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the PrevAIL study

Population screening for early signs of alcohol-related liver disease in hazardous and harmful drinkers in Liverpool and Knowsley

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1. Summary

1.1. Background

Alcohol is linked to a wide array of negative health and social outcomes. However, the direct toxic effects on the liver account for around half of all mortality attributed to alcohol in England. In the UK, mortality from liver disease has increased fivefold between 1970 and 2007, whilst it declined in Europe (from 13.25 per 100,000 in 1970 to 8.01 in 2007). Liver disease often only manifests itself once the disease is advanced, heightening the risk of mortality. Since early liver damage is reversible, the early detection of liver problems provides the opportunity to intervene to reduce the risk of mortality from liver disease, as well as other consequences of alcohol misuse.

The Preventing Alcohol Harm in Liverpool and Knowsley (PrevAIL) project was funded by Liverpool Primary Care Trust (PCT) and commissioned by the Liverpool Health Inequalities Research Institute with the aim of estimating the prevalence of early stage liver disease and identifying optimal ways of engaging people with screening.

The aims of PrevAIL were to: estimate the prevalence of early stage liver disease by age, gender, social deprivation, and history of alcohol use, using conventional markers of alcohol use and the new diagnostic tests that detect fibrosis; estimate the prevalence of hazardous and harmful drinking with particular reference to differences in level of deprivation; and to assess the test as a way of identifying and engaging people with evidence of early alcoholic liver disease in order to inform a future randomised control trial of the effectiveness of augmenting a standard alcohol brief intervention with feedback on liver health.

1.2. Methods

Participants were recruited through four general practices in Liverpool and 13 workplaces (of the 37 approached) in Liverpool and Knowsley. Recruitment through health events organised by the PCT was piloted but were not successful. Participants meeting the inclusion criteria (36 to 55 years old, resident or working in Liverpool or Knowsley) and not being treated for liver disease were asked to complete an initial alcohol consumption screen to identify increasing risk and higher risk drinkers[i] and those who reported alcohol addiction. Following this, participants were eligible to take part in a clinical exam followed by the screen for fibrosis of the liver. This entailed the collection of clinical data (height, weight, waist circumference and blood pressure) and a 20ml blood sample (for conventional liver function tests, LFTs, and fibrosis markers).

In total, 6,439 GP patients were contacted, of whom 539 (8%) returned the alcohol consumption screening questionnaire by post. Of these, 152 (28%) screened positively for risky drinking and were invited for full exam; and 27 (17%) attended. Workplace events were conducted in private rooms, with both the alcohol consumption screen and the clinical exam carried out on the day of the event. Participation level was not possible to quantify for all organisations, but was estimated to be around 2-6%, with 363 persons attending in total. Of those screened for alcohol use, 142 screened positive for being an increasing or higher risk drinker and/or reported an alcohol addiction (40%) and 129 (91%) progressed to the clinical exam and blood tests.

[i] Increasing risk drinkers are defined as males drinking between 22 and 50 units per week and females drinking between 15 and 35 units per week (one unit equalling 8mg of pure alcohol). Higher risk drinkers are defined as males drinking over 50 units per week and females drinking over 35 units per week.

Conventional liver function biomarkers measured were: gammaglutamyl transferase, aspartate aminotransferase, alanine aminotransferase, alanine phosphatase, bilirubin, albumin, total protein. A full blood count (for platelet numbers) and the international normalised ratio were also measured. Three serum biomarkers of fibrosis were measured: hyaluronic acid (HA), tissue inhibitor of matrix metalloproteinase and procollagen type III N-terminal peptide (PIIINP). Using the Southampton Traffic Light (STL) system, the risk of fibrosis in participants was categorised according to the following criteria: HA >30ng/ml or a PIIINP>5.5µg/ml = score +1; HA >75ng/ml = score +2; platelet count <150*109/l = score +1. Zero scores equated to low risk of liver fibrosis and cirrhosis (green); +1 were intermediate (amber); ≥2 were high risk (red).

1.3. Results

In total, 962 individuals completed the alcohol consumption screening questionnaire. Of these, 46.8% were male, 93.5% described themselves as White British and 85.3% as employed or self-employed. Screened individuals most commonly resided in the most deprived Index of Multiple Deprivation quintile (36.4%). Of the individuals screened, 933 individuals drank alcohol at least occasionally and 862 provided full details of quantities consumed. In total, 79% of drinkers had consumed alcohol in the last week. Their mean alcohol consumption was 22.0 units (95% confidence intervals, CI: 20.0-24.0). A total of 302 individuals were identified as being eligible for the clinical examination, and 156 increasing risk/higher risk/addicted drinkers took part in the clinical exam. Once confounding factors[ii] had been accounted for, those who were identified through their workplace had a 73-fold higher odds of completing the full study compared with those identified via the GP who returned an alcohol screening questionnaire (95% confidence intervals, CI: 28.9-182.8). Seven were flagged as 'red' using the STL algorithm, yielding a prevalence of 4.6% (95%CI 2.02-9.14%) of probable liver disease among risky drinkers. A further 26.3% (20.0-33.7%; 41 individuals) were at 'moderate risk' of liver disease (scoring 'amber' on the STL). Being red-flagged by STL was independently predicted by obesity, with those in a 'high or very high' risk category for obesity having greater than three-fold odds of being red-flagged compared to the low risk category.

1.4. Conclusions

The prevalence estimates were broadly in line with similar community surveys. If the prevalence found in this study is representative of increasing risk drinkers in the study area, we would expect that around 1,100 Liverpool residents and 200 Knowsley residents could have undetected liver disease and the same number again could be showing earlier signs of the disease. Detecting and supporting these cases in the community could avert deaths and save considerable health and social costs. Those who were overweight or obese were more likely to show signs of liver damage, in line with the known multiplicative effect of alcohol and obesity, suggesting that it could be beneficial to address these two health concerns simultaneously. The feasibility of the screening depended on setting, with workplaces being more successful once access had been granted by the employer. The recommendations that arise from this study include:

- To develop a protocol for a randomised controlled trial (RCT) to determine whether feedback from liver disease screening impacts on drinking behaviour, and ultimately alcohol-related morbidity and mortality, for submission to the National Institute of Health Research (NIHR).

- To fully explore barriers to providing screening in GPs and workplaces through consultation with GPs and employers.

[ii] This included gender, age, occupation status, ethnicity, deprivation quintile, frequency of GP/GP nurse use in the last year, drinking classification.

- To use the findings from the in-depth questionnaire used in PrevAIL to inform the advice and support given alongside the test result, for example, by providing feedback about the range of other harms experienced by those drinking more than the recommended lower risk threshold.

- To develop clear and meaningful messages around alcohol, diet and weight in order to assist people making informed choices, and to ensure that these messages are part of the feedback about liver health that are provided after a liver function test is performed.

2. Introduction

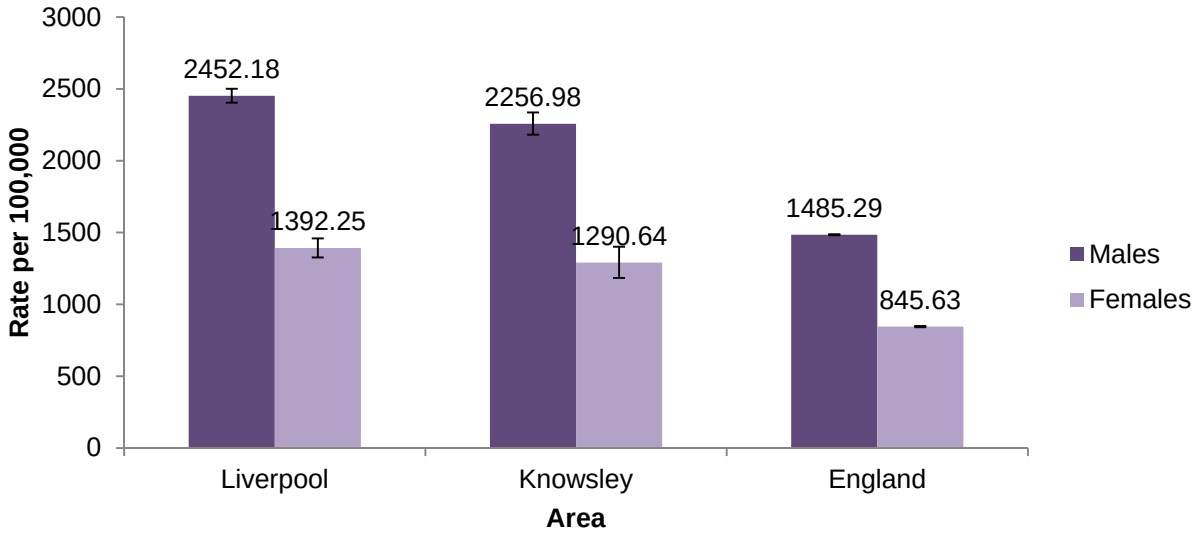
2.1. Context

The Department of Health estimated that alcohol misuse in England cost the National Health Service (NHS) £2.7bn in 2006/07 because of its involvement in hospital admissions, emergency department attendances and primary care usage.[1] Alcohol-related harms have continued to increase since then: for example, the rate of male alcohol-attributable hospital admission in England increased from 1,190 per 100,000 in 2006/07 to 1,485 in 20010/11.[2] Local authorities such as Liverpool and Knowsley, which experience high levels of deprivation,[3] are particularly negatively affected. Liverpool and Knowsley residents report two of the highest rates of alcohol-attributable hospital admission in England for both males and females (Figure 1).[2] As such, tackling alcohol harm has been identified as a key priority for Liverpool and Knowsley.[4-6] For example, Liverpool PCT aims to reduce alcohol specific hospital admissions by 5% between April 2011 and April 2014 based on their projected increase.[5] In order to achieve such targets, it is necessary to target those most at risk with appropriate and effective interventions using evidence-based information.

Although alcohol is linked to a wide array of negative health and social outcomes, its direct toxic effects on the liver account for around half of all mortality attributed to alcohol in England.[2] In the UK, mortality from liver disease increased fivefold between 1970 and 2007, whilst it declined in Europe (from 13.25 per 100,000 in 1970 to 8.01 in 2007).[7] However, liver disease often only manifest itself once disease is advanced, heightening the risk of mortality. Since early liver damage is reversible, the timely detection of liver problems provides the opportunity to intervene to reduce the risk of mortality from liver disease, as well as other consequences of alcohol misuse.

The Preventing Alcohol Harm in Liverpool and Knowsley (PrevAIL) project was funded by Liverpool Primary Care Trust (PCT) and commissioned by the Liverpool Health Inequalities Research Institute with the aim of detecting the prevalence of early stage liver disease and identifying optimal ways of engaging people with screening. Work is currently underway in southern England to increase early diagnosis of alcohol-related

Figure 1: Rate of alcohol-attributable hospital admission by geographical area by gender



Source: North West Public Health Observatory (2012).[2]

liver disease (funded by the National Institute of Health Research, NIHR, Sheron and Moore[8]), and this study incorporates some of its key principles and methodologies, with the ultimate aim of providing evidence to support an application for a multicentre trial on the effectiveness of screening in primary care. Since this project is based on a screening test for liver damage, this introduction first explores how alcohol harms the liver. This includes a consideration of the role of diet/obesity because both alcohol and diet/obesity cause similar physical damage to the liver and act together to increase the risk of liver damage.[9] We conclude this introduction by giving the full aims and objectives of the study.

2.2. Mechanisms of alcohol damage to the liver

Alcohol is rapidly absorbed in the gut and transported to the liver. All tissues and organs are exposed to alcohol via the bloodstream, but the liver is disproportionately exposed as it receives blood directly from the digestive tract.[10] In the liver, the active ingredient of alcohol, ethanol, is converted to acetaldehyde by alcohol dehydrogenase enzymes. Acetaldehyde is a highly toxic substance and in the healthy body it is converted by aldehyde dehydrogenase enzymes to harmless acetate. The liver is able to process about one unit of alcohol per hour, converting it into water, carbon dioxide and fatty acids. Alcohol absorption from the digestive tract into the bloodstream is much more rapid than the breakdown and removal of alcohol, and therefore if excess alcohol is consumed, it is transported to the rest of the organs.

As well as eliminating toxins such as alcohol, the liver performs many other vital functions. Pertinent to this discussion, it controls the levels of glucose and fats in the body. In fact, the liver and adipose (fatty) tissue interact to regulate fat homeostasis. Excess glucose is converted into fat for storage to be used when extra energy is required. The presence of obesity alongside excessive alcohol consumption can cause a synergistic effect, since excess carbohydrate consumption causes fat deposition in the liver, and alcohol ingestion in combination with a high fat diet leads to fat accumulation.[11] Obesity and alcohol together cause a greater risk of elevated liver enzymes,[5] risk of fibrosis,[12] and liver cancer[13] than either risk factor alone. The direct toxic effect of alcohol causes damage to cell membranes and stimulates the synthesis of collagen to form scar tissue.[14] Excess fat in the liver cells can also cause inflammation. The Midspan study (a Scottish cohort study) showed that, on its own, obesity in men led to only a relatively modest increase in risk for liver disease. However, in combination with alcohol use, a 'supra-additive' effect of obesity and alcohol was observed, with obese heavy drinking men being at over ten times the risk of liver disease death compared to those who were neither overweight nor drinking (Figure 2).[9] The UK Million Women Study similarly showed increasing rates of liver cirrhosis with increasing Body Mass Index (BMI) in women[iii], and yet higher rates in overweight women who drink more alcohol. The authors estimated that approximately 42% of cirrhosis in women can be attributed to alcohol consumption and 17% to having a BMI of greater or equal to 25.[17]

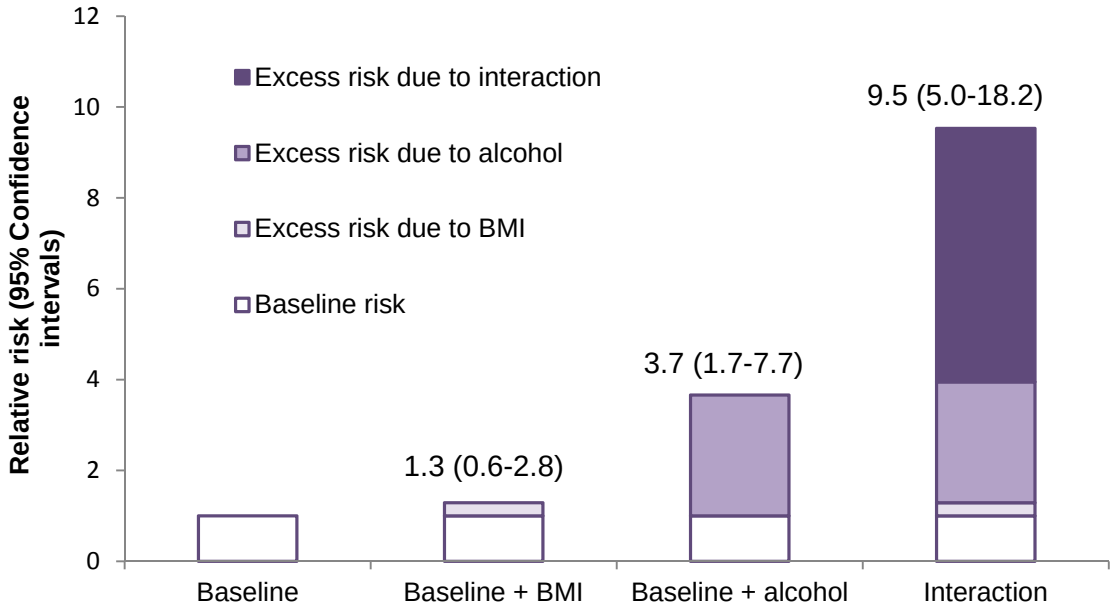
2.3. Natural history of alcohol related liver disease

The majority of harm associated with alcohol-related liver disease occurs in the relatively large number of people consuming more modest amounts of alcohol compared with the relatively small number of people drinking at very harmful levels.[18] Thus, whilst the risk of developing chronic alcohol-related conditions is highest in heavier drinkers, risk is elevated even for relatively low level drinkers.[19] This is illustrated by the fact that, in a survey of those hospitalised with alcoholic liver disease, only 9% of patients scored as 'severely'

[iii] BMI can be used to calculate the likelihood of an individual being underweight, overweight or obese. To calculate BMI, weight (kilograms) is divided by height (metres) squared. A BMI of less than 20 is classified as underweight, 25 to 30 as overweight and over 30 as obese.[9, 15] BMI does not account for muscularity and is not appropriate for some ethnic groups, young people or pregnant women.[16]

alcohol dependent, whereas 76% of those on an alcohol detoxification programme were classed as being severely dependent[iv].[20] Further, a robust meta-analysis showed that 25g of alcohol per day (equivalent to three units, the UK maximum recommended daily allowance for females) more than doubled the risk of developing liver cirrhosis compared with abstinence.[21]

Figure 2: The 'supra-additive' effect of alcohol and obesity on risk of liver disease mortality*



*Redrawn from: The Midspan Cohort Study, Hart et al. (2010)[9]

However, not all of those who drink are susceptible to liver disease.[22] While the majority (60-100%) of heavy drinkers develop fatty liver[23], only 10-35% develop liver damage,[24] and 8-20% develop cirrhosis.[25-27] Risk factors for progression to liver disease in heavy drinkers include genetic factors[24] and gender; females are more likely to progress to fibrosis or cirrhosis for a given level of alcohol intake.[23] At a population level, data from northwest England show that while rates of drinking are similar across social groups, populations in more deprived areas have significantly higher rates of alcohol-attributable hospital admissions.[28, 29] The formation of collagen to form scar tissue leads to fibrosis, which is a general scarring process caused by a number of liver diseases. At this stage, the damage to the liver is reversible. The basis of the screening tests used in PrevAIL is to detect these early changes using biochemical markers. If progressive damage occurs, fibrosis of the liver can lead to cirrhosis (after a long period of time, 10-50 years[30]). The consequences of cirrhosis include portal hypertension (complications of which comprise variceal haemorrhage, ascites and encephalopathy) and hepatocellular carcinoma (HCC; Box 1). Fibrosis is reversible upon cessation of the agent causing the liver disease, that is, in the case of alcoholic liver disease, this would entail abstinence from alcohol.[30] If liver damaged is detected only at the point when complications occur (Box 1), treatment options are limited. Liver transplantation policies often require six months of abstinence from alcohol to be demonstrated; there is a high risk of mortality during this period.

[iv] Alcohol dependence was identified through the Severity of Alcohol Dependence Questionnaire (SADQ), which collates details on individuals' consumption of alcohol and experienced effects.[20] A score of 31 or more was used to indicate severe dependence.

2.4. Detection of liver damage

The accumulation of fat in the liver, whether due to obesity, alcohol or both, is symptomless. Similarly, there are no obvious symptoms of liver fibrosis. Subsequently many patients with liver disease only present to clinicians at an advanced stage. Abnormal liver function is often first detected during routine investigations using standard liver function tests (LFTs, Box 2). Some of the LFTs measure the liver's ability to perform its normal functions of producing protein and clearing bilirubin, a blood waste product.[31] Other LFTs assess if enzymes are present that liver cells release in response to damage or disease. However, conditions other than liver disease can lead to abnormal LFT results,[31-33] and conversely results can be normal in people who have liver disease or damage.[34] The diagnosis of alcohol-related liver damage is based on excluding other causes of liver disease and having a history of drinking[v].

Liver biopsy is considered to be the gold standard for assessing the extent of liver disease. However, it is invasive and can result in serious complications (in 0.13-0.5% of cases).[35, 36] In addition, sampling error is common and the biopsy specimens are not always reliable.[37] This combination of factors (inadequate screening and diagnosis tools for early stage disease, and the lack of symptoms for early disease) means that the majority of liver disease is discovered too late.[34]

There are a number of markers of the fibrosis process, including tissue inhibitor of matrix metalloproteinase-1 (TIMP-1),[38] hyaluronic acid (HA) and procollagen type III N-terminal peptide (PIIINP),[22] which have recently been identified as useful in detecting progression to fibrosis/cirrhosis in alcoholic liver disease. The accuracy of these is increased by combining results using one of several algorithms. Examples of algorithms used to predict liver disease include the Enhanced Liver Fibrosis (ELF) test[39] and the Simple Traffic Light (STL) algorithm,[34] both of which have been validated against biopsy specimens from patients with liver fibrosis due to several causes. Another non-invasive alternative is Fibroscan (transient elastography), which assesses liver stiffness.[40] Research has evaluated their diagnostic accuracy. Here, analyses measure the 'area under the receiver operator curve' (AUROC). Here, an area of 1.0 represents a perfect test, with 0.5 being

Box 1: Natural history of alcoholic liver disease:

Fibrosis➔cirrhosis (10-50 years)➔

- ➔ Hepatocellular carcinoma (HCC) (2-3% per year);[30]
- ➔ Liver failure (5-7% per year);[30]
- ➔ Portal hypertension (variceal bleed – 12% per year);[30] and/or
- ➔ The case fatality rate of cirrhosis is 34% within a year of initial hospitalisation.[41]

Box 2: Standard liver function tests

Measures ability to perform normal functions:

- Albumin
- Total protein
- Total bilirubin

Measures enzymes released during liver damage:

- Alanine transaminase (ALT)
- Aspartate transaminase (AST)
- Alkaline phosphatise (ALP)
- Gamma glutamyl transpeptidase (GGT)

[v] The viral causes of hepatitis (e.g. hepatitis B and C) are excluded using antibody tests. In the absence of a history of drinking, because there is no observable difference in the damage to the liver caused by alcohol and that caused by diet, the damage would be attributed to diet.

diagnostically worthless and 0.9 or more being 'excellent'. Alternatives to biopsy generally fall within the range of 0.76-0.88,[42, 43] and are thus generally considered 'fair to good', leading to a reluctance to use them in primary care.[43] However, the accuracy of the biopsy itself negatively impacts on the AUROC: if a biopsy has only 80-90% specificity and sensitivity, then even a perfect alternative test would be expected to yield a fair AUROC of 0.70-0.76.[43] Given the disadvantages of comparing test performances against an imperfect 'gold standard', long-term prospective studies of markers against clinical gold standards, such as the development of end-stage liver disease are needed to assess the best markers of liver disease. Sheron et al.'s prospective study found that non-invasive markers were highly predictive of mortality and complications with varices and ascites.[34] Their study demonstrates the development of the STL (HA, PIINP and platelet counts combined using a simple algorithm), which categorises results as 'red' (a high probability of significant underlying liver disease, and the possibility of cirrhosis), 'amber' (a 50% risk of liver fibrosis) or 'green' (no sign yet of significant damage). They followed up 641 patients with suspected liver disease for an average of 3.4 years, during which time, 16% of those coded red and 3.4% of amber coded patients died from liver disease. There were no deaths among individuals categorised as green.[34]

2.5. Detection of liver disease in primary care and the community

The development of knowledge about the exact mechanisms of liver damage has led to the identification of potential biomarkers for liver damage. These serum markers of fibrosis have greater accuracy for detecting fibrosis or cirrhosis at an early stage compared to routine liver function tests.[44] This offers the opportunity for detection in primary rather than secondary care. However, to date, only a small number of studies have evaluated the detection of liver disease in community settings. A study of 7,463 individuals recruited through a community screening programme in France (using a combination of biomarkers known as the FibroTest) found a prevalence of 1.5% for confirmed fibrosis up to 3% for presumed fibrosis in all persons (i.e. regardless of drinking status).[45] The Alcohol and Liver Disease Detection Study (ALDDeS) used the STL algorithm on a community sample of 10,000 individuals recruited through general practice in Southampton.[46] Those who were drinking at risky levels were offered the screening test for liver damage. Of those who took part, 9.6% were flagged as red (high risk) and 41% amber (intermediate risk).

2.6. Rationale for the study

Liver disease has previously proved difficult to detect at an early stage. Newer diagnostic tests now make early detection possible, but as yet they are rarely used in community or primary care settings. Because both settings offer valuable opportunities for the use of such a diagnostic tool, this study explores the feasibility of rolling out a diagnostic test in primary care and the community. Primary care, in particular, could be an ideal setting in which to manage cases of suspected early liver damage and is included as a recruitment route for this study. This is because the recommended treatment in most cases would be a lifestyle intervention and 'a period of watchful waiting'.[34] Lifestyle interventions, in the form of alcohol brief interventions (BIs), are known to be effective in reducing drinking in risky drinkers:[47-49] BIs are estimated to cause one in eight risky drinkers to reduce their drinking to safe levels,[50] and are recommended for use in a variety of health, social, educational and criminal justice settings.[51] The only facilities required are a trained advisor and a private space, and a GP would be ideally placed to monitor patients and refer into secondary care, where appropriate. A liver test could augment the impact of BIs but the effectiveness of this would need to be tested against BI alone. However, there are problems with the implementation of such a test in primary care. Firstly, the incorporation of a diagnostic test would require clinically qualified personnel (for drawing blood samples) and appropriate facilities for preparation of samples. Secondly, health seeking behaviour and

participation in screening programmes is not equal across sectors of the community, with take-up varying by deprivation, gender and ethnicity.[52-54] Thus, access would not be universal.

Workplace programmes offer a promising setting to explore health in the community and will be included as a recruitment route for this study because a large proportion of people are in employment (71.8% of those aged 16-64 in England and Wales[55]), those who work spend a large amount of time in work and because employers could have a potentially large impact on staff motivation.[56] We anticipate that such a programme could be welcomed by workplaces as in a 2007 survey of Liverpool employers (n=302), 31.1% reported that alcohol consumed by their staff outside working hours negatively affected their company and 62.3% were already providing alcohol support to their employees in the form of advice, counselling and referral.[57] Previous studies have shown alcohol BIs to be moderately successful in the workplace.[58, 59] Further, evidence suggests that alcohol interventions introduced as part of general health and lifestyle screening in the workplace are feasible even when a blood sample is required.[60] Introducing alcohol as part of a general lifestyle intervention may be less stigmatising than focusing on alcohol alone and also means that other factors such as obesity, which is also a risk factor for liver disease (especially in combination with alcohol use[9, 17]), can be considered simultaneously. However, those most at risk of liver disease (those who are economically deprived and out of work[61]) would be missed by a workplace approach. As such, the community recruitment route will be boosted by recruitment through community health events. These are sessions where health initiatives are promoted with health professionals present and stands with health literature and visual aids addressing issues such as alcohol, smoking and diet. The events usually offer incentives for attending, for example child entertainment, sports activities and alternative therapies. These are therefore potentially useful occasions to engage with members of the public, who could be missed otherwise, on health issues.

The screening test selected for this study is the STL, because it uses commercially available biomarker tests and a simple algorithm designed for ease of use and interpretation in primary care. Moreover, STL is currently being evaluated in a primary care setting in a UK study, [62] the design of which was used to inform this study. As with any screening test, when moving from the higher risk secondary care setting to the general population, the prevalence of the targeted health condition is likely to be markedly lower, and this affects the positive predictive value (PPV) of the test. Sheron et al.[34] modelled the performance of the STL under a range of prevalence assumptions. The PPV of a 'red' grading could be as low as 30% in a low prevalence community sample (if the true prevalence was as low as 8% fibrosis), and 12% for an amber grade. However, the negative predictive value of a green grading was high (98%). Usually, a low PPV for a screening test would pose an ethical issue of unnecessary treatment for a condition or unnecessary worry about a condition. However, in a population of risky drinkers, the treatment (in this case, an intervention to reduce drinking) remains necessary given the range of harms attributed to alcohol[63] and the continued future liver damage.

The main co-factors that need to be considered in this study are metabolic syndrome and obesity. As well as being a cause of liver disease,[9] obesity is also a possible consequence of over consumption of alcohol because of its calorific content and effects on appetite.[64] Providing interventions that could help to tackle both health concerns simultaneously may be more cost effective and of greater interest to both participants and gatekeepers (such as workplaces and GPs). Metabolic syndrome is the combination of physiological conditions (of which obesity is a central indicator) that are precursors of cardiovascular disease and diabetes, and is a co-factor in mortality and morbidity from chronic liver disease.[65, 66] Thus, the study also aimed to collect data on obesity and metabolic syndrome. We also sought to further understand a range of alcohol-

related consequences in order to inform future interventions, since liver damage is just one of many health and social harms caused by alcohol.[63, 64, 67, 68] In a qualitative arm of the ALDDeS study, interviews with participants highlighted that some may have misunderstood the green STL results as an opportunity to maintain risky consumption levels.[69] Developing a further understanding of the wider alcohol-related harms may assist in the design of interventions that mitigate against possible misunderstanding of 'green' result in liver tests.

2.7. Aims and objectives of the project

The aims of the project are to:

- Identify levels of alcohol-related harm amongst persons aged 36 to 55 years resident in Liverpool and Knowsley, local authority areas that suffer from significantly higher levels of alcohol-attributable hospital admissions than nationally;
- Generate indicators which can be used for planning targeted interventions in order to reduce levels of alcohol misuse in Liverpool and Knowsley; and
- Inform a future randomised trial to test whether feedback on liver health can enhance the success of a brief intervention.

These will be achieved through the following objectives:

- To estimate the prevalence of early stage liver disease by age, gender, deprivation, and history of alcohol use, using conventional markers of alcohol use and the new diagnostic tests that detect fibrosis;
- To determine the clinical, demographic, and economic parameters associated with liver disease and alcohol abuse in Liverpool and Knowsley;
- To estimate the prevalence of hazardous and harmful drinking with particular reference to differences in level of deprivation;
- To facilitate the timely identification of persons drinking above recommended weekly limits[vi] who are at risk of alcohol-related liver disease;
- To identify the optimal methods for identifying and engaging with people with evidence of early alcoholic liver disease; and
- To provide Liverpool and Knowsley PCTs with tools and strategies to help protect against the consequences of alcohol misuse.

vi Consuming more than 14 units for females, more than 21 units for males (one unit equalling 8mg of pure alcohol).

3. Methods

3.1. Sampling strategy

3.1.1. Rationale

The sampling strategy for PrevAIL was designed to take a wide population approach to detecting alcohol harm for a number of reasons:

- The number of harmful drinkers in a population is closely associated with the mean level of drinking in that population.[70]
- The majority of harm occurs in the relatively large number of people consuming more modest amounts of alcohol compared with the relatively small number of people drinking at very harmful levels.[18]
- Those affected by chronic harm are getting younger: the most common age category for hospital admission for alcoholic liver disease has dropped from 55-64 years to 45-54 years (from 1989/90 to 2002/03).[21]
- Hospitals have previously been recommended as suitable settings for alcohol screening, but only 33% of a sample of 94 people who had been admitted to a hospital in southern England with alcohol-related liver damage were found to have previously been admitted to hospital for an alcohol-related episode.[71] Thus, screening in primary care might be more effective to detect those with early signs of alcohol damage.
- A large sample size was required in order to identify individuals with liver damage. For example, in a pilot screening programme in France, in 7,463 patients aged 40 years or over with no liver disease history, a FibroTest suggested fibrosis in 209 (2.8%, 95% CI 2.4%-3.2%) and presumed cirrhosis in 25 (0.3%; 95% CI 0.2%-0.5%).[45]

3.1.2. Sample size calculations

The required sample size was calculated as follows. The original intention was to select three general practices within each of three deprivation strata and to randomly select a sample of 600 persons from each practice with whom to offer a consultation. As per the NIHR established protocol being followed in southern England,[8] we assumed that 50% of 5,400 invited would take part (2,700), 30% of whom would drink above recommended weekly levels[2] and would be offered a blood test (810), 80% of whom would accept (648) providing ~100 per gender/deprivation subgroup. GPs were to be selected until the sample size was achieved in each subcategory. It was anticipated that up to 30% of heavy (harmful/dependent) drinkers would have evidence of fibrosis.[8, 72] The prevalence of liver damage among those drinking just above the recommended levels is unknown. We assume that up to 10% of all those drinking at this level could show signs of damage. Sample sizes of 100 per subcategory will be sufficient to estimate prevalence with a 6% margin of error and a 95% confidence interval (if prevalence is lower, say 1%, then the sample of 100 will be sufficient to produce an estimate with 2% error).

3.2. Screening

Screening was targeted towards those aged 36 to 55 years old and resident or working in Liverpool or Knowsley. The age range encapsulates the age group with the highest rate of liver disease mortality (45-54 years) as well as the younger age group, where the greatest percentage increase in alcoholic liver disease

mortality has been recorded.[21] Participants were screened initially for alcohol consumption (to identify those drinking above the recommended weekly limits[vii]), and recruitment into the study and then subsequently received a liver screen for full participation in the study. At each point, participants were provided with written (and where possible verbal) information, given the opportunity to ask questions and made aware of their right to withdraw from the project. Copies of the questionnaires can be found in the appendices. Here, the alcohol consumption screening questionnaire and the liver screen are referred to as Phase One and Phase Two respectively (for ease of understanding for the participants).

- ALCOHOL CONSUMPTION SCREEN: Participants completed an initial questionnaire exploring their alcohol consumption in the week prior to the survey in the form of a drinks diary (investigating quantities, types and frequency consumed), and their responses to questions based on the Alcohol Use Disorders Identification Test-C (AUDIT-C)[viii]. We used the drinks diary in order to accurately identify individuals drinking alcohol at levels which were above the recommended limits and we hypothesised that a drinks diary would be a more accurate way of doing this than AUDIT-C. However, in order to provide a comparison between the two measures and to assess which was best suited to the clinical and workplace environment, AUDIT-C was incorporated into the questionnaire. Demographic information collected included gender, ethnicity, age, postcode and employment status. Participants were also asked for details of how often they visited their GP or GP nurse (to ascertain whether a different population group were being reached through the different recruitment methods, see below) and whether they had any of a specified list of health issues (Hepatitis B or C, liver disease or cirrhosis and diabetes, for the purposes of interpreting the blood test results). Non-drinkers were asked the reasons for their non-consumption (including whether they had/have an addiction). Those who reported consuming more than the recommended weekly limits or who reported an addiction were eligible for the liver screen.

- LIVER SCREEN: Participants were asked to complete a second questionnaire (henceforth referred to as the risky drinkers' questionnaire), which asked for details of alcohol-related experiences in the last month (positive and negative)[ix] and use of illicit substances in the previous year. The risky drinkers' questionnaire also incorporated the Severity for Alcohol Dependence Questionnaire (SADQ). This asked participants to recall: frequency of effects of drinking in the last six months in a typical period of heavy drinking[x]; frequency of consuming large quantities of alcohol (such as one bottle of spirits per day); and whether (after stopping drinking for a couple of weeks and then binging) participants had experienced physical effects the next day[xi].[74] In addition, the liver screen

[vii] Consuming more than 14 units for females, more than 21 units for males (one unit equalling 8mg of pure alcohol).

[viii] The AUDIT was developed by the World Health Organization to screen for risky drinking and alcohol use disorders[73]. It consists of 10 self-report items measuring three aspects of drinking behaviour: drinking quantity and frequency; dependence; and adverse consequences.

[ix] This included the following activities after drinking: oversleeping; injuring themselves or others; visiting a GP or a nurse; driving a car; having sex that they regretted; operating heavy machinery; sleeping poorly; avoiding a boss, teacher or tutor; arguing with friends or family; arguing with a stranger; feeling tired or lethargic the next day; slept better; felt confident; relaxed; stayed out later than intended; and other such experiences.

[x] Including waking up feeling sweaty, shaky hands first thing in the morning, waking up drenched in sweat, dreading waking up, being frightened of meeting people first thing in the morning, feeling at the edge of despair when waking, liking to have a morning drink, always gulping down a morning drink as soon as possible, drinking in the morning to get rid of the shakes, having a very strong craving for a drink when waking. Where participants were unable to recall a particularly heavy period of drinking that involved such events (n=52), these participants were coded as never experiencing any of effects listed.

[xi] Included: starting to sweat, shaky hands, a shaky body, and craving a drink. In total, 129 participants had not experienced such a drinking pattern, and so these individuals were coded as never having experienced any of the effects listed.

included the collection of clinical data (height, weight, waist circumference and blood pressure) and a 20ml blood sample (see Section 3.3.4).

At each stage, participants received relevant information sheets and written details of their results. If they were identified as drinking over the recommended limits, as well as being invited to participate in the liver screen, they were also advised of this in writing, and where possible verbally. All participants were provided with a leaflet on alcohol consumption as a form of brief intervention. Those participating in the liver screen were provided with individual feedback of their blood test results. Where possible, GPs were kept informed of any concerns identified through the blood tests.

3.3. Participant recruitment

Between March 2011 and April 2012, participants were recruited through three routes: GPs, local health events and local employers. Participants for all three routes followed the standard methodological procedure, with some variations where required (see below).

3.3.1. Recruitment through general practice

Liverpool Primary Care Trust (PCT) and Liverpool Community Health identified four potential GP practices in Liverpool to participate in the study. These GPs had been involved in research before and represented different populations in the city (one in the city centre, one in the north of the city, one in the south and one in a particularly deprived area close to the city centre). All four agreed to take part. Each practice identified approximately 1,000 patients who met the following criteria: were aged 36 to 55 years old, resident or working in Liverpool or Knowsley and were not knowingly being treated for liver disease[xii]. Research information packs[xiii] were despatched from each GP practice by a member of the research team. Each pack was individually coded and participants were asked to return questionnaires even if they had decided not to participate in order to monitor refusal rates.

3.3.2. Recruitment through workplaces

Medium to large workplaces (employing more than 400 persons) and/or locations with shared offices were identified through local business networks, health promotion agencies, the Chamber of Commerce, University business links and the research team[xiv]. Attempts were made to draw on a range of employers (including white collar professionals, manufacturing, public and private sector, local and multi-national companies). Once a workplace event had been confirmed, researchers and the participating organisation worked together to maximise attendance. The project was marketed as a free health check in return for taking part. Events were conducted in private rooms, with both alcohol consumption and liver screens conducted sequentially on the day of the event. As well as receiving feedback on their level of alcohol consumption, participants were also provided with feedback on their body mass index (BMI), waist circumference and blood pressure. A trained nurse offered appropriate advice and alcohol leaflets were offered to all participants. The events were promoted through posters, flyers, e-mails and internal newsletters. Depending on the workplace, researchers either provided a drop-in clinic or pre-arranged appointments. A dedicated e-mail address was publicised for those seeking further information and/or appointments. The provision of confidentiality was stressed to participants at all stages. The times and days

[xii] This was not an eligibility criteria for workplaces or health events.
[xiii] These contained: an introductory letter; an information sheet; a form to collect their contact details and those of their GP; alcohol consumption screening questionnaire, a consent form and a pre-paid envelope for questionnaire/refusal return. All documentation is in the technical appendices.
[xiv] Small businesses were not approached because of the resources that would be required to obtain a large sample size.

of the events were co-ordinated with the individual workplace (in some locations, appointments were available up until 7pm). All events were held on weekdays; no workplaces requested weekend events.

3.3.3. Recruitment through health events

Contacts in Liverpool PCT identified six health events across the city that the research team could attend between March and December 2011[xv]. It was not possible to collect blood samples at the events themselves because of a lack of facilities and a preference from the organisers (only the alcohol consumption screen was conducted at the events). It was intended that those requiring a liver screen would be invited to attend the University. Sixty participants agreed to take part in the alcohol consumption screen (an additional 88 were approached but either declined participation or did not meet the inclusion criteria). Nine participants were eligible for the liver screen, but none of the participants chose to participate any further.

3.3.4. Biochemical analysis

Blood samples were analysed by the Department of Pathology at Alder Hey Children's Foundation Trust. A range of conventional liver function biomarkers was used,[75] namely gammaglutamyl transferase (GGT)[76] aspartate aminotransferase (AST), alanine aminotransferase (ALT), alanine phosphatase (ALP),[77] bilirubin, albumin and total protein. In addition, a full blood count was carried out to determine platelet numbers since these are conventionally used to screen for alcohol excess.[78] The international normalised ratio (INR), effectively a measure of the liver's ability to produce factors required for blood clotting, was also determined for each participant who provided a blood sample. These biomarkers are collectively referred to as the standard liver function tests (LFTs) in this report.

It had originally been intended that fasting blood glucose, triglycerides and cholesterol would be measured in order to allow the possible presence of metabolic syndrome to be detected. This would account for the known relationship between metabolic syndrome and non-alcoholic fatty liver disease,[79] and the synergistic relationship between dietary risk and alcohol as risk factors for liver disease.[9] However, collecting a fasting blood sample proved difficult in the more ad hoc recruitment settings (that is, workplaces) and only 27 blood samples were fasting (17.5% of blood samples collected where fasting status was recorded[xvi]).Thus, while we are able to provide a risk score for liver disease, we cannot rule out non-alcoholic fatty liver disease as a cause. However, since all participants had drunk more than the recommended amount of alcohol in the last week, the advice to reduce drinking would be valid regardless of the cause of the liver disease.

Three serum biomarkers of fibrosis were measured. Hyaluronic acid (HA) was measured using an ELISA kit supplied by Elitech (formerly Corgenix); similarly, tissue inhibitor of matrix metalloproteinase (TIMP-1) was measured using an ELISA kit supplied by R&D Systems. In addition, subsamples were sent to the Department of Pathology at Southampton University Hospital Trust for analysis of procollagen type III N-terminal peptide (PIIINP) by a radioactive method using kits supplied by Orion.

[xv] This recruitment route was abandoned in January 2012 because of the low numbers of recruits it generated.
[xvi] Fasting status was not recorded for two people.

3.4. Ethical considerations

Appropriate approvals were gained from Liverpool John Moores University Ethics Committee, Liverpool PCT, and NHS Ethics (reference number: 10/H1013/65). In order to minimise risk to participants, a number of procedures were carried out:

- Only appropriately trained staff were involved in the fieldwork and only trained research nurses / phlebotomists drew the blood sample. All researchers gathering data from participants recruited via health events and GPs had NHS research passports from Liverpool PCT. Passports were not required when collecting data from workplaces. All researchers adhered to the same protocols.

- Each participant was allocated a unique identity number that was placed on every participant document and blood sample. The identity number, names and contact details were stored as electronic files on file servers accessible only to key researchers and password protected on secure networks. Paper files were stored in locked filing cabinets in a secure building. Study related data and samples were labelled solely with the unique identity code.

- The GP was known for participants who were recruited via their GP, but not for participants recruited through the workplace and health event setting. These participants were asked to provide their GP details so that their GP could be informed of the results. All participants were asked for written confirmation of whether the research team was allowed to inform their GP of their test results. Of the 156 participants who completed the liver screen, 135 (86.5%) confirmed that the research team could keep their GP informed of any test results and provided their GP's contact details. All participants were provided with an appropriate alternative source of advice and referral, in case they preferred not to speak to their GP or did not have one.

3.5. Data coding and statistical analysis

Data were cleaned and analysed using SPSS v.17. Where data were available (n=913), individual postcodes were assigned to deprivation quintiles based on Index of Multiple Deprivation (IMD) 2010 Scores. Chi-square and logistic regression techniques were used to explore relationships between variables. Where means have been provided, 95% confidence intervals are shown. ANOVA was used to explore significant differences between means. For medians, non-parametric independent sample tests tested for significance and interquartile ranges are shown.

3.5.1. Alcohol consumption screening questionnaire

Analysis from the alcohol consumption screening questionnaire aimed to i) measure levels of increasing risk and higher risk drinking (see below for definitions) in the Liverpool and Knowsley population, and ii) quantify differences in demographics (gender, age employment, ethnicity and deprivation) between recruitment routes (GP, health event or workplace). Differences in alcohol consumption according to demographics and recruitment route were also examined. Participants' drinks diaries were used to classify drinkers into the following categories:

- Those who had never consumed alcohol;
- Those who did not currently consume alcohol but had done so in the past;
- Lower risk drinkers: females who drank up to and including 14 units in the last week and males who drank up to and including 21 units (including those who drink but have not done so in the last week);

- Increasing risk drinkers: females who drank over 14 units and up to and including 35 units in the last week, and males who drank over 21 units and up to and including to 50 units in the last week; and
- Higher risk drinkers: females who drank over 35 units and males who drank over 50 units in the last week.

In total, eight participants did not provide details of their gender, hampering allocation of their drinking classification. However, for five of these individuals, their level of consumption was such that their classification was the same regardless of gender (for example, an individual drinking 25 units in the last week is an increasing risk drinker whether male or female). The questionnaire also incorporated AUDIT-C styled questions;[80] response options for the frequency questions were standardised allowing participants to select from: never, less than monthly, one or two times a month, weekly, two to four times a month, daily or almost (Table 1). In total, 938 participants completed all three AUDIT-C questions, and their answers were scored and totalled. Since the frequency options differed slightly from AUDIT-C, scores for each response option were allocated from the nearest equivalent option, as shown in Table 1. Females who scored three or more and males who scored four or more were categorised as risky drinkers, following cut points recommended by an authoritative review.[80] However, alternative cut points have also been proposed (females scoring ≥4, males scoring ≥5).[81] The suitability of both will be assessed. Where gender was unknown, participants were allocated categories where there was a crossover in definition (so all participants scoring over four were categorised as risky drinkers regardless of whether gender was known). AUDIT-C participant classifications were then compared with the classifications from the drinks diary (n=927).

Table 1: Scoring for AUDIT-C

Drinks diary questions	AUDIT-C questions	Score allocated
How often do you have a drink containing alcohol?		
Never	Never	0
Less than monthly	Monthly or less	1
1 or 2 times a month	2-4 times a month	2
Weekly	-	2
2 to 4 times a week	2-3 times a week	3
Daily or almost	4 or more times a week	4
How many standard drinks containing alcohol do you have on a typical drinking day?		
1-2	1-2	0
3-4	3-4	1
5-6	5-6	2
7-9	7-9	3
10 or more	10 or more	4
How often do you have six or more drinks on one occasion?		
Never	Never	0
Less than monthly	Less than monthly	1
1 or 2 times a month	Monthly	2
Weekly	Weekly	3
2 to 4 times a week	-	3
Daily or almost	Daily or almost	4

We had considered the longer version of AUDIT, which includes questions on both consumption and consequences of alcohol consumption (e.g. 'How often during the last year have you been unable to remember what happened the night before because you had been drinking?'; 'Have you or someone else been injured as a result of your drinking?'). We ruled this out for three reasons: i) the link between quantity of alcohol consumed and risk of liver disease justifies a consumption-only approach; ii) we assumed our target population would be predominantly risky habitual drinkers who would not necessarily trigger some of the consequences; and iii) women, in particular, can drink more than the recommended limits and not trigger a positive score on AUDIT.

3.5.2. Liver screen

Risky drinkers' questionnaire

The analysis of the risky drinkers' questionnaire aimed to explore the social harms of alcohol use, which may accompany physical damage to the liver (Section 2.2). Analysis focused on differences in experiences between demography (using gender, age and deprivation only; figures in the ethnicity and employment categories were too small for any meaningful analysis), drinking classification and recruitment route.

Analysis was divided into the following subsections:

- Positive experiences of alcohol in the last month (that is relaxing, feeling more confident, sleeping better and forgetting problems).
- Harms experienced after drinking in the last month. These were grouped into: impacts on health; impacts on relationships; impacts on sleep and tiredness; impacts on diet and weight; participation in risky behaviour; and other harms (Box 3). Analysis also looked at whether those who had experienced a particular group of harms were more likely to have reported other experiences. For example, whether those who reported sleeping better after drinking in the last month were also more likely to report experiencing at least one sleep or tiredness harm in the same month.
- Use of other substances such as paracetamol, aspirin, cigarettes and illicit drugs[xvii].
- Answers from the SADQ (Section 3.2) were scored and totalled.[74] The maximum score is 60. Using the classifications from the Adult Psychiatric Morbidity Survey, a score of four to 19 indicated mild dependence, 20 to 34 indicated moderate dependence and 35 or more indicated severe dependence.[82]

Clinical examination data

The heights and weights of participants were used to calculate BMI (Table 2). Waist circumferences were also recorded. Because of the limitations of using BMI or waist circumference independently as measures of obesity (for example, BMI does not account for adults who are highly muscular), the two were used in combination to categorise risk of health complications relating to obesity.[7, 83]

Participants' systolic and diastolic blood pressure was recorded. Those with a blood pressure of less than 90mm Hg systolic and/or less than 60mm Hg diastolic were classified as having low blood pressure.[84] Those with a systolic blood pressure of 140mm Hg or higher and/or a diastolic blood pressure of 90mmHg or higher were classified as having high blood pressure.[85]

[xvii] Participants were asked whether they had used: cigarettes; cannabis; LSD, magic mushrooms; speed / amphetamines; ecstasy; Ritalin (not for medical purposes); cocaine; crack cocaine; GHB; bytmain; glue, gas or solvents; ketamine; steroids; heroin; and/or methadone. 'Bytmain' is a fictional substance included in the questionnaire to check for validity.

Box 3: Definitions of harms groupings (harms that occurred to participants in the last month after drinking

- IMPACTS ON HEALTH: Injured themselves; visited a GP or nurse; and/or attended hospital.
- IMPACTS ON RELATIONSHIPS: Injured someone else; and/or argued with friends or family.
- IMPACTS ON SLEEP AND TIREDNESS: Overslept; slept poorly; and/or felt tired or lethargic the next day.
- IMPACTS ON WORK / EDUCATION: Avoided a boss, teacher or tutor; late for work, class or lectures; avoided colleagues the next day; missed work, class or lectures; not able to concentrate at work, lectures or class; went to work, class or lectures with a hangover; went to work, class or lectures drunk; and/or avoided customers or clients at work.
- IMPACTS ON WEIGHT, DIET: Ate a kebab, chips or pizza on a night out; drank sugary or caffeinated drinks the next day; and/or ate a fry-up or a bacon sandwich the next day.
- PARTICIPATED IN RISKY BEHAVIOUR: Drove a car; had regretted sex; operated heavy machinery; and/or had been involved in a fight.
- OTHER HARMS: Stayed out later than intended; felt guilty or remorseful; failed to do what was expected; had missed an appointment; and/or had been sick or vomited.

Table 2: Categories of risk of health complications relating to obesity[7, 83]

Body Mass Index classification	Waist circumference classification		
	Low Males ≤94cm; females ≤80cm	**High** Males 94-102cm; females 80-88cm	**Very high** Males >102cm; females >88cm
Underweight or normal BMI ≤ 24.9kg/m^2	No increased risk	No increased risk	Increased risk
Overweight BMI 25.0-29.9kg/m^2	No increased risk	Increased risk	High risk
Obese BMI ≥30kg/m^2	Increased risk	High risk	Very high risk

Biochemical data

Using the Southampton Traffic Light (STL) system, the risk of fibrosis in participants was categorised according to the following criteria: HA >30ng/ml or a PIIINP >5.5 µg/ml = score +1; HA >75ng/ml = score +2; platelet count <150*109/l = score +1.[34] Those with a score of zero were categorised as having a low risk of liver fibrosis and cirrhosis (or green), those with a score of +1 were categorised as intermediate risk (amber) and those with a score of ≥2 were categorised as high risk (red).

The blood test results were also combined into an Enhanced Liver Fibrosis (ELF) algorithm (ELF score = -7.412 +(ln(HA)*0.681) + (ln(P3NP)*0.775) + (ln(TIMP1)*0.494), with cut points of 0.3576 for severe fibrosis, and values between -0.1068—0.35759 indicating moderate fibrosis.[39] This has been validated against biopsy specimens from patients with liver fibrosis due to several causes.

Thus, the statistical analysis of the biochemical data examines the following:

- Mean results from the individual standard LFT tests by gender and drinking classification.

- Likelihood of receiving at least one abnormal LFT based on demographics (age, gender and deprivation)[xviii], recruitment route, alcohol consumption, and obesity risk (using chi square and logistic regression).
- Mean levels of fibrotic markers by gender and drinking classification.
- Likelihood of being at risk of liver fibrosis or cirrhosis (using the STL and ELF scores) based on demographics, recruitment route, alcohol consumption, and obesity risk (using chi square and logistic regression).

Reference ranges for the standard liver function tests were those derived by Alder Hey Children's Foundation Trust specifically for adults. Reference ranges for serum concentrations of the three fibrosis biomarkers were those supplied by the manufacturers of the diagnostic kits used. Table 3 details the individual reference ranges used.

Table 3: Reference ranges for liver function tests and fibrotic markers

Analyte	Reference range (units)
Albumin	35-55 g/l
Total protein	65-85 g/l
Total bilirubin	0-15 µmol/l
Alkaline phosphatase (ALP)	98-279 iu/l
Aspartate aminotransferase (AST)	1-37 iu/l
Alanine aminotransferase (ALT)	1-40 iu/l
Gammaglutamyl transferase (GGT)	11-50 iu/l
Platelet count	150-400 *109 cells/l
International normalised ratio (INR)	1.0
Hyaluronic acid (HA)	0-75 ng/ml
Procollagen type III N-terminal peptide (PIIINP)	0-5.5 µg/ml
Tissue inhibitor of matrix metalloproteinase (TIMP-1)	87-524 ng/ml

Note that Sheron et al [34] have interpreted serum HA concentrations >75 ng/ml as 'very elevated' and concentrations of >30 ng/ml as 'elevated'. The work reported here has used this interpretation to derive the Southampton Traffic Light (STL) score.

[xviii] Figures in the ethnicity and employment categories were too small to allow a meaningful analysis.

4. Findings

4.1. Recruitment

In total, 6,950 contacts were identified for screening, 962 completed the initial alcohol consumption screening questionnaire (13.8% of the identified contacts), 302 were risky drinkers who were thus eligible for the liver screen (31.3% of the initial group screened) and 156 underwent the liver screen (51.7% of those eligible; Table 4). None of the nine participants identified at health events as being eligible for the liver screening presented for a liver screen.

4.1.1. Recruitment from general practice

The GP recruitment route provided the highest number of contacts (n=6,439). However, once screened for alcohol consumption, only a small proportion of GP eligible participants presented for the liver screen (17.9%). Of the 6,439 persons contacted, 23 letters were returned due to an incorrect address, 493 agreed to take part, and 375 returned the form to decline participation (Table 5). Because recruitment rates were lower than expected (in a similar study in Southampton, 37% GP patients approached agreed to participate[46]), a second distribution was organised for two of the GPs for those who had not replied. An additional 1,632 letters were disseminated, recruiting 46 people to the alcohol consumption screening questionnaire. A second dissemination was not performed for the other two GPs because of the low numbers recruited. In total, GP recruitment provided a sample of 539 who underwent the alcohol consumption screen (by returning a postal questionnaire; 8.4% of the 6,439 patients identified). Where possible, those accepting the liver screen were offered an appointment at their GP practice. Where this was

Table 4: Recruitment pathways

	GP recruitment (n=4)	Workplaces (n=13)	Health events (n=6)	Total
Alcohol consumption screen				
Contacts identified	6,439	363	148	6,950
Participants screened for risky alcohol consumption	539	363	60	962
Number of refusals	394	0	88*	482
Participants with inadequate data for initial screen	3	0	0	3
Liver screen (risk drinkers' questionnaire, health check and blood samples)				
Participants eligible for liver screen	151	142	9	302
Participants who completed liver screen	27	129	0	156
Participants who dropped out of liver screen**	124	13	9	146

*For health events, this includes those who did not meet the inclusion criteria. **Reasons for drop out included not providing contact details in the alcohol consumption screen as part of the GP recruitment (n=14), not responding to an invite to the liver screen or choosing not to participate in the liver screen (n=121) or not being able to provide sufficient blood on the day due to venepuncture issues (n=12).

Table 5: PrevAIL recruitment from general practice for the alcohol consumption screen

	First dissemination (4 GPs)	Second dissemination (2 GPs)	Total
Letters distributed	6,439	1,632	8,071
Letters returned due to an incorrect address	23	8	31
Participants recruited	493	46	539
Participants who refused participation	374	20	394
Participants who did not reply	5,548	1,558	-

not possible, appointments were offered at a university building nearby. Appointments were available from 8.30am to 7.00pm on weekdays. Of the 539 participants who completed the alcohol consumption screen, 151 (28.0%) were eligible for the liver screen. Of these, 27 completed the liver screen (14 had not provided adequate contact details, 109 did not respond and one participant was not able to provide a blood sample on the day due to venepuncture issues).

4.1.2. Recruitment from workplaces

In total, 37 organisations were approached: 13 agreed to take part, 10 declined[xix] and 14 could not be pursued[xx]. Twenty-one workplace events were arranged between February 2011 and March 2012 (one was cancelled due to low take-up – here participants were recruited via post in the same way as in the GP recruitment setting, see Section 3.3.1). Not all companies were willing/able to supply a baseline number of people who met the age criteria but of those who did, participation in the alcohol consumption screen varied between 1.8% and 5.5% of the workforce aged 36 to 55. In comparison to recruitment via the GPs, the workplace events provided a much higher completion rate: 90.8% of individuals eligible for liver screening went on to take part (Table 4).

4.1.3. Recruitment from deprived areas

The project aimed to engage with the population of Liverpool and Knowsley as a whole but also to oversample from deprived groups. Of the four GPs involved, three had a particularly deprived patient demographic. The 36-55 year old age group represents 25.2% of the total Liverpool and Knowsley population and levels of deprivation in this group are similar to levels of deprivation in the population as a whole (Table 6). In total, 913 participants in the alcohol consumption screen provided their full postcode, allowing Index of Multiple Deprivation (IMD) 2010 scores to be allocated. Whilst these individuals most commonly resided in quintile five (36.4%), this skew was not enough to accurately reflect the deprivation base of this age group in Liverpool and Knowsley as a whole (54.9%). More deprived groups were significantly more likely to be reached through GP and health event recruitment strategies compared with workplaces (Table 7). However, individuals recruited through GPs and health events were significantly less likely to complete the liver screen (Table 4).

[xix] Reasons included: other similar projects occurring/had recently occurred, other business priorities, not being able to allow employees to be away from their desk, going into administration or having internal reviews, security issues, concerns over sensitive nature of the project and employees not meeting the age criteria.
[xx] Reasons included: no response, severe delays in responding, and difficulties in identifying an appropriate contact.

Table 6: Percentage of alcohol consumption screen participants by deprivation compared with deprivation levels in Knowsley and Liverpool as a whole*

Deprivation quintile	Alcohol consumption screen participants (36-55y)	Knowsley and Liverpool population 35-54y	Knowsley and Liverpool population All ages
1 (least deprived)	6.7	0.9	0.9
2	13.1	9.0	7.3
3	24.3	18.8	16.8
4	19.5	16.4	16.9
5 (most deprived)	36.4	54.9	57.6
Total number	913	131,963	523,722

*Chi square analysis shows a significant difference between alcohol consumption screen participants and the overall Knowsley and Liverpool population for comparable ages (35-54y; P<0.001) and all ages (P<0.001). Population data were supplied by the North West Public Health Observatory (now part of Public Health England).

Table 7: Percentage of alcohol consumption screen participants recruited to the study by recruitment route and deprivation*

Deprivation quintile**	GP recruitment (n=514)	Workplaces (331)	Health events (n=50)
1 & 2 (least deprived)	12.3	33.9	24.5**
3	26.6	21.6	
4	23.1	14.7	13.2
5 (most deprived)	38.0	29.7	62.3

*Participants (n=865) recruited through workplaces were significantly more likely to reside in quintiles 1 and 2 compared with the other routes (p<0.001). **Figures have been combined for quintiles 1 to 3 for health events due to low numbers.

4.2. Findings from the alcohol consumption screening questionnaire

4.2.1. Demographics

In total, 962 individuals completed the alcohol consumption screen; 46.8% were male, 93.5% described themselves as White British and 85.3% as employed or self-employed (Table 8). The age of those screened was evenly distributed across the target age group of 36 to 55 year olds. Whilst screened individuals most commonly resided in quintile five (36.4%), this was not enough to accurately reflect the deprivation base of Liverpool and Knowsley as a whole in the target age group (see Section 4.1). (Quintiles one and two, the least deprived quintiles, have been grouped for all subsequent analyses due to the low numbers present.)

Table 8: Demographic details of individuals screened for alcohol consumption (n=962*)

	Number	Percentage**
Gender (n=953)		
Male	446	46.8
Female	507	53.2
Age (n=950)		
36-40	215	22.6
41-45	242	25.5
46-50	249	26.2
51-55	244	25.7
Occupation status (n=946)		
Employed/self-employed	807	85.3
Other***	139	14.7
Ethnicity (n=951)		
White British	889	93.5
Other****	62	6.5
Deprivation quintile (n=913)		
1 (most affluent)	61	6.7
2	120	13.1
3	222	24.3
4	178	19.5
5 (most deprived)	332	36.4
Recruitment route (n=962)		
GP	539	56.0
Workplace	363	37.7
Health event	60	6.2

*Cells may not sum to 962 due to missing data. **Percentages may not sum to 100 due to rounding. ***Other occupation includes houseperson, student, other (undefined). ****Other ethnicity includes White European, White Irish, Mixed Race, Black / Black British, Asian / Asian British, Chinese / Chinese British and other (undefined).

4.2.2. Visits to primary care

The alcohol consumption screening questionnaire asked how often individuals had visited their GP or GP practice nurse in the last 12 months: 17.2% reported never doing so; 69.9% reported doing so less than monthly and 12.9% reported doing so at least monthly. There was no significant association with gender, age or ethnicity; however, those most likely to report visiting their GP/GP nurse at least monthly in the last year included:

- Individuals who were classified as being in the other occupation category (39.4% compared with 8.3% for employed or self-employed participants; $P<0.001$);
- Those residing in the most deprived quintile (17.7% for quintile five compared with 9.0% for quintiles one and two combined; $P<0.05$); and
- Those who were recruited through the health events (21.7% compared with 14.7% for GP recruits and 8.8% for workplace recruits; $P<0.05$).

4.2.3. Alcohol consumption

Of the initial alcohol consumption screens (n=962), 29 people (3.0%) reported never having consumed alcohol. Main reasons for non-consumption included not liking the taste or feeling (n=12); being worried about the health risks or having poor health (n=9); due to religious or faith reasons (n=10); and seeing others' bad experiences (n=8). Of those individuals who had reported that they had consumed alcohol at least once, 54 people (5.8% of drinkers) reported that they now never drank alcohol. Thus, in total, 879 people reported currently drinking alcohol. Subsequent consumption analyses are limited to this group. Of these, 65.0% reported drinking at least weekly and 41.7% at least twice a week. The likelihood of drinkers reporting that they consumed alcohol at least twice weekly was significantly associated with:

- Gender: 50.8% of drinking males reported drinking alcohol at least twice weekly compared with 33.3% of females (P<0.001);
- Ethnicity: 42.5% of White British drinkers reported drinking at least twice weekly compared with 26.7% of other ethnicities (P<0.05);
- Deprivation: likelihood of drinking at least twice weekly decreased with increased deprivation: 48.5% of drinkers residing in quintiles one and two reported drinking alcohol at least twice weekly compared with 36.8% of those in quintile five (the most deprived quintile; P<0.05); and
- Recruitment route: 48.7% of those recruited through the workplace reported drinking at least twice weekly compared with 39.1% of those recruited through their GP and 18.5% of those recruited through the health events (P<0.001).

There was no significant difference in drinking at least twice weekly by age or occupation. In total, 862 drinking participants reported the number of drinks they typically consumed on a drinking day. Those who consumed up to four drinks accounted for 66.0% of drinkers; 12.8% reported typically drinking more than six drinks on one drinking day. When asked how often they drank six or more drinks on one session (n=875), 40.2% did so at least monthly and 21.6% at least weekly.

4.2.4. Alcohol consumption in the last week

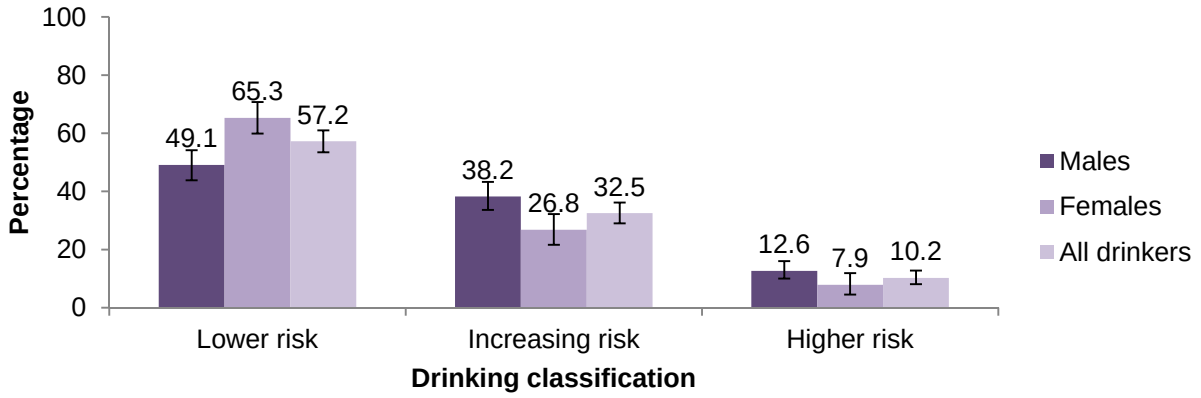
Seventy-nine per cent (78.7%; n=692) of drinkers had consumed alcohol in the last week. Consumption in the last week was significantly associated with gender (82.2% of drinking males compared with 75.9% of females; P<0.05); ethnicity (79.8% of White British drinkers compared with 62.2% of other ethnicities; P<0.01); and recruitment route (82.9% of workplace recruits compared with 76.4% of GP recruits and 72.2% of health event recruits; P<0.05). There was no significant difference associated with age, occupation or deprivation. Of those who had consumed alcohol in the last week and where full details of consumption were provided (n=688; 99.4% of last week drinkers), mean alcohol consumption was 22.0 units (95% confidence intervals, 95%CI: 20.0-24.0). Median alcohol consumption was 15.0 units (interquartile range, IQR: 4.6-25.4). Mean consumption amongst those who drank alcohol in the last week varied according to:

- Gender: mean last week consumption amongst males (28.9 units) was significantly greater than amongst females (15.3 units; P<0.001).
- Occupation: mean last week consumption was significantly higher among those classified as having an 'other' occupation (30.4 units), compared with those classified as employed or self-employed (21.0 units; P<0.01).

- Visits to primary care: mean last week consumption for those who visited primary care at least monthly (32.7 units) was significantly higher than those who never visited (21.5 units) or who visited less than monthly (20.5 units; P<0.01).

There was no significant difference in last week consumption for age, deprivation, ethnicity or recruitment source. Drinkers (n=683) were assigned classifications based on their consumption in the last week: lower risk, increasing risk and higher risk drinkers. Using the 95% confidence intervals to assess significance between groups, females (65.3%, 95%CI: 60.0-70.3%) were significantly more likely to be classified as lower risk drinkers than males (49.1%, 43.7-54.6%) and less likely to be classified as increasing risk drinkers (females: 26.8%, 95%CI: 22.2-31.8; males: 38.2%, 95%CI: 33.0-43.6%; Figure 3). There was no difference for higher risk drinkers (females: 7.9%, 95%CI: 5.3-11.2%; males: 12.6%; 95%CI: 9.3-16.7%; Figure 3).

Figure 3: Drinking classification of alcohol consumption screen participants who had consumed alcohol in the last week by gender*



*Drinking classification of last week drinkers (n=683) differed significantly by gender (Chi square, P<0.001).

4.2.5. Negative experiences of alcohol consumption

Drinkers (n=879) were asked whether they had encountered any of a number of negative experiences due to alcohol in the last year: being unable to stop drinking once they had started, failing to do what was expected, needing a drink in the morning after a heavy session, feeling guilty or remorseful about drinking and/or being unable to remember what had happened the night before. In total, 61.5% (n=519[xxi]) reported that none of these had occurred. Most commonly, drinkers reported feeling guilty or remorseful about drinking (24.5%) and experiencing memory loss (23.4%). There was no significant association with occupation, ethnicity, deprivation or recruitment source; however, having had at least once of these negative experiences in the last year was significantly associated with a number of factors:

- Gender: drinking males were significantly more likely to report at least one negative experience in the last year than females (43.3% compared with 33.9%; P<0.01);
- Age: likelihood of reporting at least one negative experience in the last year decreased with increased age (49.7% of 36-40 year olds compared with 28.8% of 51-55 year olds; P<0.001); and
- Drinking classification: increased levels of consumption were associated with a higher likelihood of reporting at least one negative experience in the last year (24.9% of lower risk drinkers compared with 82.4% of higher risk drinkers; P<0.001).

[xxi] Figures will not sum to 879 as 35 participants did not answer at least one of the negative experiences questions.

4.2.6. Identifying at risk drinkers through AUDIT-C

Using the cut point for risky drinking as recommended by an authoritative review (females scoring ≥3 and males scoring ≥4 being classified as at risk[80]), and of the total screened sample, AUDIT-C classified 672 individuals as being risky drinkers (see cut point definition 1, Table 9). If AUDIT-C had been used as a tool to differentiate drinkers, it would have provided an eligible screened population for the liver screen that would have been considerably higher than the number obtained through classifying participants using the drinks diary methodology that was used in this study (302 or 32.5% of 958 participants who completed the drinks diary). In total, AUDIT-C would have yielded an extra 385 individuals (after accounting for incomplete data and individuals missed by AUDIT). Those individuals who were highlighted as risky by AUDIT-C but not the drinks diary drank less frequently than those identified as risky by the drinks diary (38.7% typically drank less than weekly compared with 3.1%; P<0.001). They were also less likely to binge drink[xxii] regularly (10.6% reported typically binge drinking at least weekly compared with 49.8%; P<0.001). Thus, the recommended cut points appear too sensitive for use here. Exploring other validated cut points that have been used elsewhere to delineate dependence (females scoring ≥4, males scoring ≥5[81]), AUDIT-C classified 548 individuals as being at-risk (see cut point definition 2, Table 9). Again, those individuals who were highlighted as risky by AUDIT-C but not the drinks diary drank less frequently than those identified as risky by the drinks diary (38.1% typically drank less than weekly compared with 2.9%; P<0.001). They were also less likely to binge drink regularly (15.3% reported typically binge drinking at least weekly compared with 51.1%; P<0.001).

Table 9: Risk categorisation by AUDIT-C compared with the Drinks diary methodology

	AUDIT-C		Drinks diary (plus reports of addiction)
	Cut point definition 1	Cut point definition 2	
Incomplete data	20	20	4
Non-risky drinkers	270	394	656
Risky drinkers	672	548	302
Total	962	962	962

Cut point definition 1: Females scoring ≥3, males scoring ≥4. Cut point definition 2: Females scoring ≥4, males scoring ≥5.

4.3. Participation in liver screening

Of those initially screened with the alcohol consumption questionnaire, 958 provided sufficient alcohol consumption details to enable their eligibility for liver disease screening to be classified: 302 were identified as eligible, of which 156 underwent the liver disease screen. This section explores the differences between the participants who were eligible for the liver screen but did not complete it and participants who took part in liver screening. When comparing these groups, a number of differences are apparent. Those who underwent liver screening were significantly more likely to be employed or self-employed than be in the 'other occupation' category compared with those who did not complete the liver screen, they were significantly more likely to reside in the least deprived quintiles and they were significantly less likely to have been recruited through health events and GPs (Table 10). There was no association with gender, age or ethnicity. Those who did not complete the liver screen were significantly more likely to report that they had visited their GP/GP nurse at least monthly in the last year compared with those who completed the liver screen (19.9% compared with 9.0%; P<0.05; Figure 4).

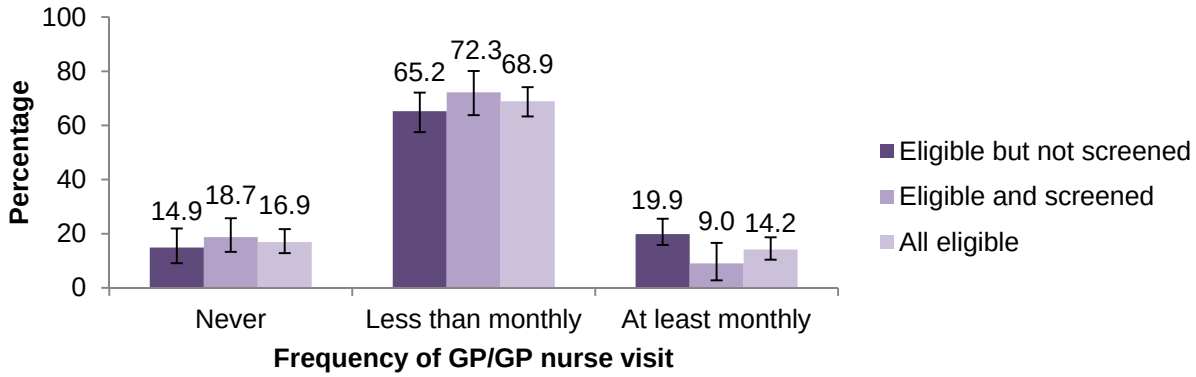
[xxii] Binge drinking here is defined as drinking six or more alcoholic drinks in one drinking session.

Table 10: Demographic details of participants eligible for the liver screen by completion status (n=302*)

	Eligible but not screened		Screened		All eligible persons		P
	N	%**	N	%**	N	%**	
Gender							
Male	81	56.3	97	62.2	178	59.3	NS
Female	63	43.8	59	37.8	122	40.7	
Age							
36-40	37	25.9	35	22.4	72	24.1	
41-45	43	30.1	44	28.2	87	29.1	NS
46-50	33	23.1	37	23.7	70	23.4	
51-55	30	21.0	40	25.6	70	23.4	
Occupation status							
Employed / self employed	111	77.6	147	94.8	258	86.6	<0.001
Other***	32	22.4	8	5.2	40	13.4	
Ethnicity							
White British	136	94.4	151	98.1	287	96.3	NS
Other****	*Data suppressed due to low numbers*				11	3.7	
Deprivation quintile							
1 & 2 (most affluent)	21	15.0	52	34.2	73	25.0	
3	30	21.4	40	26.3	70	24.0	P<0.001
4	26	18.6	23	15.1	49	16.8	
5 (most deprived)	63	45.0	37	24.3	100	34.2	
Recruitment route							
GP	124	84.9	27	17.3	151	50.0	
Workplace	13	8.9	129	82.7	142	47.0	P<0.001
Health event	9	6.2	0	0.0	9	3.0	

*Cells may not sum to 302 due to missing data. **Percentages may not sum to 100 due to rounding. ***Other occupation includes houseperson, student, other (undefined). ****Other ethnicity includes White European, White Irish, Mixed Race, Black / Black British, Asian / Asian British, Chinese / Chinese British and other (undefined). NS=not statistically significant.

Figure 4: Frequency of GP/GP nurse visits in the last year for participants eligible for the liver screen by completion status*



* There is a significant association between GP/GP nurse visits and completion status (Chi square analysis, n=296; P<0.05).

Individuals who were eligible but did not complete the liver screen reported alcohol consumption levels that were broadly similar to those reported by those who did complete the liver screen (both mean and median; Table 11). However, those who did not complete the liver screen were significantly more likely to have reported an addiction to alcohol (although numbers involved were small; P<0.05). Participants were asked whether they had encountered any of a number of negative experiences due to alcohol in the last year (being unable to stop drinking one they had started, failing to do what was expected, needing a drink in the morning after a heavy session, feeling guilty or remorseful about drinking and/or being unable to remember what had happened the night before). There was no significant difference between individuals who were eligible but did not complete the liver screen and those who were screened in their likelihood of experiencing at least one of these in the last year (Table 11). When the negative experiences were examined individually, those who did not complete the screen were significantly more likely to report needing a drink after a heavy session compared with those who did (14.1% compared with 5.3%; P<0.05); however, numbers were small. A logistic regression analysis was performed to assess the factors most likely to be related to non-completion of the liver screen (Table 12). Variables incorporated into the model included: gender, age, occupation status, ethnicity, deprivation quintile, drinking classification, recruitment route, and frequency of GP/GP nurse visits. Here, two factors were identified as having a significant relationship with liver screen completion: gender and recruitment route. Males had more than a twofold higher odds of completing the liver screen than females. Finally, those who were recruited through their workplace had a 73-fold higher odds of completion compared with those recruited through their GP.

Table 11: Alcohol consumption details for participants eligible for the liver screen by completion status

	Eligible but not screened (n=146)	Screened (n=156)	All eligible persons (n=302)	P
Mean alcohol consumption				
Mean	38.3	39.0	38.7	NS
95% confidence intervals	31.7-45.0	35.0-43.0	34.9-42.5	
Median alcohol consumption				
Median	28.0	32.5	30.0	NS
Interquartile range	10.0-46.0	8.5-56.5	8.0-52.0	
Drinking classification (%)				
Increasing risk	71.9	75.6	73.8	P<0.05
Higher risk	21.9	23.7	22.8	
Has an addiction*	6.2	0.6	3.3	
Negative alcohol-related experiences in the last year (%)	(n=132)	(n=152)	(n=284)	
At least one alcohol-related experience**	64.4	65.8	65.1	NS
	(n=135)	(n=152)	(n=287)	
Needing a drink the morning after a heavy session	14.1	5.3	9.4	P<0.05

*If a participant has reported an addiction, for the purposes of this analysis, they have been classified as such, regardless of the quantities of alcohol reportedly consumed in the last week. **Participants were asked whether they had encountered any of a number of negative experience due to alcohol in the last year: being unable to stop drinking one they had started, failing to do what was expected, needing a drink in the morning after a heavy session, feeling guilty or remorseful about drinking and/or being unable to remember what had happened the night before. NS=not significant.

Table 12: Factors associated with completion of the liver screen

Characteristic	Univariate analysis			Logistic regression			
	n	%	P	n	AOR	95% CI	P
Gender							
Male	178	54.5	NS	167	2.26	1.01-5.02	<0.05
Female	122	48.4		115	*Reference category*		
Age							
36-40	72	48.6		68	*Reference category*		
41-45	87	50.6	NS	83	0.95	0.34-2.59	NS
46-50	70	52.9		63	1.22	0.42-3.57	
51-55	70	57.1		68	1.66	0.59-4.66	
Occupation status							
Employed / self-employed	258	57.0	<0.001	246	0.46	0.22-1.98	NS
Other*	40	20.0		36	*Reference category*		
Ethnicity							
White British	287	52.6	NS	271	1.50	0.28-7.89	NS
Other**	11	27.3		11	*Reference category*		
Deprivation quintile							
1 & 2 (most affluent)	73	71.2		72	*Reference category*		
3	70	57.1	<0.001	70	0.95	0.31-2.91	NS
4	49	46.9		45	0.69	0.20-2.37	
5 (most deprived)	100	37.0		95	0.84	0.29-2.44	
Recruitment route							
GP	151	17.9	<0.001	142	*Reference category*		<0.001
Workplace	142	90.8		133	72.67	28.90-182.75	
Health event	9	0.0		7	0.00	0.00-0.00	
Frequency of GP/GP nurse use in last year							
Never	50	58.0	<0.05	47	*Reference category*		NS
Less than monthly	204	54.9		197	0.68	0.25-1.85	
At least monthly	42	33.3		38	0.37	0.09-1.59	
Drinking classification							
Increasing risk	223	52.9	NS	209	*Reference category*		NS
Higher risk or addicted	79	48.1		73	2.15	0.91-5.09	
Total	302***	51.7		282***			

*Other occupation includes houseperson, student, other (undefined). **Other ethnicity includes White European, White Irish, Mixed Race, Black / Black British, Asian / Asian British, Chinese / Chinese British and other (undefined). NS=not statistically significant. ***Univariate n may not sum to total due to missing values. ****n varies between univariate and logistic regression analysis as logistic regression only uses those cases where all data across all variables are present. AOR= Adjusted odds ratios. NS = Not significant.

4.4. Findings from the liver screen

4.4.1. Risky drinkers' questionnaire

As part of the liver screen, participants (n=156) were asked to complete a second, more detailed questionnaire about the effects of alcohol on their lives and use of illicit substances. This is referred to as risky drinkers' questionnaire.

Positive consequences of consumption

Liver screen completers reported a number of positive consequences after drinking in the last month:

- A large proportion (85.9%; n=134) reported that they had relaxed after drinking in the last month. Likelihood of relaxation was significantly associated with the 36-40 year old age group (97.1% compared with 73.0% of 46-50 year olds; P<0.05). There was no significant association with gender, deprivation, drinking classification (increasing or higher risk) or recruitment route[xxiii].
- Overall, 26.9% (n=42) reported that after drinking, they had forgotten their problems.
- Two fifths (21.8%; n=34) reported that after drinking they slept better.
- Finally, 41.7% (n=65) reported that they felt more confident after drinking.

For the latter three positive consequences examined, there was no significant association with demographics (age, gender, or deprivation), drinking classification or recruitment route.

Negative impacts on health

Participants were asked a number of questions to assess whether their alcohol consumption had impacted on their health in the last month: whether they had injured themselves, whether they had visited the doctor or nurse and whether they had attended hospital after drinking alcohol. In total, 10.9% (n=17) of liver screen completers reported at least one impact on their health in the last month. Higher risk drinkers and those who reported being addicted[xxiv] were significantly more likely to report at least one health impact than increasing risk drinkers (21.1% compared with 7.6%; P<0.05). There was no significant association between experience of such harms and demographic characteristics (gender, age or deprivation[xxv]) or route of recruitment. The most common type of health impact reported was visiting a doctor or a nurse (reported by 7.7% of liver screen completers; n=12).

Negative impacts on relationships

Participants were asked questions to assess whether their consumption had impacted on their relationships in the last month: whether they had injured someone else and whether they had argued with friends or family. None of the participants reported injuring someone else in the last month after drinking but 21.2% (n=33) had argued with friends or family at least once. There was no significant association between experience of such arguments and demographic characteristics (gender, age, or deprivation) or recruitment route. However, higher risk drinkers and those who reported being addicted were significantly more likely to report having an argument with friends or family at least once in the last month compared with increasing risk drinkers (34.2% compared with 16.9%; P<0.05). Of the 44 people who reported that after drinking, they

[xxiii] Figures in the ethnicity and employment categories were too small to allow a meaningful analysis.
[xxiv] Data for higher risk drinkers and those who reported being addicted were combined to avoid low numbers in the latter category.
[xxv] Figures in the ethnicity and employment categories were too small to allow a meaningful analysis.

had forgotten their problems at least once in the last month, 38.1% reported arguing with friends or family; this was significantly higher than the 15.0% who had not done so (P<0.01).

Negative impacts on sleep and tiredness

Participants were asked a number of questions to assess whether their consumption had impacted on their sleep and energy levels in the last month: whether they had overslept, whether they had slept poorly and whether they felt tired or lethargic the day after drinking. In total, 87.2% (n=136) felt that their alcohol consumption had impacted on their sleep and energy levels in a negative way. There was no significant association between experience of such harms and demographic characteristics (gender, age or deprivation), recruitment route or drinking classification. The most common sleep issue reported was feeling tired or lethargic the next day (83.3%; n=130), followed by sleeping poorly (55.8%; n=87), followed by oversleeping (25.0%; n=39). Of the 34 people who reported sleeping better in the last month after drinking (see Section 3.3.1), 88.2% (n=30) also reported at least one negative impact on their sleep. Further, of the 44 people who reported that after drinking, they had forgotten their problems in the last month, all reported experiencing at least one negative impact on sleep and tiredness; this was significantly higher than 83.2% who had not done so (P<0.01).

Negative impacts on work or education

Participants were asked a number of questions to assess whether their consumption had impacted on their work or education in the last month: whether they had avoided a boss, teacher, tutor; whether they had been late for work, class, or lectures; whether they had avoided colleagues the next day; whether they had avoided customers or clients at work; whether they had missed work, class, or lectures; whether they could not concentrate at work, lectures, or in class; whether they had been to work, lectures, or class with a hangover; and whether they had been in work, lectures, or class drunk. Of those who were involved in work or education (n=139), 30.2% (n=42) reported at least one impact on work or education. There was no significant association between experience of such harms and demographic characteristics (gender, age, or deprivation) or drinking classification. However, individuals recruited through their GPs were significantly more likely to report at least one work or education harm in the last month after drinking (52.9% compared with 27.0%; P<0.05[xxvi]). Attending work, lectures or class with a hangover was the most common impact reported in the last month (25.9%; n=36). Of the 44 people who reported that after drinking, they had forgotten their problems in the last month (see Section 3.3.1), 48.7% reported experiencing at least one negative impact on work or education; this was significantly higher than 23.0% who had not done so (P<0.01).

Negative impacts on weight and diet

Participants were asked a number of questions to assess whether their alcohol consumption had impacted on their diet in the last month: whether they had eaten a kebab, chips or pizza on a night out; whether they had drunk sugary or caffeinated drinks the next day; and whether they had eaten a fry-up or a bacon sandwich the next day. Overall, 86.5% (n=135) of participants reported at least one impact on their diet as a result of drinking in the last month. Such participants were significantly more likely to be male (92.8% compared with 76.3% for females; P<0.01) and be aged 36 to 45 years (for example, 94.3% of 36-40 year olds and 95.6% of 41-45 year olds compared with 67.5% of 51-55 year olds; P<0.001). There was no significant relationship with deprivation, drinking classification or route of recruitment. The most common impact on diet in the last month was eating a bacon sandwich or a fry-up the next morning (63.5%; n=99),

[xxvi] No individuals recruited from the health events completed the liver screen.

followed by drinking a sugary or caffeinated drink the next day (55.8%; n=87), followed by eating a kebab, pizza or chips on a night out (37.2%; n=58).

Participation in risky behaviour

Participants were asked a number of questions to assess whether their consumption had heightened their involvement in risky behaviour: whether they had driven a car, whether they had had sex that they regretted, whether they had operated heavy machinery and whether they had been involved in a fight in the last month after drinking. In total, 19.9% (n=31) reported at least one of these behaviours in the last month after drinking. There was no significant association between experience of such behaviours and demographic characteristics (gender, age or deprivation), or route of recruitment. However, higher risk drinkers and those who reported being addicted were significantly more likely to report participating in risky behaviour at least once in the last month compared with increasing risk drinkers (31.6% compared with 16.1%; P<0.05). The most common risky behaviour was driving a car after drinking (17.3%; n=27). Of the 65 people who reported feeling more confident after drinking in the last month (see above), 26.2% (n=17) also reported at least one risky behaviour. This was not significantly higher than those who had not felt more confident (15.7%; P=0.111).

Other harms

Participants were asked for details of other harms experienced after drinking alcohol in the last month:

- Nearly half (48.1%; n=75) of participants had stayed out later than intended. Of these, 29.3% (n=22) also reported arguing with friends or family at least once in the last month after drinking (significantly higher than those who had not stayed out later, 13.8%; P<0.05). These individuals were also significantly more likely to report experiencing an impact on their energy levels (97.3% compared with 78.8% of those who had not stayed out later than intended; P<0.001). In addition, of those who were involved in work or education (n=139), 40.9% reported staying out later as well as at least one negative impact on their work or education (significantly higher than those who had not stayed out later, 21.6%; P<0.05). Overall, staying out later than intended decreased significantly with age (68.6% of 36-40 year olds to 33.3% of 51-55 year olds; P<0.05). Finally those recruited through their GP were significantly more likely to report staying out later than intended (70.4% compared with 43.8% recruited through the workplace; P<0.05). There was no significant association with gender, deprivation or drinking classification.

- One quarter (25.0%; n=39) of participants reported that they had felt guilty or remorseful after drinking. Of these, 38.5% (n=15) also reported arguing with friends or family at least once in the last month after drinking (significantly higher than those who had not felt guilty or remorseful, 15.5%; P<0.01). These individuals were also significantly more likely to report an impact on their health in the last month after drinking (12.8% compared with 9.6% of those who had not felt guilty or remorseful; P<0.05). There was no significant association with demographic characteristics (gender, age or deprivation) or recruitment route. However, individuals who were higher risk drinkers or who had reported an addiction were significantly more likely to report feeling guilty or remorseful compared with increasing risk drinkers (35.1% compared with 22.0%; P<0.05).

- Finally, 10.9% (n=17) reported that they had failed to do what was expected of them after drinking at least once in the last month; 9.0% (n=14) of participants reported being sick or vomiting; and less than five reported missing an appointment.

Indicators of alcohol dependency

None of the 156 liver screen participants were classified as having a severe dependence on alcohol using the SADQ. Forty-two (26.9%) participants were classified as having a mild or moderate dependence[xxvii] and 114 (73.1%) as having no dependence. The likelihood of liver screen completers being classified as having a mild or moderate dependence was significantly associated with (Table 13):

- Deprivation: 40.5% of those residing in the most deprived quintile (quintile 5) and 47.8% of those residing in the fourth most deprived quintile (quintile 4) were classified as having a mild or moderate dependence compared with 13.5% of those residing in the least deprived quintiles (quintiles 1 and 2; P<0.01).
- Recruitment route: 55.6% of those who were recruited through their GP were classified as classified as having a mild or moderate dependence compared with 20.9% of those recruited through the workplace (P<0.001).
- Drinking classification: Those who were classified as higher risk drinkers or who had reported an addiction to alcohol were significantly more likely to be classified as having a mild or moderate dependence than increasing risk drinkers (47.4% compared with 20.3%; P<0.05).

There was no significant association with gender, age, or frequency of contact with primary care[xxviii]. A logistic regression analysis was performed to assess the factors most likely to be related to being classified as having a mild or moderate dependence (Table 13). Variables incorporated into the model included: gender, age, deprivation quintile, drinking classification, recruitment route, and frequency of GP/GP nurse visits. This confirmed the findings of the univariate analysis.

4.4.1. Clinical exam

Indicators of obesity

All 156 participants who completed their liver screen were measured for their height and weight. Their mean BMI was 27.1kg/m^2 (95%CI: 26.4-27.9), which sits within the criteria for overweight (see Section 3.5.2 for criteria).[83] Waist circumferences were available for 154 participants: the mean waist circumference for men was 95.9cm (95%CI: 93.9-98.0) and for women was 86.6cm (95%CI: 83.0-92.3), putting the average for both genders in the increased risk of obesity-related health complications category.[83] BMIs and waist circumferences were combined as described in Section 3.5.2 to provide an overall assessment of health risk relating to obesity (n=154). Overall, 22.1% (n=34) of participants were classified as being at increased risk of health complications relating to obesity, 17.5% (n=27) were at high risk and 13.6% (n=21) were at very high risk. Females were significantly more likely to be at high risk (22.0%) and very high risk (15.3%) compared with males (14.7% and 12.6% respectively); males were more likely to be at increased risk (30.5% compared with 8.5% for females; P<0.05). For the sample as a whole, there was a decreasing proportion of individuals in successively riskier obesity categories; however, for higher risk/addicted drinkers there appears to be a J-shaped relationship, whereby individuals are either have no obesity risk or high/very high risk: there are relatively few in the intermediate 'increasing risk' category (Figure 5). However, accompanying confidence intervals were wide. There was no significant association with age, deprivation[xxix], recruitment route or alcohol dependency.

[xxvii] Participants classified as having a mild or moderate dependence are discussed in unison due to low numbers.
[xxviii] Figures in the ethnicity and employment categories were too small to allow a meaningful analysis.
[xxix] Figures in the ethnicity and employment categories were too small to allow a meaningful analysis.

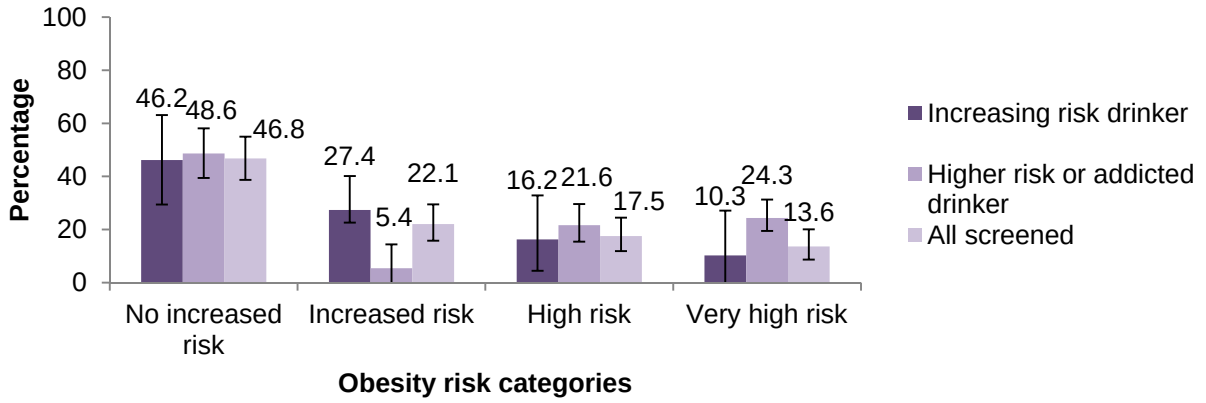
For those recruited in the workplace, obesity data were available for all participants (regardless of drinking status) because height, weight and waist circumference measurements were offered as part of a health check (which was used as an incentive in this settings). This provides an opportunity, in this workplace subsample, to compare the obesity characteristics of risky drinkers with low risk drinkers/abstainers. Thus. the data enable an assessment of whether those individuals who received the liver screen were significantly different from those who only completed the alcohol consumption screening tool in terms of obesity risk. Here, there was no significant difference in mean BMI (n=142 increasing/higher risk drinkers compared to n=351 abstainers/low risk drinkers), mean waist circumference (by gender, n=353 waist circumference measurements for abstainers/low risk drinkers) or level of health risk in relation to obesity according to study completion status (workplace recruits only).

Table 13: Factors associated with having a mild/moderate dependence on alcohol for individuals completing the liver screen

Characteristic	Univariate analysis			Logistic regression			
	n	%	P	n	AOR	95% CI	P
Gender							
Male	97	29.9	NS	93	1.51	0.61-3.74	NS
Female	59	22.0		58	*Reference category*		
Age							
36-40	35	40.0		34	*Reference category*		
41-45	44	22.7	NS	42			NS
46-50	37	27.0		36			
51-55	40	20.0		39			
Deprivation quintile							
1 & 2 (most affluent)	52	13.5		51	*Reference category*		
3	40	20.0	<0.01	40	0.90	0.25-3.23	<0.05
4	23	47.8		23	4.79	1.38-16.66	
5 (most deprived)	37	40.5		37	3.09	0.96-9.97	
Recruitment route							
GP	27	55.6	<0.001	27	3.94	1.39-11.21	<0.05
Workplace	129	20.9		124	*Reference category*		
Frequency of GP/GP nurse use in last year							
Never	29	13.8	NS	28	*Reference category*		NS
Less than monthly	112	28.6		109	2.81	0.74-10.72	
At least monthly	14	42.9		14	8.26	1.34-51.01	
Drinking classification							
Increasing risk	118	20.3	<0.01	115	*Reference category*		<0.05
Higher risk or addicted	38	47.4		36	2.80	1.11-7.04	
Total	156*	26.9%		151**			

Those scoring four to 34 using the Severity of Alcohol Dependence Questionnaire were classified as having a mild or moderate dependence on alcohol (no participants scored above 34, which would have been defined as severely dependent). *Univariate n may not sum to total due to missing values. **n varies between univariate and logistic regression analysis as logistic regression only uses those cases where all data across all variables are present. AOR= Adjusted odds ratios. NS = Not significant.

Figure 5: Percentage of drinkers completing the liver screen in each obesity risk category by drinking category *



*There is a significant association between obesity risk category and drinking category (Chi square analysis, n=154; P<0.05).

Blood pressure

In total, both systolic and diastolic blood pressure were taken from 151 liver screen completers. Of these, 31.1% (n=47) had high blood pressure and a small number (<5) had low blood pressure. Males were significantly more likely to have high blood pressure than females (39.6% compared with 16.4%; P<0.01). There was no significant association with age, deprivation, recruitment route, drinking classification[xxx] or alcohol dependency. As with indicators of obesity (see above), blood pressure measurements were also collected from all those workplace recruits regardless of alcohol consumption screen questionnaire results. Here, a total of 347 blood pressure measurements were recorded. For workplace recruits, there was no significant difference in likelihood of having a high blood pressure reading in relation to study completion status.

4.4.2. Liver function tests

Higher risk drinkers and those who reported an addiction to alcohol had received significantly higher levels of AST and GGT compared with increasing risk drinkers (AST 27.7 and 23.8iu/L respectively; P<0.05; GGT 51.1 and 35.9iu/L respectively; P<0.01; Table 14). For males, a significant difference was only found for GGT while for females, higher risk and addicted drinkers had significantly higher levels of ALT and AST compared with increasing risk drinkers (Table 15).

Of the 156 participants who completed the liver screen, 29.5% (n=46) had at least one abnormal liver function test (LFT) result (as defined by the reference ranges given in Section 3.5.2). The likelihood of individuals completing the liver screen having an abnormal LFT was significantly associated with:

- Gender: 39.2% of males had an abnormal LFT compared with 13.6% of females (P<0.001).
- Drinking classification: Those who were classified as higher risk drinkers or who had reported an addiction to alcohol were significantly more likely to have an abnormal LFT than increasing risk drinkers (44.7% compared with 24.6%; P<0.05).
- Overweight and obesity classifications: Whilst the relationship was not linear, the probability of having an abnormal LFT result was highest for those in the very high risk obesity risk category (Figure 6).

[xxx] Figures in the ethnicity and employment categories were too small to allow a meaningful analysis.

There was no significant association with age, deprivation, recruitment source, alcohol dependency, frequency of contact with primary care or high blood pressure.[xxxi] A logistic regression analysis was performed to assess the factors most likely to be independently related to receiving at least one abnormal LFT result (Table 14). Variables incorporated into the model included: gender, age, deprivation quintile, drinking classification, alcohol dependency, recruitment route, frequency of GP/GP nurse visits, obesity risk classification and blood pressure classification. Findings of this multivariate analysis confirmed the univariate analysis results, with gender, drinking classification and obesity risk classification remaining significant.

Table 14: Mean liver function test results by gender and drinking classification (95% confidence intervals)

	Albumin g/L	Protein g/L	Total bilirubin umol/L	ALP iu/L	ALT iu/L	AST iu/L	GGT iu/L
All							
Increasing risk (n=118)	44.5 (44.0-44.9)	72.7 (72.0-73.5)	11.4 (10.6-12.3)	174.3 (165.8-182.9)	27.9 (25.3-30.4)	23.8 (22.5-25.1)	35.9 (31.2-40.6)
Higher risk or addicted (n=38)	44.4 (43.8-45.0)	72.4 (71.2-73.7)	13.0 (10.9-15.2)	172.9 (156.3-189.4)	31.5 (26.8-36.2)	27.7* (22.5-33.0)	51.1** (38.2-63.9)
All (n=156)	44.4 (44.1-44.8)	72.7 (72.0-73.3)	11.8 (11.0-12.6)	174.0 (166.4-181.5)	28.8 (26.5-31.0)	24.8 (23.2-26.4)	39.6 (34.9-44.4)
Male							
Increasing risk (n=73)	45.0 (44.5-45.5)	73.6 (72.6-74.5)	12.4 (11.3-13.6)	177.0 (166.8-187.3)	32.2 (28.8-35.6)	25.9 (24.2-27.7)	41.0 (34.9-47.0)
Higher risk or addicted (n=24)	44.7 (43.9-45.5)	73.5 (72.1-74.9)	13.9 (10.9-16.8)	183.4 (161.8-205.0)	33.8 (27.5-40.1)	30.0 (21.9-38.2)	61.6** (42.9-80.3)
All (n=97)	44.9 (44.5-45.4)	73.6 (72.8-74.3)	12.8 (11.7-13.9)	178.6 (169.4-187.8)	32.6 (29.7-35.5)	26.9 (24.6-29.3)	46.1 (39.6-52.7)
Female							
Increasing risk (n=45)	43.6 (42.8-44.4)	71.3 (70.1-72.5)	9.8 (8.8-10.9)	170.0 (154.4-185.6)	20.8 (18.0-23.7)	20.4 (18.8-22.0)	27.8 (20.8-34.7)
Higher risk or addicted (n=14)	43.8 (42.8-44.8)	70.6 (68.5-72.8)	11.5 (8.3-14.8)	154.9 (128.8-181.0)	27.6* (20.3-34.8)	23.4* (20.5-27.1)	33.1 (22.5-43.7)
All (n=59)	43.6 (43.0-44.3)	71.1 (70.1-72.1)	10.2 (9.1-11.3)	166.4 (153.3-179.6)	22.4 (19.7-25.2)	21.2 (19.7-22.6)	29.0 (23.3-34.8)

ALP = Alkaline phosphatise. ALT = Alanine aminotransferase. AST = Asparate aminotransferase. ALP = Alkaline phosphatase. GGT = gammaglutamyl. T-tests were used to assess significance between increasing risk and higher risk drinkers (and those who reported an addiction). P values are shown as follows: * P<0.05; ** P<0.01; *** P<0.001.

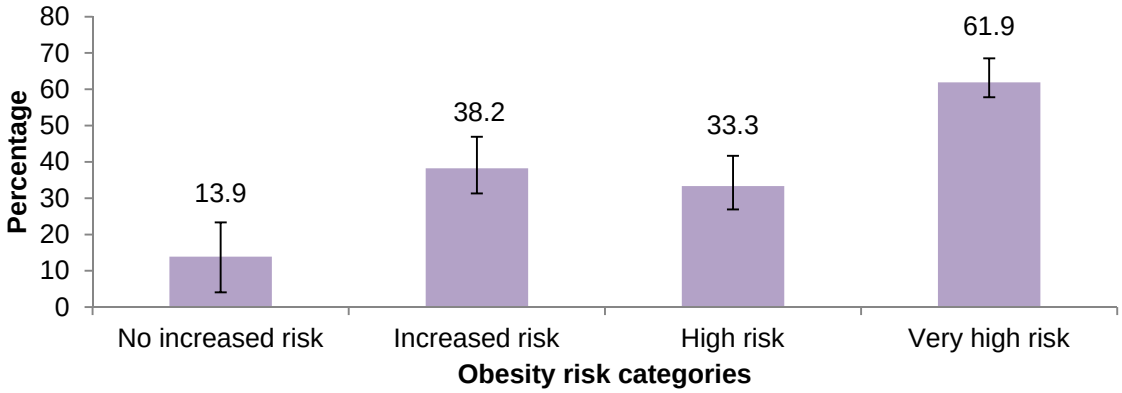
[xxxi] Figures in the ethnicity and employment categories were too small to allow a meaningful analysis.

Table 15: Mean liver function test results by gender and drinking classification – haematology tests (95% confidence intervals)

	Platelet counts 10*9/L	INR
All		
Increasing risk (n=118)	247.8 (24.3-267.3)	1.03 (1.0-1.1)
Higher risk or addicted (n=38)	241.7 (226.3-257.0)	1.0 (1.0-1.0)
All (n=156)	253.9 (245.8-262.0)	1.0 (1.0-1.1)
Male		
Increasing risk (n=73)	249.3 (237.4-261.1)	1.1 (1.0-1.1)
Higher risk or addicted (n=24)	229.3 (209.3-249.2)	1.0 (1.0-1.0)
All (n=97)	244.5 (234.3-254.6)	1.0 (1.0-1.1)
Female		
Increasing risk (n=45)	272.6 (257.1-288.1)	1.0 (1.0-1.0)
Higher risk or addicted (n=14)	262.1 (239.4-284.8)	1.0 (1.0-1.0)
All (n=59)	270.0 (257.3-282.6)	1.0 (1.0-1.0)

INR = International Normalised Ratio. T-tests were used to assess significance between increasing risk and higher risk drinkers (and those who reported an addiction). There were no significant differences (P>0.05).

Figure 6: Likelihood of having at least one abnormal liver function test result by obesity health risk classification*



*There was a significant association between having at least one abnormal liver function test and obesity risk (Chi square, n=154; p<0.001). It was not possible to calculate a level of obesity risk for two participants due to missing data.

Table 16: Factors associated with having at least one abnormal liver function test result*

Characteristic	Univariate analysis			Logistic regression			
	n	%	P	n	AOR	95% CI	P
Gender							
Male	97	39.2	<0.001	90	8.56	2.45-29.89	<0.01
Female	59	13.6		54	*Reference category*		
Age							
36-40	35	37.1		32	*Reference category*		
41-45	44	25.0	NS	39	0.43	0.11-1.65	NS
46-50	37	24.3		35	0.59	0.15-2.36	
51-55	40	32.5		38	1.13	0.29-4.45	
Deprivation quintile							
1 & 2 (most affluent)	52	17.3		48	*Reference category*		
3	40	35.0	NS	39	3.89	1.05-14.40	NS
4	23	34.8		22	4.54	1.05-21.62	
5 (most deprived)	37	37.8		35	6.21	1.43-26.89	
Recruitment route							
GP	27	37.0	NS	25	*Reference category*		NS
Workplace	129	27.9		119	2.67	0.74	
Frequency of GP/GP nurse use in last year							
Never	29	24.1	NS	27	*Reference category*		NS
Less than monthly	112	28.6		103	1.24	0.33-4.60	
At least monthly	14	50.0		14	3.43	0.75-10.20	
Drinking classification							
Increasing risk	118	24.6	<0.05	109	*Reference category*		<0.05
Higher risk or addicted	38	44.7		35	3.66	1.20-11.23	
Alcohol dependency							
No dependence	114	25.4	NS	105	*Reference category*		NS
Mild or moderate dependence	42	40.5		39	1.17	0.39-3.58	
Obesity risk classification							
No increased risk	72	13.9		66	*Reference category*		
Increased risk	34	38.2	<0.001	33	5.15	1.50-17.68	<0.01
High risk	27	33.3		26	4.40	1.21-16.06	
Very high risk	21	61.9		19	20.04	4.24-104.37	
Blood pressure							
Low or normal blood pressure	104	26.0	NS	99	*Reference category*		NS
High blood pressure	47	38.3		45	2.23	0.74-6.70	
Total	156*	29.5		144**			

Participants had at least one abnormal test result from the following: alkaline phosphatase (ALP), alanine aminotransferase (ALT), asparate aminotransferase (AST), gammaglutamyl transferase (GGT), international normalised ratio (INR), platelet count, albumin, total protein and total bilirubin. * Univariate n may not sum to total due to missing values. ** n varies between univariate and logistic regression analysis as logistic regression only uses those cases where all data across all variables are present. AOR= Adjusted odds ratios. NS = Not significant.

4.4.3. Fibrotic marker test results

The mean level of HA in risky drinkers was 26.0ng/ml (95% CI 22.7-29.2); this did not differ significantly between genders or drinking classifications (Table 17). Of the 156 participants who completed the liver screen, 29.5% (n=46) had an elevated HA level (>30ng/ml), of whom seven had a very elevated level (>75ng/ml, 4.5% of the total sample of increasing and high risk drinkers). All seven of these individuals were in the 'increasing risk' drinking category. Mean levels of PIIINP and TIMP-1 did not differ between genders and alcohol consumption groups. For PIIINP, three participants had an elevated result (<5.5µg/ml).

Table 17: Mean fibrotic marker levels by gender and drinking classification (95% confidence intervals)

	HA ng/ml	PIIINP µg/ml	TIMP-1* ng/ml
All			
Increasing risk (n=118)	27.7 (23.6-31.7)	2.8 (2.7-3.0)	146.6 (140.9-152.4)
Higher risk or addicted (n=38)	20.7 (16.3-25.0)	2.9 (2.5-3.3)	138.8 (128.2-149.4)
All (n=156)	26.0 (22.7-29.2)	2.9 (2.7-3.0)	144.7 (139.7-149.7)
Male			
Increasing risk (n=73)	28.7 (23.3-34.2)	2.9 (2.7-3.1)	147.2 (139.8-154.6)
Higher risk or addicted (n=24)	21.4 (15.2-27.5)	2.8 (2.4-3.1)	138.2 (122.9-153.6)
All (n=97)	26.9 (22.6-31.3)	2.9 (2.7-3.1)	145.0 (138.3-151.6)
Female			
Increasing risk (n=45)	25.9 (19.6-32.2)	2.7 (2.5-2.9)	145.7 (136.3-155.1)
Higher risk or addicted (n=14)	19.4 (13.3-25.6)	3.2 (2.4-4.1)	139.8 (125.6-154.1)
All (n=59)	24.4 (19.4-39.3)	2.8 (2.6-3.1)	144.3 (136.6-152.1)

HA = Hyaluranic acid. PIIINP = Amino-terminal propeptide of type III collagen. TIMP-1 = Tissue inhibitor of matrix metalloproteinase. It was not possible to split the reference range results by gender as no such details were provided. T-tests were used to assess significance between increasing risk and higher risk drinkers (and those who reported an addiction). There was no significant difference in HA, PIIINP or TIMP-1 result by gender or drinking classification. *TIMP-1 was not measured for four individuals due to insufficient blood sample.

Blood test results from the three fibrotic marker tests were combined using the STL diagnostic algorithm (section 3.5.2) to estimate whether or not the participants had signs of early liver disease. The algorithm classifies individuals according to level of risk of liver fibrosis and cirrhosis (high, intermediate and low risk). In total, seven participants were classified as being of high risk. All of these individuals were increasing risk drinkers. An additional 41 participants were classified as intermediate risk (104 were low risk; four individuals could not be classified as their blood sample was insufficient to allow for all the analytes to be measured).[xxxii] Univariate analysis suggested that likelihood of being at intermediate or high risk of liver fibrosis and cirrhosis was significantly associated with deprivation, frequency of GP/GP practice nurse visits

[xxxii] Figures in the ethnicity and employment categories were too small to allow a meaningful analysis.

and obesity risk classification (Table 18). However, when confounding variables were accounted for using logistic regression techniques, only obesity risk classification remained significant. Here, level of liver fibrosis and cirrhosis risk increased with obesity risk classification: with a high or very high risk of obesity related harm having a three-fold higher odds of being at risk for liver fibrosis or cirrhosis compared with those at no increased risk of obesity related harm.

Of the 44 participants who had received at least one abnormal LFT result and full data for the STL analysis, 40.9% (n=18) were also classified as being at intermediate or increased risk of liver fibrosis or cirrhosis. This was comparable with the proportion of individuals with normal LFTs who were at intermediate or increased risk of liver fibrosis or cirrhosis (27.8% of 108 individuals did so) and thus there was no significant association between the two (P=0.114).

An alternative fibrosis marker algorithm that also incorporates the TIMP-1 marker, the ELF score[39], was also calculated. The scores ranged from -3.08 to -0.72. The cutoff point for 'moderate fibrosis' is -0.1 or greater, and thus no patients were categorised as having 'moderate' or 'severe' fibrosis.

Table 18: Factors associated with being at intermediate or high risk of liver fibrosis and cirrhosis (using the Southampton Traffic Light classification system)

Characteristic	Univariate analysis			Logistic regression			
	n	%	P	n	AOR	95% CI	P
Gender							
Male	96	34.4	NS	90	1.39	0.58-3.31	NS
Female	56	26.8		52	*Reference category*		
Age							
36-45	75	29.3	NS	69	*Reference category*		NS
46-55	77	33.8		73	1.12	0.49-2.48	
Deprivation quintile							
Quintiles 1 & 2 (most affluent)	50	30.0		47	*Reference category*		
Quintile 3	40	40.0	0.049	39	1.30	0.49-3.44	NS
Quintile 4	23	8.7		22	0.18	0.03-1.03	
Quintile 5 (most deprived)	36	38.9		34	1.05	0.36-3.11	
Recruitment route							
GP	27	40.7	NS	25	*Reference category*		NS
Workplace	125	29.6		117	0.64	0.22-1.85	
Frequency of GP/GP nurse use in last year							
Never	28	17.9	0.035	27	*Reference category*		NS
Less than monthly	109	31.2		101	2.20	0.70-6.98	
At least monthly	14	57.1		14	4.95	1.05-23.46	
Drinking classification							
Increasing risk	115	33.9	NS	107	*Reference category*		NS
Higher risk or addicted	37	24.3		35	0.511	0.18-1.45	
Drinking classification							
No dependence	111	30.6	NS	103	*Reference category*		NS
Mild or moderate dependence	41	34.1		39	1.54	0.58-4.08	
Obesity risk classification							
No increased risk	70	20.0	0.018	65	*Reference category*		0.040
Increased risk	34	38.2		33	2.58	0.92-7.25	
High risk or very high risk	46	43.5		44	3.15	1.23-8.09	
Blood pressure							
Low or normal blood pressure	101	32.7	NS	97	*Reference category*		NS
High blood pressure	47	31.9		45	0.60	0.24-1.49	
Total	152*	31.6		142**			

*Univariate n may not sum to total due to missing values. **n varies between univariate and logistic regression analysis as logistic regression only uses those cases where all data across all variables are present. AOR = Adjusted odds ratios. NS = Not significant.

5. Discussion

5.1. Main findings

A total of 156 people, identified as having consumed more than the government recommended levels of alcohol in the previous week (and therefore deemed at 'increasing or higher risk' of alcohol related harm) donated a blood sample for this study. Of these, seven were found to be at high risk of liver disease (i.e. were flagged as 'red' using the STL algorithm). This gives a prevalence of 4.6% (95%CI 2.02-9.14%) probable liver disease among risky drinkers in the sample. A further 26.3% (20.0-33.7%; 41 individuals) were at 'moderate risk' of liver disease (scoring 'amber' on the STL). Previous research has found that those flagged as red and amber have a significantly increased mortality risk compared to individuals in the green category: Sheron et al. followed up 641 patients with suspected liver disease for an average of 3.4 years, during which time, 16% of red flagged and 3.4% of amber flagged patients died from liver disease. There were no deaths among individuals categorised as green.[34] If the prevalence estimates found in PrevAIL are applied to the population of Liverpool and Knowsley (Table 19), an estimated 2249 Liverpool and 403 Knowsley residents could have signs of liver disease, with around half this number (i.e. 1120 and 201 respectively) potentially having more advanced disease.

Table 19: Estimates of number of drinkers, risky drinkers, and drinkers with alcohol-related liver disease in Liverpool and Knowsley

	KNOWSLEY		LIVERPOOL		Total
Numbers drinking in population	**%**	**n**	**%**	**n**	**n**
Total population	100.0	18 456	100.0	113 507	131 963
Number of drinkers[a]	93.4	17 238	84.1	95 459	112 697
Number at increasing risk[a]	18.7	3 224	18.5	17 660	20 884
Number at high risk[a]	6.6	1 138	7.0	6 682	7 820
Estimated prevalence of liver disease					
High risk (STL Red)	4.6[b] (2.02-9.14)	201 (88-399)	4.6[b] (2.02-9.14)	1 120 (492-2 225)	1 320 (580-2 624)
Moderate risk (STL Red/Amber)	9.2[c] (7.1-11.4)	403 (308-497)	9.2[c] (7.1-11.4)	2 249 (1 716-2 775)	2 652 (2 024-3 272)

STL=Southampton Traffic Light test. [a]Estimates of numbers of drinkers, increasing risk and high risk drinkers are from the Local Alcohol Profiles for England.[2] [b]Red estimate is based on the prevalence found in this study. [c]Red/Amber prevalence was 30.8% in this study, but this estimate is reduced to account for the relatively low positive predictive value of a red/amber STL in a community setting (30%).[34] Numbers in brackets are 95% confidence intervals.

Whilst previous studies have been carried out in clinical settings,[34] less is known about community settings. The Alcohol and Liver Disease Detection Study (ALDDeS) used the STL algorithm on a community sample of 10,000 individuals recruited through general practice.[46] In ALDDeS, 9.6% were flagged as red and 41% amber. Compared with PrevAIL, ALDDES used a higher risk population comprising those screening positive screen on AUDIT (compared to PrevAIL's drinks diary measure). A study of individuals recruited through a community screening programme in France (using an alternative combination of biomarkers, known as FibroTest) found a prevalence of 1.5% for confirmed fibrosis up to 3% for presumed fibrosis in all persons (i.e. regardless of drinking status).[45] Thus our prevalence estimates fall within those for the higher risk ALDDES population and the low risk French study, as would be expected.

At the outset, this study aimed to recruit individuals from workplaces as well as primary care, in line with other lifestyle intervention programmes.[60, 86, 87] This study is unique in identifying workplaces as potentially cost effective settings for such screening interventions, although individuals recruited through the GPs were more likely to reside in more deprived areas. Whilst blood tests (including for the liver function indicator GGT) have been carried out in workplaces in Sweden as part of a brief intervention,[60] PrevAIL is the first study to incorporate the fibrosis biomarkers in this setting. Workplace programmes have considerable potential for engaging with their employees on lifestyle issues because of the amount of time employees spend in work, and because of the influence of employers on staff motivation.[56] Further, in a survey of employers in Liverpool (n=302), 31.1% reported that alcohol consumed by their staff outside working hours negatively affects their company and 62.3% provided alcohol support to their employees in the form of advice, counselling and referral.[57]

5.2. Predictors of presumed fibrosis

As has been reported elsewhere, the study found no relationship between STL status and abnormal standard liver function test (LFT) results.[34] Thirty percent of participants had one or more elevated LFT reading. As per protocol, these individuals received a letter from the study team (copied to their GP if they had given permission for us to do so) to inform them of their abnormal result. This is because such individuals should be monitored by their GP (most individuals with persistently raised ALT or AST have signs of some form of liver damage[88]). However, it must also be remembered that not all individuals with biopsy-proven cirrhosis have raised LFTs[32, 33] and LFTs are often criticised for generating too many false negatives.

In this population of risky drinkers, being 'red flagged' by STL was predicted by obesity, with those in the 'high or very high' risk category for obesity being over three-fold more likely to be red flagged compared with the low risk category. This is consistent with the reported multiplicative effect of alcohol and obesity on the probability of liver damage.[9] Strategies are required that act jointly to reduce alcohol consumption and obesity as this would provide greater potential to reduce liver disease than tackling each issue separately. Further, because of the calorific content of alcohol and the associations between drinking alcohol and consuming food,[64] reducing alcohol consumption can aide weight reduction. However, associations between STL status and other predictors should be treated with caution since the sample size is small. Moreover, we are unable to evaluate the relationship between obesity and liver damage in non- or low risk drinkers.

Although not widely used in the UK, there are several non-invasive biomarkers available that perform well in the detection of alcoholic liver disease. It was not the aim of this study to evaluate the STL or any other test, since this has already been done.

5.3. Feasibility of screening in workplaces and general practice

The most significant factor to influence participation was the setting. Almost all eligible employees recruited through the workplace were willing to take part in the full study (99%: although 8.6% of these were unable to do so because of difficulty in drawing a blood sample). The convenience of performing the screening alongside the fully study is likely to have boosted recruitment in workplaces. The overall response rate is unknown because of the difficulty in calculating the baseline population represented by the non-participating organisations. Even for those participating, not all were able to tell us the total number of their employees in the target age range. Where data were available, between 1.8-5.5% of employees were screened. This was considerably lower than the Swedish study (~15% of ~6,000 staff were recruited), which

also collected blood samples in workplaces as part of a brief intervention.[60] However, a walk to work intervention based in three employers in Glasgow only recruited 3.5% of the combined workforces (n=~8,350).[86] Gaining access to workplaces was time consuming. Of the 37 workplaces contacted, thirteen took part. Employers refused participation for a range of reasons: employees not being able to leave their desks, the uncertain economic climate (with some employers being businesses that were going into administration or having internal reviews), the co-occurrence of similar health-related projects, and perceptions of alcohol being seen as too sensitive to bring up in the workplace. Success within an organisation depended on how actively employees were encouraged to take part, and how flexible employers were with working arrangements. Despite our best efforts to emphasise the confidentiality of the data, one anecdotal reason provided for not participating was fear of disclosure of alcohol use to the employer. The importance of confidentiality to the participants is further illustrated by the fact of the participants recruited to the liver screen through the workplace, 13.5% (n=21) did not provide their GP's contact details.

For the GP recruitment, sampling effort calculations were based on the early results from the Southampton study, ALDDeS. We invited 6,439 eligible individuals by post, 8.4% of whom responded to the initial screening survey. This was significantly lower than that achieved by the ALDDeS study (37%).[46] This low response rate for PrevAIL was despite the second distribution that was organised for two of the GPs. Analysis of responses to this initial screening questionnaire suggests that those declaring themselves to be regular users of primary care services also consumed alcohol in greater quantities, demonstrating that general practice could be a good setting for identifying heavier drinkers. However, only 18% of those declaring an interest in the study responded to our invitation to the clinical examination (none of the nine people recruited through the health events attended the clinical examination), compared with 32% in the ALDDeS study.[46] The poor response rate in this study may be due to the fact that our sample was drawn from GPs serving particularly deprived locations in Liverpool. In a study in Bristol, recruiting women living in deprived areas with depression to a cognitive behavioural therapy randomised controlled trial, 27% of the 499 individuals identified as being eligible through GP notes expressed an interest in the study.[89] The relative poor performance of the recruitment from GPs compared with the workplace led to a lower representation of individuals residing in the poorer areas (as GP recruits were more likely to be from the more deprived areas than those recruited through the workplace). The requirement to provide a blood sample to fully participate in the study may also have discouraged participation. We note that the recent Health Survey for England (2009) had an option to provide a blood sample, and of 4,645 interviews, only around half provided a blood sample.[90]

Participants who were screened as being eligible for the full study did not go through for the full study (i.e. blood test and clinical examination) reported alcohol consumption levels that were broadly similar to those reported by those who fully participated, in terms of average last week consumption (both mean and median) and in terms of subsequent drinking classification. Males were more likely to complete the full study than females. There was no difference in terms of deprivation.

5.4. Measuring alcohol consumption

This study used a drinks diary measuring tool to screen for risky drinking (based on the quantity consumed in the previous week). The disadvantage of this approach is that inclusion (or not) in the study could be influenced by unusually heavy (or light) drinking weeks. An alternative approach would have been to use a tool such as AUDIT, which asks about typical drinking behaviour. Some AUDIT questions were also included in our initial screening questionnaire for comparison, although for reasons of space the full AUDIT was not

reproduced. The short form, AUDIT-C, classified 71% of the participants as risky drinkers, compared with 32% using the drinks diary measure. Those classified as low risk by the diary but risky by AUDIT-C were less likely to be binge drinkers or frequent drinkers. Further research is required to assess whether these individuals, who were missed by the drinks diary classification system, are also at risk of liver disease. We had considered the longer version of AUDIT, which includes questions on both consumption and consequences of alcohol consumption (e.g. 'How often during the last year have you been unable to remember what happened the night before because you had been drinking?'; 'Have you or someone else been injured as a result of your drinking?'). We ruled this out for three reasons: i) the quantity of alcohol consumed has a linear relationship with the risk of cirrhosis of the liver,[19] while the AUDIT other indicator questions are consequences rather than causes of liver damage; ii) we hypothesised that our target population may be predominantly risky habitual drinkers who would not necessarily trigger some of the consequences; and iii) women, in particular, can drink more than the recommended limits and not trigger a positive on AUDIT. The consumption diary approach also gives potentially useful information on consumption patterns, which, with a larger sample, could be used to elucidate the relationship between total quantity, pattern of drinking, and risk of liver disease.

We found that although the total quantity of alcohol consumed in the previous week did not differ by deprivation, those from less deprived areas drank more frequently, thereby spreading their weekly units over more occasions. Such differences in drinking patterns could be a factor in the 'paradox' whereby the most deprived suffer the most alcohol harm (in terms of hospital admissions), despite the fact that alcohol consumption is relatively evenly distributed across the social gradient.[91] Future studies on liver disease risk should account for both drinking patterns and deprivation to further elucidate this apparent paradox.

5.5. Other alcohol harms

We recorded other potential impacts of alcohol on the increasing and higher risk drinkers. These insights could be used to inform the feedback given to recipients of liver screening. This may be particularly important to mitigate the effect of receiving a 'green' flag, which could be interpreted as a 'green light' for continued drinking.[69] The majority (87%) felt that their alcohol consumption had impacted on their sleep and energy levels in a negative way in the last month. Even those who reported sleeping better in the last month after drinking were highly likely to also report at least one negative impact on their sleep. A literature review of alcohol's relationship with sleep supports this contradiction, suggesting that alcohol may improve sleep in non-alcoholics in the initial half of the night, but at high alcohol doses, individuals may experience more disturbances in the second half of the night.[92] Further, tolerance to this initial sedative effect can develop quite quickly (for example, after three nights of consecutive consumption).[92] It is important to develop clear and meaningful messages around alcohol and its contradictory impacts on sleep in order to assist people making informed choices.

Over half of our sample of increasing and higher risk drinkers were also at risk of obesity-related health complications (as defined by clinical guidelines for detecting obesity related complications,[83] from combinations of BMI and waist circumference measurements), with 22% being rated as at 'increased risk of health complications relating to obesity', 18% at 'high risk' and 14% at 'very high risk'. This was especially true for females and higher risk drinkers. The majority (87%) of the participants declared that alcohol influenced their dietary choices in the previous month. Segmentation analysis in Great Britain shows that dieting is a key issue for women in affluent and family groups, and that 41% of women in the MOSAIC segmentation group 'Upwardly Mobile Families' report trying to lose weight most of the time (compared with 20% for males).[93] This may explain why in our increasing and higher risk drinker group, males were

significantly more likely to report at least one impact on their diet (92.8% did so) compared with females; females may have been more wary of allowing alcohol consumption to affect their diet and weight. However, despite the potential for such concerns, 76.3% of females still reported at least one negative impact on their diet. Further, the segmentation analysis for Great Britain shows that only two fifths of participants believed that drinking alcohol makes them put on weight[93] despite the evidence available that shows that alcohol affects both how food is consumed and which types of food are consumed.[64] Thus, the development of clear and meaningful messages around alcohol, diet and weight are required in order to assist people making informed choices, and these messages should be part of the feedback about liver health.

Negative impacts on sleep and diet were the main harms reported but increasing and higher risk drinkers were affected by a range of social consequences. A fifth reported that their consumption had impacted on their relationships in the last month through arguing with friends and family and 30% reported at least one negative impact on work or education. Attending work, lectures or class with a hangover was the most common impact reported. 19.9% (n=31) reported participating in at least one risky behaviour in the last month after drinking. However, not all experiences with alcohol were negative: 85.9% of increasing and higher risk drinkers reported that they had relaxed after drinking in the last month; 26.9% reported that after drinking, they had forgotten their problems; 21.8% reported that after drinking they slept better and 41.7% reported that they felt more confident after drinking. These help show the motivations for consumption. They should be considered as part of any health promotion campaign aiming to reduce alcohol consumption in order that appropriate alternative mechanisms can be developed which provide participants with equivalent outcomes (relaxation, good quality sleep, stress relief and confidence).

Whilst the data analysed here highlight the variety of negative and positive experiences around alcohol consumption, in order to make any messages delivered through, for example a social marketing campaign, as effective and as meaningful as possible, further work should be done to understand which population groups are most affected by these issues. Segmentation analysis could be used to identify which population groups are most affected by the experiences discussed,[93, 94] followed by qualitative analysis to further understand the issues involved.

5.6. Screening for liver disease as part of the alcohol intervention

National clinical guidance recommends that GPs and other primary healthcare professionals should opportunistically identify hazardous and harmful drinkers and deliver a brief (ten minute) intervention.[51] Brief interventions can be an effective means of targeting at-risk drinkers in settings such as primary care,[47] and have also been successfully carried out in the workplace.[60] A meta-analysis of the effectiveness of brief interventions delivered in general practice revealed significant reductions in alcohol consumption,[49, 62] which provided evidence in support of brief interventions in reducing alcohol consumption. For every eight people who receive alcohol advice, research suggests one person will reduce their drinking to within low-risk levels.[50] This study aimed to understand the feasibility of providing such screens supplemented with a liver screen in a primary care and working population. Here, we identified that workplaces were an appropriate and effective means of engaging with people, more so than the patients identified through their GP practices or individuals attending health events. We hope to further develop this study by evaluating whether additional feedback for those with signs of early liver damage could augment the brief advice currently provided. It has been suggested that while those at high risk (i.e. red flagged) could be appropriately investigated by liver specialists, those at lower risk could receive lifestyle interventions and be monitored in the community.[34]

5.7. Limitations

Surveys are known to considerably under-report alcohol consumption, for example, when compared with other statistics such as those on alcohol taxation,[95] and because of this levels of alcohol consumption and related harm experienced documented in this report may also be an under-estimate. The original aim of PrevAIL was to estimate the prevalence of alcohol-related liver disease in Liverpool and Knowsley. This would have necessitated using a random sample. However, the practicalities of enlisting GPs who were willing to collaborate meant that we used a non-random sample of GPs known to be supportive of research initiatives. More importantly, the profile of those who took part in the full screen was biased towards those recruited at their place of work. As a result, the less affluent, heavier drinkers were less likely to take part. Thus the true prevalence of liver disease is likely to be higher.

The project aimed to oversample from deprived groups. In total, 913 participants provided their full postcode, allowing Index of Multiple Deprivation (IMD) 2010 scores to be allocated. Whilst PrevAIL participants most commonly resided in the most deprived quintile (36.4%), this skew was not enough to accurately reflect the deprivation base of Liverpool and Knowsley as a whole (63.5%). More deprived groups were significantly more likely to be reached through GP and health event recruitment strategies compared with workplaces. However, individuals recruited through GPs and health events were significantly less likely to complete the full screen and blood test.

5.8. Next steps

Further research is required to understand the long-term efficacy of using a liver screen as part of a brief intervention. The concept has shown initial success in Southampton, where qualitative research (n=30) has highlighted how those with positive STL results felt motivated to reduce their consumption.[69] However, the STL test is less sensitive to the earliest stages of fibrosis, and some individuals with a negative/green test felt less inclined to reduce their drinking. Further work should develop tools to enable participants need to understand that this "is not a 'green light' to continue drinking, but a reassurance that there is no sign yet of significant damage with time to modify risky drinking".[69] Findings from the in-depth questionnaire used in PrevAIL could be used to inform the advice and support given alongside the test result, for example, by providing feedback about the range of other harms experienced by those drinking more than the recommended lower risk threshold.

The design of PrevAIL was informed by the Southampton ALDDeS study.[46] The findings from both PrevAIL and ALDDeS will provide the baseline knowledge required for developing a trial into the effectiveness of non-invasive tests for the detection and management of liver disease in primary care/occupational settings. Our strong national team will collaborate to apply to the NIHR for funding to develop a definitive, large scale randomised controlled trial (RCT) to determine whether feedback from liver disease screening impacts on drinking behaviour, and ultimately alcohol-related morbidity and mortality. The RCT will assume that early detection of liver disease may prevent the need for referral to secondary care on the basis of abnormal LFTs alone (since many persons with raised LFTs have a benign non-alcoholic fatty liver condition).[96] As part of the RCT protocol, we will analyse referral rates between primary and secondary care, and the proportion due to late stage alcohol-related liver damage. This will allow us to demonstrate whether a significant burden to secondary care would be prevented by the provision of early liver screening in primary care/occupational settings.

Prior to the development of the RCT protocol, we will need to identify barriers to screening in various settings. We will interview Liverpool GPs to evaluate the possibility of delivering enhanced liver disease management in their surgeries taking into account current NHS restructures. We will also engage with a wide range of employers to explore the acceptability and feasibility of carrying out this type of intervention in their workplace. Our experience in workplaces suggests that an intervention targeting both obesity and alcohol is more desirable than one that targets these issues in isolation. This more general public health and wellbeing approach is supported by the literature, which shows that the combination of obesity and alcohol consumption is a more potent risk factor to health compared to each factor considered alone.[9, 17] However, more work is required to define the nature of the intervention and follow-up support to be delivered for those with those with liver results graded red or amber by STL.

Biopsy of the liver is currently the gold standard for assessing liver damage, but is risky and uncomfortable for patients, and costly to the NHS. It would not be justified to perform a biopsy in the absence of any symptoms for liver damage. However, non-invasive tests (such as the blood tests proposed here) are not universally accepted as being appropriate for the detection and management of liver disease either by hospitals or GPs.[97, 98] Thus, work is required to: i) share PrevAIL and ALDDeS findings; ii) review the literature on non-invasive diagnostic tools for alcoholic liver disease; iii) review other contemporary research on screening for liver disease; iv) disseminate findings to experts in order to promote the value of non-invasive liver tests; and v) develop the protocol for the definitive large scale study.

5.9. Conclusions and recommendations

The prevalence estimates were broadly in line with similar community surveys. If the prevalence found in this study is representative of increasing risk drinkers in the study area, we would expect that around 1,100 Liverpool residents and 200 Knowsley residents could have undetected liver disease and the same number again could be showing earlier signs of the disease. Detecting and supporting these cases in the community could avert deaths and save considerable health and social costs. Those who were overweight or obese were more likely to show signs of liver damage, in line with the known multiplicative effect of alcohol and obesity, suggesting that it could be beneficial to address these two health concerns simultaneously. Finally, the feasibility of the screening depended on setting, with workplaces being more successful once access had been granted by the employer.

5.9.1. Recommendations

- To develop a protocol for an RCT to determine whether feedback from liver disease screening impacts on drinking behaviour, and ultimately alcohol-related morbidity and mortality, for submission to the NIHR.

- To fully explore barriers to providing screening in GPs and workplaces through consultation with GPs and employers.

- To use the findings from the in-depth questionnaire used in PrevAIL to inform the advice and support given alongside the test result, for example, by providing feedback about the range of other harms experienced by those drinking more than the recommended lower risk threshold.

- To develop clear and meaningful messages around alcohol, diet and weight in order to assist people making informed choices, and to ensure that these messages are part of the feedback about liver health that are provided after a liver function test is performed.

6. Appendices

6.1. Appendix 1: Alcohol consumption screen

SECTION A. Drinking alcohol

Centre for Public Health

Participant code:

1. Have you ever drunk alcohol? Yes ☐ No ☐

If you have never drunk, please go to Section C.

2. How often do you drink alcohol? *(Please tick one)*

Never	Less than monthly	1 or 2 times a month	Weekly	2-4 times a week	Daily (or almost)
☐	☐	☐	☐	☐	☐

If you never drink, please go to Section C.

3. How many drinks do you have on a typical drinking day? *(Please tick one)*

1-2	3-4	5-6	7-9	10 or more
☐	☐	☐	☐	☐

4. How often do you have six or more drinks in one session? *(Please tick one)*

Never	Less than monthly	1 or 2 times a month	Weekly	2-4 times a week	Daily (or almost)
☐	☐	☐	☐	☐	☐

5. Did you drink alcohol in the last week? Yes ☐ No ☐

If yes, please complete the table below. If no, please go to Section B.

	Mon	Tue	Wed	Thu	Fri	Sat	Sun
Did you drink alcohol on...? (Please tick)	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐
If so, what did you drink? *Please complete the table below, entering the number of drinks in the spaces provided for*							
EXAMPLE DRINK	1	0	2	0	3	7	0
Pints of low alcoholic beer/lager/cider							
Pints of normal strength beer/lager/ shandy/stout/cider							
Pints of strong beer/ lager/cider							
Bottles of alcopops (330ml)							
Single glasses of spirits (25ml)							
Standard glasses of wine (175ml)							
Single glasses of fortified wine e.g. sherry/port/martini							

SECTION B. Consequences

1. Thinking about the last year, how often has the following happened to you because of drinking?
(Please tick the appropriate box)

	Never	Less than monthly	1 or 2 times a month	Weekly	2-4 times a week	Daily (or almost)
I was unable to stop drinking after I started	☐	☐	☐	☐	☐	☐
I failed to do what was expected of me	☐	☐	☐	☐	☐	☐
I needed a drink in the morning after a heavy session	☐	☐	☐	☐	☐	☐
I felt guilty or remorseful about drinking	☐	☐	☐	☐	☐	☐
I was unable to remember what happened the night before	☐	☐	☐	☐	☐	☐

Please go to Section D.

SECTION C. For non-drinkers

1. Why do you choose not to drink alcohol? *(Please tick all)*

I do not like the taste	☐	I do not like the feeling	☐
I am worried about the health risks	☐	My doctor advised me not to drink	☐
For religious or faith reasons	☐	I have seen other people's bad experiences	☐
I have poor health	☐	Other *(please specify)*	☐
I have / had an addiction to alcohol	☐		

SECTION D. About you

1. Are you...? *(Please tick one)*

White British ☐
White European ☐
White Irish ☐
Mixed race ☐
Black / black British ☐
Asian / asian British ☐
Chinese / Chinese British ☐
Other ☐

2. Are you...? *(Please tick one)*

Male ☐ Female ☐

3. What is the initial of your first name? ____

4. What is the initial of your surname? ____

5. How old are you?

36-40 years ☐ 46-50 years ☐
41-45 years ☐ 51-55 years ☐

6. What is your postcode? ____

7. How would you describe your main occupation? *(Please tick one)*

Employed / self-employed ☐
Student ☐
Housewife / husband ☐
Retired ☐
Unemployed ☐
Other ____

8. How often have you attended your GP or GP nurse in the last 12 months? *(Please tick one)*

Never ☐
Less than monthly ☐
Monthly ☐
2-4 times a month ☐
Weekly or more ☐

9. Do you have any of the following health issues?

Hepatitis B or C ☐
Liver disease or cirrhosis ☐
Diabetes ☐

END OF QUESTIONNAIRE—THANK YOU!

6.2. Appendix 2: Risky drinkers' questionnaire

SECTION A: About you

Centre for Public Health

Participant code:

1. Are you...? *(Please tick one)*

Male ☐ Female ☐

2. What is your postcode? _____

3. What is the initial of your first name? _____

4. What is the initial of your surname? _____

SECTION B: After drinking...

1. Have you drunk alcohol in the last month? Yes ☐ No ☐

If you have not drunk alcohol in the last month, please go to Section C.

2. Thinking about the last month, has the following happened to you after drinking?

	Yes	No	N/A
You overslept	☐	☐	
You injured myself	☐	☐	
You visited your GP or nurse	☐	☐	
You drove a car	☐	☐	
You had sex that you regretted	☐	☐	
You injured someone else	☐	☐	
You operated heavy machinery	☐	☐	
You slept poorly	☐	☐	
You avoided a boss/teacher/ tutor	☐	☐	☐
You argued with friends/family	☐	☐	
You were involved in a fight	☐	☐	
You argued with a stranger	☐	☐	
You felt tired or lethargic the next day	☐	☐	
You were late for work/class/ lectures	☐	☐	☐
You avoided colleagues the next day	☐	☐	☐
You stayed out later than intended	☐	☐	
You missed work/class/lectures	☐	☐	☐
You relaxed	☐	☐	

	Yes	No	N/A
You were sick/vomited	☐	☐	
You failed to do what was expected of you	☐	☐	
You could not concentrate at work/lectures/class	☐	☐	☐
You missed an appointment	☐	☐	
You went to work/lectures/class with a hangover	☐	☐	☐
You could not remember what happened the night before	☐	☐	
You ate a kebab/chips/pizza on a night out	☐	☐	
You attended hospital after drinking (e.g. because of an injury)	☐	☐	
You went to work/lectures/class drunk	☐	☐	☐
You forgot your problems	☐	☐	
You slept better	☐	☐	
You avoided customers/clients at work	☐	☐	
You drank sugary or caffeinated drinks the next day	☐	☐	☐
You felt confident	☐	☐	
You felt guilty or remorseful	☐	☐	☐
You ate a fry-up or a bacon sandwich the next morning	☐	☐	

SECTION C: Substance use

1. Are you using any of the following?

If so, how often? *(Please tick the appropriate box)*

	Never	Less than monthly	Monthly	2-4 times a month	Weekly	2-4 times a week	Daily (or almost)
Alcohol	☐	☐	☐	☐	☐	☐	☐
Cigarettes	☐	☐	☐	☐	☐	☐	☐
Paracetamol	☐	☐	☐	☐	☐	☐	☐
Aspirin	☐	☐	☐	☐	☐	☐	☐
Cannabis	☐	☐	☐	☐	☐	☐	☐
LSD	☐	☐	☐	☐	☐	☐	☐
Magic mushrooms	☐	☐	☐	☐	☐	☐	☐
Speed / amphetamines	☐	☐	☐	☐	☐	☐	☐
Ecstasy	☐	☐	☐	☐	☐	☐	☐
Ritalin *(not for medical reasons)*	☐	☐	☐	☐	☐	☐	☐
Cocaine	☐	☐	☐	☐	☐	☐	☐
Crack cocaine	☐	☐	☐	☐	☐	☐	☐
GHB	☐	☐	☐	☐	☐	☐	☐
Bytmain	☐	☐	☐	☐	☐	☐	☐
Glue, gas or solvents	☐	☐	☐	☐	☐	☐	☐
Ketamine	☐	☐	☐	☐	☐	☐	☐
Steroids	☐	☐	☐	☐	☐	☐	☐
Heroin	☐	☐	☐	☐	☐	☐	☐
Methadone	☐	☐	☐	☐	☐	☐	☐

2. **<u>If you do not drink alcohol,</u>** when was the last time you drank alcohol? *(Please tick one)*

In the last month	In the last 2 months	In the last 6 months	In the last year	Over a year ago
☐	☐	☐	☐	☐

<u>If you do not drink alcohol,</u> please go to Section E.

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