of this study was the absence of information on alcohol consumption, smoking, and metabolic syndrome, known to influence the risk of liver disease, so we cannot examine whether differences in these factors contributed to our findings. Differences in alcohol drinking patterns across socioeconomic strata in England are the most plausible explanation for the inequality in ALD incidence that we report: extreme drinking (>24 units per day) and alcohol dependence were more common in those of lower socioeconomic position in studies from the UK and England (26,33). In addition, obesity, smoking, poor nutrition, and other risk factors that are more prevalent in individuals of lower socioeconomic position and associated with increased risk of ALD may also contribute to the inequality in ALD incidence that we observed in this study (1,2). Of note, studies on total alcohol-related disease and death found that obesity and smoking played only a minor role in mediating the socioeconomic inequality in this outcome (27,34).

As for the inequality in mortality after ALD diagnosis, patients of lower socioeconomic position have lower levels of social support, which is an important factor for the ability to stay alcohol abstinent and have compliance with medical care (35). In England, the number of people entering alcohol addiction treatment has fallen during the study period (36). Liver transplantation could not explain our findings because this happened to fewer than 0.6% of the study cohort during follow-up (see Supplementary Table S8, Supplementary Digital Content 2, http://links.lww.com/AJG/D186). Metabolic syndrome, if it varied between groups, could also contribute to the difference in mortality risk according to socioeconomic position; however, we found a similar proportion with diabetes (Table 2) in each deprivation quintile, and including BMI in the mortality analysis did not affect the deprivation gradient for mortality risk (see Supplementary Table S10, Supplementary Digital Content 2, http://links.lww.com/AJG/D186). Chronic hepatitis C infection was more common in the most deprived but only found in 3.7% of patients with ALD. Excluding those infected with hepatitis C did also not alter the deprivation gradient in mortality risk (HR 1.22, 95% CI 1.17–1.27, when excluding patients with hepatitis C and still HR 1.22, 95% CI 1.17–1.27, when including them). Severity of liver disease at diagnosis was also similar according to deprivation quintile in our study, and this was also true when we stratified ALD severity by deprivation quintile in each calendar period 2001–2018 (data not shown). The weaker association between deprivation index and liver-related mortality than was seen for deprivation index and all-cause mortality in our study suggests that other causes than liver disease are important to explain the higher mortality in the most deprived (see Supplementary Table S9, Supplementary Digital Content 2, http://links.lww.com/AJG/D186). This finding further indicates that earlier diagnosis of ALD is not enough to eliminate the socioeconomic inequality in mortality after ALD diagnosis.

The picture of an increased ALD incidence in England that we report is very different from the ALD time trends in Denmark. While England and Denmark had comparable standardized ALD incidence in 2001, the Danish ALD incidence has decreased considerably since then (see Supplementary Table S11, Supplementary Digital Content 2, http://links.lww.com/AJG/D186) (1). A simple explanation for the ALD time trend in Denmark is the substantial decrease in the average liters of pure alcohol per capita since 2000. In England, the decrease in the average liters of pure alcohol has been smaller and probably mainly in those younger than 50 years judged by the figures for alcohol-specific mortality by age (see Supplementary Figures S6 and S7, Supplementary Digital Content 2, http://links.lww.com/AJG/D186). Non-invasive screening for ALD in high-risk individuals in England may also contribute to its increasing incidence, while this practice has not been implemented in Denmark.

This study should motivate government and health care institutions to act now to tackle the increasing but preventable burden of ALD on those of lower socioeconomic position in England. For instance, alcohol control policies such as minimum unit pricing have greater impact among groups of lower socioeconomic position than educational programs, the current main approach to tackle harmful alcohol consumption in England (1,6). Limiting the availability of alcohol by restricting licenses to sell alcohol in deprived areas may be another useful approach (37). Furthermore, there is a need for initiatives to ensure that patients with ALD receive appropriate clinical care and addiction treatment, regardless of socioeconomic position.

CONFLICTS OF INTEREST

Guarantor of the article: Joe West, PhD

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Study Highlights

WHAT IS KNOWN

- ✓ Socioeconomic variation in alcohol-related liver disease incidence and mortality was found in Scandinavian countries, but the pattern may be unique in every country.
- ✓ Despite a reduction in alcohol consumption per capita in England since 2001, age-standardised deaths due to alcohol-related liver disease have increased by more than 40%.

WHAT IS NEW HERE

- ✓ Individuals living in the most deprived quintile in England have a three-fold higher incidence of alcohol-related liver disease than those living in the least deprived quintile and they also have a 20% higher mortality risk after diagnosis of alcohol-related liver disease.
- ✓ The incidence rate of alcohol-related liver disease increased substantially for 55–74-year-olds during 2001 and 2018 in England while it was nearly unchanged for other age-groups.

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