BMJ Open Gastroenterology

Association between behavioural risk factors for chronic liver disease and transient elastography measurements across the UK: a cross-sectional study

Ceyhun Aksel Oztumer ⁽¹⁾,^{1,2} Rayhan Mehmood Chaudhry ⁽¹⁾,³ Laith Alrubaiy ⁽¹⁾,³

To cite: Oztumer CA, Chaudhry RM, Alrubaiy L. Association between behavioural risk factors for chronic liver disease and transient elastography measurements across the UK: a cross-sectional study. *BMJ Open Gastro* 2020;**7**:e000524. doi:10.1136/ bmjgast-2020-000524

Additional material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/ bmjgast-2020-000524).

Received 22 August 2020 Revised 13 October 2020 Accepted 27 October 2020

Check for updates

© Author(s) (or their employer(s)) 2020. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

¹Department of Gastroenterology and Hepatology, Imperial College London, London, UK ²Department of Medicine, Brighton and Sussex Medical School, Brighton, UK ³Department of Gastroenterology, St Mark's Hospital and Academic Institute, London, UK

Correspondence to

Dr Laith Alrubaiy; Laith.al-rubaiy@nhs.net

ABSTRACT

Objective Chronic liver disease (CLD) is a largely preventable condition with increasing burden on National Health Service resources. We aimed to determine the prevalence of behavioural risk factors for CLD and their association with liver stiffness and socioeconomic status in the UK.

Design In this cross-sectional study, adults aged ≥18 years were invited to complete a liver health screener and have a liver stiffness measurement (LSM) by transient elastography (TA) to screen for alcohol intake, obesity and viral hepatitis risk across different areas in the UK. Index of Multiple Deprivation (IMD) scores were used as a measure of socioeconomic status. We performed binary logistic regression, adjusting for age, gender, alcohol consumption, body mass index, diet and viral hepatitis risk to determine the factors associated with LSM and IMD.

Results We analysed the data from 2150 individuals across 25 UK areas. Of those, 24.1% had high-risk alcohol consumption, 29.6% had high-risk diets, 24.7% were obese and 32.7% had risk factors for viral hepatitis. LSMs were available for 1043 participants, of which 16.2% were \geq 7 kPa. Independent predictors of an LSM \geq 7 kPa were an age≥40 years (OR, 1.986; 95% Cl, 1.280 to 3.081), male gender (OR, 1.599; 95% CI, 1.128 to 2.266), obesity (OR, 2.526; 95% CI, 1.383 to 4.614) and high-risk diet (OR, 2.197; 95% CI, 1.000 to 4.826). Five-unit increases in IMD score were an independent predictor of obesity (OR, 1.110; 95% CI, 1.028 to 1.200), but not high-risk alcohol consumption (p=0.88) or viral hepatitis risk (p=0.05). **Conclusions** We identified a high prevalence of risk factors for CLD, most of which are addressable through raising public awareness to inculcate healthy habits. More studies are needed to assess longitudinal outcomes of liver screening using TA, accounting for societal factors and comorbidities, to help inform resource allocation and policy-making in the future.

INTRODUCTION

Chronic liver disease (CLD) is thought to be a largely preventable condition, with the three major risk factors of alcohol, obesity and viral hepatitis accounting for more than 90% of all cases.¹ The Lancet Liver Commission² identified the late diagnosis of liver disease as the most important clinical issue, with

Summary box

What is already known about this subject?

- The UK has seen a 400% increase in liver disease mortality since 1970.
- Over 90% of all chronic liver disease (CLD) cases are caused by three modifiable risk factors: alcohol, obesity and viral hepatitis.
- Despite the well-described association between liver disease and socioeconomic status, there are limited population-based data that have examined the relationship between behavioural risk factors for CLD, transient elastography measurements and socioeconomic deprivation.

What are the new findings?

- A large proportion of the screened UK population have at least one high-risk factor for CLD.
- There is great variability in risk behaviours between different areas of the UK.
- ► Age, gender, diet and body mass index are significant independent predictors of a high liver stiffness measurement (≥7 kPa).
- People in areas of higher deprivation are more likely to have unhealthy diets and be obese.

How might it impact on clinical practice in the foreseeable future?

- Understanding the risk patterns of the UK population in terms of alcohol, diet and viral hepatitis risk will help to inform resource allocation and policymaking in the future in an attempt to reduce the burden of CLD on healthcare resources.
- Increasing awareness regarding these three major modifiable risk factors can help to educate the public about early recognition and diagnosis of CLD.

an estimated 75% of people with cirrhosis unaware of their condition until presenting as an emergency with acute-on-chronic liver failure when there are limited treatment options available.

The UK has seen a 400% increase in liver disease mortality since 1970. The opposite is true for other European countries, such as France and Italy, where liver disease mortality has declined over this period, mainly due to effective policy and population-level measures.³ The rise in number of liver-related hospital admissions by 50% in England over the past decade has led to an increasing burden on the National Health Service resources.⁴ Understanding the UK risk patterns of alcohol consumption, diet and viral hepatitis needs to be considered in an attempt to reduce this burden.

The prognosis and management of CLDs are largely influenced by the severity of hepatic fibrosis,⁵ with metaanalyses finding increased liver stiffness to be correlated with liver-related events and all-cause mortality.⁶⁷ Transient elastography (TE) is a novel, non-invasive method for assessment of liver stiffness, which is a surrogate marker of fibrosis. With its ease of use as a bedside tool that provides immediate results,⁸ TE can be used by healthcare professionals with minimal training to stage fibrosis and assess its progression over time.⁹

To our knowledge, previous studies have not assessed the prevalence and geographical variation of alcohol, diet and viral hepatitis risk at a wide scale across the UK and their effects on liver stiffness. Moreover, the association between socioeconomic deprivation and CLD risk has not been clearly identified. While people in the UK's most deprived areas may have higher liver-related mortality than those in the least deprived areas,¹⁰ it is unclear whether this is due to increased high-risk behaviours or other factors such as poor access to healthcare.

This study aimed to collect and analyse data from the UK population to identify the prevalence and geographical variation of the three biggest modifiable risk factors for CLD; alcohol, diet and viral hepatitis. We also aimed to identify the factors associated with increased liver stiffness. We hypothesised that people from areas of higher deprivation have more risk factors for CLD compared with those from less-deprived areas. Moreover, we predicted that excess alcohol consumption, unhealthy diets and viral hepatitis risk would be determinants of an increased liver stiffness.

METHODS

Study design and population

We conducted a population-based study between 21 April 2018 and 22 May 2019 based on a self-reported health questionnaire in the UK. As part of the 'Love Your Liver' campaign by the British Liver Trust (BLT), we visited different areas in England, Northern Ireland and Scotland in a mobile liver unit over the study period. Members of the public aged 18 years old and above were invited from the town centres to complete a liver health screener and have an onsite measurement of their liver stiffness.

Liver health screener

Participants completed a liver health screener¹¹ at private computer terminals in the mobile liver unit. The liver health screener, comprised of five main sections, was

developed by the BLT after extensive consultations with hepatologists and patients. The first section collected general demographic data, including age, gender and region of birth. The second section obtained information regarding diabetes, hypertension and whether participants were concerned about liver damage. The third, fourth and fifth sections focused on alcohol consumption, diet and viral hepatitis risk.

Participants were stratified according to a three-category ordinal variable, separating low-risk drinkers (≤ 14 units/ week), medium-risk drinkers (14.1-29.9 units/week) and high-risk drinkers (≥ 30 units/week). Likewise, we separated those with high-risk diets (diet score ≥ 4), mediumrisk diets (score 2–3) and low-risk diets (score ≤ 1). Viral hepatitis risk was assessed as a two-category ordinal variable of either low (no viral risk factors) or cautious (viral score ≥ 1). The full criteria can be found in online supplemental table 1. Height and weight measurements were taken to calculate body mass index (BMI).

Assessment of socioeconomic status

Socioeconomic status for participants in England was determined using the Index of Multiple Deprivation (IMD).¹² We obtained the 2019 IMD average scores for the Local Authority District from which each participant completed the liver health screener. For Scotland, we used the 2020 Scottish IMD,¹³ which highlights the percentage of data zones within each area that are among the most deprived 20% of the country. Similarly, the 2017 Multiple Deprivation Measure for Northern Ireland¹⁴ was used to indicate the percentage of data zones within each area that are among the most deprived 100 in the country.

Liver stiffness measurement (LSM)

After completing the liver health screener, participants were offered an LSM by TE (FibroScan, Echosens, Paris, France). From 24 March 2019, we linked participants' LSMs to their liver health screener. Examinations were performed by trained healthcare professionals using the standard M or XL probes, in line with the manufacturer's instructions.¹⁵ We used an LSM≥7kPa to signify an abnormal LSM for the purposes of this study.¹⁶ Participants who had previously received a liver transplant, and those previously informed of having a liver condition, were not offered an LSM.

Statistical analysis

All continuous variables were deemed to have nonnormal distribution, with averages expressed as median (IQR). Categorical variables were compared using χ^2 tests and continuous variables were compared using a Mann-Whitney U or Kruskal-Wallis test.

Univariable logistic regression models were used to predict factors associated with liver damage, abnormal LSMs and socioeconomic status. Results are expressed as an OR with a corresponding 95% CI. IMD scores were divided by 5 to calculate ORs for each 5-unit increase in IMD score. Multivariable logistic regression was used to calculate adjusted ORs while accounting for confounders with a significance of p<0.20. All significance tests were two tailed, with p<0.05 considered significant. All analyses were performed using SPSS V.26.

Role of the BLT

The BLT was responsible for creation of the liver health screener and data collection over the study period. They had no role in data analysis, data interpretation or writing of the report.

RESULTS

Between 21 April 2018 and 22 May 2019, 2642 participants completed the liver screener across 25 UK areas. We excluded 492 participant responses due to incomplete demographics or risk factor data, so a total of 2150 participants' data were included for analysis. Characteristics of all 2150 participants are shown in table 1.

Participants were equally split between males (50.8%) and females (49.2%), with most being 40–59 years old (39.9%). The majority of participants were screened in England (70.3%). Overall, 24.1% had high-risk alcohol consumption, 29.9% had high-risk diets and 32.7% had risk factors for viral hepatitis. Only 7.4% were low risk for liver disease across all three risk categories.

A combined 65.3% of participants were either overweight (40.6%) or obese (24.7%). Of those with a lowrisk diet, no participants were obese. In contrast, 68.6%of individuals with a high-risk diet were obese, and the majority of participants with a medium-risk diet (61.5%) were overweight.

Geographical variation of risk factors Countries

Table 2 displays the risk factors of participants from different regions in the UK. There were significant differences in risk between the countries for alcohol (p<0.001), diet (p=0.008) and viral hepatitis (p<0.001), with Scotland having the lowest prevalence across all three categories (35.8%, 74.1% and 25.9%, respectively) (figure 1). The proportion of participants with viral hepatitis risk factors was greatest in England (35.5%). Northern Ireland had the highest prevalence of both high-risk alcohol consumption and high-risk diets (35.5% and 31.4%, respectively). Full data for each region and its areas can be found in online supplemental table 2.

England

Overall, 1511 individuals were screened over 19 areas in England. Of those, 24.2% were high-risk alcohol consumers, 29.3% had high-risk diets and 35.5% had risk factors for viral-induced liver disease. Only 6.4% were low risk across all three risk categories. Within England, the North West had the highest prevalence of both alcohol and diet risk factors (41.4% and 83.4%, respectively). The prevalence of viral hepatitis risk factors was significantly different across the different regions in England (p<0.001). London had the highest risk of viral hepatitis
 Table 1
 Characteristics of participants who completed the liver health screener

Characteristic	n (%) or median (IQR)
Age category-n (%)	
18–24 years	90 (4.2)
25–39 years	427 (19.9)
40–59 years	857 (39.9)
60+ years	776 (36.1)
Gender-n (%)	
Male	1092 (50.8)
Female	1058 (49.2)
Country-n (%)	
England	1511 (70.3)
Northern Ireland	315 (14.7)
Scotland	324 (15.1)
Median BMI* (IQR)-kg/m ²	26.0 (23.0–29.0)
BMI category-n (%)	
Underweight (<18 kg/m²)	20 (0.9)
Normal weight (18 to <25 kg/m ²)	725 (33.7)
Overweight (25 to <30 kg/m ²)	873 (40.6)
Obese (≥30 kg/m²)	532 (24.7)
Alcohol risk—n (%)	
Low	1272 (59.2)
Medium	360 (16.7)
High	518 (24.1)
Diet risk—n (%)	
Low	429 (20.0)
Medium	1084 (50.4)
High	637 (29.6)
Viral hepatitis risk-n (%)	
Low	1447 (67.3)
Cautious	703 (32.7)
Median LSM* (IQR)-kPa	4.9 (4.0–6.2)

*BMI and LSM were only available as continuous variables for 1043 (48.5%) individuals.

BMI, body mass index; LSM, liver stiffness measurement.

(45.7%), with Harrow and Brixton being the areas with the highest prevalence overall (69.8% and 58.8%, respectively). Out of all 25 areas screened, Brixton also had the highest prevalence of a high-risk diet (52.9%) and the second-highest prevalence of high-risk alcohol consumption (32.4%).

Scotland

Of the 2150 individuals screened, 15.1% were from Scotland. Of those, 16.7% were at high risk of alcohol-related liver disease (ALD), 29.6% had high-risk diets and 25.9% had risk factors for viral hepatitis. Only 11.4% of individuals were low risk across all three categories. The percentage of participants with either high-risk alcohol, diet or viral hepatitis risk factors increased alongside the local share of deprived areas.

across different regions in the UK						
	Medium risk	High risk	Total at risk*			
Region	Number of participants (% of region)					
Scotland 2018 (n=324)						
Alcohol	62 (19.1)	54 (16.7)	116 (35.8)			
Diet	144 (44.4)	96 (29.6)	240 (74.1)			
Viral hepatitis			84 (25.9)			
England 2018 (n=	783)					
Alcohol	115 (14.7)	182 (23.2)	297 (37.9)			
Diet	390 (49.8)	231 (29.5)	621 (79.3)			
Viral hepatitis			249 (31.8)			
London 2019 (n=2	269)					
Alcohol	45 (16.7)	65 (24.2)	110 (40.9)			
Diet	142 (52.8)	73 (27.1)	215 (79.9)			
Viral hepatitis			123 (45.7)			
Northern Ireland 2	2019 (n=315)					
Alcohol	67 (21.3)	98 (31.1)	165 (52.4)			
Diet	163 (51.7)	99 (31.4)	262 (83.2)			
Viral hepatitis			83 (26.3)			
North West England 2019 (n=459)						
Alcohol	71 (15.5)	119 (25.9)	190 (41.4)			
Diet	245 (53.4)	138 (30.1)	383 (83.4)			
Viral hepatitis			164 (35.7)			
England combined† (n=1511)						
Alcohol	231 (15.3)	366 (24.2)	597 (39.5)			
Diet	777 (51.4)	442 (29.3)	1219 (80.7)			
Viral hepatitis			536 (35.5)			

Table 2 Prevalence of behavioural risk factors for CLD

*Participants with viral hepatitis risk factors are displayed in the 'Total at risk' column.

†England combined includes England 2018, London 2019 and North West England 2019.

Northern Ireland

A total of 315 individuals completed the questionnaire in Belfast and Derry City combined. Overall, 31.1% had high-risk alcohol consumption, 31.4% had highrisk diets and 26.3% had risk factors for viral hepatitis. Only 7.9% of individuals identified as low risk across all three categories. Out of all UK areas screened, Belfast had the highest prevalence of high-risk alcohol consumption (33.8%) and second highest prevalence of obesity (33.3%). Compared with Derry City, Belfast has a higher proportion of its data zones in the most deprived 100 areas on the country (29% vs 27%).

Attitudes regarding liver damage

We analysed a subgroup of 976 participants for whom we had responses to the question, 'Are you worried that your liver could be damaged?' The frequency of responses was approximately equal across the options, with 32.8% being concerned, 32.2% not concerned and 35.0% unsure of whether their liver could be damaged. After adjusting for confounding variables, factors such



Figure 1 Prevalence and geographical variation of chronic liver disease risk factors across the UK. A χ^2 test was used to show that the proportion of participants displaying risk behaviours for alcohol, diet and viral hepatitis were significantly different across England, Northern Ireland and Scotland.

as age, alcohol consumption, diet and viral hepatitis risk were significantly associated with whether participants were concerned about liver damage. Those with highrisk alcohol consumption were six times more likely to be concerned about their liver being damaged compared with those with low-risk consumption (OR, 5.992; 95% CI, 4.116 to 8.722; p<0.001). Likewise, those with high-risk diets were over three times more likely to be concerned (OR, 3.321; 95% CI, 1.858 to 5.935; p<0.001). Neither hypertension nor diabetes was significant in determining participants' concern (table 3).

Factors associated with a high LSM

LSMs were available for 1043 participants (48.5%) across 11 areas (median, 4.9 kPa; IQR, 4.0–6.2 kPa). LSMs were not available for the remaining 1107 participants because we began recording the measurements and linking them to participants' liver health screeners from 24 March 2019, which is after the study commenced in 21 April 2018.

There were significant differences in LSMs between genders, BMI categories and diet risk groups (p<0.001 for all). There were no significant differences in LSMs between the different alcohol groups (p=0.62) or the viral hepatitis groups (p=0.81). Overall, 16.2% had an LSM \geq 7 kPa and 8.1% had an LSM \geq 9.1 kPa.

On univariable analysis, age \geq 40 years, male gender, BMI and diet risk were significantly associated with an LSM \geq 7kPa. Alcohol consumption, viral hepatitis risk factors and IMD were not significantly associated with an abnormal LSM (figure 2A). A multivariable logistic regression model was developed to adjust for age, gender, BMI and diet (figure 2B). Age \geq 40 years (OR, 1.986; 95% CI, 1.280 to 3.081; p=0.002), male gender (OR, 1.599; 95% CI, 1.128 to 2.266; p=0.008) and obesity

Table 3 Participants' concern regarding liver damage					
	Concerned— n (%)	Unadjusted OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Gender					
Female	142 (29.6)	Reference	-	Reference	-
Male	178 (35.9)	1.332 (1.019 to 1.743)	0.036	0.887 (0.653 to 1.205)	0.44
Age category-years					
60+	95 (23.6)	Reference	-	Reference	-
40–59	139 (38.5)	2.030 (1.485 to 2.775)	<0.001	1.649 (1.151 to 2.363)	0.006
25–49	74 (45.7)	2.726 (1.855 to 4.008)	<0.001	2.399 (1.513 to 3.804)	< 0.001
18–24	12 (24)	1.024 (0.514 to 2.038)	0.95	0.907 (0.423 to 1.947)	0.80
BMI category					
Normal	99 (29.6)	Reference	-	Reference	-
Overweight	114 (29.5)	0.991 (0.719 to 1.366)	0.96	0.752 (0.507 to 1.117)	0.16
Obese	103 (41.9)	1.710 (1.210 to 2.415)	0.002	0.825 (0.500 to 1.361)	0.45
Alcohol risk					
Low	151 (24.0)	Reference	_	Reference	-
Medium	48 (32.4)	1.516 (1.027 to 2.239)	0.036	1.788 (1.183 to 2.703)	0.006
High	121 (60.5)	4.838 (3.453 to 6.780)	<0.001	5.992 (4.116 to 8.722)	<0.001
Diet risk					
Low	15 (20.8)	Reference	-	Reference	-
Medium	140 (29.9)	1.480 (1.015 to 2.158)	0.041	1.853 (1.149 to 2.989)	0.011
High	165 (37.9)	2.870 (1.933 to 4.261)	<0.001	3.321 (1.858 to 5.935)	<0.001
Viral hepatitis risk					
Low	201 (29.1)	Reference	-	Reference	-
Cautious	119 (41.6)	1.734 (1.301 to 2.309)	<0.001	1.663 (1.200 to 2.304)	0.002
Hypertension					
No	242 (31.4)	Reference	-	Reference	-
Yes	78 (37.9)	1.330 (0.965 to 1.831)	0.08	1.393 (0.945 to 2.055)	0.09
Diabetes					
No	298 (32.6)	Reference	_		
Yes	22 (36.1)	1.168 (0.680 to 2.005)	0.57		

Logistic regression models were used to identify the factors associated with participants' concern of possible liver damage. All variables with a significance level of p<0.20 in univariable analysis were included in the multivariable regression model. Variables were adjusted for gender, age, BMI, alcohol risk, diet risk, viral hepatitis risk and hypertension. BMI, body mass index.

(OR, 2.526; 95% CI, 1.383 to 4.614; p=0.003) maintained significance as independent predictors of an abnormal LSM. Compared with low-risk diet, participants with a medium-risk and high-risk diet were more likely to have an abnormal LSM (OR, 2.063; 95% CI, 1.070 to 3.975; p=0.031 and OR, 2.197; 95% CI, 1.000 to 4.826; p=0.049, respectively). When BMI was used as a continuous variable, each 1 kg/m² increase in BMI remained a significant predictor of an abnormal LSM in both univariable (OR, 1.141; 95% CI, 1.104 to 1.180; p<0.001) and multivariable logistic regression analysis (OR, 1.139; 95% CI, 1.082 to 1.198; p<0.001) after adjusting for age, gender and diet.

Socioeconomic status and CLD risk factors

Across the 19 locations in England, Harrow had the lowest IMD score (15.0) and Blackpool had the highest

IMD score (45.0). The median IMD score was 29.6 (IQR, 20.3–34.5). In univariable analysis, each 5-unit increase in IMD score had a significant association with obesity (OR, 1.110; 95% CI, 1.028 to 1.200; p=0.008) and highrisk diet (OR, 1.088; 95% CI, 1.012 to 1.170; p=0.023), but not with high-risk alcohol consumption (OR, 1.006; 95% CI, 0.931 to 1.086; p=0.88) or viral hepatitis risk (OR, 0.933; 95% CI, 0.871 to 1.000; p=0.05). After adjusting for age, gender and diet, each 5-unit increase in IMD score remained an independent predictor of obesity (OR, 1.116; 95% CI, 1.004 to 1.240; p=0.042).

DISCUSSION Risk factors for CLD

This is the first population-based study analysing the prevalence of the three major risk factors for CLD in the

А

Variable			Unadjusted OR (95	% CI)	Unadjusted OR (95% CI)	<i>p</i> value
Age – years	<40				Reference	-
	≥40				1.870 (1.221–2.864)	0.004
Gender	Female				Reference	-
	Male				1.503 (1.076–2.100)	0.017
BMI	Normal				Reference	-
	Overweigh	t —			1.183 (0.758–1.845)	0.46
	Obese			*	3.607 (2.341–5.558)	<0.001
Alcohol risk	Low				Reference	-
	Medium				0.875 (0.546–1.401)	0.58
	High				1.166 (0.801–1.699)	0.42
Diet risk	Low				Reference	-
	Medium		*	—	2.161 (1.171–3.988)	0.014
	High				4.397 (2.366–8.170)	<0.001
Viral hepatitis risk	Low				Reference	-
	Cautious				1.001 (0.710–1.413)	0.99
IMD score		-	-		1.084 (0.942–1.247)	0.26
		0.5 1	.0		10.0	
		Favours LSM <7 kP	a Favours LS	M ≥7 kPa		

В

Variable		Adjusted OR (95% CI)	Adjusted OR (95% CI)	<i>p</i> value
Age – years	<40		Reference	-
	≥40		1.986 (1.280–3.081)	0.002
Gender	Female		Reference	-
	Male		1.599 (1.128–2.266)	0.008
BMI	Normal		Reference	-
	Overweight		0.832 (0.514–1.346)	0.45
	Obese	*	2.526 (1.383-4.614)	0.003
Diet risk	Low		Reference	-
	Medium	*	2.063 (1.070–3.975)	0.031
	High	*	2.197 (1.000–4.826)	0.049
	0.5	1.0	10.0	
	Favours LSM	<7 kPa Favours LSM ≥7 kPa		

Figure 2 Forest plots of the (A) univariable and (B) multivariable logistic regression models used to identify the variables associated with a liver stiffness measurement $(LSM) \ge 7 kPa$. Variables with a significance level of p<0.20 in univariable analysis were included in the multivariable regression model. Variables were adjusted for age, gender, body mass index (BMI) and diet. Index of Multiple Deprivation (IMD) scores are shown per 5-unit increase. ORs are presented on a logarithmic scale.

UK, as well as identifying the factors associated with LSMs and socioeconomic status in England. A unique strength of our study was the large sample size across a wide range of areas in the UK.

We found that there were great variations in risk factors between the different areas. Overall, 65.7% of the study population had at least one high-risk factor for CLD, while only 7.4% were low risk across all three risk categories. This finding could explain the increasing numbers of people with liver disease across the UK.

While participants with higher alcohol, diet and viral hepatitis risk were more likely to be concerned regarding liver damage compared with those at low risk, diabetics were not more likely to be concerned compared with non-diabetics. This highlights a lack of awareness of the association between diabetes and liver disease, emphasising the need for routine screening and counselling regarding lifestyle choices for these high-risk individuals and those with metabolic syndrome and diabetes. We suggest a tailored approach to addressing this public health problem. By distributing these results and continuing our work with the BLT, we aim to raise public awareness of the importance of liver health, particularly targeting the areas identified to be most at risk. We have already worked with some of the local councils and hospitals to provide lifestyle workshops, gym memberships and diet advice, but we plan to continue to do so on a larger scale across the UK.

Liver stiffness

The proportion of participants with possible fibrosis using cut-offs of 7 kPa (16.2%) and 9.1 kPa (8.1%) was greater than that reported by previous studies with similar cut-offs,^{16 17} possibly due to self-selection bias. This may also be explained by the high proportion of participants aged 60+ (39.1%), since increasing age is a major risk factor for CLD¹⁸ and development of fibrosis.¹⁹

The main determinant of a high LSM was obesity. Lallukka *et al*²⁰ found liver fat content and waist circumference to be independent predictors of non-alcoholic fatty liver disease (NAFLD) and increased liver stiffness. Additionally, the severity of steatosis directly influences LSMs in NAFLD.²¹ Furthermore, males were significantly more likely to have a higher LSM than females. These results support those from a recent population-based study in Europe,²² which could be explained by the protective effect of female sex hormones on the progression of hepatic fibrosis.²³

After adjusting for BMI and other confounding variables, the association between diet risk and high LSMs was borderline significant. Although BMI and diet passed our collinearity checks, there was a high pairwise correlation between these two variables which may have caused this finding. While the mechanism by which unhealthy diets cause increased LSMs is likely to be through obesity, previous studies have found BMI-adjusted associations between NAFLD and lower-density lipoproteins,²⁴ increased processed meat consumption.²⁶

Increased alcohol consumption was not associated with higher LSMs in this study. This is surprising given that ALD is a major cause of cirrhosis and one of the most common indications for liver transplantation.²⁷ This finding is likely to be an anomaly due to the low sample size of participants with both high-risk alcohol consumption and an LSM \geq 7 kPa. This could also be explained by the low cut-off for high-risk alcohol use. Also, the self-reported and subjective nature of the questions related to alcohol use could have resulted in under-reporting of alcohol consumption.

Although TE is useful in diagnosing fibrosis in participants with ALD,²⁸ the effect of increased alcohol consumption on LSMs of healthy individuals remains unclear. In patients without ALD, Wong *et al*²⁹ found that increased alcohol consumption was not associated with higher LSMs. A recent UK-based population study by Abeysekera *et al*^{δ^0} also found no difference in odds of having fibrosis between patients with self-reported low or hazardous alcohol consumption. A significantly greater risk was, however, observed when participants were diagnosed with alcohol use disorder using the Diagnostic and Statistical Manual of Mental Disorders-5 criteria. This may suggest that more objective measurements and higher cut-offs are required to correctly classify these high-risk patients if we wish to assess their risk of developing fibrosis using TE.

Ultimately, this raises questions regarding the use of TE as a screening tool for fibrosis in individuals without established liver disease. Not only are there various cutoffs for different aetiologies, there is also variation in cutoffs proposed by different studies for the same aetiology.⁸ These cut-offs are derived from studies which are biopsy controlled and based on a population either at high risk or already diagnosed with CLD. Extrapolating these results to the general UK population would, therefore, lead to spectrum bias. Where the actual prevalence of fibrosis is likely to be smaller than that observed in this study, the positive predictive value of TE would be very low.

Several meta-analyses have confirmed that TE has much higher accuracy for diagnosis of cirrhosis compared with fibrosis.^{31–33} Additionally, it is better at ruling out than ruling in cirrhosis, with negative and positive predictive values of 96% and 74%, respectively.³⁴ A high LSM suggesting fibrosis may, therefore, be insufficient to inform clinical decision-making, so a histological sample by liver biopsy will still be required to confirm a diagnosis in these patients.

More studies are required to validate the use of noninvasive markers and TE by assessing longitudinal outcomes to determine whether these tools can be used in the clinical decision-making process without the need for invasive histological confirmation. Additionally, costeffectiveness studies are required to assess whether these screening tools are feasible and worthwhile on a large scale.

Socioeconomic status

IMD score was an independent predictor of obesity. Studies have found an association between deprivation and obesity in paediatric populations,^{35 36} though none have clearly explored this concept in adults. The trend we identified between deprivation and obesity is supported by results from the Health Survey for England 2018.³⁷ This may be explained by better education to increase physical activity levels, or being able to afford gym memberships to aid weight loss.

We found no association between deprivation and alcohol consumption or viral hepatitis risk. Despite participants from more deprived areas having similar levels of alcohol consumption, they may be subject to disproportionate alcohol-related harm compared with those from less-deprived areas.³⁸ This may be explained by the pattern of drinking whereby people with lower socioeconomic status may be more likely to binge, despite consuming a similar number of units of alcohol.³⁹⁴⁰ Additionally, lack of psychosocial support and poorer access to healthcare may play a role.⁴¹

Limitations

The biggest limitation of our study was with regards to missing confounding variables. Although we obtained information regarding ethnicity, diabetes and hypertension, these variables were lost during data exportation and were, therefore, missing for our main analysis. Additionally, we had data from only four areas in Scotland, two areas in Northern Ireland and we did not have any data for Wales. Lastly, each country uses a different deprivation scoring system, so it was not possible to directly compare them.

CONCLUSIONS

UK towns displayed noteworthy disparity in the prevalence of CLD risk factors, which was not fully explained

Open access

by levels of deprivation. Further studies are required to explain this disparity, accounting for societal factors and comorbidities, to inform resource allocation and policymaking. Overall, a large proportion of the screened population had risk factors for liver disease. New policies are required to address this, with the hope of reversing the increasing burden of CLD in the UK.

There is a continued need for large-scale population studies to assess the accuracy of TE and non-invasive markers as a screening tool for liver disease in general population settings. Additionally, cost-effectiveness analyses are required to assess whether these are feasible and worthwhile options for large-scale screening in the future.

Acknowledgements We would like to thank Jonathan Worsfold from the British Liver Trust for providing us with the data from their 'Love Your Liver' campaign. We would also like to thank all of the patients who participated in the study to help make this entire research project possible.

Collaborators Jonathan Worsfold from the British Liver Trust.

Contributors LA planned the study and helped with data collection. CA0 and RMC analysed the data. All authors contributed to writing and editing of the manuscript. The British Liver Trust collected data over the study period. LA is responsible for the overall content as guarantor.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information. This study uses deidentified participant data that were obtained via an anonymous, self-completed questionnaire. Data are available upon reasonable request.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.

ORCID iDs

Ceyhun Aksel Oztumer http://orcid.org/0000-0002-5353-3375 Rayhan Mehmood Chaudhry http://orcid.org/0000-0001-9721-8425 Laith Alrubaiy http://orcid.org/0000-0002-6340-8244

REFERENCES

- 1 Public Health England. Liver disease profiles: statistical commentary, February 2020. Available: https://www.gov.uk/government/ publications/liver-disease-profiles-february-2020-update/liverdisease-profiles-statistical-commentary-february-2020 [Accessed 13 April 2020].
- 2 Williams R, Aithal G, Alexander GJ, *et al*. Unacceptable failures: the final report of the Lancet Commission into liver disease in the UK. *Lancet* 2020;395:226–39.
- 3 Pimpin L, Cortez-Pinto H, Negro F, et al. Burden of liver disease in Europe: epidemiology and analysis of risk factors to identify prevention policies. J Hepatol 2018;69:718–35.
- 4 Public Health England. The 2nd atlas of variation in risk factors and healthcare for liver disease in England. Available: https://fingertips. phe.org.uk/profile/atlas-of-variation [Accessed 21 Apr 2020].
- 5 Pinzani M, Rombouts K, Colagrande S. Fibrosis in chronic liver diseases: diagnosis and management. *J Hepatol* 2005;42 Suppl:S22–36.
- 6 Singh S, Fujii LL, Murad MH, Hassan M, et al. Liver stiffness is associated with risk of decompensation, liver cancer, and death in

patients with chronic liver diseases: a systematic review and metaanalysis. *Clin Gastroenterol Hepatol* 2013;11:1573–84.

- 7 Wang J, Li J, Zhou Q, *et al.* Liver stiffness measurement predicted liver-related events and all-cause mortality: a systematic review and nonlinear dose-response meta-analysis. *Hepatol Commun* 2018;2:467–76.
- 8 European Association for Study of Liver, Asociacion Latinoamericana para el Estudio del Higado. EASL-ALEH clinical practice guidelines: non-invasive tests for evaluation of liver disease severity and prognosis. J Hepatol 2015;63:237–64.
- 9 Boursier J, Konate A, Guilluy M, et al. Learning curve and interobserver reproducibility evaluation of liver stiffness measurement by transient elastography. *Eur J Gastroenterol Hepatol* 2008;20:693–701.
- 10 Foster HME, Celis-Morales CA, Nicholl BI, et al. The effect of socioeconomic deprivation on the association between an extended measurement of unhealthy lifestyle factors and health outcomes: a prospective analysis of the UK Biobank cohort. *Lancet Public Health* 2018;3:e576–85.
- 11 British Liver Trust. Love your liver health screener. Available: https:// britishlivertrust.org.uk/information-and-support/liver-health-2/ love-your-liver/love-liver-health-screener/love-liver-health-screener/ [Accessed 2 May 2020].
- 12 National Statistics. English indices of deprivation 2019. Available: https://www.gov.uk/government/statistics/english-indices-ofdeprivation-2019 [Accessed 5 May 2020].
- 13 Scottish Government. Scottish index of multiple deprivation 2020. Available: https://www.gov.scot/collections/scottish-index-ofmultiple-deprivation-2020/ [Accessed 5 May 2020].
- 14 Northern Ireland Statistics and Research Agency. Northern Ireland multiple deprivation measure 2017 (NIMDM2017). Available: https://www.nisra.gov.uk/statistics/deprivation/northern-irelandmultiple-deprivation-measure-2017-nimdm2017 [Accessed 5 May 2020].
- 15 Echosens. FibroScan® recommendations. Available: https://www. echosens.com/en/fibroscan/recommendations [Accessed 29 Apr 2020].
- 16 Wong VW-S, Vergniol J, Wong GL-H, et al. Diagnosis of fibrosis and cirrhosis using liver stiffness measurement in nonalcoholic fatty liver disease. *Hepatology* 2010;51:454–62.
- 17 Serra-Burriel M, Graupera I, Torán P, et al. Transient elastography for screening of liver fibrosis: cost-effectiveness analysis from six prospective cohorts in Europe and Asia. J Hepatol 2019;71:1141–51.
- 18 Sheedfar F, Di Biase S, Koonen D, *et al*. Liver diseases and aging: friends or foes? *Aging Cell* 2013;12:950–4.
- 19 Iwaisako K, Brenner DA, Kisseleva T. What's new in liver fibrosis? the origin of myofibroblasts in liver fibrosis. J Gastroenterol Hepatol 2012;27 Suppl 2:65–8.
- 20 Lallukka S, Sädevirta S, Kallio MT, et al. Predictors of liver fat and stiffness in non-alcoholic fatty liver disease (NAFLD) - an 11-Year Prospective Study. Sci Rep 2017;7:14561.
- 21 Petta S, Maida M, Macaluso FS, et al. The severity of steatosis influences liver stiffness measurement in patients with nonalcoholic fatty liver disease. *Hepatology* 2015;62:1101–10.
- 22 Caballería L, Pera G, Arteaga I, et al. High prevalence of liver fibrosis among European adults with unknown liver disease: a populationbased study. *Clin Gastroenterol Hepatol* 2018;16:1138–45.
- 23 Lee C, Kim J, Jung Y. Potential therapeutic application of estrogen in gender disparity of nonalcoholic fatty liver disease/nonalcoholic steatohepatitis. *Cells* 2019;8:1259.
- 24 Sun D-Q, Wu S-J, Liu W-Y, et al. Association of low-density lipoprotein cholesterol within the normal range and NAFLD in the non-obese Chinese population: a cross-sectional and longitudinal study. BMJ Open 2016;6:e013781.
- 25 Zelber-Sagi S, Ivancovsky-Wajcman D, Fliss Isakov N, Isakov NF, et al. High red and processed meat consumption is associated with non-alcoholic fatty liver disease and insulin resistance. J Hepatol 2018;68:1239–46.
- 26 Noureddin M, Zelber-Sagi S, Wilkens LR, et al. Diet associations with nonalcoholic fatty liver disease in an ethnically diverse population: the Multiethnic cohort. *Hepatology* 2020;71:1940–52.
- 27 Marroni CA, Fleck AM, Fernandes SA, et al. Liver transplantation and alcoholic liver disease: history, controversies, and considerations. *World J Gastroenterol* 2018;24:2785–805.
- 28 Moreno C, Mueller S, Szabo G. Non-Invasive diagnosis and biomarkers in alcohol-related liver disease. J Hepatol 2019;70:273–83.
- 29 Wong VW-S, Chu WC-W, Wong GL-H, et al. Prevalence of nonalcoholic fatty liver disease and advanced fibrosis in Hong Kong Chinese: a population study using proton-magnetic resonance spectroscopy and transient elastography. *Gut* 2012;61:409–15.

<u>d</u>

- 30 Abeysekera KWM, Fernandes GS, Hammerton G, et al. Prevalence of steatosis and fibrosis in young adults in the UK: a populationbased study. Lancet Gastroenterol Hepatol 2020;5:295–305.
- 31 Friedrich-Rust M, Ong M-F, Martens S, et al. Performance of transient elastography for the staging of liver fibrosis: a metaanalysis. Gastroenterology 2008;134:960–74.
- 32 Stebbing J, Farouk L, Panos G, et al. A meta-analysis of transient elastography for the detection of hepatic fibrosis. J Clin Gastroenterol 2010;44:214–9.
- 33 Tsochatzis EA, Gurusamy KS, Ntaoula S, et al. Elastography for the diagnosis of severity of fibrosis in chronic liver disease: a metaanalysis of diagnostic accuracy. J Hepatol 2011;54:650–9.
- 34 Ganne-Carrié N, Ziol M, de Ledinghen V, et al. Accuracy of liver stiffness measurement for the diagnosis of cirrhosis in patients with chronic liver diseases. *Hepatology* 2006;44:1511–7.
- 35 White J, Rehkopf D, Mortensen LH. Trends in socioeconomic inequalities in body mass index, underweight and obesity among English children, 2007-2008 to 2011-2012. *PLoS One* 2016;11:e0147614.
- 36 Twaits A, Alwan NA. The association between area-based deprivation and change in body-mass index over time in primary

school children: a population-based cohort study in Hampshire, UK. *Int J Obes* 2020;44:628–36.

- 37 NHS Digitial. Health survey for England 2018: overweight and obesity in adults and children. Available: https://files.digital.nhs.uk/ 52/FD7E18/HSE18-Adult-Child-Obesity-rep.pdf [Accessed 26 Apr 2020].
- 38 Jones L, Bates G, McCoy E, et al. Relationship between alcoholattributable disease and socioeconomic status, and the role of alcohol consumption in this relationship: a systematic review and meta-analysis. BMC Public Health 2015;15:400.
- 39 Lewer D, Meier P, Beard E, et al. Unravelling the alcohol harm paradox: a population-based study of social gradients across very heavy drinking thresholds. BMC Public Health 2016;16:599.
- 40 Jefferis BJMH, Manor O, Power C. Social gradients in binge drinking and abstaining: trends in a cohort of British adults. *J Epidemiol Community Health* 2007;61:150–3.
- 41 Kontopantelis E, Mamas MA, van Marwijk H, et al. Chronic morbidity, deprivation and primary medical care spending in England in 2015-16: a cross-sectional spatial analysis. BMC Med 2018;16:19.