Faculty of Medicine and Health Sciences

Alcohol use disorder epidemiology and interventions to support behaviour change

By

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Publications

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The work performed as part of my doctoral thesis has led to the following peer-reviewed publications.

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2. **Subhani M**, Sheth A, Unitt S, Aithal GP, Ryder SD, Morling JR. The Effect of Covid-19 on Alcohol Use Disorder and the Role of Universal Alcohol Screening in an Inpatient Setting: A Retrospective Cohort Control Study. Alcohol and alcoholism (Oxford, Oxfordshire). 2021. (Chapter 4)

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   Subhani M, Morling JR, Ryder SD. Alcohol use disorder data, trials and Covid-19

Poster

1. UEG: United European Gastroenterology annual conference Vienna, Austria, 2022
   Subhani M, Aithal GP, Ryder SD, Morling JR. The epidemiology of alcohol use disorder and Validation of AUDIT-C in secondary care: a retrospective cohort control study

2. BSG: British Society of Gastroenterology annual conference Birmingham, UK, 2022
   Subhani M, Talat U, Knight H, Morling JR, Jones KA, Aithal GP, et al. Characteristics of alcohol recovery narratives: Systematic review and narrative synthesis.

3. ESBRA: European Society for Biomedical Research on Alcoholism annual conference Timisoara, Romania 2021
   Sheth A, **Subhani M,** Sahota S, Ryder SD. Impact of Covid-19 pandemic on hospital admissions for alcohol-specific conditions

4. BSG: British Society of Gastroenterology virtual annual conference 2020
   Elleray MR, **Subhani M,** Ryder S, Bethea J. O25 Alcohol-related liver disease: delayed diagnosis and missed opportunities for intervention. Gut. 2021;70(Suppl 1):A13-A4.

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   Subhani M, Knight H, Morling J, Ryder S. P76 Effectiveness of advice based on liver disease diagnostic tests on managing high-risk drinking behaviour in patients with alcohol misuse: a systematic review with metanalysis. Gut. 2020;69(Suppl 1):A43-A.

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيم

المعرفة لا تأتي ولكن عليك أن تذهب إليها
"Knowledge does not come but you have to go to it"
Malik Ibn Anas

لقليل من المعرفة يزيل الكثيرمن الجهل
"A little knowledge removes a lot of ignorance"
Ali Ibn Talib (R.A.)

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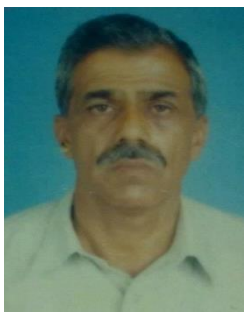
I dedicate my PhD work to my late father, Mohammed Akbar.



“The greatest glory in living lies not in never falling, but in rising every time we fall”. - Nelson Mandela

Author's Declaration

I, Mohsan Subhani, declare that this thesis has been composed solely by myself and that it has not been submitted, in whole or in part, in any previous application for a degree. Except where states otherwise by reference or acknowledgement, the work presented is entirely my own. Any views expressed in the thesis are those of the author.

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Abstract

Alcohol is a preventable leading cause of liver disease. In the United Kingdom (UK) 25% of the population drinks above the recommended level and 10% are harmful drinkers. Alcohol-related liver disease (ARLD) progresses silently, over 50% of patients are first diagnosed with liver disease after an emergency hospital admission at a stage when the scope of any medical and behavioural intervention is limited. Though the prevalence of alcohol use disorder is disproportionately higher among hospitalised patients as compared to the community, it is persistently underdiagnosed and undertreated in hospital settings.

There is a large burden of undiscovered, asymptomatic, but clinically significant liver disease in patients attending community substance misuse services. Early detection of liver disease followed by targeted interventions is a logical and effective way to reduce the risk of late presentation of liver disease and other alcohol-related end organ damage. Although, providing tailored feedback based on non-invasive tests (NITs) for liver disease to people at risk of liver disease may affect their drinking behaviour, at present these markers are not widely incorporated into alcohol treatment settings. Hence, the potential of combining early diagnostic interventions and advice has not been extensively explored in alcohol services.

First, I conducted a retrospective observational study to explore the epidemiology of alcohol use disorder among hospitalised patients. I demonstrated that one in six hospitalised were screened positive for alcohol use disorder (AUD) based on AUDIT-C alcohol assessment. Patients with AUD were more likely to be male, white, admitted as an emergency, and cared for by surgical specialities compared to those without AUD. Although there was an overall reduction in the number of hospital admissions, patients admitted during the pandemic compared to pre-pandemic were more likely to have possible alcohol dependence and mental disorders due to alcohol. Covid-19-positive patients with AUD died at a younger age compared to Covid-19-positive patients without AUD.

I then, conducted a systematic review and meta-analysis to determine the effectiveness of non-invasive tests (NITs) based advice compared to routine care in changing high-risk drinking behaviour. Twenty papers comprising 14 RCTs, 2 observational studies, and n=3763 participants were included. The meta-analysis demonstrated a greater reduction in self-reported alcohol intake and liver biomarkers for the intervention compared to the control group: the mean difference for weekly alcohol intake was -74.4 grams per week (95%CI -126.1, -22.6, p=0.005); and mean

difference for gamma-glutamyl transferase (GGT) -19.7 IU/L (95% CI -33.1, -6.4, p=0.004). There was a higher incidence of alcohol-attributed mortality, number of days spent in the hospital, physician visits and sickness absence in the non-intervention group.

In addition to NITs based advice, I planned to include alcohol recovery video stories (ARVS) as part of the intervention in my future feasibility RCT. I conducted a systematic review and narrative synthesis and proposed a conceptual framework characterising alcohol recovery narratives. Based on the three-stage narrative synthesis approach I determined that alcohol recovery narratives are composed of eight principle narrative dimensions (genre, identity, recovery setting, drinking trajectory, drinking behaviours, stages, spirituality and religion, and recovery experience) each with types and subtypes. All dimensions were present in most subgroups. *Shame* was a prominent theme for female narrators, as a *lack of sense of belonging* for LGBTQ+ narrators, and *alienation* and *inequality* for indigenous Alaskan and Australian narrators. Moreover, spiritual awakening was more commonly sought rather than a religious affiliation in LGBTQ+ narratives.

Finally, I conducted a feasibility randomised control trial (KLIFAD) at three community settings in Nottingham, including adult patients presenting to any of these services with a primary problem of alcohol use disorder. Participants were randomised (1:1) to either continue routine care (control group) or in addition to routine care have feedback based on transient elastography results and watch alcohol recovery video stories (intervention group). I demonstrated that the integration of transient elastography into community alcohol services is feasible. Over 76% of eligible participants agreed to be part of the trial and gave informed consent and were randomised, 65% stayed in services for three months, and a six-month follow-up was available in 59%. Implementing opportunistic screening in otherwise asymptomatic high-risk individuals showed one in five had raised liver stiffness measure (LSM), and of concern one in seven of them were in the cirrhotic range. The provision of feedback based on transient elastography results was associated with higher rates of completion of the allocated treatment program, reduction in self-reported alcohol intake, or complete cessation of alcohol consumption. A normal liver stiffness measure did not provide false reassurance to study participants.

Table of contents

Table of Figures

Table of Tables

Abbreviations

AA	Alcohol Anonymous
A&E	Accident & emergency
AD	Alcohol Disorders
AIBA	Alcohol identification and Brief Advice
APC	Annual per capita
ARD	Alcohol-related disorders
ARLD	Alcohol-related liver disease
ARNCF	Alcohol recovery narrative conceptual framework
AUD	Alcohol Use Disorder
AUDIT	Alcohol Use Disorders Identification Test
BA	Brief Advice
CI	Confidence Interval
CQUIN	Commissioning for Quality and Innovation
EBM	Evidence-based medicine
ELF	Enhanced liver fibrosis
ENT	Ear Nose Throat
GCS	Glasgow coma scale
GGT	Gamma-glutamyl transferase
ICD	International classification of diseases
ICF	Informed Consent Form
ICU	Intensive care unit
IMDD	Index of multiple deprivation decile
ISRCTN	International Standard Randomised Controlled Trials Number
kPa	Kilopascal
LFTs	Liver function tests
LSM	Liver stiffness measure

LSOAs	Lower Super Output Areas
MCV	Mean corpuscular volume
NCEPOD	The National Confidential Enquiry into Patient Outcome and Death
NHS	National Health Services
NICE	The National Institute for Health and Care Excellence
NITs	Non-invasive tests
NRN	Nottingham Recovery Network
NUH	Nottingham University Hospital
ONS	The Office of National Statistics
PHE	Public Health England
RCT	Randomised Control Trial
REC	Research Ethics Committee
RfPB	Research for Patient Benefit
SADQ	Severity of Alcohol Dependence Scale
SD	Standard deviation
STLT	Southampton traffic light test
T&O	Trauma & Orthopaedics
TE	Transient elastography
UAS	Universal alcohol screening
UK	United Kingdom
WHO	World Health Organisation
WP	Work Package

Chapter 1. Introduction

Alcohol is a leading, but preventable cause of liver disease, and has been an important commodity of human culture for centuries, both due to its perceived positive influence on social experience and financial contribution to the economy (1, 2). Alcohol consumption varies across societies and ethnicities, with men often higher alcohol consumers compared to women (3). Europe is among the highest in the world for age-standardised heavy alcohol consumption rates and the proportion of alcohol use disorders (AUD) (4).

1.1 Alcohol use disorder

1.1.1 Epidemiology of Alcohol use disorder:

The World Health Organisation (WHO) estimated that in 2018 worldwide nearly 2.3 billion people were current alcohol drinkers, of these approximately 240 million were alcohol dependent (5). Globally annual per capita (APC) alcohol intake in the age group 15 years and over is 6.4 litres of pure alcohol and is twice as high (15 litres of pure alcohol per annum) in the current drinkers which is equivalent to 237 grams of alcohol per week per person (5). In Europe, 14.8% of men and 3.5% of women consume alcohol harmfully (5). In the United Kingdom (UK) 25% of the population drinks above the recommended level and 10% are harmful drinkers, the total per capita pure alcohol intake in the age group 15 years and over is 11.4 litres per annum averaging 175 grams of alcohol per week per person (6).

Excess alcohol use is related to over 200 acute or chronic medical conditions (5). Diseases including malignancies, heart diseases, alcohol-related liver disease, musculoskeletal injury, behaviour and alcohol-induced mental disorders, alcohol-induced acute and chronic pancreatitis, fetal alcohol syndrome, alcohol-induced brain disorders, myopathy and polyneuropathy are wholly or highly attributed to harmful alcohol intake (7).

According to WHO 2018 statistics, globally alcohol-related disorders (ARD) are the cause of over 3 million deaths a year, contributing to 7% of premature deaths (age ≤65 years), and 132.6 million disability-adjusted life years (DALYs). Overall, alcohol-related mortality is ahead of other common causes like diabetes, HIV, and tuberculosis (5). Among the deaths attributed to alcohol, injuries are the most common cause (29%), followed by digestive diseases (21%), cardiovascular (19%) and cancer (13%) (5). In England, in 2018, there were 5,698 alcohol-specific deaths, the alcohol-

specific age-standardised death rate/100,000 was 11.9 (male=16.4 female=7.6), Nottingham has one of the highest (total=18.6, male=26.8, female 10.2) alcohol-specific age-standardised death rate/100,000 in the country (8).

Over the last three decades, the UK has observed a 400% rise in mortality due to liver disease, it is now the third common cause of premature death, and the second common cause of working life years lost in men and fifth in women (5, 9). According to Office for National Statistics (ONS) for England and Wales, in 2020, the death rate due to wholly alcohol-attributable conditions reached 14.0 deaths per 100,000, the highest since 2001. In 2020 there were 8,974 alcohol-specific deaths compared to 7,565 deaths for a similar period in 2019, an 18.6% increase (10). A recent study from the United States predicted if no appropriate measures are taken, there will be an estimated 75% increase in age-standardised alcohol-related annual mortality and a 65% increase in decompensated cirrhosis in high-income countries over the next two decades (11).

1.1.2 Alcohol-related disorders (ARD) and hospitalisation

Alcohol-related disorders (ARD) are among the commonest reason for hospitalisation, in 2019, 7.4% of all hospital admissions in England were alcohol-related (9, 12, 13). Among the hospitalised patients, 1 in 5 have a history of harmful alcohol use and 1 in 10 are alcohol dependent (14). Those with alcohol dependence (9%) account for 59% of all alcohol-attributable hospital admissions (9, 13). Accident and Emergency (A&E) is the most common source of admission, 21% of all emergency presentations are due to alcohol, of these up to 74% are due to chronic alcohol dependence and 24% are due to acute alcohol intoxication (13). This has a huge cost implication for National Health Services (NHS). It is estimated that an annual 1.3 million alcohol-related hospital admissions are costing £3.5 billion to NHS (5, 6).

According to Nottinghamshire Health and Wellbeing Board report 2018 for England, Nottingham has a higher level of alcohol dependence (Nottingham 2.2%, England 1.4%), years of life lost to alcohol (Nottingham 843 per 100,000, England 624 per 100,000), and number of hospital admissions (Nottingham 1000 per 100,000, England 647 per 100,000) (15). Nottingham University Hospital (NUH) data from 2019 showed that, based on the AUDIT-C score, 18% of hospitalised patients were screened positive for alcohol use disorder (AUDIT-C Score ≥5) of which 4% were alcohol dependent (16, 17).

Though the prevalence of harmful alcohol use is disproportionately higher among hospitalised patients as compared to the community, it is persistently underdiagnosed and undertreated in hospital settings (18-20). Of people with underlying alcohol-related liver disease, 80% die during hospital admission (20). Post-hospital admission alcohol-related liver disease mortality is 23.4% at 60 days and reaches 61.8% at five years, which is seven times higher than stroke and eight times higher than acute myocardial infarction (21).

1.1.3 Alcohol harm paradox

The socioeconomic disparity is another aspect of alcohol-related disorders known as the “alcohol harm paradox”, an observation that shows, that though people from both the least deprived and most deprived neighbourhoods of a community drink alcohol harmfully, the alcohol-related worst outcomes are disproportionately higher in those from most deprived areas and often involve the younger and male population (22, 23). Socioeconomic inequalities have also been observed in hospitalised patients due to alcohol and become more prominent in alcohol-related mental health issues and alcohol-related liver disease (23). Public Health Scotland 2016 data showed, that in Scotland, the most deprived areas compared to the least deprived areas, had seven times higher ARLD mortality and eight times higher alcohol-related hospital admissions (20). According to the Ministry of Housing, Communities & Local Government 2019 report, Nottingham is among the top ten most deprived areas in England; over half of Nottingham city population live in 20% of the most deprived areas nationally, compared to 14.1% in Nottinghamshire County (24).

1.1.4 Screening for alcohol use disorder

National Institute of Clinical Excellence (NICE) guidelines recommend that adults with a high level of alcohol intake should be screened for alcohol use disorder (AUD), and be offered intensive structured community-based interventions (with or without medical therapy) as these provide the best chance of achieving and maintaining abstinence from alcohol (25).

National Confidential Enquiry into patient outcome (NCEPOD) national audit done in 2013 and 2021 highlighted the inadequacy in the screening and management of hospitalised patients for alcohol misuse (26, 27). A recent UK hepatology trainee-led audit in 2021 showed similar findings (28). The recommendations from NCEPOD included that every patient presented to a hospital should be screened for alcohol and referred to specialist alcohol services as indicated.

The accuracy of self-reported alcohol intake is questionable and decreases as the consumption of alcohol increases (29, 30). There are multiple alcohol identification tests available, both for community and hospital care settings, to effectively screen for harmful alcohol use. Public Health England (PHE) suggests using the following alcohol identification and screening tests (31);

a) Alcohol use disorders identification test (AUDIT)
b) Alcohol use disorders identification test for primary care (AUDIT PC)
c) Alcohol use disorders identification test for consumption (AUDIT C)
d) Fast alcohol use screening test (FAST)
e) Single question alcohol use test (M SASQ)

Public Health England (PHE) and the NHS Long Term Plan advocate for maximising every contact with patients with a focus on preventative medicine. The burden of such contacts has implications for both individuals and healthcare services. The UK Commission for Quality and Innovation (CQUIN) give incentives for screening patients for alcohol and initiating an appropriate response. Both CQUIN and National Institute for Health and Care Excellence (NICE) recommend using AUDIT-C as an initial alcohol screening tool.

1.2 Alcohol-related liver disease (ARLD):

1.2.1 Epidemiology of ARLD

Among active drinkers; the cumulative incidence of ARLD is 20,000 per 100,000 persons (32), whereas, the prevalence of ARLD varies with age, in the age group 25 to 44 years the prevalence of ARLD is 604 per 100,000 persons, and in the age group 45 to 64 years 948 per 100, 000 person (33, 34).

Most of the consumed alcohol (90%) is metabolised in the liver by enzymatic pathways involving alcohol dehydrogenase (ADH), cytochrome P4502E1 and catalase (35). Acute or chronic insult to the liver impact hepatic alcohol oxidation. Due to sex related disparities in factors, such as body fat distribution, gastric alcohol dehydrogenase activity, cytochrome P4502E1 activity, dopamine system, exposure of Kupffer cells and insulin like growth factors to oestrogen, there is an increased risk of alcohol-related end-organ damage in females compared to males (35, 36).

Among lifelong drinkers, 20-30% develop cirrhosis, and the risk proportionally rises with an increase in the volume of alcohol consumed (20, 37). ARLD has a positive dose-response relationship with the volume of alcohol consumed, the risk of liver

disease starts from alcohol consumption as low as 84 grams per week in women and 168 grams per week in men (38, 39). As compared to long-term abstainers the consumption of one drink a day (12 grams of pure alcohol) significantly increased the risk of liver disease in women (relative risk 1.64, 95% CI 1.07, 2.51) (39). For an alcohol consumption of 5-6 drinks per day, the relative risk (RR) of cirrhosis both in men and women was 6.26 (95% CI 2.38, 16.50), and for more than 7 drinks per day was 10.70 (95% CI 2.95, 38.78) (39). A prospective population-based study comprising 130,558 person-years of follow-up demonstrated that for an alcohol intake of 336 to 492 grams per week the relative risk (RR) of developing cirrhosis in men was 7.0 (95% CI 3.8, 12.8) and in women was 17.0 (95% CI 6.8, 40.8) (38).

In people with chronic alcohol use disorder (AUD), 90-95% have hepatic steatosis, of these 40 - 50 % will develop alcoholic hepatitis and up to 10% progress to liver cirrhosis (40). The risk significantly rises with the presence of other comorbidities; especially metabolic diseases such as diabetes and obesity (41). Abstinence from alcohol is key for recovery, in the biopsy proven alcohol-related cirrhosis cohort, 7-year survival in abstainers was 72% compared to 44% in active drinkers (42). The evidence shows, after cessation of chronic alcohol drinking, liver function tests start improving in two weeks and hepatic steatosis in 2-6 weeks (43, 44). To mitigate the health hazards of alcohol use the United Kingdom (UK) Chief Medical Officer's drinking guidelines recommend both for men and women to limit alcohol intake to 14 units per week and spread it over 3 days a week (45).

Excess alcohol intake causes a spectrum of liver injuries ranging from haptic steatosis, steatohepatitis, alcoholic hepatitis, liver fibrosis and cirrhosis. A recent systematic review reported, among the cohort of harmful alcohol users who had a liver biopsy for any reason, a quarter had hepatic steatosis, a quarter had steatohepatitis, and quarter had cirrhosis (46). Amongst hazardous alcohol drinkers, based on histological features at baseline, the annualised progression rates to cirrhosis were 1% (95% CI 0-8%) for a normal liver biopsy, 3% (95% CI 2-4%) for hepatic steatosis, 10% (95% 6-17%) for steatohepatitis and 8% (95% 3-19%) for any grade of fibrosis. Annual mortality was 6% and 8% in hepatic steatosis and cirrhosis respectively, whereas in patients with alcoholic steatohepatitis annual mortality was higher if they were hospitalised (15% vs 5%) (46). Once the patient has established cirrhosis the rate of progression from compensated to decompensated chronic liver disease is 5 to 7% per year, and the median survival drops from 12 years to below 2 years (47). The liver has a remarkable recovery potential; stopping drinking is the key factor in improving outcomes and survival for those with liver damage and remains

the mainstay of treatment (48). Abstinence from alcohol leads to complete resolution of alcoholic-related fatty liver disease and improves survival both in early and advanced ARLD (49, 50).

1.2.2 The rationale for non-invasive tests-based advice

ARLD often causes no symptoms in its earlier stages, over half of the patients are unaware they have it and are first diagnosed after an emergency hospital admission (51). This results in only a few patients presenting at a stage when interventions can avert alcohol-related liver damage (6, 20). ARLD is twelve times more likely to present late compared to other aetiologies of liver disease (52). Once patients with alcohol misuse develop cirrhosis the prognosis becomes exceptionally poor, the mortality rate for alcohol-related cirrhosis has been reported as high as 75% at 5 years and 91% at 15 years (53).

A recent study showed, in 5 years before their death, ARLD patients had a median of five hospital admissions (interquartile range 3–10), 4 A&E attendances (interquartile range 2–8) and 16 outpatient attendances (interquartile range 7–29) (54). Yet over half of these were only diagnosed with liver disease in the last six months of their life. Emergency presentation at first ARLD diagnosis and white ethnicity were significantly associated with a delay in diagnosis. Each of these interactions with healthcare services presents an opportunity missed (55). This also presents a teachable moment whereby patients can be more receptive to health messages (48). Evidence has demonstrated, if current treatment figures for alcohol dependence can be increased from 8% to 40%, it will reduce alcohol-related mortality in men by 13% and women by 9%, though current constraints on health services draw limitations on how much of this can be realistically achieved (56).

Although systematic reviews of Randomised Controlled Trials (RCTs) have established that delivering brief advice to harmful drinkers helps to reduce alcohol consumption (57, 58). Most studies were conducted in settings where the prevalence of liver disease is likely to be lower than in specialist alcohol treatment services. In alcohol services high levels of physical and psychological dependence on alcohol are frequent. NICE guidelines state that adults with alcohol dependency should be assessed and offered intensive structured community based interventions (with or without medical therapy) as these provide the best chance of achieving and maintaining abstinence from alcohol (25). Despite several behavioural interventions for alcohol misuse that have been in clinical practice for over two decades alcohol-related harm is on an alarming rise (6). There is a pressing need to optimise existing

interventions to reduce harmful alcohol intake and examine effective alternative options.

Early diagnosis of liver fibrosis provides an opportunity to intervene and reduce or stop alcohol intake. This is known to be the most effective way of preventing liver disease progression (21). Though, several non-invasive tests (NITs) such as transient elastography, and enhanced liver fibrosis (ELF) tests are now available which can reliably test for the presence or absence of significant liver fibrosis (59). These tests are not widely embedded in high-risk community services including outreach alcohol services (9, 20). Transient elastography by FibroScan (Echosens, France) has been used in primary care (General Practice) settings to detect liver disease in populations identified as having liver disease risk (heavy drinkers and those with type 2 diabetes). These studies showed that screening asymptomatic individuals based on risk for liver disease doubles the rates of cirrhosis diagnosis in the primary care populations studied (60, 61). Moreover, a recent systematic review suggested providing feedback to patients based on non-invasive tests (NITs) for liver disease can be an effective way to reduce harmful alcohol intake (62). In contrast, concerns have also been raised regarding the risks of NITs based feedback methods potentially providing false reassurance leading to unintended negative consequences such as exacerbating alcohol drinking (63). Although, providing tailored NITs based feedback to people at risk of liver disease may affect their drinking behaviour (64), at present these markers are not widely incorporated into alcohol treatment settings (9). Hence, the potential of combining early diagnostic interventions and advice has not been extensively explored in alcohol services.

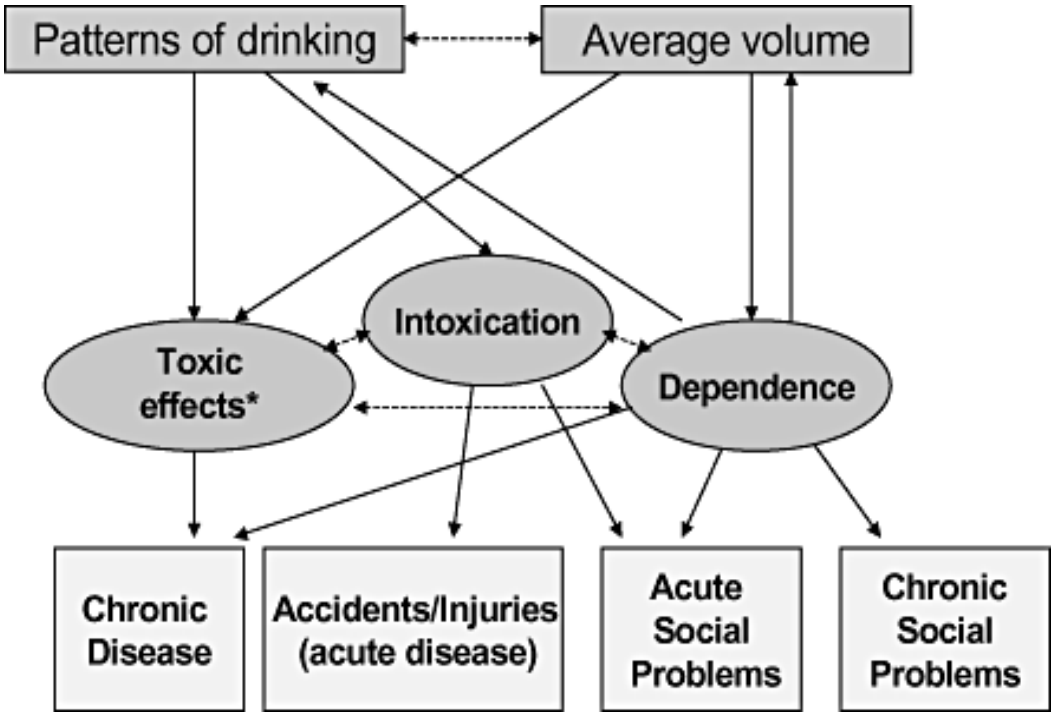
1.3 Alcohol harm reduction: interventions to reduce alcohol intake

Alcohol-related harm either at the individual or population level can be determined by the volume of alcohol drunk, patterns of drinking, and frequency of drinking (2, 65). Thomas F. Babor, (2010); explained the complex correlation between patterns of alcohol drinking, average volume consumed, and alcohol-related harm (Figure 1-1).

Interventions to reduce alcohol-related harm are targeted at the individual and population levels. To effectively mitigate the risk of harmful drinking The National Institute for Health and Clinical Excellence (NICE) advocates for both (66-68).

I will provide a brief overview of population based interventions; the focus of this doctoral thesis will be individual level interventions mainly non-invasive tests (NITs) for liver disease based advice.

Figure 1-1. “Why alcohol is no ordinary commodity; relationships among alcohol consumption, mediating factors and alcohol-related consequences”



Alcohol: No Ordinary Commodity – a summary of the second edition (Addiction, Volume: 105, Issue: 5, Pages: 769-779, First published: 08 April 2010, DOI: 10.1111/j.1360-0443.2010.02945.x). Reprint permission was obtained (date 10/01/2022, License number 5225320329410, Publisher John Wiley, and Sons

1.3.1 Population based interventions

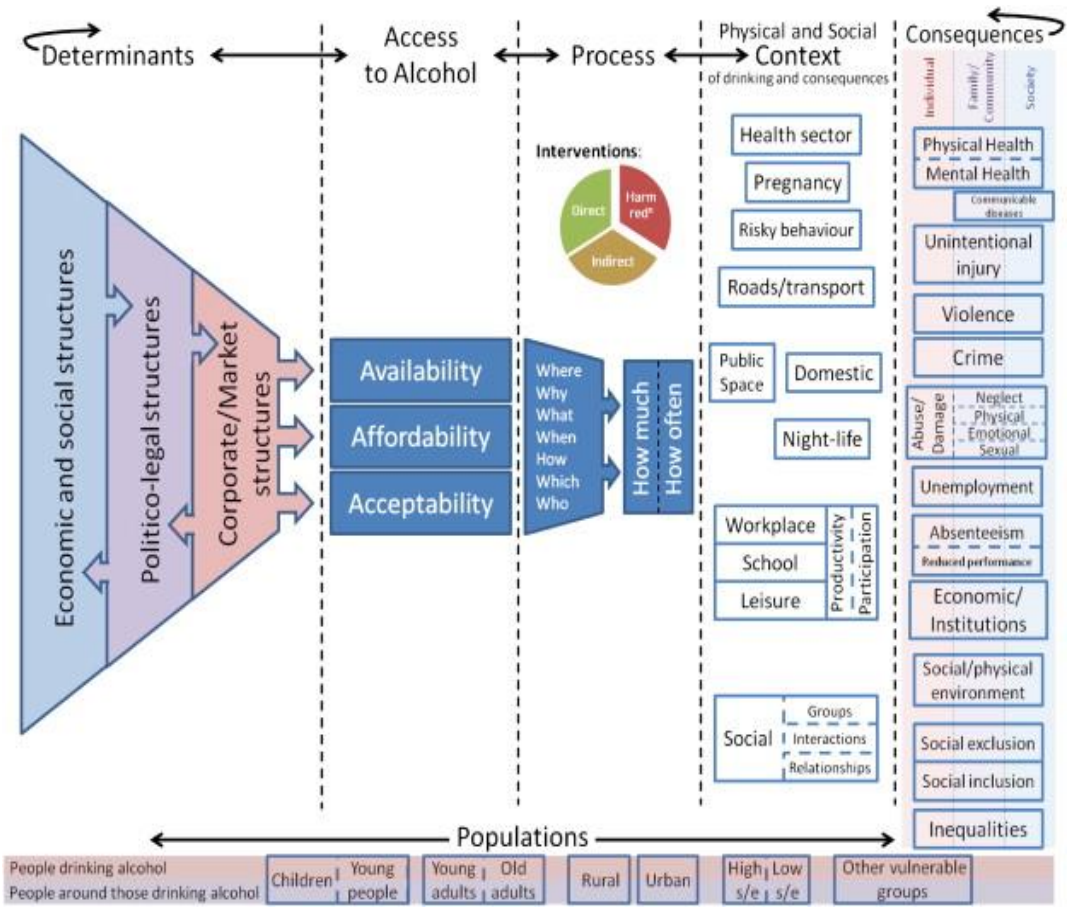
Unhealthy lifestyle choices such as smoking and alcohol have a significant impact on health related outcomes (69). There is growing interest in modifying high-risk lifestyles by implementing population based interventions (70). Researchers have previously shown by implementing preventive measures and modifying major risk factors for non-communicable diseases (NCDs) would increase global healthy life expectancy by 9.3 years (range 4.6-16.1 years) (70, 71).

Leading drivers for alcohol-related harm that can be intervened at the population level are alcohol affordability, availability, and acceptability (65, 72). Martineau et al., (2013) presented a framework summarising determinants, drivers, moderators, and consequences of alcohol-related harm at a population level (Figure 1-2) (72). The existing evidence on population-level interventions supports regulatory and statutory enforcement policies e.g., minimum legal drinking age, increasing taxation, restricting days or hours of sale, local non-regulatory strategies e.g., on-premises server training, family interventions, school, or workplace-based interventions (72).

There is an increasing body of evidence demonstrating that policies like minimum unit pricing (MUP) are effective in mitigating alcohol-related harm (73, 74). In Canada, a 10% increase in MUP resulted in a 9% reduction in alcohol-related hospital admissions and a 32% reduction in alcohol-related mortality (75). Similarly, limiting alcohol availability e.g., by reducing alcohol outlet density, and changing alcohol social acceptability e.g., by controlling labelling and advertisement has shown to be beneficial in decreasing alcohol-related harm (76, 77).

Population-based approaches are effective in lowering overall alcohol consumption and dampening alcohol-related harm (66). Implementing effective population-based interventions to reduce alcohol-related should be among the top public health priorities and key components of health and social care policies surrounding alcohol (71). Despite most evidence supporting their effectiveness population level interventions are not widely adopted. This could be due to perceived economic contribution in the remit of alcohol tax revenue and the influence of the alcohol industry on shaping these policies (78).

Figure 1-2. Conceptual framework of the causative pathways linking proximal drivers of alcohol consumption with distal health and social outcomes"



Population-level interventions to reduce alcohol-related harm: An overview of systematic reviews (Preventive medicine, Volume 57, Issue 4, October 2013, Pages 278-296, First published: 27 June 2013, DOI: 10.1016/j.ypmed.2013.06.019) Reprint permission was obtained (date 10/01/2022, License number 5225340349331, Publisher Elsevier.

1.3.2 Individual-level interventions

As per NICE guidelines, alcohol screening should be followed by individual-level interventions such as brief advice (66). For the purpose of this thesis, the individual-level interventions are broadly divided into two subtypes: non-NITs based advice (standard advice), and NITs-based advice.

1.3.2.1 Non-NITs based advice (standard advice)

The non-NITs based advice is defined as a “form of advice where no non-invasive tests (NITs) of liver disease were performed, and advice was given purely based on the history of alcohol misuse”. From now onwards, I will refer to non-NITs based advice as standard advice.

Most of these interventions such as brief interventions (BI) are designed to reduce harmful drinking and can be delivered in non-specialist settings across primary and secondary care. They employ techniques of motivational interviewing and the concept of the “teachable moment” designed to achieve behaviour change (79). Although brief interventions have been proven beneficial in reducing hazardous alcohol intake both in primary and secondary care settings they are most effective in increased and high-risk alcohol drinkers while evidence to support effectiveness in the alcohol dependent group is limited (57, 58). Majority of patients presenting to specialist alcohol services are alcohol dependent (80).

The community alcohol services in Nottingham are run by Nottingham Recovery Network (NRN). For adult drug and alcohol services, there are three main categories of standard advice offered by the NRN:

a) Psychological which include motivational interventions, family and social network interventions, and cognitive and behavioural-based relapse prevention interventions (substance misuse specific).
b) Recovery Support includes 12-step work and counselling.
c) Pharmacological which involves prescribing medication for drug and/or alcohol relapse prevention support. For example, naltrexone, acamprosate, disulfiram as part of alcohol or opioid relapse prevention therapy and Chlordiazepoxide for acute alcohol withdrawal.

1.3.2.2 Non-invasive tests (NITs) for liver disease-based advice

The non-invasive tests-based advice is defined as a “form of advice where no non-invasive tests (NITs) for the liver disease were performed (including but not limited to; Transient elastography, Liver function tests (LFTs), Enhanced Liver Fibrosis (ELF) Test, FIB-4 score, APRI score) and advice was given based on results of non-invasive tests”.

The advice based on biological markers, such as diagnostic tests, indicating exposure to a harmful substance, increased susceptibility or the presence of a disease is more likely to promote behaviour change (81, 82). The tailored advice based on the results of the tests demonstrating the degree of lung injury has been successfully used to

promote smoking cessation (83). Similarly, including the results of point-of-care diabetes tests in patient feedback has been associated with improvement in compliance with treatment and improved glycaemic control (84, 85). There is emerging evidence that the addition of biomarker-based advice to personalised healthcare communications enhances motivation to overcome addictive behaviour (86, 87). For hazardous and harmful alcohol users, a simple liver fibrosis test and personalised feedback prompted reductions in alcohol use in those with and without evidence of liver damage (88).

1.3.2.3 Alcohol recovery narratives

Recovery narratives are personal stories of health problems and recovery, which can be shared with others and can provide recipients with insights into the phenomenology of recovery (89-91). In the context of alcohol misuse, the recovery narratives can be defined as “first-person lived experience accounts, which include elements of adversity, struggle, strength, success, and survival related to alcohol misuse, and refer to events or actions over a period” (92, 93). Sharing alcohol recovery narratives has been an important component of the Alcoholics Anonymous (AA) 12-step programme (94). Moreover, recovery narratives have been used to promote and encourage engagement with health services (95), where they might be used to extend clinical practice, including as a resource for clients who are struggling to recover (96).

Access to recovery stories can help address mental health problems and support recovery from addiction (97, 98). Peer support from people who have recovered from alcohol misuse is beneficial in modifying high-risk drinking behaviour (99).

Chapter 2. Thesis outline

2.1 Aim

The overarching aim of this thesis is to describe the epidemiology of alcohol use disorder (AUD) in secondary care and to evaluate the feasibility of delivering NITs based advice in community alcohol services.

2.2 Objectives

- To systematically review the literature to determine the effect (beneficial or adverse) of the addition of advice based on liver disease diagnostic tests compared to standard advice on high-risk drinking behaviour
- To systematically review the literature and produce a conceptual framework describing the characteristics of alcohol recovery narratives to inform the development of alcohol recovery video stories (ARVS) for the KLIFAD trial
- To determine the prevalence and characteristics of alcohol use disorder (AUD), describe the distribution of alcohol use disorder in non-alcohol-specific or non-alcohol-related admissions, ascertain the relationship between them and discuss the impact of the Covid-19 pandemic on alcohol use disorder in the secondary care setting.
- To evaluate the feasibility and extent of efficacy of NITs (transient elastography) based advice and alcohol recovery video stories (ARVS) in changing high-risk drinking behaviour in community alcohol services common to the UK practice
- To summarise the findings of the above projects, discuss salient findings, and highlight key recommendations for implementation into clinical practice

2.3 Thesis overview

The aim and objectives of this thesis are addressed in six chapters.

Chapter 3 discusses the epidemiology of alcohol use disorder (AUD) and associated shared high-risk characteristics among hospitalised patients. It further explores the distribution of alcohol use disorder in non-alcohol-related hospital admissions and ascertains the relationship between them. It also outlines the impact of the Covid-19 pandemic on alcohol use disorder in the secondary care setting. The findings from chapter 4 highlighted the burden of AUD and led to the KLIFAD trial. To inform the KLIFAD trial I conducted a systematic review with a meta-analysis which is presented in chapter 4.

Chapter 4 outlines the systematic review and meta-analysis evaluating existing literature on the impact of adding advice based on diagnostic tests for liver disease (intervention-based advice) to routine care to prevent alcohol misuse and compares the effectiveness of intervention-based advice to non-intervention-based advice in reducing alcohol consumption amongst people with high-risk drinking behaviour. While conducting the literature search for this systematic review I came across evidence discussing the role of lived experience in mental health recovery. This led me to explore the role of alcohol recovery narratives in AUD and informed chapter 5.

Chapter 5 outlines the finding of the systematic review with narrative synthesis and proposes a conceptual framework describing the characteristics of alcohol recovery narratives that have been reported in the research literature. The proposed alcohol recovery narrative conceptual framework (ARNCF) will facilitate identifying gaps in knowledge (e.g., narratives or narrators who have not been considered in research analyses), summarising the range of methods that have been used to collect and analyse narratives to date, understanding potential biases of these methods, informing the content of educational courses that support people in sharing a narrative as a part of the recovery process and enabling collective approaches that draw on sets of narrative knowledge to influence the health system.

Chapter 6 provides an outline of the KLIFAD (Knowledge of LIver Fibrosis Affects Drinking) study. Much of this thesis is both informs the KLIFAD study and constitutes parts of it. The KLIFAD study comprised of three work packages (WP). **WP1:** consists of developing standardised scripts for transient elastography operators to deliver liver disease-specific advice to eligible participants having transient elastography. **WP2:** consists of collecting alcohol recovery video stories (ARVS) and creating a video library of ARVS for use in the feasibility RCT (WP3). **WP3:** is a feasibility RCT testing the transient elastography scripts and ARVS developed in WP1 and WP2 in a 1:1 randomised control trial in community alcohol services. WP 2 and WP 3 are presented in detail in Chapters 7 and 8. There is no dedicated analysis and chapter for WP 1.

Chapter 7 validated the ARNCF proposed in chapter 5 by applying it to alcohol recovery narratives generated through semi-structured interviews in KLIFAD WP 2. It assessed the relevance of existing dimensions and types, identified additional dimensions and types, and extended the pre-existing subgroups of ARNCF. It also outlines the preliminary understanding of the types of knowledge that can be developed by applying the framework to narratives. The work from chapters 5 and 7

informed the creation of alcohol recovery video stories which were used as part of the intervention in KLIFAD WP 3.

Finally, Chapter 8 presents KLIFAD WP 3 outlining the feasibility of integrating scripted feedback based on transient elastography results and alcohol recovery video stories as behavioural interventions in addition to usual care in community alcohol services.

Chapter 3. Epidemiology of alcohol use disorder among hospitalised patients and the impact of Covid-19 pandemic

3.1 Rationale and Overview

Alcohol is among the leading causes of hospital admission in the UK. However, alcohol use disorder (AUD) detection rates in secondary care remain poor. This could be due to inadequate knowledge, awareness and negative attitudes toward patients with alcohol use disorder (100, 101). In patients with AUD understanding the common reasons for hospitalisation can facilitate early identification of ARLD and improve patient engagement (102). An in-depth understanding of AUD in hospital settings, and associated high-risk patient and environment-related factors are critical in developing targeted alcohol services (103).

The covid-19 pandemic has severely influenced health behaviours, imposed financial difficulties, ongoing social isolation and uncertainty about the future has resulted in an increase in harmful alcohol consumption. Simultaneously, the redistribution of health care resources could mean less help was accessible to those with AUD (104). During Covid-19, the tertiary liver units reported a more than two-fold increase in referral burden for ARLD (48% versus 19%, p=<0.0001) and critically unwell cases (24% versus 11%) (105). The Global Drug Survey on Covid-19 showed almost half (48%) of the UK participants reported an increase in the quantity of alcohol consumed, and 54% stated an increase in frequency (106). Although hospitals in the UK have observed a spike in alcohol-related hospital admissions, detailed and more representative data on the impact of Covid-19 on alcohol use disorder among hospitalised patients is lacking (107).

In this chapter, I have presented routinely collected NHS data on retrospective cohorts of adult patients admitted to Nottingham University Hospitals (NUH) and had alcohol assessment by AUDIT-C. I first analysed the cohort admitted to NUH between 1st April 2019 to 31st March 2020 to determine the prevalence of alcohol use disorder (AUD) among hospitalised patients. Using the same data, I then compared the characteristics of patients with AUD to patients with no AUD, to identify the high-risk shared characteristics related to AUD. I analysed individual ICD-10 discharge diagnosis codes to describe the distribution of AUD among non-alcohol-related hospital admissions, and ascertain the relationship between them. Finally, I compared pre-pandemic (1st April 2019 to 31st October 2019-derived from cohort one) and pandemic (1st April 2020 to 31st October 2020) cohorts to evaluate the impact of the Covid-19 pandemic on AUD detected in secondary care settings.

3.2 Methods

3.2.1 Study population

Nottinghamshire is a county in the East Midland region of England with a population of 817,900 (mid-2017). This includes Nottingham which is the biggest city in Nottinghamshire with a mid-2017 population of 329,200 (108). The study was conducted at Nottingham University Hospitals (NUH), England, UK, which is the regional tertiary centre for many services including hepatology. Local institutional ethical approval was obtained (Registration Number: 20-728C).

3.2.2 Cohorts

To determine the epidemiology of AUD among hospitalised patients the cohort was defined as

1. **Cohort one**: patients admitted to NUH between 1st April 2019 to 31st March 2020.

To evaluate the impact of the Covid-19 pandemic on AUD in secondary care settings two time periods were chosen and cohorts were defined as

2. **Pre-pandemic**: patients admitted to NUH between 1st April 2019 to 31st October 2019. This cohort was derived from cohort one.
3. **Pandemic**: patients admitted to NUH between 1st April 2020 to 31st October 2020. This was an independent cohort from cohort one.

3.2.2.1 Eligibility criteria

The following eligibility criteria were applied

a) Adult patients aged 18 and over admitted to NUH during study defined periods

3.2.3 Definitions

As per Public Health England (2014 and 2020) guidance, the conditions were defined as non-alcohol related where alcohol was not a contributory or sole cause of the admission (109).

The term alcohol use disorder (AUD) was used to represent and discuss the results of the AUDIT-C score and alcohol-related disorders (AD) to encompass broader alcohol-related problems including ARLD.

3.2.4 Universal alcohol screening

Universal alcohol screening by AUDIT-C score has been implemented at NUH since 2018. All patients, except the ones admitted directly to intensive care, have a mandatory electronic alcohol assessment by the admitting staff nurse. The AUDIT-C is an alcohol harm assessment tool consisting of three questions on alcohol consumption (

Table 3-1). An AUDIT-C score of 0-4 is screened negative for AUD whereas a score of ≥5 is screened positive for AUD (increased risk score 5-7, high-risk score 8-10, possible dependence score 11,12) (110). As local practice in NUH patients with an AUDIT-C score ≥ 8 get automatically referred to an onsite alcohol care team.

Table 3-1. Alcohol use disorder identification test consumption (AUDIT-C)

Question	**score**				
	0	1	2	3	4
How often do you have a drink containing alcohol?	Never	Monthly or less	2 to 4 times per month	2 to 3 times per week	4 or more times per week
How many units of alcohol do you drink on a typical day when you are drinking?	0 to 2	3 to 4	5 to 6	7 to 9	10 or more
How often have you had 6 or more units if female or 8 or more if male, on a single occasion in the last year?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily
			Final AUDIT-C score:		

Interpretation of AUDIT C score	**score**
Screened positive for alcohol use disorder	≥ 5
Low risk	0-4
Increased risk	5-7
High risk	8-10
Possible dependence	11-12

3.2.5 Data source and variables

Access to NUH electronic medical records was gained as part of local ethical approval, and hospital-based activity and the access team facilitated the data extraction. Electronic medical records hold information on the patient's discharge diagnosis, alcohol assessment, and demographics. Anonymised data on age, sex, ethnicity, civil status, mode of admission, AUDIT-C score at admission, discharge diagnosis (ICD-10 version 5), inpatient speciality of care, length of stay, number of

hospital admissions, Lower Super Output Area (LSOA) and Indices of Multiple Deprivation (IMD).

The following variables were coded as binary

- Sex: male vs female
- Ethnicity: White vs Minority ethnicity
- Civil status: In a relationship (married, in a civil partnership or in a long-term relationship) vs not in a relationship (single, divorced, separated, dissolved civil partnership, widowed, or surviving civil partner)
- Mode of admission: Accident & Emergency (A&E) vs Non-A&E (elective, from an outpatient clinic, from GP).
- Inpatient speciality of care: Medicine vs Surgery (Table 3-2)

Table 3-2. List of medical and surgical specialities

Medical specialities	**Surgical specialities**
General Medicine	Trauma & Orthopaedics
Respiratory Medicine	General Surgery
Cardiology	Urology
Stroke Medicine	Neurosurgery
Health Care for Older People	Otorhinology
Clinical Oncology	Thoracic Surgery
Clinical Haematology	Spinal Surgery Service
Gastroenterology	Gynaecology
Infectious Diseases	Maxillo-Facial Surgery
Nephrology	Cardiac Surgery
Adult Cystic Fibrosis Service	Vascular Surgery
Diabetic Medicine	Colorectal Surgery
Neurology	Hepatobiliary & Pancreatic Surgery
Hepatology	Upper Gastrointestinal
Endocrinology	Breast Surgery
Palliative Medicine	Burns Care
Rheumatology	Ophthalmology
Medical Oncology	Transplantation Surgery
Pain Management	Cardiothoracic Surgery
Rehabilitation	Interventional Radiology
Genitourinary Medicine	Cleft Lip & Palate
	Oral Surgery
	Blood & Marrow Transplantation

The length of stay (LOS) was calculated as the number of days between the date of admission and the date of discharge. The number of admissions was the total number of hospital inpatient visits a patient had during the study specified period.

The Lower Super Output Areas (LSOAs) are produced by the Office for National Statistics (ONS) to describe statistics of a small area with an average of approximately 1,500 residents or 650 households. As per the 2011 Census, there are 32,844 LSOAs in England which were used to determine indices of multiple deprivations 2015 (111).

Deprivation was assigned by using the index of multiple deprivations 2015 (IMD) quintiles as provided by PHE based on the LSOAs of residence at the time of hospital admission. The index of multiple deprivation decile (IMDD) combines information from seven domains and produces an overall measure of deprivation. IMD ranks the scores to produce quintiles with 1 equal to the most deprived 20% and 5 equal to the least deprived 20% of neighbourhoods nationally.

3.2.6 Outcomes

3.2.6.1 For cohort one

- The primary outcomes were: (a) to describe the prevalence and characteristics of AUD among hospitalised patients, (b) to determine the distribution of AUD in patients with a non-alcohol specific or alcohol-related ICD-10 discharge diagnosis and ascertain the relationship between them.
- The secondary outcomes were to identify high-risk shared characteristics associated with AUD and to establish acceptance rates of universal alcohol screening among these patients.

3.2.6.2 For pre-pandemic and pandemic cohorts

- The primary outcome was to evaluate the impact of the Covid-19 pandemic on AUD among hospitalised patients.
- The secondary outcome was to compare pandemic cohort Covid-19 positive and negative patients, including inpatient mortality analysis between Covid-19 positive AUD vs Covid-19 positive low risk for AUD.

During the study period, the diagnosis of Covid-19 at NUH was confirmed by accepted molecular tests and/or by radiology.

3.2.7 Statistical analysis plan

3.2.7.1 Normality of data

The normality of quantitative data was assessed by visual inspection of histograms. The normally distributed quantitative variables were summarised as mean ± standard

deviation (SD) and the quantitative variables which did not follow a normal distribution as median ± interquartile range (IQR). The correlation between AUDIT-C Score and normally distributed quantitative variables was assessed by parametric tests (Pearson's correlation coefficient, unpaired T-test, ANOVA test) and non-normally distributed by non-parametric tests (Spearman's correlation coefficient, Mann-Whitney U test).

3.2.7.2 Categorical data

All the categorical variables included in the study were coded as ordinal or nominal and were summarised as numbers (percentages). Categorical variables were analysed by the Chi-Squared test, with results reported as absolute and relative frequencies ± 95% confidence interval.

3.2.7.3 Logistic regression analysis

Logistic regression analysis was carried out to ascertain if primary and secondary outcomes influenced AUD. The low-risk group was set as a control to compare increased-risk, high-risk and alcohol-dependent groups to predict the possibility of different outcomes. A complete case analysis model was used, and cases with missing data were excluded. The variables of interest (age, gender, IMD, ethnicity) and variables with a P-value ≤0.05 were included in the final model. The variables were mutually adjusted for each other The results were presented as an adjusted odds ratio (OR) with a 95% confidence interval and p-value.

3.2.7.4 Statistical tools and reporting guidelines

Statistical analysis was conducted using Statistical Package for the Social Sciences (SPSS version 26.0) and Prisma GraphPad (version 8.0). Strengthening the reporting in observational studies in epidemiology (STROBE) reporting guidelines for reporting observational studies in epidemiology were used throughout the article (112).

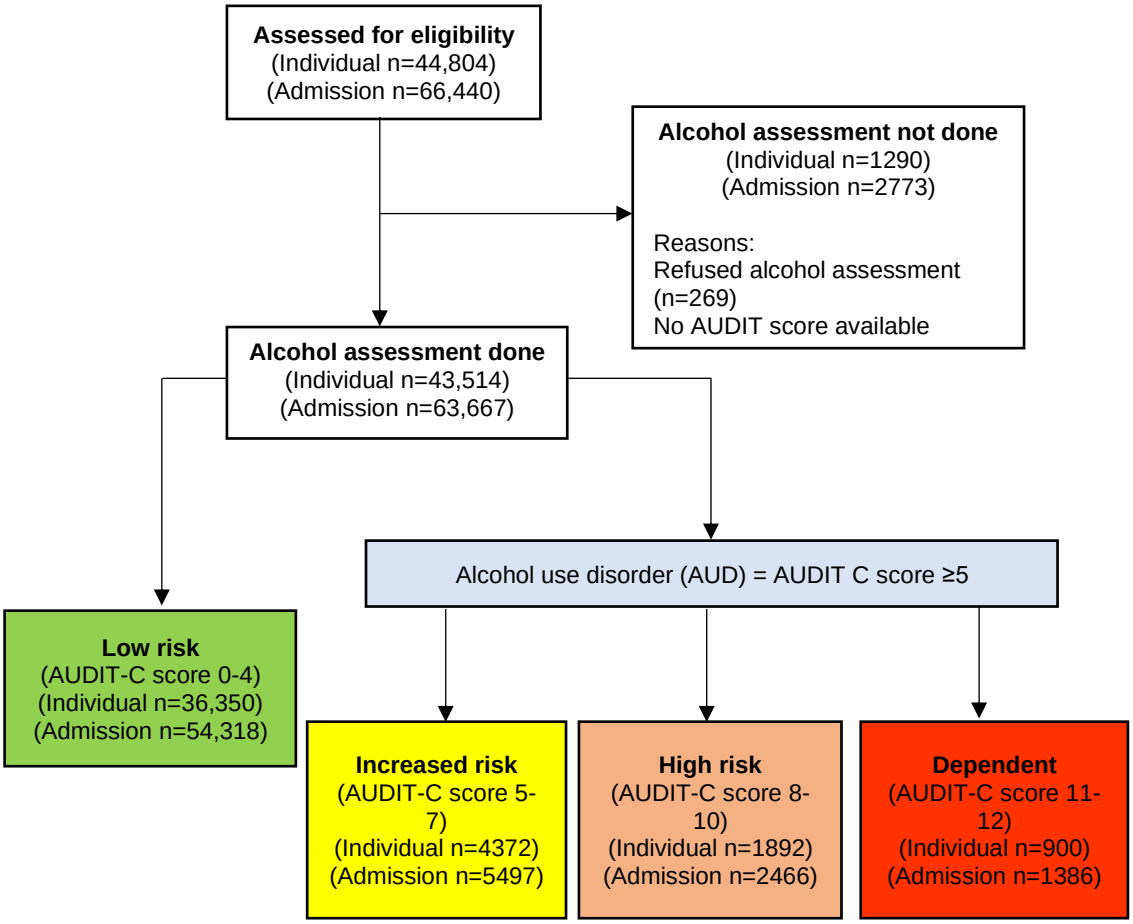
3.3 Results Cohort one

3.3.1 Description of cohort and epidemiology of alcohol use disorder (AUD)

A total of 44,804 patients accounting for 66,440 admissions were offered alcohol assessment by AUDT-C. Of them, 269 (0.60 %) declined to complete the alcohol assessment and 1021 (2.28%) were excluded for not having an AUDIT-C

assessment. The final cohort included 63,667 admissions involving 43,514 patients (Figure 3-1).

Figure 3-1. Consort flow diagram for participant's inclusion



The mean age of the cohort was 63.1 years (SD±19.9), 48.0% (n=20,863) were male, 71.2% (n=30,994) were white, and 44.7% (n=17,819) were from top two most deprived quintiles. In the whole cohort based on the AUDIT-C score, 16.5% (n=7,164) had AUD, of them, 10.7% (n=4,372) were increased risk, 4.4% (n=1,892) were high risk, 2.1% (n=900) were alcohol dependent. The baseline characteristic of the cohort are provided in Table 3-3

Table 3-3. Baseline characteristics of the cohort

	No AUD (n= 36,350)*	AUD (n=7,164)*	p
All admissions	54,318 (85.3)	9,349 (14.7)	<0.001
Male	16,017 (44.1)	4846 (67.7)	<0.001
Age years (SD)	64.6 (± 20.0)	56.0 (± 14.2)	<0.001

Ethnicity				<0.001
	White	2,5826 (89.9)	5,168 (94.5)	
	BAME	2,914 (10.1)	300 (5.5)	
	Missing	7,610	1,696	
IMD quintiles				0.195
	1 (most deprived)	8,797 (26.4)	1,759 (26.9)	
	2	6,094 (18.3)	1,169 (17.9)	
	3	5,749 (17.2)	1,056 (16.2)	
	4	5,475 (16.4)	1,094 (16.7)	
	5 (least deprived)	7,222 (21.7)	1,455 (22.3)	
	Missing	3,013	631	
Civil status				<0.001
	In a relationship[a]	18,108 (60.4)	2,783 (48.0)	
	Not in a relationship[b]	11,853 (39.6)	5,792 (52.0)	
	Missing	6,389	1,372	
Mode of admission				0.421
	Emergency	21,355 (58.7)	4,172 (49.2)	
	Other	14,995 (41.8)	2,992 (50.8)	
Speciality				<0.001
	Medicine	20,591 (56.6)	3,522 (49.2)	
	Surgery	15,759 (43.4)	3,642 (52.2)	
	Other or unknown	647	187	
Length of Stay (days)		4 (1-268)	3 (1-178)	<0.001

Data are number (%), mean (SD) or median (range),

AUDIT-C score: 0-4 (low risk), 5-7 (increased risk), 8-10 (high risk), 11-12 (alcohol dependent)

[a]In a relationship includes married, in a civil partnership or in a long-term relationship

[b]Not in a relationship includes single, divorced, separated, dissolved civil partnership, widowed, or surviving civil partner

*Number of individual patients

3.3.2 Comparison of patients with alcohol use disorder (AUD) to those without AUD

3.3.2.1 Univariable analysis

The patients with AUD were significantly younger than those without AUD, with a mean age difference of 8.6 years (SD± 0.25, p<0.001). Patients with AUD compared

to those without AUD were more likely to be male (p <0.001), of white ethnicity (p<0.001), not in a relationship (p <0.001), cared for by surgical specialities (p <0.001) and had a shorter length of stay (p <0.001). The difference between deprivation quintiles and mode of admission were non-significant.

3.3.2.2 Multivariable analysis

The results of fully adjusted multivariable logistic regression (MLR) demonstrated that based on AUDIT-C assessment, females compared to males were 66% less likely to have AUD (Odds ratio OR 0.34, p<0.001), minority ethnicity compared to white ethnicity were 61% less likely to have AUD (OR 0.39, p<0.001), patients were less likely to be from a lower index of multiple deprivations (1^{st}, 2^{nd},3^{rd}, 4^{th} quintile) compared to 5^{th} quintile, and less likely to be cared for by medical specialities (OR 0.85, p<0.001). Among all age groups patients in the age group, 60-69 years were more likely to be screened positive for AUD (OR 4.19, p<0.001). AUD compared to low risk were more likely to be single (OR 1.18, p<0.001), and admitted as an emergency (OR 1.21, p<0.001) (Table 3-4). The multivariable logistic regression for individual AUD risk groups is given in Appendix 1.

Table 3-4. Multivariable logistic regression analysis

		Unadjusted	p	Adjusted	p
Age group (years)					
	18-29	1		1	
	30-39	0.98 (0.86-1.10)	0.702	1.48 (1.29-1.69)	<0.001
	40-49	0.88 (0.79-0.97)	0.011	2.52 (2.19-2.89)	<0.001
	50-59	1.29 (1.16-1.43)	<0.001	3.86 (3.32-4.49)	<0.001
	60-69	0.99 (0.89-1.10)	0.864	4.19 (3.53-4.99)	<0.001
	>70	0.39 (0.36-0.44)	<0.001	2.88 (2.33-3.55)	<0.001
Sex					
	Female	0.38 (0.35-0.39)	<0.001	0.34 (0.35-0.39)	<0.001
	Male	1		1	
Ethnicity					

	Unadjusted	p	Adjusted	p
Minority ethnicity	0.51 (0.46-0.58)	<0.001	0.39 (0.35-0.45)	<0.001
White	1		1	
IMD quintiles				
1 (most deprived)	0.99 (0.92-1.07)	0.846	0.79 (0.74-0.86)	<0.001
2	0.95 (0.87-1.03)	0.254	0.80 (0.73-0.88)	<0.001
3	0.91 (0.84-0.99)	0.036	0.78 (0.72-0.86)	<0.001
4	0.99 (0.91-1.08)	0.851	0.92 (0.84-1.01)	0.072
5 (least deprived)	1		1	
Civil status				
Not in a relationship[a]	1.65 (1.56-1.74)	<0.001	1.18 (1.11-1.26)	<0.001
In a relationship[b]	1		1	
Mode of admission				
Emergency	0.98 (0.93-1.03)	0.421	1.21 (1.14-1.29)	<0.001
Other	1		1	
Speciality				
Medicine	0.72 (0.68-0.76)	<0.001	0.85 (0.80-0.90)	<0.001
Surgery	1			
Length of Stay (days)				
	0.98 (0.97-0.99)	<0.001	0.99 (0.98-1.00)	<0.001

Odds ratio (95% CI), No AUD (low risk) was set reference category, variables were mutually adjusted

[a] Not in a relationship includes married, in a civil partnership or in a long-term relationship

[b] In a relationship includes single, divorced, separated, dissolved civil partnership, widowed, or surviving civil partner

3.3.2.3 Individual AUD risk groups

Among individual AUD risk groups (increased risk, high risk, dependent), the alcohol-dependent group was the youngest (mean age 53.8 years ±14.2), had the highest proportions of males (73.1%), and white ethnicity (93.6%). The alcohol-dependent patients compared to low risk were from the most deprived neighbourhoods (IMDQ-1

38.3%), were more likely to be not in a relationship (65.7%), admitted as a medical emergency (76.8%) and cared for by medical specialities (69.7%). In increased and high-risk groups surgery compared to medicine was the most common inpatient speciality of care (56.7% vs 43.3% and 52.2% vs 47.8%) (Table 3-5)

Table 3-5. Characteristics of alcohol use disorder (AUD) risk groups

	Low risk (n=36,350)	Increased risk (4,372)	High risk (1,892)	Dependent (900)	P[c]
All admissions	54,318 (85.3)	5,497 (8.6)	2,466 (3.9)	1,386 (2.2)	
Male	16,017 (44.1)	2,833 (64.8)	1,355 (71.7)	658 (73.1)	<0.001
Age years (SD)	64.6 (± 20.0)	57.1 (± 18.5)	54.5 (± 17.3)	53.8 (± 14.2)	<0.001
Ethnicity					<0.001
White	2,5826 (89.9)	3,121 (94.8)	1,376 (94.4)	671 (93.6)	
BAME	2,914 (10.1)	172 (5.2)	82 (5.6)	46 (6.4)	
Missing	7,610	1,079	434	183	
IMD quintiles					<0.001
1 (most deprived)	8,797 (26.4)	927 (23.2)	523 (30.2)	309 (38.3)	
2	6,094 (18.3)	682 (17.1)	311 (18.0)	176 (21.8)	
3	5,749 (17.2)	668 (16.7)	274 (15.8)	114 (14.1)	
4	5,475 (16.4)	725 (18.1)	269 (15.6)	100 (12.4)	
5 (least deprived)	7,222 (21.7)	995 (24.9)	352 (20.4)	108 (13.4)	
Missing	3,013	375	163	93	
Civil status					<0.001
In a relationship[a]	18,108 (60.4)	1,832 (52.3)	695 (35.0)	256 (34.3)	
Not in a relationship[b]	11,853 (39.6)	1,669 (47.7)	850 (65.0)	490 (65.7)	
Missing	6,389	871	347	154	
Mode of admission					<0.001
Emergency	21,355 (58.7)	2,334 (53.4)	1,147 (60.6)	691 (76.8)	
other	14,995 (41.3)	2,038 (46.6)	745 (39.4)	209 (23.2)	
Speciality					<0.001
Medicine	19,942 (55.9)	1,850 (43.3)	879 (47.8)	606 (69.7)	
Surgery	15,761 (44.1)	2,420 (56.7)	959 (52.2)	263 (30.3)	
Other or unknown	647	102	54	31	
Length of Stay (days)	4 (1-268)	3 (1-177)	3 (1- 127)	4 (1-157)	<0.001
Number of admissions	2.5 (± 3.8)	2.1 (± 2.9)	2.1 (± 3.4)	2.2 (± 2.3)	<0.001

Data are number (%), mean (SD) or median (range), IMD-index of multiple deprivations

[a]In a relationship includes married, in a civil partnership or in a long-term relationship

[b]Not in a relationship includes single, divorced, separated, dissolved civil partnership, widowed, or surviving civil partner

[c]p for the difference in low risk versus; increased-risk, high risk and alcohol dependent

3.3.2.4 Inpatient speciality of care

A significantly higher proportion of patients cared for by surgical specialities (n=3,642, 52.2%) were screened positive for AUD compared to patients cared for by medical specialities (n=3,522, 49.2%) (p<0.001). The most common medical specialities of care for patients with AUD were general medicine (n=1,856, 40.2%), respiratory medicine (n=392, 11.2%), cardiology (n=386, 11.0%), and surgical specialities were trauma & orthopaedics (n=1,015, 27.9%), general surgery (n=631, 17.3%), urology (n=285, 7.8%). The top five inpatient medical and surgical specialities cared for AUD patients are provided in Figure 3-2. A detailed comparison of inpatient specialities between patients with AUD to those without AUD is provided in Table 3-6 and for individual AUD risk groups in Table 3-7.

Figure 3-2. Top five inpatient medical (blue bars) and surgical (red bars) specialities of care for AUD patients

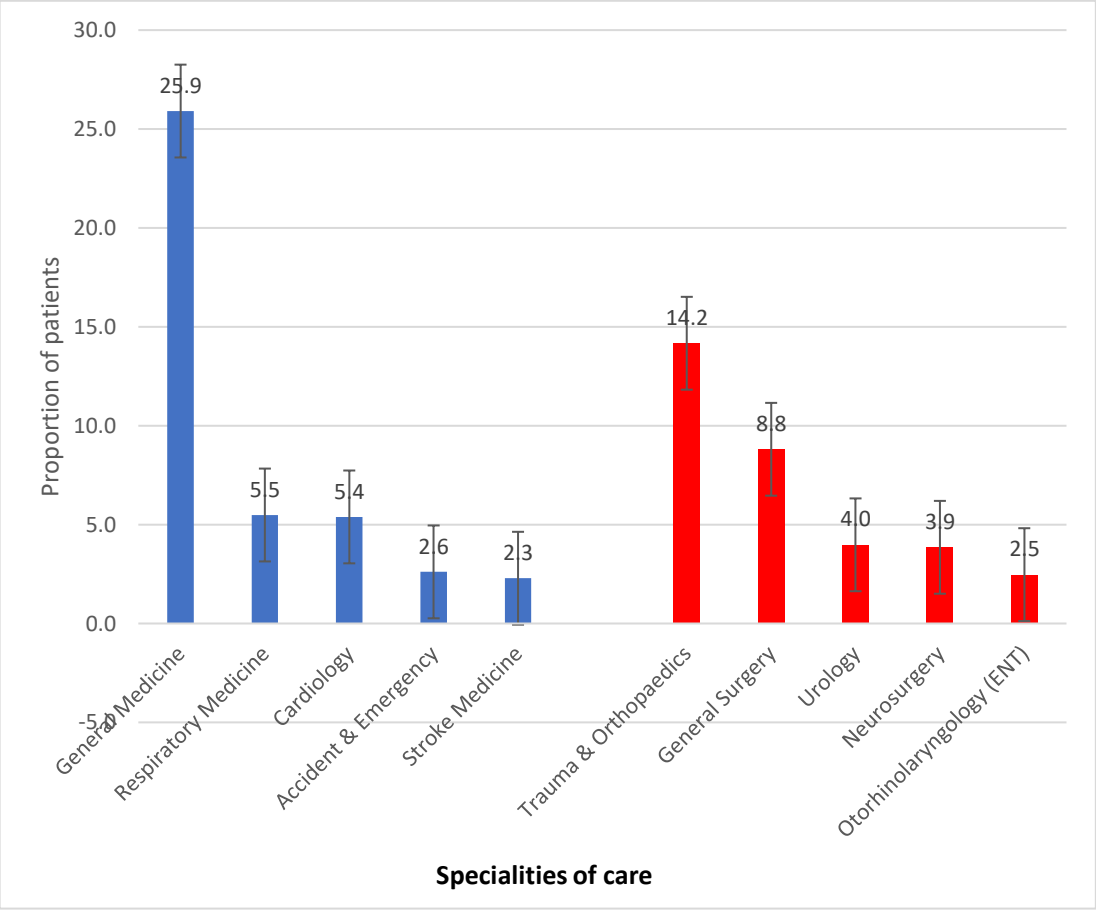


Table 3-6. Inpatient specialities of care for patients with alcohol use disorder (AUD) compared to those without AUD

Medical specialities	Low risk (n=20,591)	AUD (n=3,522)	Surgical specialities	Low risk (n=15,759)	AUD (n=3,642)
General Medicine	8269 (40.2)	1856 (52.7)	Trauma & Orthopaedics	3478 (22.1)	1015 (27.9)
Respiratory Medicine	2302 (11.2)	393 (11.2)	General Surgery	2566 (16.3)	631 (17.3)
Cardiology	1515 (7.4)	386 (11.0)	Urology	1566 (9.9)	285 (7.8)
Accident & Emergency	647 (3.1)	187 (5.3)	Neurosurgery	1304 (8.3)	276 (7.6)
Stroke Medicine	771 (3.7)	164 (4.7)	ENT	667 (4.2)	177 (4.9)
Health Care for Older People	3805 (18.5)	131 (3.7)	Thoracic Surgery	490 (3.1)	159 (4.4)
Clinical Oncology	1211 (5.9)	96 (2.7)	Plastic surgery	552 (3.5)	144 (4.0)
Clinical Haematology	531 (2.6)	73 (2.1)	Spinal Surgery Service	752 (4.8)	140 (3.8)
Gastroenterology	422 (2.0)	64 (1.8)	Gynaecology	1336 (8.5)	131 (3.6)
Infectious Diseases	285 (1.4)	57 (1.6)	Maxillo-Facial Surgery	371 (2.4)	116 (3.2)
Nephrology	377 (1.8)	31 (0.9)	Cardiac Surgery	334 (2.1)	104 (2.9)
Adult Cystic Fibrosis Service	85 (0.4)	22 (0.6)	Vascular Surgery	467 (3.0)	104 (2.9)
Diabetic Medicine	63 (0.3)	20 (0.6)	Colorectal Surgery	487 (3.1)	99 (2.7)
Neurology	155 (0.8)	20 (0.6)	Hepatobiliary & Pancreatic Surgery	407 (2.6)	66 (1.8)
Hepatology	35 (0.2)	14 (0.4)	Upper Gastrointestinal	265 (1.7)	54 (1.5)
Endocrinology	9 (0.0)	3 (0.1)	Breast Surgery	311 (2.0)	49 (1.3)
Palliative Medicine	76 (0.4)	2 (0.1)	Burns Care	76 (0.5)	36 (1.0)
Rheumatology	11 (0.1)	2 (0.1)	Ophthalmology	159 (1.0)	35 (1.0)
Medical Oncology	11 (0.1)	1 (0.0)	Transplantation Surgery	150 (1.0)	17 (0.5)
Rehabilitation	6 (0.0)		Cardiothoracic Surgery	9 (0.1)	2 (0.1)
Genitourinary Medicine	5 (0.0)		Interventional Radiology	12 (0.1)	2 (0.1)

*Number of individual patients

Table 3-7. Speciality distribution for individual alcohol use disorder (AUD) groups

Medical specialities	Dependent (n=637)	High risk (n=933)	Increased risk (n=1,952)
General Medicine	444	487	925
Respiratory Medicine	43	111	239
Accident & Emergency	31	54	102
Stroke Medicine	31	43	90
Cardiology	30	115	241
Health Care for Older People	16	37	78
Gastroenterology	12	13	39
Infectious Diseases	6	17	34
Nephrology	6	4	21
Hepatology	5	4	5
Clinical Haematology	3	10	60
Neurology	3	3	14
Clinical Oncology	2	21	73
Diabetic Medicine	2	7	11
Adult Cystic Fibrosis Service	1	4	17
Endocrinology	1	1	1
Rheumatology	1	1	
Palliative Medicine			2
Medical Oncology		1	

Surgical specialities	Dependent (n=263)	High risk (n=959)	Increased risk (n=2,420)
Trauma & Orthopaedics	68	264	683
General Surgery	59	157	415
Neurosurgery	22	87	167
Thoracic Surgery	16	33	110
Urology	15	59	211
ENT	15	53	109
Plastic Surgery	11	49	84
Maxillo-Facial Surgery	11	37	68
OBG	10	30	91
Spinal Surgery Service	9	37	94
Cardiac Surgery	6	34	64
Vascular Surgery	6	28	70
Colorectal Surgery	4	26	69
Upper Gastrointestinal	4	11	39
Burns Care	4	10	22
Hepatobiliary & Pancreatic Surgery	2	17	47
Breast Surgery	1	8	40
Ophthalmology		13	22
Transplantation Surgery		4	13
Cardiothoracic Surgery		2	
Interventional Radiology			2

3.3.2.5 ICD-10 discharge diagnosis

On analysing ICD-10 discharge diagnosis, injury, poisoning and other consequences of the external causes were the most common discharge diagnosis (19.4%, n=1,390), followed by diseases of the circulatory system (13/6%, n=971), diseases of the digestive system (11.5%, n=824), neoplasm (10.7%, n=765), and diseases of the respiratory system (8.8%, n=632). On further evaluation, 30.9% (n=213) of patients were admitted with mental behaviour disorders. A detailed distribution of ICD_10 discharge diagnoses for patients with and without AUD is given in Table 3-8 and for individual AUD risk groups in Table 3-9.

Table 3-8. Distribution of ICD-10 discharge diagnosis amongst the patients with and without AUD

	AUD (n=7,164)	No AUD (n=3,6350)
Mental and Behaviour Disorders	213 (30.9)	476 (69.1)
Injury, poisoning and certain other consequences of the external causes	1,390 (23.8)	4,454 (76.2)
Congenital malformations, deformities, and chromosomal abnormalities	24 (20.5)	93 (79.5)
Diseases of digestive system	824 (19.6)	3,387 (80.4)
Diseases of eye and adnexa	35 (17.6)	164 (82.4)
Diseases of circulatory system	971 (17.5)	4,582 (82.3)
Diseases of MSK and connective tissue	615 (16.4)	3,131 (83.6)
Diseases of the skin and subcutaneous tissue	138 (15.7)	739 (84.3)
Neoplasm	765 (15.2)	4,258 (84.8)
Endocrine, nutritional and metabolic diseases	137 (14.4)	815 (85.6)
Symptoms, signs and abnormal Clinical and laboratory findings, not elsewhere classified	562 (14.0)	3446 (86.0)
Diseases of respiratory system	632 (13.5)	4,042 (86.5)
Diseases of the nervous system	150 (12.8)	1022 (87.2)
Factors influencing health status and contact with health services	32 (12.7)	219 (87.3)
Diseases of the genitourinary system	347 (12.6)	2,403 (87.4)
Disease of ear and mastoid	22 (11.9)	163 (88.1)
Certain infection and parasitic disease	254 (10.7)	2,113 (89.3)
Codes for special purposes (Covid 19)	13 (10.0)	117 (90.0)
Diseases of Blood and blood forming organs and certain disorders of immune system	28 (7.9)	325 (92.1)
Pregnancy, childbirth, and the puerperium	12 (2.9)	401 (97.1)

Data are number (%)

Table 3-9. Top 10 ICD-10 discharge diagnosis groups for individual AUD risk groups

Increased risk			High risk
Injury, poisoning and certain other consequences of the external causes	763 (17.5)	Injury, poisoning and certain other consequences of the external causes	432 (22.8)
Diseases of circulatory system	601 (13.7)	Diseases of circulatory system	273 (14.4)
Neoplasm	550 (12.6)	Diseases of digestive system	220 (11.6)
Diseases of digestive system	465 (10.6)	Diseases of respiratory system	177 (9.4)
Diseases of MSK and connective tissue	449 (10.3)	Neoplasm	165 (8.7)
Diseases of respiratory system	388 (8.9)	Symptoms, signs and abnormal Clinical and laboratory findings, not elsewhere classified	160 (8.5)
Symptoms, signs and abnormal Clinical and laboratory findings, not elsewhere classified	326 (7.5)	Diseases of MSK and connective tissue	131 (6.9)
Diseases of the genitourinary system	236 (5.4)	Diseases of the genitourinary system	87 (4.6)
Certain infection and parasitic disease	164 (3.8)	Certain infection and parasitic disease	60 (3.2)
Diseases of nervous system	104 (2.4)	Mental and Behaviour Disorders	48 (2.5)
Dependent			
Injury, poisoning and certain other consequences of the external causes	195 (21.7)		
Diseases of digestive system	139 (15.4)		
Mental and Behaviour Disorders	135 (15.0)		
Diseases of circulatory system	97 (10.8)		
Symptoms, signs and abnormal Clinical and laboratory findings, not elsewhere classified	76 (8.4)		
Diseases of respiratory system	67 (7.4)		
Neoplasm	50 (5.6)		
Diseases of MSK and connective tissue	35 (3.9)		
Certain infection and parasitic disease	30 (3.3)		
Diseases of the genitourinary system	24 (2.7)		

Data are number (%)

3.3.2.5.1 AUD amongst the patients admitted with non alcohol-specific or alcohol-related discharge diagnosis codes

Among the whole cohort, 35,080 (80.6%) had primary ICD-10 discharge diagnosis codes which were neither alcohol-specific nor alcohol-related, of them, based on AUDIT-C, 29,454 (84.0%) had no AUD (low risk), and 5,626 (16.0%) had AUD. Chronic obstructive pulmonary disease with acute lower respiratory infection was the most common (n=108) discharge diagnosis in this group, followed by Coxarthrosis unspecified (n=105), Gonarthrosis unspecified (n=97), poisoning (n=93), and sepsis (n=66) (Table 3-10).

Table 3-10. Top 25 non alcohol specific or alcohol-related discharge diagnoses for patients with AUD

Description of primary diagnosis	AUD	No AUD	All
Chronic obstructive pulmonary disease with an acute lower respiratory infection	108	469	577
Coxarthrosis, unspecified	105	376	481
Gonarthrosis, unspecified	97	541	638
Poisoning: 4-Aminophenol derivatives	93	134	227
Sepsis, unspecified	66	908	974
Acute appendicitis, other and unspecified	65	145	210
Cellulitis of other parts of limb	65	378	443
Fractures of other parts of lower leg closed	58	123	181
Multiple fractures of ribs closed	52	114	166
Pain localized to upper abdomen	52	200	252
Syncope and collapse	52	310	362
Fracture of neck of femur closed	49	370	419
Gastroenteritis and colitis of unspecified origin	48	294	342
Headache	48	255	303
Malignant neoplasm of prostate	47	186	233
Unspecified acute lower respiratory infection	47	484	531
Pain localized to other parts of lower abdomen	43	196	239
Urinary tract infection, site not specified	43	510	553
Fracture of mandible closed	41	35	76
Gastrointestinal haemorrhage, unspecified	39	161	200
Malignant neoplasm: Upper lobe, bronchus or lung	39	180	219
Tubulointerstitial nephritis, not specified as acute or chronic	39	174	213
Acute renal failure, unspecified	38	292	330
Traumatic subdural haemorrhage without open intracranial wound	35	237	272
Acute appendicitis with localized peritonitis	34	73	107

3.4 Results pre-pandemic and pandemic cohorts

3.4.1 Description of the cohorts

During the study period, there were 69,764 admissions to NUH involving 50,578 patients. Of these 1,789 (3.5%) declined to complete the alcohol assessment and 835 (1.6%) were excluded for not having an AUDIT-C score. The final study cohort included 63,927 admissions from 47,954 patients, pre-pandemic 27,356 and pandemic 20,598 (Figure 3-3 and Figure 3-4).

Figure 3-3. Description of pre-pandemic and pandemic cohorts; AUDIT-C score risk categories

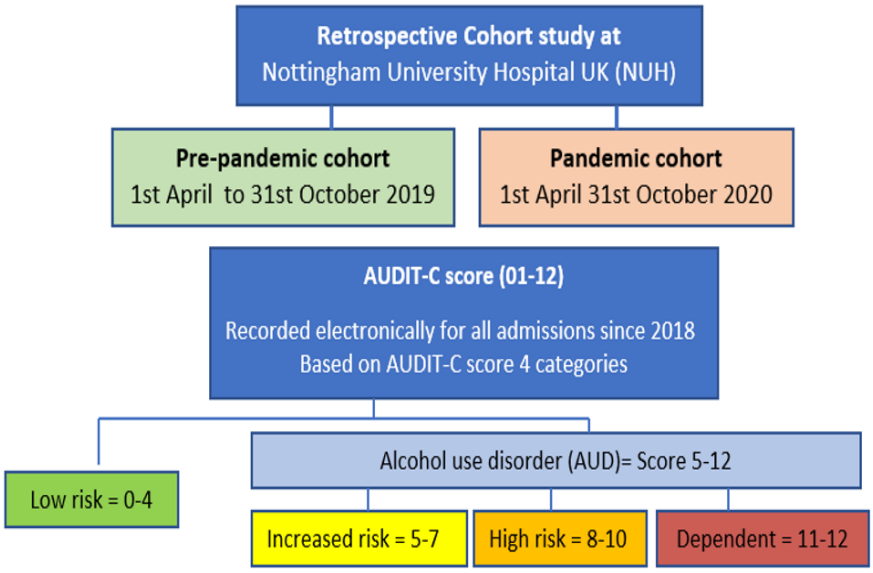
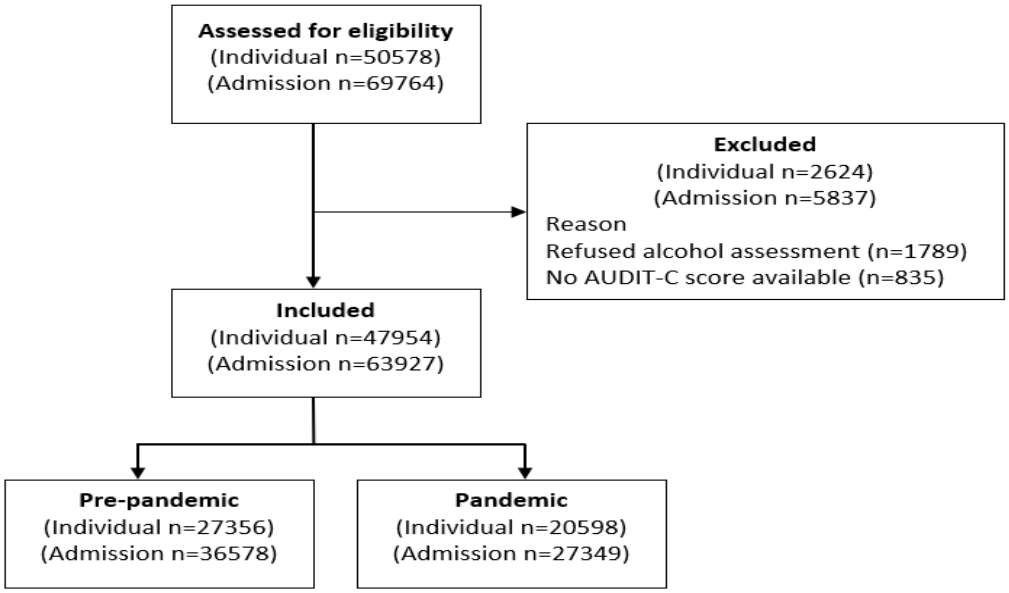


Figure 3-4. Consort flow diagram for participant inclusion



There were 36,578 (57.2%) admissions in the pre-pandemic period and significantly fewer, 27,349 (42.8%) in the pandemic period (p<0.001). The differences between the pre-pandemic and pandemic cohorts are shown in Table 3-11.

Table 3-11. Characteristics of pre-pandemic and pandemic cohorts

	Pre-pandemic (n=27,356)	**Pandemic (n=20,598)**	***p***
Admissions	36,578 (57.2%)	27,349 (42.8%)	<0.001
Male	13024 (47.6%)	10160 (49.3%)	<0.001
Age years (SD)	63.0 (+/-19.9)	64.0 (+/- 19.7)	<0.001
Ethnicity			0.920
White	19778 (90.8%)	14845 (90.7%)	
Minority ethnicity	2014 (9.2%)	1517 (9.3%)	
Unknown	5564	4236	
IMD quintiles			<0.001
1 (most deprived)	7249 (26.6%)	4571 (23.1%)	
2	4923 (18.0%)	3513 (17.1%)	
3	4635 (17.0%)	3445 (16.8%)	
4	4556 (16.7%)	3639 (17.7%)	
5 (least deprived)	5922 (21.7%)	5200 (25.3%)	
Missing data	71	50	
Civil status			<0.001
In a relationship[a]	13207 (58.1%)	10816 (63.3%)	
Not in a relationship[b]	9509 (41.9%)	6276 (36.7%)	
Unknown	4640	3506	
Mode of admission			<0.001
Emergency	15272 (55.8%)	13390 (65.0%)	
Other	12084 (44.2%)	7208 (35.0%)	
Speciality			<0.001
Medicine	13937 (52.1%)	11880 (59.4%)	
Surgery	12791 (47.9%)	8106 (40.6%)	
Other or unknown	628	612	
Length of Stay (days)	4 (1-320)	4 (1-173)	<0.001
Number of readmissions	1 (1-17)	1 (1-13)	0.879

Data are number (%), mean (SD) or median (range)

[a] In a relationship includes married, in a civil partnership or in a long-term relationship

[b] Not in a relationship includes single, divorced, separated, dissolved civil partnership, widowed, or surviving civil partner

Those in the pandemic cohort were more likely to be male (49.3% vs 47.6%, p<0.001), older (mean 64.0 vs 63.0 years, p<0.001), more likely to be in a relationship (63.3% vs 58.1%, p<0.001) and were from more affluent socioeconomic quintiles (43.0% vs 38.4%, p<0.001) compared to the pre-pandemic cohort. Ethnic distribution did not differ between the two cohorts.

Patients in the pandemic cohort were more likely to be admitted as an emergency (65.0% vs 55.8%, p<0.001) to a medical speciality (rather than surgical) (59.4% vs 52.1%), p<0.001). The median length of stay (LOS) for the pre-pandemic and pandemic cohorts was unchanged at 4 days. There was no difference in the median number of readmissions (median 1, p=0.879) between the cohorts.

3.4.2 Characteristics of low-risk alcohol drinkers and those with alcohol use disorder

Based on the AUDIT-C assessment 17.9% (n=4,895) of individual patients in the pre-pandemic and 17.0% (n=3,500) in the pandemic cohort had AUD. In both cohorts patients with AUD had several shared characteristics. Compared to low risk (no AUD), those with AUD were significantly younger (p<0.001), more likely to be male (p<0.001), of white ethnicity (p<0.001), have mental and behavioural disorders due to alcohol (p<0.001), less likely to be in a relationship (p<0.001) and cared for by surgical specialities (p<0.001) (Table 3-12 and Figure 3-5).

On comparing patients with AUD in the pre-pandemic versus the pandemic cohort, a number of characteristics differed. Those with AUD in the pandemic cohort (as compared to pre-pandemic AUD) were more likely to be of higher socioeconomic background (IMD quintile 1: 21.6% vs 27.1%, IMD quintile 5: 27.7% vs 21.8%, p<0.001), admitted as an emergency (66.3% vs 56.0%, p<0.001), cared for by medical specialities (54.3% vs 46.6%, p<0.001) (Table 2). Patients with AUD in the pandemic cohort had a significantly higher proportion of mental and behavioural disorders due to alcohol (3.5% vs 2.4%, p=0.002) compared to the pre-pandemic cohort (Figure 3-5)

Table 3-12. Characteristics of low risk for AUD and those screening positive for AUD

	Pre-pandemic (n=27356)		p	Pandemic (n=20598)		p	p[c]
	Low risk (n=22461)	**AUD (n=4895)**		**Low risk (n=17098)**	**AUD (n=3500)**		
Admissions	29855 (81.6%)	6723 (18.4%)		22539 (82.4%)	4810 (17.6%)	<0.001	?p
Male	9767 (43.5%)	3257 (66.5%)	<0.001	17098 (49.3%)	2436 (69.6%)	<0.001	0.003
Age years (SD)	64.4 (20.1)	56.3 (17.8)	<0.001	65.1 (19.8)	56.7 (17.7)	<0.001	0.278
Ethnicity			<0.001			<0.001	0.028
White	16173 (90.0%)	3605 (94.5%)		12218 (89.7%)	2627 (95.7%)		
Minority ethnicity	1806 (10.0%)	208 (5.5%)		1400 (10.3%)	117 (4.3%)		
Unknown	4482	1082		3480	756		
IMD quintiles			0.146			0.006	<0.001
1 (most deprived)	5931 (26.5%)	1318 (27.1%)		3995 (23.4%)	756 (21.6%)		
2	4050 (18.1%)	873 (17.9%)		2918 (17.1%)	595 (17.0%)		
3	3864 (17.2%)	771 (15.8%)		2879 (16.9%)	566 (16.2%)		
4	3711 (16.6%)	845 (17.4%)		3027 (17.8%)	612 (17.5%)		
5 (least deprived)	4860 (21.7%)	1062 (21.8%)		4233 (24.8%)	967 (27.7%)		
Missing data	71			50			
Civil status			<0.001			<0.001	<0.001
In a relationship[a]	11279 (60.3%)	1928 (47.9%)		9283 (65.3%)	1533 (53.2%)		
Not in a relationship[b]	7414 (39.7%)	2095 (52.1%)		4929 (34.7%)	1347 (46.8%)		
Unknown	3768	872		2886	620		
Mode of admission			0.768			0.068	<0.001
Emergency	12530 (55.8%)	2742 (56.0%)		11068 (64.7%)	2322 (66.3%)		
Other	9931 (44.2%)	2153 (44%)		6030 (35.3%)	1178 (33.7%)		
Speciality			<0.001			<0.001	<0.001
Medicine	11719 (53.3%)	2218 (46.6%)		10065 (60.5%)	1815 (54.3%)		
Surgery	10252 (46.7%)	2539 (53.4%)		6577 (39.5%)	1529 (45.7%)		
Other or unknown	490	138		456	156		

	Pre-pandemic (n=27356)		p	Pandemic (n=20598)		p	p[c]
Length of stay (days)	4 (1-320)	4 (1-178)	<0.001	5 (1-174)	4 (1-135)	<0.001	0.033
Number of readmissions	1 (1-17)	1 (1-11)	<0.001	1 (1-13)	1 (1-13)	0.012	0.0676

Data are number (%), mean (SD) or median (range),

[a] In a relationship includes married, in a civil partnership or in a long-term relationship,

[b] Not in a relationship includes single, divorced, separated, dissolved civil partnership, widowed, or surviving civil partner,

[c]Significance of difference between Pre-pandemic and Pandemic AUD.

Figure 3-5. Mental and behavioural disorders due to alcohol.

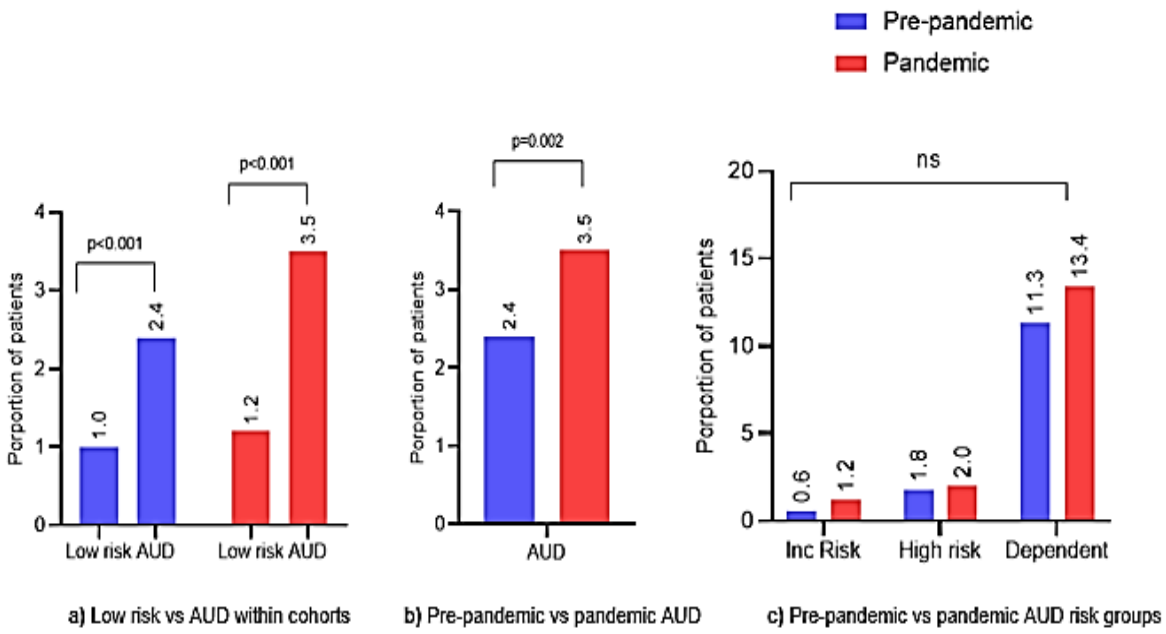


Figure 3-5 legend: (a) comparison of the prevalence of mental and behavioural disorders due to alcohol in patients low risk for AUD (no AUD) vs patients with AUD in pre-pandemic and pandemic cohorts, (b) comparison of the prevalence of mental and behavioural disorders due to alcohol patients with AUD in pre-pandemic cohort vs patients had AUD in the pandemic cohort, (c) prevalence of mental and behavioural disorders due to alcohol in individual AUD risk groups for pre-pandemic and pandemic cohort

3.5 AUD individual risk groups

On further dividing AUD screened-positive into individual risk groups, significantly higher proportions with AUD in the pandemic cohort were alcohol dependent (3.7% vs 3.0%, p<0.001) compared to the pre-pandemic cohort. The variation in proportion for increased risk was 10.4% vs 9.3% (p=0.640), and high risk 5.1% vs 4.7% (p=0.018) for the pre-pandemic and pandemic cohorts, respectively. For both cohorts, the detailed characteristic distribution for each risk group is given in Table 3-13.

Table 3-13. Pre-pandemic versus pandemic-cohort comparison between AUD risk groups (Low risk, Increased risk, High Risk and Alcohol dependent)

		Pre-Pandemic	Pandemic	p
Admissions				
	Low Risk	29855 (81.6%)	22539 (82.4%)	0.001
	Increased Risk	3788 (10.4%)	2538 (9.3%)	0.640
	High Risk	1851 (5.1%)	1273 (4.7%)	0.018
	Dependent	1084 (3.0%)	999 (3.7%)	<0.001
Age years (SD)				
	Low Risk	64.4 (20.1)	65.1 (19.8)	<0.001
	Increased Risk	57.3 (18.5)	58.1 (18.7)	0.190
	High Risk	55.1 (17.5)	56.4 (17.2)	0.080
	Dependent	53.9 (14.2)	52.7 (14.1)	0.110
Male				
	Low Risk	9767 (43.5%)	7724 (45.2%)	0.050
	Increased Risk	1838 (64.0%)	1304 (67.2%)	0.020
	High Risk	944 (69.9%)	706 (73.2%)	0.720
	Dependent	475 (70.7%)	426 (71.6%)	0.070
White				
	Low Risk	16173 (90.0%)	12218 (89.7%)	0.490
	Increased Risk	2096 (94.8%)	1437 (96.1%)	0.070
	High Risk	1001 (92.9%)	712 (95.6%)	0.500
	Dependent	508 (94.5%)	478 (95.0%)	0.140
Civil status in relationship[a]				
	Low Risk	11279 (60.3%)	9283 (65.3%)	<0.001
	Increased Risk	1225 (52.8%)	935 (58.6%)	<0.001
	High Risk	517 (46.2%)	407 (52.7%)	0.005
	Dependent	186 (32.0%)	191 (37.3%)	0.060
Emergency mode of admission				
	Low Risk	12530 (55.8%)	11068 (64.7%)	<0.001
	Increased Risk	1493 (52.0%)	1208 (62.3%)	0.010
	High Risk	763 (56.5%)	653 (67.7%)	<0.001
	Dependent	486 (72.3%)	461 (77.5%)	0.049
Inpatient speciality medicine				
	Low Risk	11719 (53.3%)	10065 (60.5%)	<0.001
	Increased Risk	1176 (42.0%)	917 (49.4%)	<0.001
	High Risk	613 (46.5%)	503 (54.3%)	<0.001
	Dependent	429 (66.8%)	395 (70.7%)	0.150
Length of stay				
	Low Risk	4 (1-320)	5 (1-174)	<0.001
	Increased Risk	3 (1-178)	4 (1-108)	0..002
	High Risk	4 (1-126)	4 (1-135)	0.990
	Dependent	5 (1-131)	5 (1-68)	0.150

Data are n (%), mean (SD) or median (range)

[a] In a relationship includes married, in a civil partnership or in a long-term relationship

3.5.1 Subgroup analysis

3.5.1.1 Covid-19 negative vs Covid-19 Positive whole subcohort

Among all individuals in the pandemic cohort, 994 (4.8%) were diagnosed with Covid-19 infection accounting for 1456 admissions (5.3%). As would be expected, patients diagnosed with Covid-19 infection, compared to those without Covid-19, were older (mean age 69.0 vs 63.0 years, p<0.001), more likely to be admitted as an emergency (83.1% vs 64.1%, p<0.001), cared for by medical specialities (89.2% vs 57.9%, p<0.001), had a longer median length of stay (7 vs 4 days, p<0.001) and more likely to die as an inpatient (26.6% vs 7.6%, p<0.001) (Appendix 2).

3.5.1.2 Covid-19 positive with AUD vs Covid-19 positive without AUD

Of those diagnosed with Covid-19 infection, 88 (8.9%) had AUD based on AUDIT-C assessment. The group with Covid-19 were significantly younger (mean age 62 vs 70 years, p<0.001), more likely to be male (72.7% vs 52.1%, p<0.001), white ethnicity (98.5% vs 85.0%, p<0.001) and died as an inpatient at a significantly younger age (mean age 63.1 vs 71.6 years, p<0.001) compared to those with Covid-19 infection and but without AUD (Figure 3-6). There was no significant difference in the index of multiple deprivation IMD, civil status, mode of admission, length of stay, number of readmissions and inpatient mortality between the two groups (Table 3-14).

Figure 3-6. The difference in mean age for inpatient mortality based on Covid-19 and AUD status (*p significant)

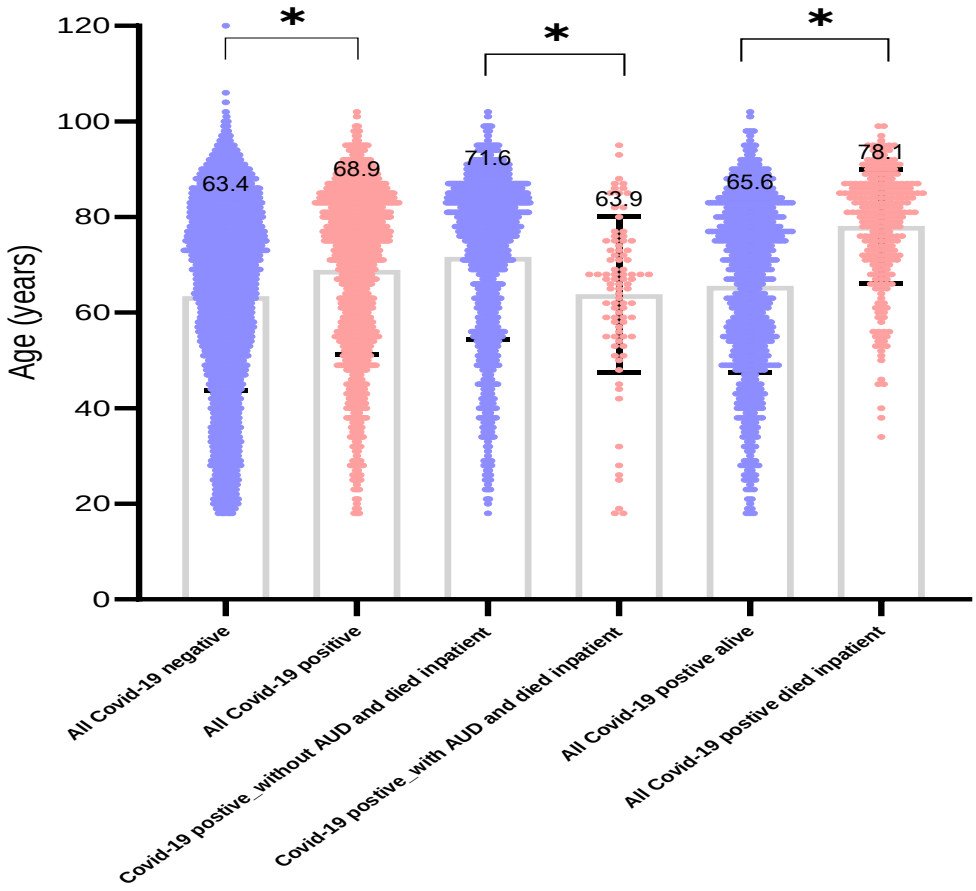


Table 3-14. Covid 19-Positive low risk vs AUD

	Low risk (n=906)	AUD (n=88)	p
Male	472 (52.1%)	64 (72.7%)	<0.001
Age (years)	70.0 (18.0)	62.0 (16.0)	<0.001
Ethnicity			<0.001
White	645 (85.0%)	66 (98.5%)	
Minority ethnicity	114 (15.0%)	1 (1.5%)	
Unknown	147	21	
IMD quintiles			0.941
1 (most deprived)	202 (22.6%)	19 (21.6%)	
2	123 (13.8%)	14 (15.95)	
3	148 (16.6%)	16 (18.2%)	
4	166 (18.65)	17 (19.35)	
5 (least deprived)	254 (28.4%)	22 (25.0%)	
missing	13		
Civil status			0.376
In a relationship[a]	223 (24.6%)	25 (28.4%)	
Not in a relationship[b]	549 (60.6%)	49 (55.7%)	
Unknown	134 (14.8%)	14 (15.9%)	
Mode of admission			0.458
Emergency	750 (82.8%)	76 (86.4%)	
Other	156 (17.2%)	12 (13.65)	
Speciality			0.002
Medicine	804 (88.7%)	76 (86.4%)	
Surgery	106 (10.7%)	1 (1.1%)	
Other or unknown	8 (0.8%)	11 (12.5%)	
Length of stay (days)	7 (1 – 147)	10 (1-43)	0.112
Number of readmissions	1 (1- 8)	1 (1-8)	0.767
Inpatient death	243 (26.8%)	22 (25.0%)	0.801

Data are number (%), mean (SD) or median (range)

[a] In a relationship includes married, in a civil partnership or in a long-term relationship

[b] Not in a relationship includes single, divorced, separated, dissolved civil partnership, widowed, or surviving civil partner

3.6 Discussion

3.6.1 Summary of key findings

The study demonstrated universal alcohol screening by AUDIT-C in secondary care is feasible and improves the detection rate of alcohol use disorder (AUD) in these settings. One in six (16.5%) admitted patients screened positive for AUD based on AUDIT-C. Alcohol use disorder (AUD) was identified in all discharge diagnosis groups irrespective of their alcohol-attributable fraction. In the alcohol-specific group majority (81.6%) had alcohol use disorder, and among those (18.4%) who had no AUD, alcohol-related liver disease was the leading diagnosis. A significant proportion of patients who had an ICD-10 discharge diagnosis of non-alcohol-specific or non-alcohol-related disorders (16.0%) had concomitant AUD.

I noted, although almost half of the included participants in all cohorts were female, over 70% of those with AUD were male, in their 50s, and of white ethnicity. It is noteworthy though overall the majority of all cohorts were admitted under medical specialities, a higher proportion of patients with AUD were cared for by surgical specialities, predominantly general surgery, and trauma & orthopaedics.

The study demonstrated a largely similar overall pattern of alcohol use disorder between pre-pandemic and pandemic cohorts. Of note, a significantly higher proportion of hospital admissions during the pandemic based on AUDIT-C had possible alcohol dependence. The alcohol-dependent group in the pandemic cohort had a higher, but non-significant, recurrent admission rate. A significantly higher proportion of patients in the pandemic with alcohol use disorder (AUD) had mental and behavioural disorders. Covid-19 positive patients with concomitant AUD died as an inpatient at a significantly younger age. It is important to highlight that the total number of admissions reduced during the pandemic, and this was noted across all risk groups. However, a significantly higher proportion presented as an emergency during the pandemic.

3.6.2 Strengths and limitations

This is one of the largest contemporaneous cohort studies to evaluate the epidemiology of AUD and determine the impact of Covid-19 on alcohol use disorder (AUD) among hospitalised patients. The study provides an important insight into the complex relationship between AUD, mental health, demographic characteristics, and Covid-19,

which has implications for policymakers to manage alcohol use disorders in hospital settings. For example, my study helps to identify hospital specialities with a high burden of patients with AUD, common modes of hospital admission and ICD-10 discharge diagnoses for patients with AUD. This in turn can help to build targeted alcohol services and provide a foundation to engage with healthcare professionals and make every contact matter. Another strength of the study is the use of the AUDIT-C score as a screening tool for AUD, the use of AUDIT-C has been extensively validated (110, 113). The National Institute for Health and Care Excellence (NICE) advocate using of AUDIT-C as an alcohol screening tool both in primary and secondary care (114).

The main limitation of this study is its retrospective design. The risk of information and selection bias was mitigated by using an independent person to extract data, unaware of the outcomes, by clearly defining the study population, risk stratifying alcohol groups using a validated tool (AUDIT-C) and representing an internal comparison group. The confounders (Age, Ethnicity, Sex, socioeconomic status) were adjusted to establish an accurate association between critical variables and AUDIT-C score. The lack of long-term follow-up in this study hinders my ability to extrapolate accurate long-term outcome predictions.

3.6.3 Other evidence

The prevalence of AUD among hospitalised patients based on AUDIT-C was significantly higher than the previously reported 7.4% of alcohol-related hospital admissions in the UK (12). The acceptance rates for alcohol screening by AUDIT-C were similar to previously reported community studies on the validation of AUDIT-C (113). Universal alcohol screening provides a unique opportunity for early detection of AUD followed by intervention to effectively mitigate future risk of harm. NICE recommends that those at high risk of AUD should be assessed and undergo intensive structured interventions (with or without medical therapy) as these provide the best chance of achieving and maintaining abstinence from alcohol (25).

A significant proportion of patients who had an ICD-10 discharge diagnosis of non-alcohol-specific or non-alcohol-related disorders had concomitant alcohol use disorder. This might be due to the ICD-10 codes for alcohol misuse do not consider the level or pattern of alcohol consumption but rather focus on the consequences of harmful alcohol intake (115). Whereas the AUDIT-C score assesses the risk of alcohol use disorder and

based on the responses categories one into four risk categories (110, 116). The issue of the ICD-10 code underestimating alcohol misuse has been shown previously, in a cohort of injury-related hospital admissions only 38% had alcohol-specific diagnostic codes (117). Although the proportion of patients with alcohol use disorder in these groups was smaller, in the context of absolute number these were much larger cohorts.

By highlighting the most common inpatient specialities these cohorts encountered during hospitalisation, we have helped to identify areas where the implementation of alcohol identification and brief advice (AIBA) could have the most impact. The use of AIBA has a proven role in reducing alcohol consumption and subsequent harm (118). Over the last decade, there has been a drive in the UK to promote AIBA across a range of services (119, 120). NICE 2011 guidelines state that staff working in the NHS and involved in caring for people at risk of alcohol misuse should be competent in identifying harmful alcohol intake and delivering a brief intervention (25).

I assume the observed phenomena of an overall reduction in hospital admissions during the pandemic could be due to a reduction in routine hospital services as part of pandemic contingency planning. A similar reduction in hospital admissions during the Covid-19 pandemic has been reported by other researchers (121). The socioeconomic disparity is a well-described aspect of alcohol use disorder known as the "alcohol harm paradox" an observation that shows, though people from upper socioeconomic class drink more, worse alcohol-related outcomes are higher in lower socioeconomic class and often noted among the younger and male population (22, 23). This study demonstrated a similar alcohol use disorder and mortality trend for age; however, a different socioeconomic disparity distribution was observed between pre-pandemic and pandemic patients with AUD. One possible explanation for this observation could be the ease of access to alcohol in more affluent socioeconomic groups due to lower financial constraints compounded by social isolation perpetuating a yearning for alcohol to provide respite. Classically substance and alcohol misuse has been associated with worse outcomes when hospitalised (122, 123). Therefore, universal alcohol screening and risk stratification need to become a key component of the admission pathway.

The gender and ethnic data were consistent with previously reported data defining at-risk groups for alcohol use disorder in western populations (6, 9, 13, 124, 125). It is important to note that the evidence shows an increase in harmful drinking among females (126, 127). At the same time, females often suffer from higher levels of shame and social

stigma related to AUD which can act as a barrier to seeking help (128, 129). Alcohol use disorder is associated with an increased burden of mental health and behavioural disorders. In addition, the Covid-19 pandemic has severely impacted people's mental well-being. There is a mutual relationship between a negative effect on mental health with increasing alcohol intake and vice versa (130, 131). My findings emphasise the importance of commissioning targeted services for mental health and alcohol support to at-risk populations to stem the tide of multi-morbidity as highlighted by a recent report from The Royal College of Psychiatry (132). Previous epidemiological studies have demonstrated a high prevalence of psychiatric disorders concomitant with AUD and subsequent poorer outcomes (133). The lifetime prevalence of AUD in major depressive disorders ranges from 27%-40%, anxiety disorders range from 20-40%, and post-traumatic stress disorders range from 34%-55% (133). This highlights the importance of integrated treatment strategies addressing both AUD and mental health which have been reported to improve outcomes (134, 135).

3.6.4 Implications

Universal alcohol screening of hospitalised patients by AUDIT-C provides a useful tool to screen for AUD and to identify the change when facing sudden health crises. Alcohol contributes to over two hundred different medical conditions and of these, at least twenty-five are wholly attributable to alcohol (136). To manage these conditions patients often require hospitalisation which presents a distinct opportunity for effective intervention in alcohol use disorder (AUD) (101). The brief interventions provided by healthcare workers are proven to reduce alcohol-related harm (137). This puts healthcare staff in a unique position to intervene in the alcohol-related disease process, facilitate recovery, and prevent future harm (138). However, AUD detection rates both in primary and secondary care are poor. This could be due to inadequate knowledge, awareness and negative attitudes toward patients with AUD (100). The study presents a strong case that universal alcohol screening of hospitalised patients should be adopted nationwide as it enhances the pickup rate of AUD and creates a window of opportunity to intervene.

The message that health improvement is the responsibility of all healthcare professionals is not yet fully embedded, despite assurances to the contrary. The 2010 position statement from The Royal College of Surgeons of England, stressed the surgeon's role in capitalising on "teachable moments" by screening patients for alcohol misuse followed by a brief intervention (139). In order to address alcohol misuse treatment services must

be more accessible and education for healthcare professionals on how to integrate early diagnosis of alcohol misuse and interventions into their practice should be mandatory (140). There is a growing body of evidence supporting clinician lead integrated multidisciplinary care models to provide person-centred care for alcohol misuse (141, 142).

3.7 Conclusion

Alcohol assessment by AUDIT-C in secondary care is feasible and has high acceptance and completion rates. It provides an effective tool to screen hospitalised patients for alcohol use disorder and identify the change when facing sudden health crises like Covid-19. One in six admitted patients were screened positive for alcohol use disorder based on AUDIT-C assessment. Universal alcohol screening provides a unique opportunity for early detection of AUD followed by intervention to effectively mitigate future risk of harm.

The pattern of alcohol misuse recorded during the Covid-19 pandemic was largely similar to the pre-pandemic era but a higher proportion of admissions during the pandemic were alcohol dependent. There was an overall reduction in admissions during the pandemic likely due to the closure of elective services which could account for a higher proportion of being admitted as an emergency. Patients with alcohol use disorder during the pandemic were more likely to have mental disorders. Of concern, if admitted to the hospital and diagnosed with Covid-19 and alcohol use disorder, it significantly increased the risk of mortality at a relatively younger age than Covid-19 positive patients without alcohol use disorder.

Healthcare professionals should keep a high index of suspicion for alcohol-related disorders among hospitalised patients. A clinician-led integrated multidisciplinary approach accepting referrals based on both validated alcohol assessment tools and physician diagnosis should be adopted.

Chapter 4. Does advice based non-invasive tests for liver disease impact high-risk drinking behaviour: A systematic review with meta-analysis

4.1 Rationale and Overview

The use of alcohol screening and brief interventions has been advocated for by the World Health Organisation (WHO) over the last twenty years and has been recommended by the National Institute for Health and Care Excellence (NICE) for a decade (25, 143). Despite the existence of multiple alcohol behaviour interventions, their use does not appear to have been optimised in the UK, as illustrated by a significant rise in alcohol-related mortality (6).

Advice based on biological markers, such as diagnostic tests, indicating exposure to a harmful substance, increased susceptibility or the presence of a disease is more likely to promote behaviour change (81, 82). The addition of biomarker based advice to personalised healthcare communications can enhance motivation to overcome addictive behaviour (86, 87). In respiratory medicine, providing tailored advice based on the degree of lung injury has been successfully used to promote smoking cessation (83). Similar changes in alcohol consumption in response to advice based on non-invasive tests (NITs) for liver disease have been previously reported in patients with hazardous alcohol consumption (144-146).

Most heavy drinkers at risk of liver disease and in contact with alcohol services at present do not have access to testing for the identification and assessment of liver disease severity (9, 147). Current screening strategies to detect clinically significant liver fibrosis rely on serum liver function tests (LFTs), which are known to have poor sensitivity. The yield of significant liver disease following the investigation of abnormal LFTs in the community is less than 3% (148). Several non-invasive tests such as TE, and ELF tests are now available which can reliably test for the presence or absence of significant liver fibrosis (59). The use of these tests is not widely embedded in alcohol treatment settings (9, 20). Hence, the potential of combining early diagnostic interventions and advice has not been extensively explored in alcohol services. In this chapter, I aim to determine the impact of adding advice based on diagnostic tests for liver disease (intervention-based advice) to routine care and to compare the usefulness of intervention-based advice to non-intervention-based advice on reducing alcohol consumption amongst people with high-risk drinking behaviour.

4.2 Methods

4.2.1 Checklist and protocol registration

To keep the transparency of reporting, the systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) process (Appendix 5) (149).

The PRISMA is an evidence-based guide that consists of a list of minimum items, that authors are required to report as part of a systematic review and meta-analysis (150). Most journals required authors to submit a PRISMA checklist as part of the submission. It helps to improve the accuracy of reporting, enhance the validity of findings, and keep reporting process uniform and fairer (150).

A pre-defined systematic review protocol was registered on the International prospective registration of systematic reviews (PROSPERO). Protocol registration number: CRD42020164185

PROSPERO is an international open-access database produced by the University of York Centre for Research and Dissemination and supported by the National Institute for Health Research (NIHR). It accepts prospective registration of systematic review protocols. The purpose of the database is to avoid duplication, reduce reporting bias and encourage transparency in reporting systematic reviews (151).

4.2.2 Review question

Formulating a well-focused research question is a key step in evidence-based medicine (EBM) (152). Depending upon the type of systematic review, for example, effectiveness review, economic evaluation review, diagnostic test accuracy review, or epidemiology review, there are multiple frameworks available to facilitate drafting a well-structured research question and search strategy. The population, intervention, comparator, and outcome (PICO) model is one of the operational frameworks built on four core elements (population, intervention, control, outcomes) and has been primarily used in systematic reviews assessing the effectiveness of an intervention (153). PICO was used to create the review question: “Does the addition of NITs based advice compared to routine advice and care impact high-risk drinking behaviour”.

The detailed breakdown of PICO (Table 4-1) concerning the current systematic review is as follows

- **P**= Participants or Population or Patients. The target population was defined as participants with a diagnosis of alcohol use disorder (AUD). Within the study, this was defined as alcohol consumption exceeding 14 units/week, a physician diagnosis of an alcohol use disorder, or where available a diagnosis defined by the Alcohol Use Disorder Identification Test (AUDIT) score of greater than 8, ICD-10 or DSM-5 criteria.
- **I**= Intervention or interest or exposure (intervention group). The intervention of interest was the "addition of NITs based advice to routine care". For purpose of the current study, NITs based advice was defined as "advice based on any non-invasive measure of liver disease including (but not limited to): imaging e.g. transient elastography (Fibroscan) (154), serum liver biochemistry, or other markers of fibrosis e.g. enhanced liver fibrosis (ELF) test, FIB-4 score, APRI score.
- **C**= Comparator (control group). The comparator was routine advice called non-intervention based advice which was defined as "advice that does not include feedback on liver disease diagnostic tests including but not limited to; brief advice (BA), simple advice (SA), alcohol identification and brief advice (AIBA), identification and brief advice (IBA), and standard Care.
- **O**= Outcomes. The outcomes of interest were a change in self-reported alcohol intake, changes in liver blood markers, and alcohol-related health outcomes.

Table 4-1. PICO for systematic review

Population	Adult participants ≥16 years
	All gender
	History of alcohol misuse (>14 units/week), a physician diagnosis of alcohol misuse or where available a diagnosis based on AUDIT score, ICD, or DSM V criteria
Intervention group	The group received NITs based advice in addition to routine care and advice.
Control group	The group only received routine advice and care without NITs based advice
Outcomes	Change in self-reported alcohol intake
	Change in alcohol assessment scores e.g., AUDIT, AUDIT C
	Change in LFTs
	Change in liver fibrosis score
	Change in alcohol-specific mortality and morbidity

4.2.3 Literature search

4.2.3.1 Search strategy

An electronic search was conducted using Ovid Medline, PubMed, EMBASE, Psychinfo, and CINAHL to identify articles published from the inception of databases to the end of February 2020. As per the Cochrane systematic review handbook, I included more than two databases to optimise the scope of the search strategy (155). The evidence has shown by combining Medline with EMBASE produces over 90% of unique references related to the primary review question and adding google Scholar further increases the accuracy (155). Psychinfo and CINHHAL were included as specialist databases on the subject of alcohol misuse and behavioural intervention to increase the scope of the literature search. Additionally, to optimise the search strategy the grey literature was searched in conference proceedings, Ethos, Google Scholar, and Clinicaltrials.gov. For included studies, a citation search was undertaken, and reference lists were hand examined.

To identify all relevant evidence the databases were searched from their inception. The stop date of the end of February 2020 was chosen because the systematic review was done as part of the KLIFAD trial to identify pre-existing evidence before starting the trial (156).

To finalise the search strategy, I took advice from a local expert librarian. The search was restricted to the English language due to my limited proficiency in other languages, and the availability of translation services. The search strategy syntax was customised to individual databases. Different combinations of Boolean operators, parenthesis, field codes and truncation were used.

4.2.3.2 Search terms

Different combinations of following search terms were used: “alcoholism”, or “alcoholic*”, or “alcoholic liver disease”, or “binge drinking”, or “alcohol intoxication”, or “alcohol related disorders”, or “alcohol misuse”, or “alcohol dependence”, or “alcohol abuse”, or “harmful drinking”, and “fibroscan”, or “fibro scan”, “fibrotest”, or “liver fibrosis scan”, or “transient elastography”, or “Elastography”, or “enhanced liver function test”, or “ELF markers”, or “liver function tests”, or “liver function$”, or “Liver enzymes”, or “liver biomarkers”, or “liver tests”, and “counselling”, or “Advice”, or “brief advice”, or “simple

advice", or "alcohol identification and brief advice", or "patient education", or "Brief alcohol intervention*", "alcohol intervention*", or "motivational intervention", "advice.ab", or "brief adj2 advice", or "brief adj2 intervention", or "brief adj2 intervention*", and "alcohol Abstinence", or "reduction in alcohol use", or "self-reported alcohol intake", or "change in Behaviour", or "Behavio?r", or "Alcohol drinking behaviour", or "Change in drinking".

4.2.4 Study selection

The following eligibility criteria were applied.

4.2.4.1 Inclusion criteria

- Studies of the following design: randomised control trials, prospective and retrospective observational studies. These study designs were chosen considering the hierarchy of evidence and the availability of robust methods to assess the quality and evaluate internal validity (157).
- Studies recruited adult participants with a self-reported history of alcohol misuse, a physician diagnosis of alcohol misuse or AUD, or a diagnosis defined by alcohol assessment scores e.g., AUDIT, ICD10. Or DSM-5 criteria. The diagnostic criteria were kept broad to minimise the risk of missing relevant studies.
- Studies report a comparison between NITs based advice to routine advice and care (non-intervention-based advice).
- The studies in which the non-invasive tests (NITs) for liver disease were performed prior to an advice and the results were incorporated into final advice. The study protocol was reviewed, and if required lead authors were contacted to ensure these criteria were met.
- Studies report a primary outcome of change in self-reported alcohol intake or alcohol assessment scores such as alcohol use disorder identification test (AUDIT) score. And secondary outcomes of change in liver blood markers, alcohol-related mortality, sickness days, and any other outcomes directly related to harmful consumption of alcohol.

4.2.4.2 Exclusion criteria

- Case reports and case series were excluded due to the lack of a robust process to determine quality and concerns regarding the validity of results. Moreover, after running the search I identified sufficient higher hierarchical evidence to answer the review question.
- Studies which included participants with known diagnoses of ARLD or have previously been seen in liver services before receiving intervention base advice were excluded. This was to reduce the bias (information and selection) as the participants who are known to have ARLD compared to participants who are never known to have ARLD will have a different response to NITs based advice and this would have impacted the results.
- Studies with a follow-up of less than 3 months. The 3-month cut-off was decided as evidence has shown this is the minimum period to see any effective change in addictive behaviour (158, 159). In those, the duration of treatment for addictive behaviour was less than 90 days 35% relapse compared to 17% in those with a treatment duration of greater than 90 days (158). Moreover, most alcohol treatment programs including one at Nottingham Recovery Network are of twelve week duration.

4.2.5 Study screening

The titles and abstracts of all potentially relevant articles after removing duplicates were reviewed independently for inclusion. Rayyan-QRCI systematic review software, Endnote (version-X9) and Microsoft Excel (2019) were used to screen, remove duplicate entries, and record the reviewer's decisions.

4.2.6 Data extraction

Data were extracted on an adapted Cochrane data extraction form. In view of the review question, new sections were added, and irrelevant sections were deleted (Appendix 3).

The details on the following variables were collected; author name and year of publication, study design, country and setting, sampling technique, method of recruitment, eligibility criteria, study duration, ethical approval, participants' demographics, sample size, baseline alcohol intake and laboratory parameters and if available alcohol use scores, type of advice given to intervention and control group, outcome measures, the key conclusion by author, and the studies strengths and

limitations. Pre and post-changes in self-reported alcohol intake and laboratory parameters were also collected.

Where available, data on other outcomes (e.g., mortality and sickness days) were also extracted. Where information was missing the corresponding author of the study was contacted. Data on alcohol use was converted to grams per week of pure alcohol and for gamma-glutamyl transferase (GGT) to IU/Litre.

4.2.7 Risk of bias (ROB) and Quality Assessment

The Cochrane Risk of Bias tools “Rob 2 version 2019” and the Risk Of Bias In Non-randomized Studies of Interventions “ROBIN 1” were used to assess the risk of bias (ROB) and quality of included studies (160).

Rob 2 assesses the risk of bias in randomised control trials and consists of five domains: selection of the results, measurement of the outcome, missing outcome data, deviations from intended interventions, and randomisation process. Each domain has a set of specific questions regarding the design, conduct and reporting of a randomised control trial. The responses to signalling questions are yes, probably yes, probably no, and no information. Based on the responses to the signalling questions the risk of bias is labelled as low risk, some concerns, and high risk. The results are graphically displayed (161).

The ROBINS-1 tool is specifically designed to assess ROB in non-randomised studies related to the following domains: pre-intervention, at-intervention and post-intervention stages (162). Like Rob 2 it has a set of specific signalling questions for each domain. Based on the responses to questions individual studies' risk of bias is labelled as low risk, moderate risk, serious risk, critical risk, or no information.

Studies with low risk of bias were deemed high quality, with moderate risk of bias or some concern as medium quality, and with high risk or serious risk or critical risk as low quality.

4.2.8 Data synthesis and statistical analysis

Cochrane Review Manager (RevMan version 5.3) was used to complete the statistical analyses.

Analysis was undertaken on all studies for the intended primary outcome of change in self-reported alcohol consumption and repeated for the following subgroups: (i) sex (male vs female); (ii) baseline alcohol intake (>250 grams per week vs <250 grams per week);

(iii) study type (RCT vs observational); and (iv) diagnostic method (liver blood test vs fibrosis marker). The subgroups were decided in priori.

Where available, main data were analysed per protocol for secondary outcomes of change in GGT, MCV, non-invasive liver fibrosis score, impact on alcohol-related significant episodes e.g., hospital or emergency admission per year, mortality, and sickness.

There was insufficient data to undertake subgroup analyses by study type, diagnostic method, and change in non-invasive liver fibrosis score.

To calculate effectiveness where available pre, post and mean difference data on weekly self-reported alcohol intake and liver blood markers were extracted. A p-value of <0.05 was considered significant. Due to expected heterogeneity among the included studies, a random-effects meta-analysis with weighted average differences, standard deviation (SD), and a 95% confidence interval was performed. For studies without evidence of heterogeneity, fixed-effects models were used. Forest plots were used for the graphical display of estimated study results and funnel plots for publication bias. Where the data were not suitable for meta-analysis, a narrative description was performed.

4.2.9 Sensitivity analysis

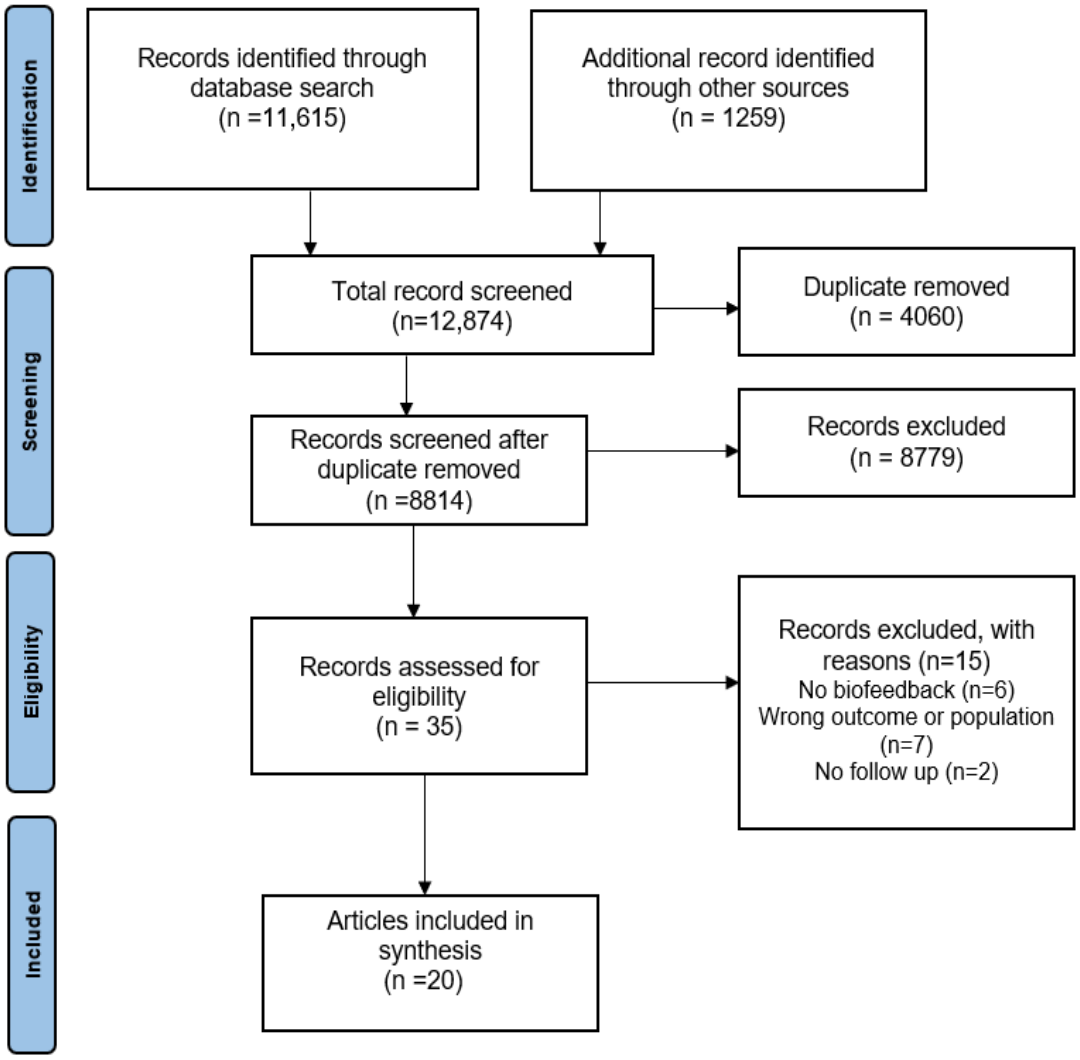
Given the variability of control conditions and heterogeneity between studies, a sensitivity analysis was undertaken for the following outcomes, change in self-reported alcohol, change in GGT, and change in MCV.

The sensitivity analysis was performed by restricting the meta-analysis to compare different forms of control conditions to the intervention group: **(a)** no advice vs intervention-based advice, **(b)** brief advice (BI) vs intervention-based advice, **(c)** brief advice at request vs intervention-based advice, (**d)** no advice and BI and brief advice at request vs intervention-based advice.

4.3 Results

After the screening of titles and abstracts, 35 studies were selected for further search. After full-text reading, 15 articles were excluded as the content did not meet the inclusion criteria (Figure 4-1).

Figure 4-1. PRISMA flow diagram for study selection



Of the 20 included articles 16 were different studies 14 RCTs and two observational. Kristenson et al., (137, 163-165) published four studies using the same cohort but at different intervals of follow-up. Nilssen et. al. (1991, 2004) published one year and nine years of follow-up on the same cohort (166, 167). The repeated publications of the same cohort were managed by taking data on the primary outcomes of interest up to three years of follow-up and taking mortality and morbidity data from later publications. The characteristics of included studies are summarised in Table 4-2

4.3.1 Participants

A total of n=3,763 participants were recruited consisting of n=3,291 from RCTs, and n=472 from the observational studies. The pooled dropout rate in the intervention group was 33% and, in the control group was 34%, the individual study recruitment and dropout rates are provided in Table 4-2. The mean age of participants was 43.2 years (SD+/- 4.4). In the RCTs 80% of participants were male, and seven studies (163, 168-173) included only a single sex as described in Table 4-2. The studies were predominantly performed in Caucasian populations, but a detailed ethnic distribution was missing in most studies.

4.3.2 Interventions

In the intervention group, the advice was given based on non-invasive tests (NITs) for liver disease concerning alcohol intake. The studies used the following biomarkers as part of the feedback: GGT and MCV (163, 166, 168-171, 173-179), FIB-4 score (172), Southampton traffic light test (STLT) score (88), and transient elastography (Fibroscan) (180). The advice was tailored using these markers in relation to alcohol intake. Across control groups, participants either received no advice, advice which did not include NITs based advice or brief advice at request (Table 4-2).

Table 4-2. Characteristics of the included studies

Author (year)	Sample	Design	Interventions	Results/Findings[c]
	Age[a] (years) Size (n[b]) Sex Dropout ITT	(Setting/Country Starting Year Follow-up Duration)	(IG= Intervention group/s CG= Control group)	(As per study measures of outcome) GGT=IU/Litre Alcohol intake=g/week
Kristenson et al. (1981-1985, 2002) (137, 163-165)	46 n=585 M=585 F=0 n=177 Yes	RCT Community Malmo Sweden Screening from 1975-1981 2, 3, 5,13 years	**Intervention Group:** Tapered counselling and biofeedback based on GGT. **Control Group:** An invitation letter was sent for a repeat blood test in 2 years	**Change in Gamma GT:** A significant reduction within but not between groups **Sickness Days** Significant increase in CG **Hospital days** CG spent more days **Mortality at 13 years** Twice as high alcohol-related deaths in the control group

Author (year)	Sample	Design	Interventions	Results/Findings[c]
Poika et al. (1988) (168)	39 n=120 M=120 F=0 n=31 No	RCT Inpatient Helsinki Finland Started 1985 6 Months	**Intervention Group:** Brief counselling, biofeedback on blood tests concerning alcohol **Control Group:** No advice was given, and a follow-up was offered at 6 months	**Alcohol Use** IG- significantly reduced CG- Significantly worsen Improved- IG 50%, CG 20% **Change in Gamma GT:** No statistically significant difference noted both between and within groups
Persson et al. (1989) (176)	44 n=78 M=61 F=17 n=23 No	RCT Somatic Outpatient Karlstad Sweden Started 1982 1- 2 year	**Intervention Group:** Brief counselling, and biofeedback based on labs concerning alcohol. **Control Group:** No contact or discussion about alcohol. All participants were invited at 1 year for a repeat	**Alcohol Use:** IG- 21 out of 36 reduced CG- No follow-up data **Change in gamma GT:** A non-significant reduction in both groups **Sickness days:**

Author (year)	Sample	Design	Interventions	Results/Findings[c]
			blood sample	Significant reduction in IG Physician Consultations: Non-significant decrease in IG and an increase in CG
Romelsjo et al. (1989) (177)	46 n=83 M=70 F=13 n=21 No	RCT Community Stockholm Sweden 1984 1 year	**Intervention Group:** GP provided biofeedback on GGT concerning alcohol. **Control Group:** GP advised to cut down on alcohol intake	**Alcohol Use:** No significant change between or within groups **Change in gamma GT:** No significant ($p > 0.05$) change between or within groups.
Scott et al. (1990) (173)	45 n=72 M=0 F=72 n=22 Yes	RCT Community Oxford UK 1989 1 year	**Intervention Group:** GP delivered Brief (10 minutes) advice plus biofeedback on blood tests concerning alcohol intake	**Alcohol use:** There was a significant reduction in the whole study group **Change in gamma GT:** No significant change within or

Author (year)	Sample	Design	Interventions	Results/Findings[c]
			Control Group: No advice from GP except at their request.	between groups **Dependence score:** Significant improvement in both groups.
Nilssen et al. (1992,2004) (166)	41 n=338 M=290 F=48 n=18 Yes	RCT Community Tromso Norway - 1 & 9 year	**Intervention Group:** Major Intervention Group: 15 minutes intervention, biofeedback on GGT concerning alcohol intake Minor Intervention Group: 10 minutes intervention, possible reasons for elevated GGT discussed, a booklet containing information on GGT and alcohol. **Control Group:** No Intervention	**Alcohol use:** IG- significant improvement in CG- increase Change in gamma GT: IG- a significant reduction CG- increase **Change in gamma GT at 9 years:** All three groups receiving treatment (control, minor and major) displayed significant GGT reduction. No significant difference between groups

Author (year)	Sample	Design	Interventions	Results/Findings[c]
Anderson et al. (1992) (169)	44 n=154 M=154 F=0 n=54 Yes	RCT Community Oxford UK - 1 year	**Intervention Group:** GP delivered Brief (10 minutes) advice plus biofeedback on blood tests concerning alcohol intake. **Control Group:** No advice from GP except at their request.	**Alcohol Use:** At 1 year Follow up 18% of men in IG reduced their alcohol intake compared with 5% in CG **Change in gamma GT/MCV:** No significant change within or between groups
Seppa et al. (1992) (178)	54 n=178 M=140 F=38 n=83 No	RCT Community Tampere Finland - 1 year	**Intervention Group:** Brief advice and biofeedback on MCV concerning alcohol. Follow up every 3 months with repeat brief sessions and biofeedback **Control Group:** Counselling but no biofeedback	**Alcohol use:** Men- 7% stated a reduction in the whole cohort Women- 11% stated a reduction in the whole cohort. **Change in MCV:** No significant reduction both within and between groups

Author (year)	Sample	Design	Interventions	Results/Findings[c]
Israel et al. (1996) (175)	30-60[d] n=105 M=46 F=59 n=32 No	RCT Community Cambridge Ontario Canada - 1 year	**Intervention Group:** Received 30-minute cognitive behaviour treatment biofeedback on GGT concerning alcohol. **Control Group:** Received brief advice on reducing alcohol intake and a Pamphlet.	**Alcohol Use:** IG group had a 70% reduction in mean alcohol intake per four weeks and CG had a 46% reduction **Change in gamma GT:** IG showed a 32% mean reduction from baseline. No significant reduction in CG **Physician Visits:** IG mean reduction of 34% CG no significant change
Tomson et al. (1998)[e] (179)	45 n=222 M=(61)[f] F=(14)[f] n=147 Yes	RCT Community Stockholm Sweden - 2 years	**Intervention Group:** A nurse-delivered Intervention focussed on factors that facilitated controlled drinking. GGT was used as biomarker feedback.	**Alcohol Use:** IG- Significant reduction CG- no data at baseline Change in gamma GT:

Author (year)	Sample	Design	Interventions	Results/Findings[c]
			Control Group: GP discussed the possible causes of elevated GGT. No alcohol-specific advice was given.	IG-Significant reduction CG- Non-significant increase **Sickness days** No significant reduction in the whole cohort **Mortality** IG- No death CG- 3 deaths
Gentilello et al. (1999) (174)	36 n=762 M=625 F=137 n=353 Yes	RCT Inpatient Washington USA October 1994 1 year	**Intervention Group:** A 30-minute motivational interview with a psychologist comprises personalised feedback and biofeedback on abnormal laboratory values. **Control Group:** Control patients requesting help for a drinking problem were assisted in obtaining it.	**Alcohol use:** Significant reduction of weekly alcohol intake in IG as compared to CG (p=0.03) **Trauma Recurrence:** The intervention group had a 47% reduction in new injuries **Mortality:**

Author (year)	Sample	Design	Interventions	Results/Findings[c]
				No difference in death rate between 2 groups (2.7% in intervention, 2.3% in controls) Traffic Violation: Fewer in IG
Aalto et al. (2000) (170)	41 n=118 M=0 F=118 n=40 Yes	RCT Community Tampere Finland 1994 3 years	**Intervention Group:** Group A: received sessions at baseline, 2, 6, 12, 18, 24, and 30 months. Group B: received brief intervention at baseline, 12, and 24 months. Both groups received biofeedback on blood test concerning alcohol **Control Group:** GP provided general advice	**Alcohol Use:** The change was not statistically significant in all groups **Change in gamma GT:** GGT decreased in IG A and B but increased CG, the difference was not significant **Change in MCV:** Significant reduction in MCV in the whole study group. Self-estimation of Mental health:

Author (year)	Sample	Design	Interventions	Results/Findings[c]
				Poorer in intervention groups A and B
Aalto et al. (2001) (171)	42 n=296 M=296 F=0 n=94 Yes	RCT Community Tampere Finland 1994 3 years	**Intervention Group:** Group A: received sessions at baseline, 2, 6, 12, 18, 24, and 30 months. Group B: received brief intervention at baseline, 12, and 24 months. Both groups received biofeedback on blood tests concerning alcohol **Control Group:** GP provided general advice	**Alcohol Use:** 25-53% reduce alcohol intake in the whole cohort. **Change in gamma GT:** No significant change within or between groups **Change in MCV:** A significant change in MCV between baseline and 3 years follow-up in each group (all significant at ($p < .01$)
Sheron et al. (2013) (144)	34 n=393 M=229 F=164 n=90	Prospective observational Community Southampton UK	Liver fibrosis was checked by using the Southampton Traffic light (STL) test[g], results were sent to GP who provided biofeedback.	**Alcohol use (AUDIT score):** 42% had reduced their drinking, and participants receiving amber/red grades were significantly more likely to reduce than the green group

Author (year)	Sample	Design	Interventions	Results/Findings[c]
	Yes - 1 year			
Kahler et al. (2018) (172)	42 n=180 M=180 F=0 n=19 No	RCT Outpatient Boston USA 2011 1 year	**Intervention Group:** Motivational intervention and biofeedback on Fib-4 score[h]. **Control Group:** Assessment only	**Alcohol use:** Significant reduction of alcohol intake in the intervention group ($p<0.04$) **FIB-4 score[*]:** No Significant change
Mathews et al. (2018)[e] (180)	79 - - - - Yes	Prospective observational study Edinburgh UK 2014 1 year	Individuals who self-identified as harmful drinkers attended for a Fibroscan.	Compliance with further assessment: 100% engaged in further assessment Attendance at specialist services: 92 % attended the first medical appointment Attendance at 6 months:

Author (year)	Sample	Design	Interventions	Results/Findings[c]
				90% attended 6 months follow up

ITT, intention to treat.
[a]Age—mean, sex—F = female, M = male distribution of total recruited.
[b]Number recruited.
[c]Not all findings are included.
[d]Age range.
[e]Tomson *et al*. and Mathews *et al*., no information on sex distribution at recruitment.
[f]Number of the participant at follow-up, no information on distribution at recruitment.
[g]STL test: Combines several different tests and clinical markers, which are given a score that indicates the patient's likelihood of developing liver fibrosis and cirrhosis. Green—No evidence of severe fibrosis but early damage cannot be excluded. Amber—Liver fibrosis likely but not certain. Red—Fibrosis almost certain, possible severe fibrosis or cirrhosis.
[h]FIB-4 score: The score combines patient age, platelet count, AST and ALT to give a fibrosis score.

4.3.3 Outcomes

4.3.3.1 Self-reported alcohol consumption

Pooled mean self-reported alcohol intake for the intervention group at baseline (pre-intervention) was 307 grams per week (SD+/-155.7) and post-intervention was 198.2 grams per week (SD+/- 76.7). The post-intervention reduction in alcohol consumption was 108 grams per week (36.0%). Pooled mean self-alcohol intake for the control group at baseline (pre-intervention) was 316.1 grams per week (SD+/-166.6 range), and post-intervention was 294 grams per week (SD+/- 174). The post-intervention reduction in alcohol consumption was 22 grams per week (7.0%).

Pre- and post-intervention data on self-reported alcohol intake in both groups were available in nine studies (168-175, 177) (Figure 4-2). The mean difference in individual studies varied from -505.0 grams per week (95%CI -785.8 to -224.2) to 24.3 grams per week (-44.8 to 93.39). A meta-analysis revealed the weighted mean average difference of weekly alcohol intake between the intervention and control (Brief and/or no advice) groups was -74.4 grams per week (95%CI -126.1 to -22.6). The results favoured the positive effect of intervention-based advice including feedback on laboratory tests or markers of liver fibrosis to reduce alcohol intake (p=0.005). There was statistically significant heterogeneity between studies (I^2=98%) and there was no evidence of publication bias (Figure 4-3).

Figure 4-2. Forest plot for meta-analysis of change in self-reported alcohol intake (grams per week)

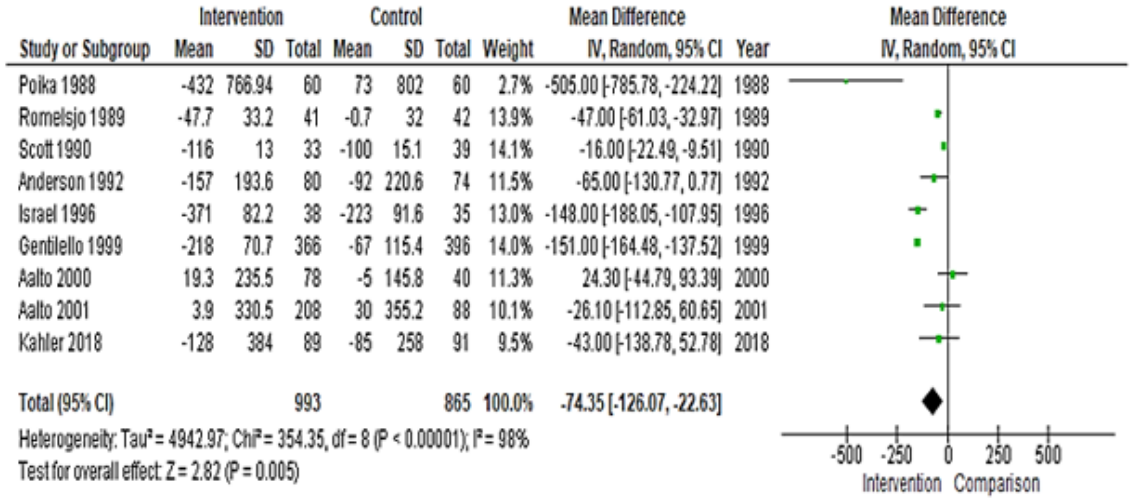
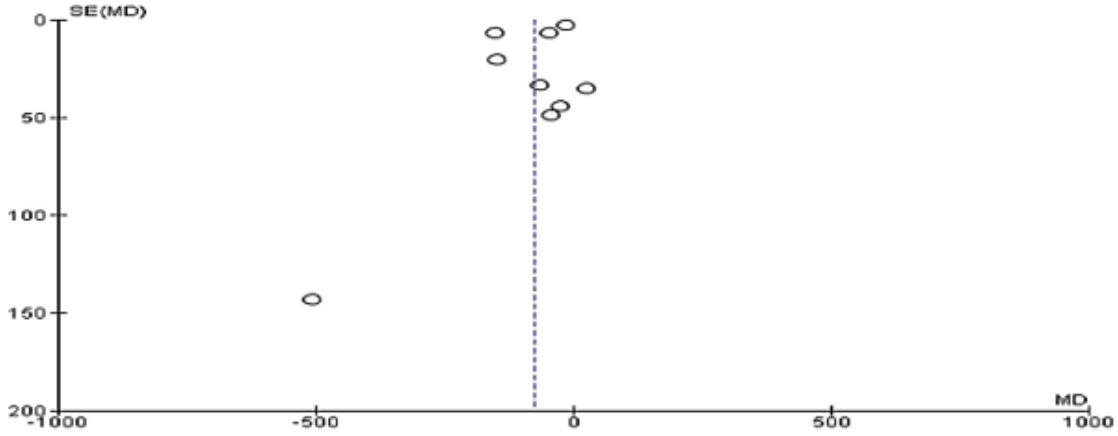


Figure 4-3. Funnel plot for publication bias

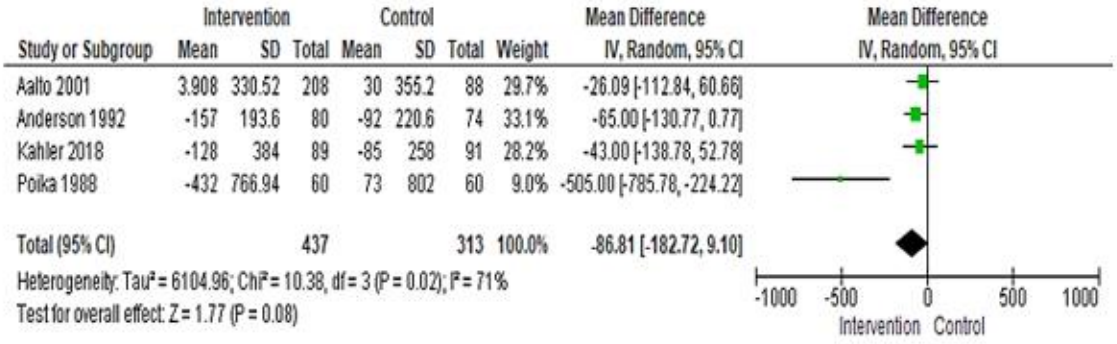


The following RCTs (137, 163, 166, 176, 178, 179) were excluded from the meta-analysis as pre- and post-intervention data on self-reported alcohol intake was not collected in both groups. Kristenson et al.(1983; 1981) did not collect follow-up data on alcohol intake post-intervention. In the Persson and Magnusson. (1989) study post-intervention data was only reported in the intervention group (n=36), of whom 21 reduced their alcohol intake (176). The studies by Nilssen et al.(1991) (166) and Tomson et al.(1998) (179) showed significant reductions in alcohol use in the intervention group, but pre-intervention data in controls was not collected. In the Seppa et al.(1992) trial, quantitative data on alcohol consumption was not collected but 7.0% of men and 11.0% of women from the study cohort reported a general reduction in alcohol intake (178).

4.3.3.1.1 Sex-based analysis for change in self-reported alcohol intake

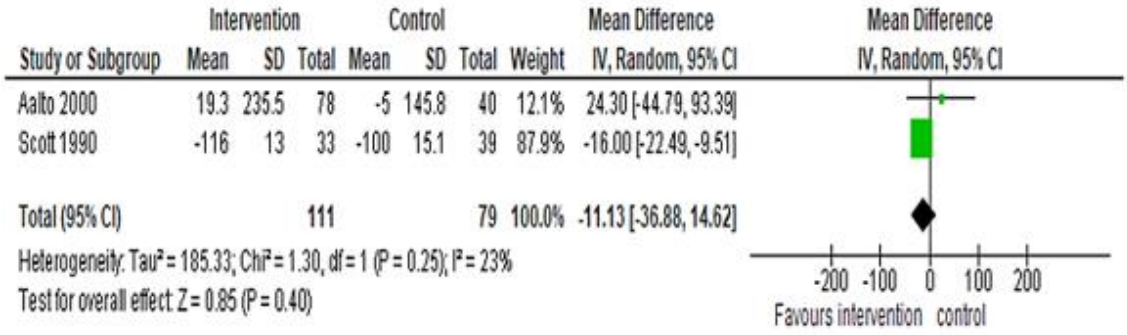
On restricting the analysis to specific sex: The male only participant studies (168, 169, 171, 172) analysis demonstrated a weighted mean average difference in weekly alcohol intake between the intervention and control groups of -86.8 gram/week (95% CI -182.7 to 9.1) but was not statistically significant (p=0.08). The I^2 was 71% (p = 0.02) indicating statistically significant heterogeneity between studies (Figure 4-4)

Figure 4-4. Forest plot for meta-analysis of change in self-reported alcohol intake (gram per week) in male only studies



Analysis of the female only studies (170, 173) showed a significant (p<0.01) reduction in alcohol intake across the whole study group but no significant difference between groups with a weighted mean average difference of weekly alcohol intake between the groups was -11.1g/week (95% CI -36.9 to 14.6), (p=0.4). The I^2 was 23% (p = 0.25) indicating no significant heterogeneity between studies (Figure 4-5)

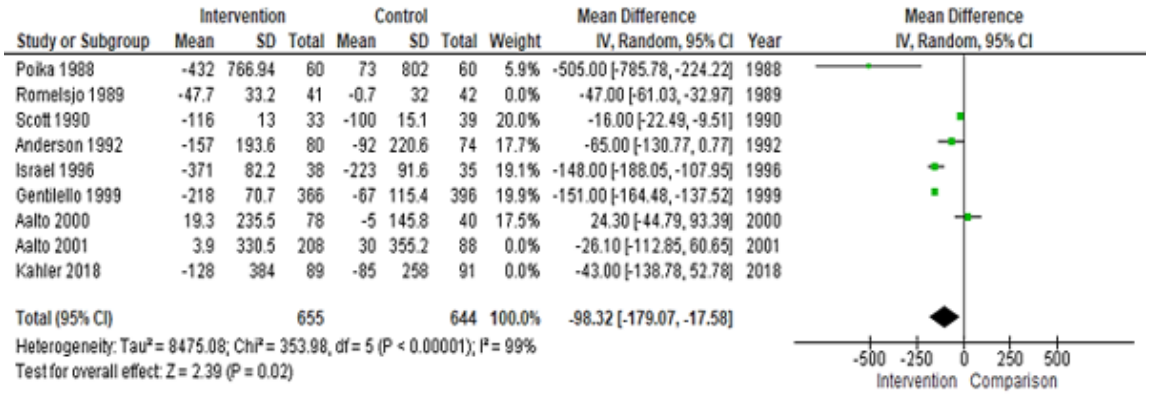
Figure 4-5. Forest plot for meta-analysis of change in self-reported alcohol intake (gram per week) in female-only studies



4.3.3.1.2 Volume of alcohol consumed per week

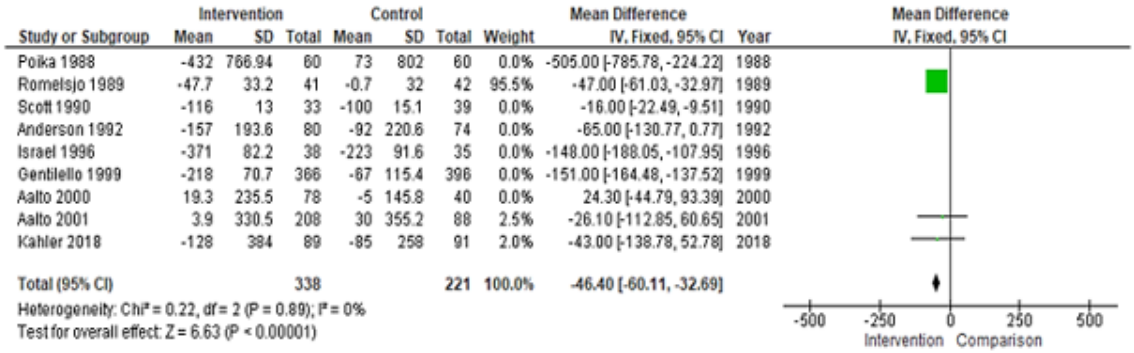
On stratifying studies using baseline alcohol intake above or below 250 grams per week, the effect of the intervention remained significant irrespective of participant baseline alcohol intake. On analysing the studies with baseline alcohol intake >250 grams per week, the weighted mean average difference of weekly alcohol intake between the intervention and control was -98.32 grams per week (95% CI -179.07 to -17.58, p=0.02). The I^2 was 99% (p <0.001) indicating significant heterogeneity between studies (Figure 4-6).

Figure 4-6. Forest plot for meta-analysis of alcohol intake >250 grams per week



On analysing the studies with baseline alcohol intake <250 grams per week, the weighted mean average difference of weekly alcohol intake between the intervention and control was -46.40 grams per week (95% CI -60.11 to -32.67, p=<0.0001). The I^2 was 0% (p <0.89) indicating no significant heterogeneity between studies (Figure 4-7)

Figure 4-7. Forest plot for meta-analysis of alcohol intake <250 grams per week



4.3.3.2 AUDIT score

The study by Sheron et al.(2013) used the Southampton traffic light test (STLT) as part of biofeedback and reported a change in the AUDIT category (harmful to hazardous, or, hazardous to low risk) (88).

STLT combines the results of serum blood tests (platelet count, hyaluronic acid, collagen P3NP, viral hepatitis serology), units of alcohol consumed per week, patient age, sex, body mass index (BMI), and diagnosis of underlying liver disease, and generate a score that indicates the patient's likelihood of developing liver fibrosis and cirrhosis (181). Based on scores patients were divided into green (no evidence of severe fibrosis but early damage cannot be excluded), amber (liver fibrosis likely but

not certain) and red (fibrosis almost certain, possible severe fibrosis or cirrhosis) groups.

Out of 393 patients who had liver fibrosis measured by SLTL follow-up AUDIT data at 12 months was available in 303 patients (red n=31, amber n=122, and green n=150). The mean change in AUDIT score was, green -1.9 (SD +/- 3.6), amber and red -3.0 (SD +/- 4.5). At the 12-month follow-up, in the whole cohort, 42.2% (n=128) had reduced and 2.6% (n=8) increased their drinking by one AUDIT category. In patients with evidence of liver damage (amber and red group), 49.6% (n=76/153) reduced their AUDIT by one category compared to 35.0% (n=52/150) with no evidence of liver damage (green group). Participants receiving amber and red results (possible or probable liver fibrosis) were significantly more likely to reduce the AUDIT category than those with a green result (liver fibrosis unlikely) (p =.011). In the green group, 3.3% (n=5/303) reported an increase in the AUDIT category compared to 2.0% (n=3/153) in the amber and red groups, the difference was non-significant (p=0.498).

4.3.3.3 Liver blood markers

The GGT and MCV were used as a marker of excess alcohol intake and a decline in their results were taken as an indication of a reduction in alcohol intake. Data concerning pre- and post-changes in GGT for both groups were available in ten studies and for MCV in fine studies.

4.3.3.3.1 Gamma-glutamyl transferase (GGT)

The pooled mean pre and post-intervention GGT levels for the intervention group were 86.2 IU/L (SD+/- 39.5) and 76.2 IU/L (SD+/-44.7), and for the control group were 65.4 IU/L (SD+/-24.1) and 71 IU/L (SD+/-39.7).

Meta-analysis on the studies providing pre-and post-data on change in GGT between the intervention and control groups showed the mean difference between the two groups varied from -81.0 (95% CI -98.89, -63.11) to 19.84 (95% CI -21.32, 61.0). The weighted mean average difference in GGT between intervention and control groups was -19.7 IU/L (95% CI -33.0, -6.4) (Figure 4-8). The change was statistically significant (p=0.004) and favoured the intervention over the control group. The I^2 was 93% (p<0.001) indicating statistically significant heterogeneity between studies. The publication bias is given in Figure 4-9.

Figure 4-8. Forest plot for meta-analysis for change in GGT

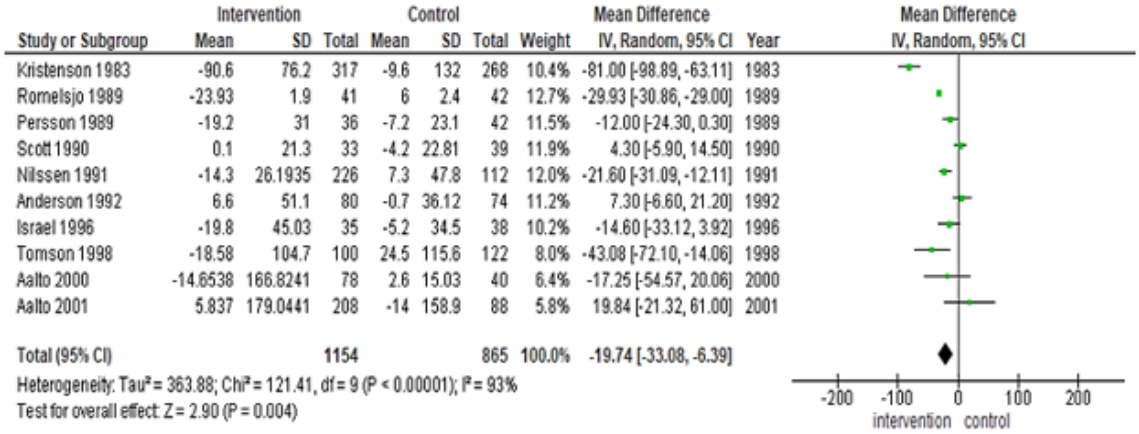
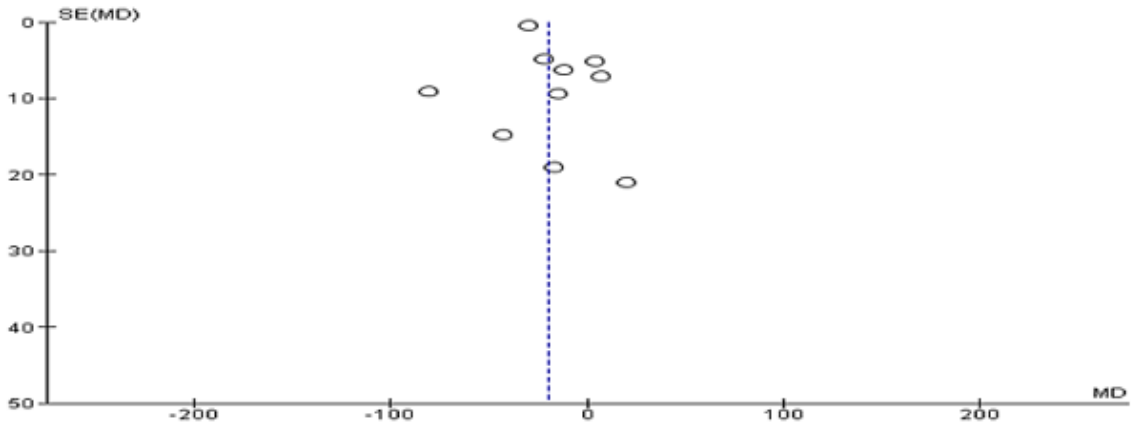


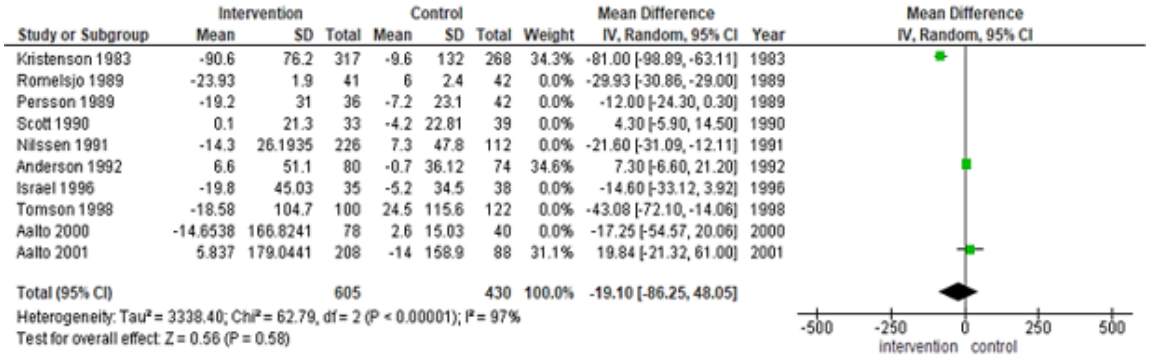
Figure 4-9. Funnel plot for publications bias



4.3.3.3.2 Sex-based analysis for change in GGT

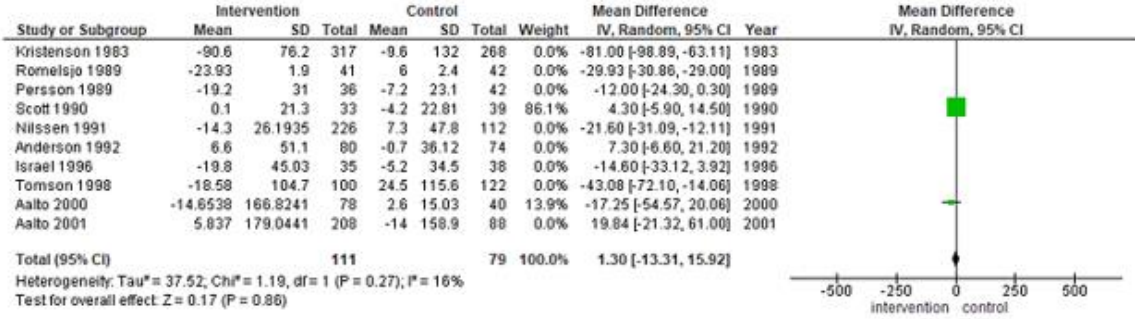
On restricting the analysis to specific sex: The male only participant studies analysis demonstrated a weighted mean average difference in GGT between the intervention and control groups was -19.10 (95% CI -86.25, 48.05), the difference was statistically non-significant (p=0.58). The I^2 was 97% (p<0.001) indicating significant heterogeneity between the studies (Figure 4-10).

Figure 4-10. Forest plot for meta-analysis of change in GGT in male only studies



The female only participant studies analysis demonstrated a weighted mean average difference in GGT between the intervention and control groups was -1.30 (95% CI -13.3, 15.92), the difference was statistically non-significant (p=0.86). The I^2 was 16% (p=0.27) indicating no significant heterogeneity between the studies (Figure 4-11).

Figure 4-11. Forest plot for meta-analysis of change in GGT in female only studies

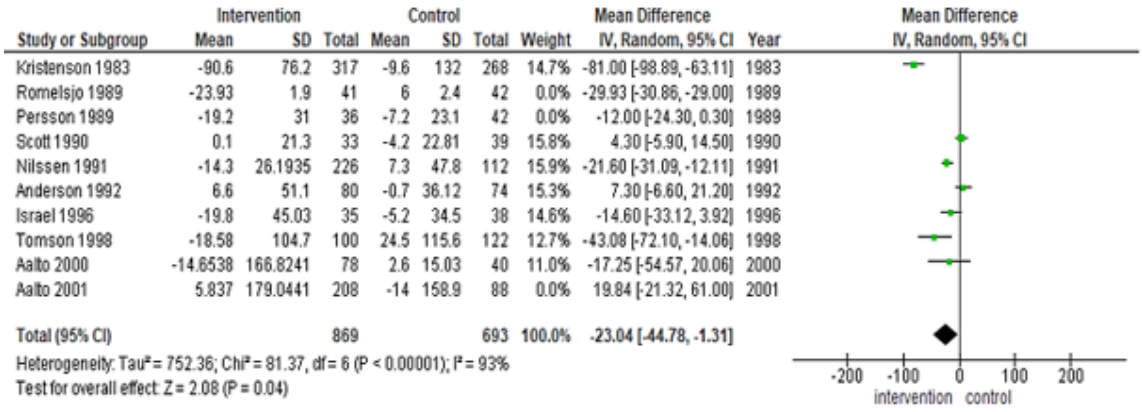


4.3.3.3.3 Volume of alcohol consumed per week

On stratifying studies using baseline alcohol intake above or below 250 grams per week, the effect of the intervention was only significant if baseline alcohol intake was greater than 250 grams per week (p 0.04).

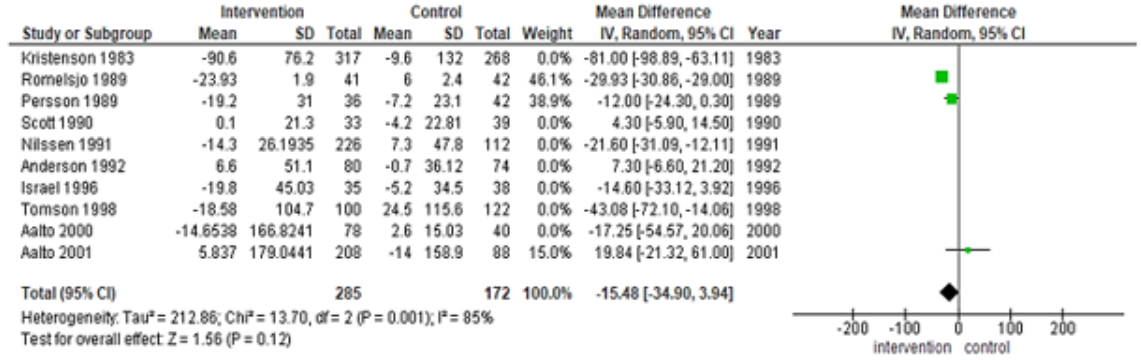
On restricting the analysis to studies with baseline alcohol intake >250 grams per week the weighted mean average difference in GGT between the intervention and control groups was -23.04 (95% CI -44.78, -1.31). The difference was statistically significant (p=0.04). The I^2 was 93% (p<0.001) indicating significant heterogeneity between studies (Figure 4-12).

Figure 4-12. Forest plot for meta-analysis of alcohol intake >250 grams per week



On analysing studies with baseline alcohol intake <250 grams per week the weighted mean average difference in GGT between the intervention and control groups was -15.48 (95% CI -34.90, 3.94). The difference was statistically non-significant (p=0.12). The I^2 was 85% (p<0.001) indicating significant heterogeneity between studies (Figure 4-13)

Figure 4-13. Forest plot for meta-analysis alcohol intake < 250 grams per week



4.3.3.4 Mean corpuscular volume (MCV)

The pooled mean pre and post MCV values for the intervention group were 95.6 femtoliter/cell (SD+/-2.4) and 94.8 femtoliter/cell (SD+/-2.8). For the control group, these values were 95.4 femtoliter/cell (SD+/-3.3) and 94.9 femtoliter/cell (SD+/-3.5) respectively.

Meta-analysis on the studies providing pre-and post-data on change in MCV between the intervention and control groups showed the mean difference between the two groups varied from -0.20 (95% CI –1.70, 1.30) to 0.80 (95% CI -1.13, 2.73).

Given that heterogeneity was not evidenced (I2 = 0%; p = 0.94) a fixed-effects meta-analysis was conducted on the studies (n=5) using MCV values as an outcome

measure. The weighted mean average difference in MCV between intervention and control groups was 0.36 femtoliter/cell (95% CI -0.27, 0.99). The difference was statistically non-significant (p=0.26) (Figure 4-14). The publication bias is provided in Figure 4-15.

Figure 4-14. Forest plot for meta-analysis of change in MCV

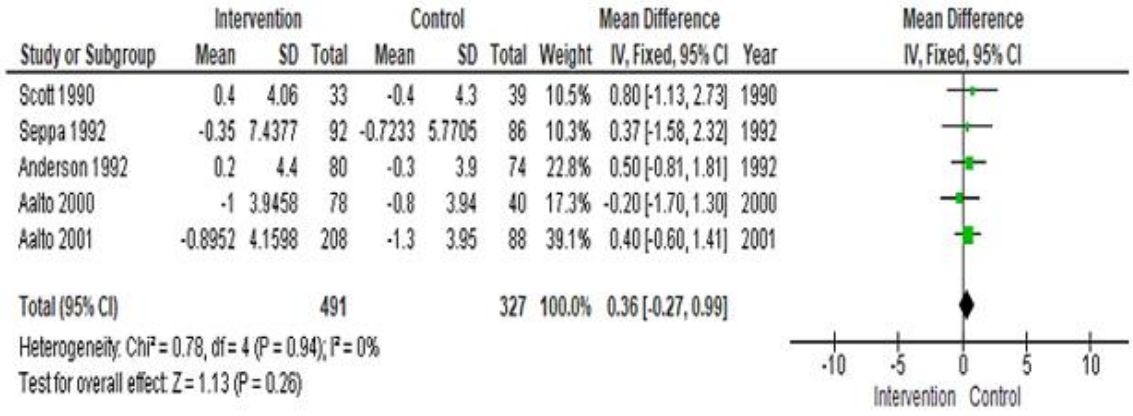
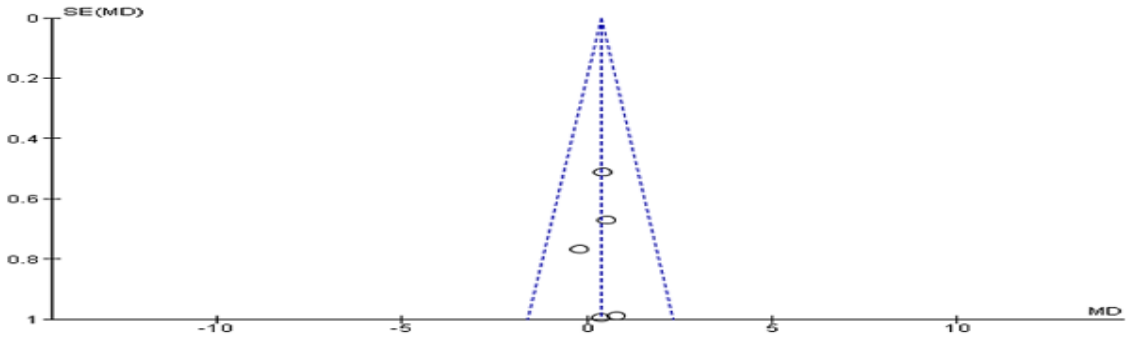
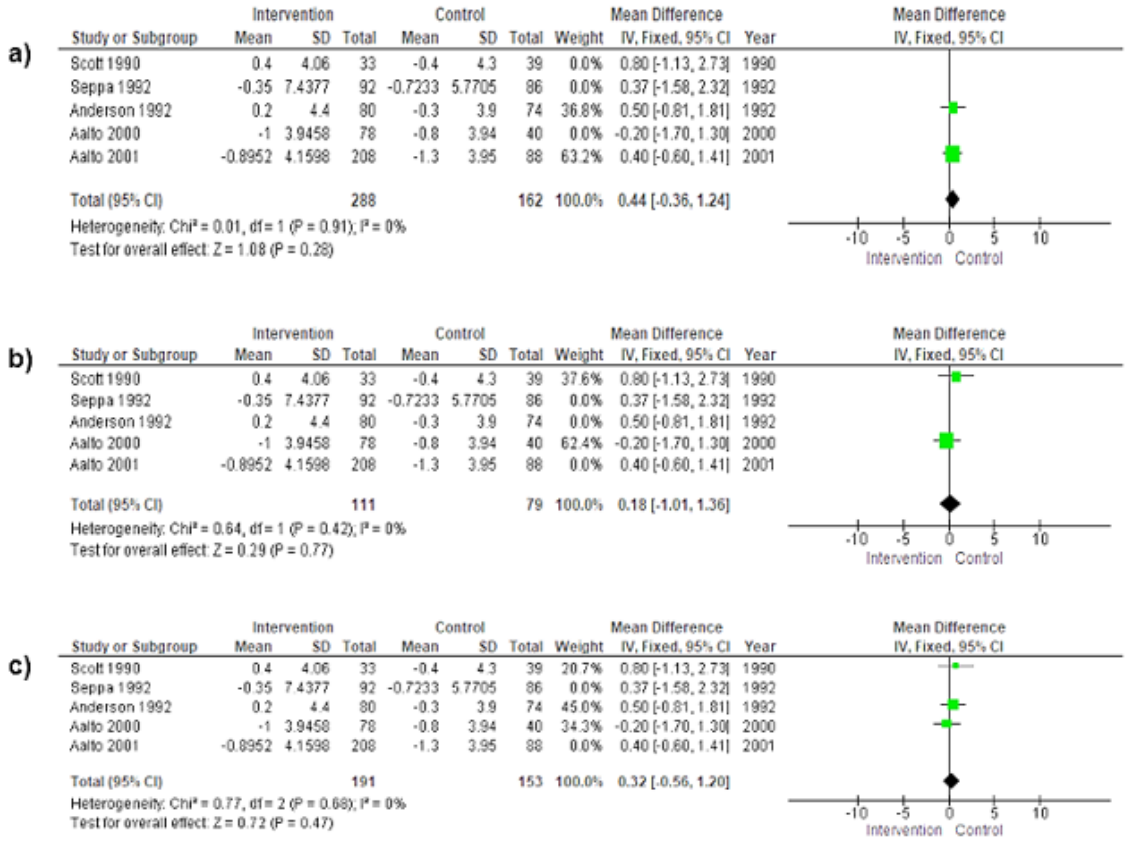


Figure 4-15. Funnel plot for publication bias



The weighted mean average difference in MCV between intervention and control groups remained non-significant on restricting the analysis to male (0.44, 95% CI -0.36, 1.24, p=02.8), female (0.18, 95% CI -1.01, 1.36, p=0.77), and baseline alcohol intake >250 grams per week (0.32, 95% -0.56, 1.20, p=0.47) subgroups (Figure 4-16). The data was insufficient for baseline alcohol intake <250 grams per week subgroup analysis.

Figure 4-16. Meta-analysis for change in MCV: a) Male only studies, b) female only studies, d) Alcohol intake > 250 grams per week



4.3.3.5 Mortality

In the study, Kristenson et al. (2002) conducted follow-up at 13 years (median) and reported 37% of deaths in the intervention group and 48% of deaths in the control group were alcohol-related (165). The authors reported a statistically significant difference in alcohol-related survival curves (risk ratio 1.9, 95% CI 1.0 – 3.8).

The study by Tomson et al.(1998) reported two deaths in the control group over two years but none in the intervention group, the cause of death was not specified (179). Whereas the study by Gentilello et al.(1999) reported no significant difference in death rates (Intervention group 2.7%, Control group 2.3%) at 12 months (174).

4.3.3.6 Sickness absence

At four year follow-up, Kristenson et al.(1985, 1983) reported the number of sickness days in the control group significantly rose from a mean of 24.7 days per year to 51.9

days per year, (p <0.05) (137, 164). The change in the intervention group was minimal and non-significant (p>0.05).

In Persson and Magnusson. (1989) study, the intervention group demonstrated significant (p<0.05) reduced total sickness absence, change was more marked in female participants (176). The study by Tomson et al.(1998) reported no significant change in sickness absence in the whole study cohort (179). In both above studies, the control group received no advice.

4.3.3.7 Engagement with secondary care liver services

In a prospective observational study conducted in community alcohol services, Matthews et al. (2019) recruited individuals who self-identified as harmful drinkers (180). Individuals who consented to participate were invited to attend an appointment to have liver stiffness measured by transient elastography (Fibroscan). Participants with liver stiffness measure (LSM) of >7.1 kilopascals (kPa) were referred to a nurse lead clinic for further assessment based on which a secondary care referral was made. The authors showed high patient engagement with secondary care liver services in those going through the pathway, however, this study lacked a control condition or comparison group.

4.3.3.8 Other outcomes

On average, control group participants spent more days in the hospital (ratio 2.2) and had more physician visits. In contrast, overall, the intervention group reduced the total number of physician visits, had a 47% reduction in new injuries, and a smaller number of traffic violations and police arrests (137, 174-176) (Table 4-2).

4.3.4 Sensitivity analysis

4.3.4.1 Control conditions

Separate analyses by control group type (intervention versus no advice; intervention versus brief advice; intervention vs brief advice at request is provided in Table 4-3.

Table 4-3. Sensitivity analysis

Analysis	Mean Difference	95% CI	I^2	P
Change in self-reported alcohol intake (gram/week)[a]				
IBA vs No advice	-254.37	-705.49, 196.74	0.89	0.27
IBA vs BI	-54.18	-120.21, 11.85	0.89	0.11
IBA vs BI at request	-77.71	-185.41, 29.98	0.99	0.16
IBA vs No advice or BI at request	-103.02	-195.04, -11.0	0.99	0.03*
Change in gamma-glutamyl transferase (GGT) (IU/Litre)[a]				
IBA vs No advice	-37.41	-71.16,-3.67	0.95	0.03*
IBA vs BI	-22.21	-36.54, -7.89	58	0.02*
IBA vs BI at request	5.35	-2.87, 61.0	0	0.2
IBA vs No advice or BI at request	-19.92	-43.89, 4.04	0.95	0.1
Change in Mean Corpuscular Volume MCV (femtoliters/cell)[a]				
IBA BI at request	0.59	-0.49, 1.68	0	0.28
IBA vs BI	0.24	-0.52, 1.01	0	0.53

IBA-intervention based advice, BI-Brief advice

[a]Random effect Meta-analysis

[b]Fixed effects Meta-analysis, data was insufficient to compare IBA to no advice

*Statistically significant ($p<0.05$)

The weighted mean average difference in weekly self-reported alcohol intake for intervention versus no advice was -254.4 grams per week; for intervention versus brief advice -54.2 grams per week, and intervention vs brief advice at the request was -77.7 grams per week respectively, the change was non-significant (p=0.27, p=0.11, p=0.16). However, the difference was statistically significant when comparing intervention to combined groupings of no advice and BI at request, with a weighted mean average difference in weekly self-reported alcohol intake of -103 grams per week (95% CI -195.04, -11.0, p=0.03).

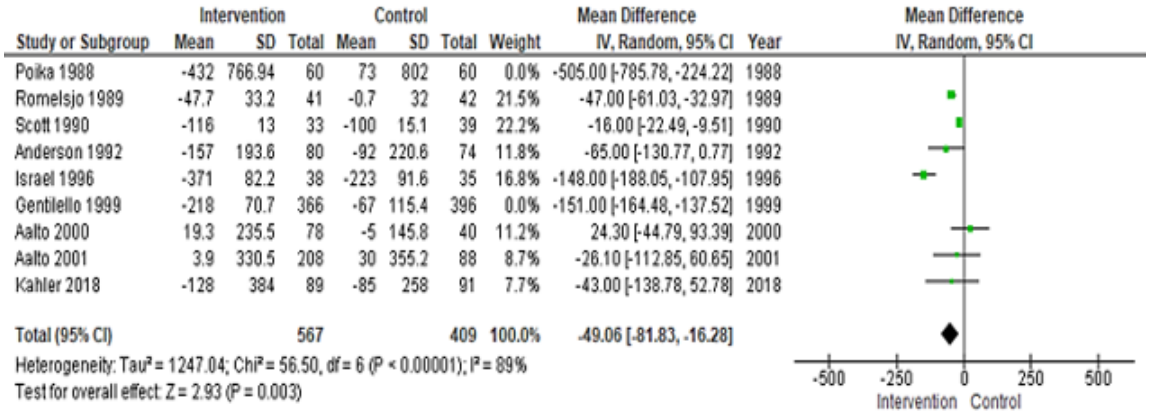
In the case of GGT, the change was significant both for comparing intervention to no-advice, with weighted mean average difference -37.41 IU/Litre (95% CI -71.2, -3.7, p=0.03) and intervention versus BI, the weighted mean average difference -36.54 IU/Litre (95%CI -36.6, -7.9, p=0.002).

For MCV data was insufficient to compare the intervention to no advice and change was non-significant on comparing intervention to BI or BI at request (p=02.8, p=0.53).

4.3.4.2 Study settings

On restricting the analysis to studies done in the community setting, comprising nine studies and n=976 participants, the weighted mean average difference of weekly alcohol intake between the intervention and control (Brief and/or no advice) groups was -49.06 grams per week (95%CI –81.83 to -16.28). The results remained significant (p=0.003) and favoured the positive effect of intervention-based advice including feedback on laboratory tests or markers of fibrosis to reduce alcohol intake in community settings (Figure 4-17).

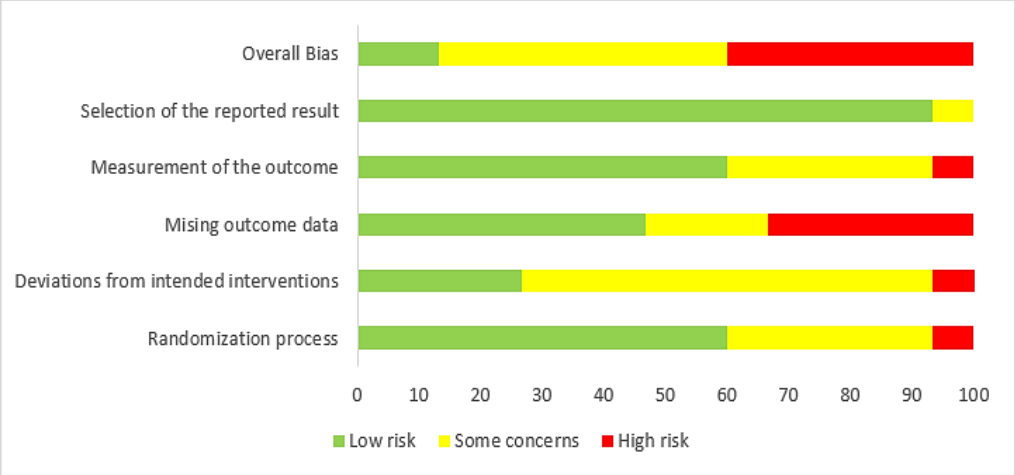
Figure 4-17. Meta-analysis for change in self-reported alcohol intake (grams per week) for studies done in community settings

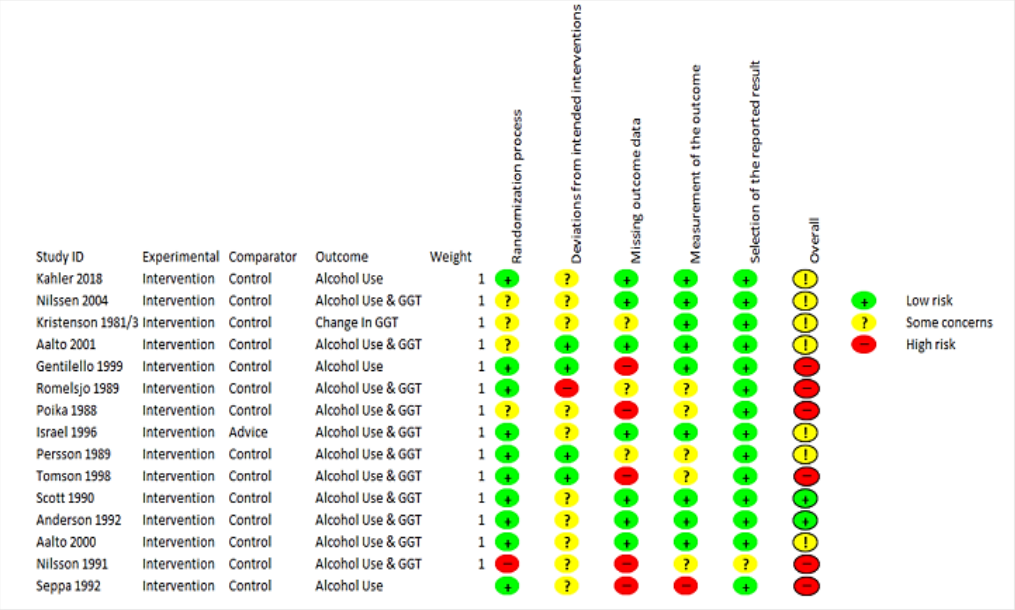


4.3.5 Risk of Bias Assessment(ROB)

The risk of bias assessment (ROB) for the RCTs is given in (Figure 4-18). Most authors described the method used for randomisation, apart from Nilssen et al. (1991) (166). Due to the nature of the studies, blinding was not possible. The main area for high concern was missing outcome data; few studies reported high rates of missing data but failed to satisfactorily describe how the missing data was handled. The study by Sheron et al.(2013) had a moderate risk of bias as GPs were advised to refer patients with moderate to high-risk drinking behaviour which might have introduced selection bias and in turn confounded AUDIT score outcomes (88). The study by Matthews et al.(2019) study had a low risk of bias (180).

Figure 4-18. Risk of bias and quality assessment for randomised control trials.





4.4 Discussion

4.4.1 Summary of key findings

The systematic review of the literature demonstrated a significant beneficial effect on alcohol consumption with a 36% decrease in self-reported alcohol consumption in the group that received advice based on non-invasive tests (NITs) of liver disease compared to 7% with standard care (control). This substantial effect was mirrored by a similar fall in GGT in the intervention group compared to the control (Figure 4-8). Although the number of studies reporting these outcomes was smaller, non-invasive test based advice was more effective in reducing alcohol-attributed sickness absence, the number of days spent in the hospital, the number of physician visits and long-term mortality, compared to routine care or non-intervention-based advice. Reducing alcohol consumption reduces liver injury and is well known to improve the outcome of physical health problems such as liver disease which result from it.

The sensitivity analysis for non-invasive tests based advice against no advice and brief advice showed a non-significant change in self-reported alcohol but a significant change in GGT (Table 4-3). However, when control conditions were pooled a significant interaction effect was observed. This is likely due to small sample sizes for each type of control condition and methodological nuances such as cross-contamination. The interaction effect remained significant irrespective of baseline alcohol intake. As no group received biofeedback without brief advice, I attempted to investigate this by looking at biofeedback plus brief advice versus a range of alternatives. I found that the biofeedback plus brief advice only had an alcohol consumption change mean difference of -78 grams per week (p=0.16) suggesting that biofeedback does have a role to play (although I note the lack of statistical significance and a small number of studies n=3).

4.4.2 Strengths and limitations

This is the first systematic review to evaluate the effectiveness of advice based non-invasive tests (NITs) for liver disease (NITs based advice) on alcohol intake in high-risk drinkers. As no group received biofeedback without brief advice, I conducted a sensitivity analysis to confirm the finding. The sensitivity analysis did confirm that NITs base advice in addition to routine care doses helps to change high-risk drinking behaviour. The age, gender, and ethnic distribution match the UK population with alcohol use disorder. This makes the finding very relevant and generalisable to primary care in the UK.

Included RCTs had some methodological uncertainties. In Israel et al.(1996) and Tomson et al.(1998) studies, participants in the control group received brief initial feedback on GGT levels which might have caused cross-contamination among groups (175, 179). This should, however, be a bias away from NITs based advice being beneficial. The studies used varying behaviour interventions like motivational interventions and counselling sessions. Most trials in this review used GGT and MCV values as a marker of alcohol misuse and to assess the effectiveness of the intervention. However, both of these markers have very low sensitivity and specificity as diagnostic tools for alcohol abuse (182), perhaps explaining the small changes. Their utility is hampered by the variability of results among different age groups, sex, and ethnicity, and by the potential of false-positive results due to other conditions like diabetes, smoking, obesity, vitamin B12 or folate deficiency and haematological diseases (182, 183). In this context, the potential impact of such biomarkers in the diagnosis of liver injury due to alcohol is limited, although the size of the impact seen on markers and alcohol intake in this review is impressive. Most studies in this review only reported short term outcomes and therefore there is uncertainty over the validity of the longer-term change. Only two studies reported outcomes beyond five years (165, 167). This lack of long term outcomes is not however limited to the impact of intervention based advice; previous systematic reviews on alcohol brief advice faced similar deficiencies related to the long term effect of alcohol interventions (184).

Limitations to the review are noted. First, there was significant heterogeneity between the trials in self-reported alcohol intake and laboratory tests (GGT) which has been reflected in our meta-analysis. A random effect analysis was used assuming the estimated reduction in alcohol consumption of 74.4 grams per week is averaged across populations and settings, providing support for the observed reduction. The lack of adequate concealment might have caused an overestimation of the treatment effect (185), though it would not always have been possible to blind participants or the person providing advice due to the nature of interventions. Another potential source of bias was a loss to follow up or drop out. However, most trials (Table 4-2) adopted an intention to treat analysis which likely overcomes this bias. The studies which lacked this method might have introduced reporting bias but the overall estimated reduction in alcohol consumption is substantial. Further, the accuracy of self-reported alcohol intake might be questionable; it decreases as consumption of alcohol increases, which might have caused self-report biases in the outcomes (29, 30). The review may not generalise to non-Caucasian populations as all the studies were done in white predominant countries with minimal information on ethnic

distribution and the search strategy was restricted to the English language. Finally, despite the inclusion of sex-specific analyses, female patients were underrepresented in the data. Future research should focus on the greater inclusivity of diverse populations.

4.4.3 Other evidence

The findings are consistent with those in respiratory medicine, which showed that by providing smokers with the results of their doppler ultrasound demonstrating atherosclerotic plaques, or results of spirometry improved smoking cessation (81, 82). Similarly, including the results of point-of-care diabetes tests in patient feedback has been associated with improvement in compliance treatment and glycemic control (84, 85). The evidence in past has demonstrated strong support for use of personalised feedback to prompt reductions in alcohol use and alcohol-related problems (186, 187). Personalised feedback involves the provision of objective data regarding alcohol misuse, risk of alcohol-related problems, and comparisons to normative drinking patterns. Motivation to change behaviour may depend on the perceived likelihood of a negative health outcome occurring and a belief that behaviour change can reduce their risk of harm (188). Providing personalised biomarker feedback could increase risk awareness and therefore the likeliness that an individual will change their behaviour. The change in alcohol consumption is backed up by previous evidence that providing personalised healthcare communications has been shown to enhance the motivation to overcome addictive behaviour (86, 87). For hazardous and harmful alcohol users, providing feedback based on a simple liver fibrosis test prompts a reduction in alcohol consumption for both with and without evidence of liver damage (88).

The concerns of NITs based advice potentially providing false reassurance to some participants leading to unintended negative consequences such as exacerbating pre-existing addictive behaviours are of clinical relevance. The literature to answer this specific question is scarce. . The studies have reported adding biofeedback based on fibroscan results increased patient uptake to a specialist clinic but lacked information on any harmful impact when the fibroscan result was negative (180, 189). The study of Sheron et al. (2013) using STLT for biofeedback when assessing liver fibrosis demonstrated a significant reduction of AUDIT score across all risk groups, the reduction being greater among intermediate and high-risk groups. In the test negative group (green) 3.3% reported an increase in the AUDIT category compared to 2.0% in intermediate and high-risk groups (amber and red), the difference was statistically

non-significant (p=0.498) (88). In Nottingham, within the SCARRED Liver Project, researchers found that only participants with normal liver stiffness (TE readings <8 kPa) significantly reduced their consumption (190). Overall, these studies are reassuring regarding the use of biofeedback amongst people who consume alcohol excessively.

Overall, 80% of participants in RCTs were male. A sex based analysis for self-reported alcohol intake did reveal a reduction in alcohol for the intervention group in both sexes as compared to controls, but the difference did not reach statistical significance. This might be because of a lack of statistical power due to the limited number of studies that included single gender and studies that included both genders were excluded from sex based analysis. The sex and ethnic distribution, however, reflect the population trends observed across Europe and high-income countries (191, 192).

4.4.4 Implications

Early diagnosis of liver fibrosis provides an opportunity to intervene and reduce or stop alcohol intake. This is known to be the most effective way of preventing liver disease progression (21). There is also the potential that earlier engagement of individuals with significant liver disease in secondary care services, which was demonstrated here, allows the implementation of NICE approved interventions, such as endoscopy for varices, potentially improving outcomes.

The results are relevant and applicable to the high-risk drinking population of the UK and Europe, with a well-matched age range and ethnicity distribution (191, 193). The studies were undertaken in routine clinical settings which makes its application suitable in day-to-day primary medical practice, although there is minimal data on the use of such advice in emergency settings.

The review provided conceptual ground for my future feasibility trial “KLIFAD”. The trial is specifically designed to assess the feasibility and extent of efficacy of NITs based advice on top of routine care.

4.5 Conclusion

This systematic review strongly suggests that NITs based advice is effective in reducing harmful alcohol intake. However, future work should explore the relative effect of different components of an intervention and types of brief advice, which patient or delivery related factors are needed to successfully implement the

interventions, and finally to develop interventions that are appropriate across diverse ethnic populations, sexes, and clinical settings.

Chapter 5. Characteristics of alcohol recovery narratives: a systematic review and narrative synthesis

5.1 Rationale and Overview

Recovery narratives can be defined as personal stories of health problems and of recovery (89), which can be shared with others (90), and which can provide recipients with insights into the phenomenology of recovery (91). In this regard, the Social Identity Model of Recovery (SIMOR) identifies alcohol recovery as "a process of social identity transitioning, wherein an individual becomes a member of a recovery-orientated group, and in doing so internalizes the values and beliefs of the group which, in turn, leads to a new sense of self (or recovery identity) that strongly guides their attitudes and behaviours" (page 113) (194, 195). The act of sharing alcohol narratives has been an important component of the Alcoholics Anonymous (AA) 12-step programme (94). In part, the sharing of narratives is important because this method provides the context of personal recovery from addiction, opening opportunity for recognizing and working on behaviours in a group setting.

Narrative approaches have been applied in health research (196-198), where they "allow for the intimate and in-depth study of the individual's experiences over time and in context" (199). For example, recovery in people with stroke was facilitated by identity transformation using a metaphor of change in physical functioning and self-identity (200). In another study sharing cancer stories and narratives of illness helped cancer patients to make choices and enabled a sense of belonging to the group (201). Moreover, recovery narratives have been used to promote and encourage engagement with health services (95), where they might be used to extend clinical practice. In particular, narratives are a resource for people who are finding recovery challenging (96). Alcohol misuse recovery narratives have been studied by researchers to understand different processes of change (202), how people can recover in both the presence or absence of treatment (194) and how people differ on individual factors (e.g., age, gender, ethnicity) in the recovery process (203).

Amongst the body of literature on narrative typologies available for use, a recent systematic review synthesised evidence on the characteristics of mental health recovery narratives and generated a framework to describe how these narratives have been conceptualised by the research community (92). The framework identified nine dimensions: genre, positioning, emotional tone, relationship with recovery, trajectory, use of turning points, narrative sequence, protagonists, and use of metaphor. Dimensions such as genre, relationship with recovery, turning points, and

trajectory can apply to narratives of recovery from a range of other health conditions including alcohol misuse.

As part of the KLIFAD trial, I planned to record alcohol recovery video stories (ARVS) describing lived experiences of people's recovery from AUD and receiving transient elastography. The ARVS were used as part of KLIFAD. Whilst recovery from alcohol misuse is possible, and researchers have demonstrated successful models and real-world outcomes over the years, little remains known at the individual level regarding the characteristics of recovery narratives and their related dimensions (195, 204, 205). In view of poor knowledge of the narrative methods in their application to alcohol use disorder, in this chapter, I aim to develop a conceptual framework describing the characteristics of alcohol recovery narratives that have been reported in the research literature.

5.2 Methods

5.2.1 Checklist and protocol registration

This systematic review and narrative synthesis were conducted following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidance (206). The protocol was prospectively registered with the Prospective Register of Systematic Reviews (PROSPERO). Protocol registration number: CRD42021235176

The systematic review was conducted as part of the KLIFAD (Does knowledge of liver fibrosis affect high-risk drinking behaviour?) study (NIHR201146) (156).

A mapping/scoping search was conducted in order to identify relevant evidence that offers a discussion about alcohol narratives and to inform the research question for a systematic review proposing a framework characterising alcohol recovery narratives. The finding from the systematic review supplemented the drafting of a guide for recording alcohol recovery video stories (207).

5.2.2 Review question

Based on the results from the initial mapping search following review question was formulated: "How have alcohol recovery narratives been characterized in the research literature?"

The alcohol recovery narratives were defined as "first-person lived experience accounts, which include elements of adversity, struggle, strength, success, and survival related to alcohol misuse, and refer to events or actions over a period of time".

This is a modified definition of mental health recovery narratives in the study by Llewellyn-Beardsley et al. (2019).

5.2.3 Literature search

5.2.3.1 Search strategy

The search strategy was refined based on the results of the initial mapping search and primary review questions. The final search strategy was designed in consultation with a librarian with expertise in literature search for a systematic review. Due to the multidisciplinary nature of the review question, a combination of databases from health and social sciences were searched.

Electronic database searches were conducted using Ovid Medline, Embase, CINHAL, PsychInfo, and AMED. A grey literature search was conducted using ProQuest, SCOPUS, and ClinicalTrials.gov. To identify relevant articles the included databases were searched from inception to March 2021. A backwards citation search was conducted by examining the reference list in each included publication.

5.2.3.2 Search terms

Different combinations of Boolean operators, parenthesis, field codes and truncation were applied using the following search terms: exp Alcoholism/, or exp Alcoholics/, or exp Liver Diseases/, exp Alcoholic/, or exp Alcohol Abstinence/, or exp Alcohol Drinking in College/, or exp Alcohol Drinking/, or exp Alcohol-Related Disorders/, or exp Binge Drinking/, or exp Alcoholic Intoxication/, or ("alcohol misuse" or "Alcohol misuse" or "alcohol abuse" or "alcohol dependence").mp, or ("Alcohol use disorder" or "abstinence" or "alcohol abstinence" or "cessation" or "alcohol cessation" or "reduce drinking"), and, ("Recovery Story" or "lived experience" or "recovery narratives" or "alcohol recovery story" or "alcohol recovery" or "alcohol recovery narrative").ti,ab, Or (Recover* or transform* or resilien* or surviv* or thriv* or endur* or rebuild* or hope* or conquer* or reclaim*).ti,ab, Or Personal Narratives/or Narration/or Narrative therapy/ or (narrat* or story or stories or storytelling or telling or tale* or restory* or counter-narrative* or disnarrat* or memoir* or testimon* or biograph* or autobiograph* or auto-biograph* or autoethnograph* or auto-ethnograph* or photovoice).ti,ab.or (typol* or classif* or genre* or theme* or structur* or categor* or framework* or dimension* or format*)

A sample search from Ovid Medline is provided in Appendix 4, which was specialised in each database.

5.2.4 Study selection

The eligibility criteria were based on the following three components of the primary review question

- Participants: People who can account for their first hand lived experience of alcohol recovery.
- Phenomena of interest: Alcohol recovery narratives
- The outcome of interest: Characteristics, structure, or framework describing alcohol recovery narratives

5.2.4.1 Inclusion criteria

- The studies included participants of any sex who had a self-reported history of alcohol misuse or alcohol-related disorders, a physician diagnosis of alcohol misuse, or where available a diagnosis defines by AUDIT score, ICD 10, or DSM 5 Criteria. The diagnostic criteria were kept broad to minimise the risk of missing relevant studies.
- The study advances an original framework of typologies and/or themes of alcohol misuse recovery narratives.
- The framework is produced through an analysis of empirical evidence. The empirical evidence is based on a verified observation or experimentation, rather than on logic or theory. In empirical evidence, information is received by utilizing the senses, this includes observing patterns and behaviours of interest, that are experienced in the real world.

5.2.4.2 Exclusion criteria

- The study is about narratives, but it is not possible to identify from the title or abstract, whether they are alcohol misuse recovery narratives.
- The study is about narratives where the narrator does not have personal experience of alcohol misuse for example the narratives are of family members of people who have misused alcohol. This was because the review focused to characterise the personal alcohol recovery stories rather than witnessed accounts, secondary source information, or third person account.

5.2.5 Study screening

Two reviewers (the author MS and UT) independently screened titles and abstracts for eligibility. A candidate list of included studies was crosschecked by both reviewers, along with a randomly selected 10% of excluded studies. Any conflicts in study

inclusion were resolved through discussion with three further reviewers (SRE, KJ and JLB). Rayyan-QRCI systematic review software, Endnote (Version-X9) and Microsoft Excel were used to screen articles, remove duplicate entries, and record reviewers' decisions.

5.2.6 Data abstraction

A modified data abstraction table (DAT) was designed using Llewellyn-Beardsley et al. (2019) as an example (Appendix 6) (92).

The DAT included information about the lead author, academic discipline, country of study, participant demographics (age, gender, country), study design, how alcohol recovery stories were named and defined by the authors, key characteristics of the study and alcohol recovery narrative 'types' (as identified by study authors) was extracted. Microsoft Excel (2019) and Nvivo (version 12) were used for data abstraction, preliminary synthesis, and data synthesis.

5.2.7 Risk of bias and quality assessment

Quality assessment of qualitative evidence synthesis has been a matter of debate for many decades (208). Cochrane Qualitative and Implementation Methods Group recommendations are to use a tool that takes the multi-dimensional concept of qualitative evidence into account (208).

Keeping this in view, the quality of included studies and risk of bias was assessed using the Critical Appraisals Skills Programme (CASP) tool for qualitative research (209). The CASP tool focuses on three domains, study design, results validity, and generalisability. Each domain has a set of questions. Based on the response to these questions the studies were marked as low, medium, or high quality. The studies which provided satisfactory information in all domains were marked as high quality, with missing or unsatisfactory information in one domain as medium quality, and with missing or unsatisfactory information in two or more domains as low quality.

5.2.8 Data synthesis

Analysis was taken on all studies for the intended primary outcome of developing a conceptual framework of over arching narrative typologies (structures) and themes (content) characterizing alcohol recovery narratives.

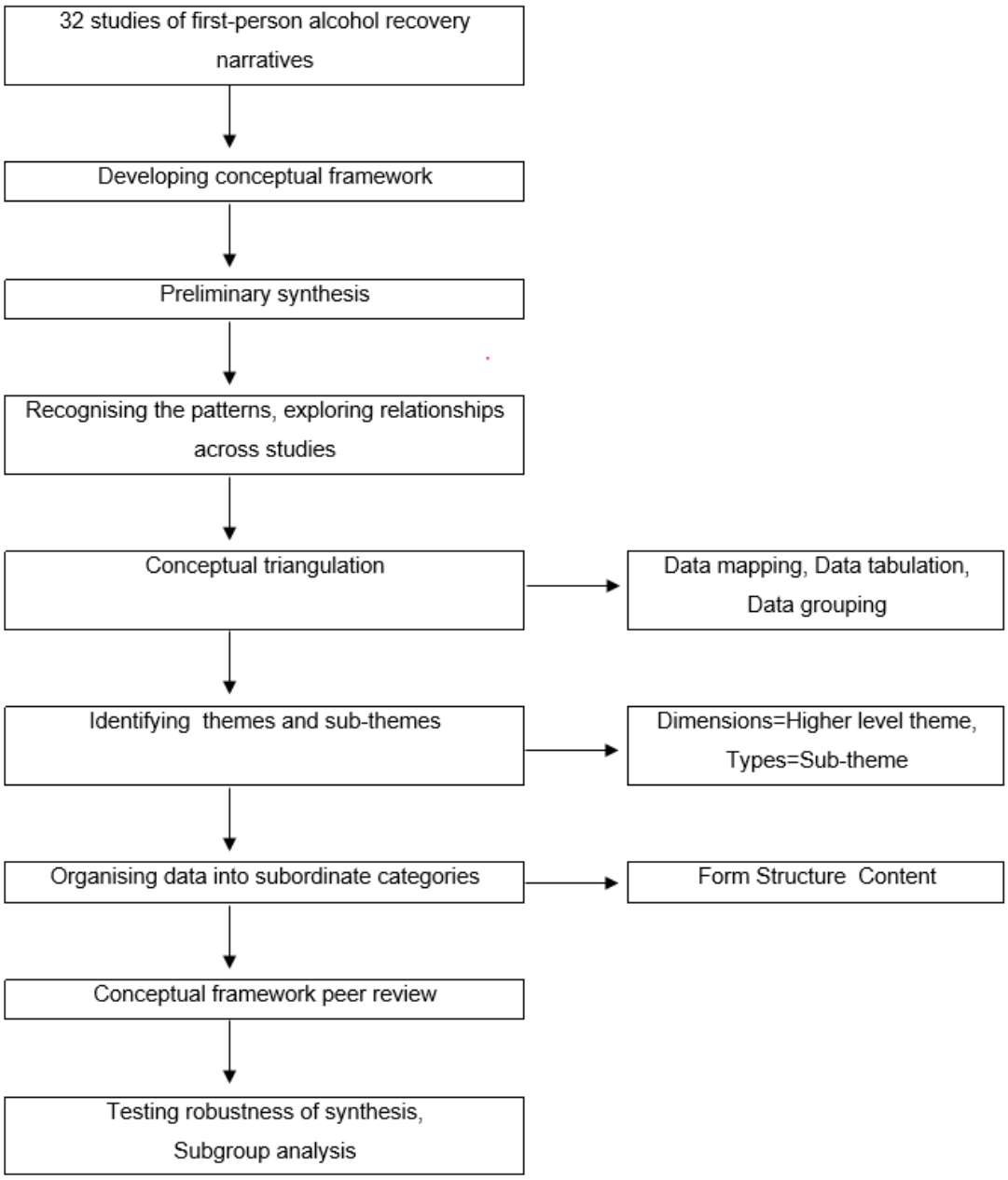
The following three-stage narrative synthesis approach was adopted, modified from Popay (2006) (92, 207).

- An initial conceptual framework presenting a preliminary synthesis of findings from included studies was formed.
- The conceptual framework was reviewed by the rest of the review team, and relationships between entities in the framework were explored
- The robustness of the synthesis was assessed by conducting selected subgroup analyses

Figure 5-1 describes the steps for data synthesis.

1. Data abstracted into themes
2. Themes organised into sub-themes
3. Sub-themes are explainable through subordinate categories.
4. Categories have form, structure, and content
5. The conceptual framework organises steps 1-4
6. Test the robustness of the framework via sub-group analysis.

Figure 5-1. Data synthesis flow chart



5.2.8.1 Conceptual framework

A preliminary synthesis of results from individual studies was conducted to recognise patterns in findings and to explore relationships across the studies. The variability among the included studies' characteristics, findings, and outcomes was also explored. The conceptual triangulation approach was adopted to identify key concepts relevant to the review question and create the preliminary framework (210, 211).

In producing the initial conceptual framework, concepts from included studies were organised into themes and sub-themes. Sufficiently similar concepts were merged. Abstracted higher-level themes were organised into a three-level framework of - form, structure, and content - informed by narrative theory (212). The framework was further categorised as dimensions and sub-theme types. The dimension and types were tabulated and a narrative synthesis of each of them was provided.

5.2.8.2 Peer review of conceptual framework

The initial conceptual framework was reviewed by the rest of the review team. The subordinate categories and the relationship between themes and subthemes were discussed. The reflexive thoughts were

- How to best describe harmful drinking that has the least stigma associated
- How to maintain the clarity of synthesis by preserving the original author's language
- How to best present the LGBTQ+ community
- To adopt gender neutral language and use the term sex instead of gender.

5.2.9 Subgroup analyses

The subgroups were assimilated through an inductive thematic analysis of the content of included studies, which engaged social, cultural, and demographic aspects. Where available the extracted data were analysed for the following subgroups narrator's age, gender, sexuality, ethnicity, and mental health.

5.2.10 Original author language

Where possible the language used by the original authors was preserved while maintaining the clarity of synthesis of dimensions and characteristics of alcohol recovery narratives. Where the terms "alcoholic" or "alcoholism" were used by the original authors to describe alcohol misuse, these have been retained.

The review group acknowledges heterogeneity in the language used to describe alcohol use and the stigma associated with some of these terms, which itself can act as a barrier to change (213). After thoughtful discussion between the review group, we opted for the term 'alcohol misuse' to describe excess alcohol intake, harmful alcohol intake, drinking problems, alcohol dependence, and alcohol use disorder.

5.3 Results

A total of 11,332 records were initially identified. After applying the eligibility criteria 32 documents were included in the final narrative synthesis (Figure 5-2). Most studies described in these documents were conducted in the United States (46.9% *n*=15), followed by Europe (34.4%, *n*=11). No included studies were from low-income countries. Of the included studies (*n*=32), 29 used qualitative and 3 mixed methods. The characteristics of included studies are given in Table 5-1.

Figure 5-2. Prisma flow diagram for studies selection

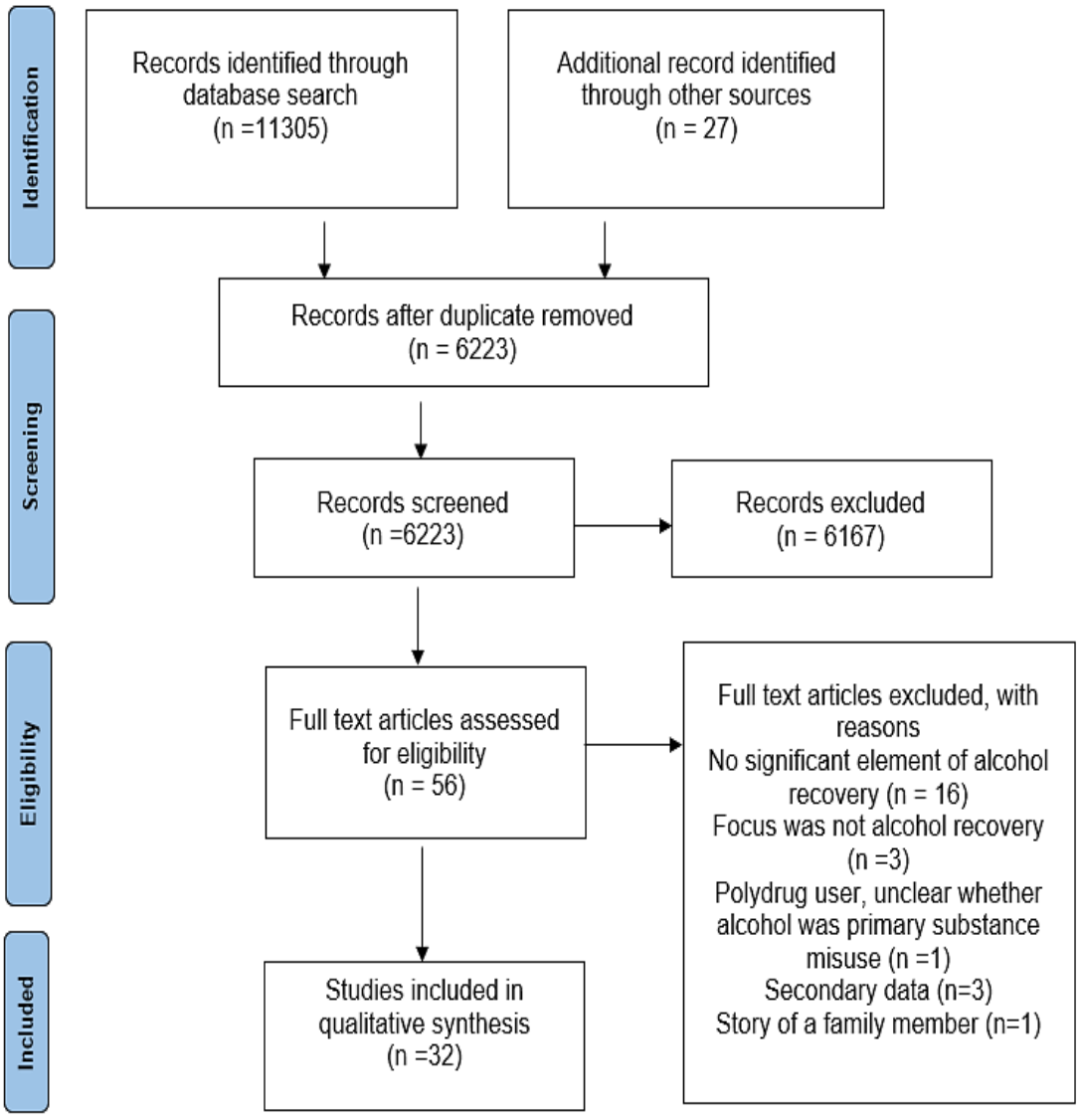


Table 5-1. Characteristics of included studies and participants

Lead Author			Methods		Participants			
Study ID	**Academic discipline**	**Country**	**Setting of recovery**	**Study design, Data collection**	**Sample size** (Male)	**Age** (years)[e]	**Ethnicity**	**Length of sobriety** (years)
Best et al. (2016) (195)	Social and health research	UK, USA	Glasgow addiction services	Quantitative, Structured interview	205 (M=137)	42	-	1-3 (n=121) 3-5 (n=26) >5 (n=58)
Burman, 1997 (214)	Social Work	USA	Natural recovery[a]	Qualitative, Semi-structured interview	38 (M=24)	22-73	White=34 Black=3 Other=1	1-26
Cain, 1991 (215)	Anthropology	USA	Alcoholics Anonymous (AA)	Qualitative, Unstructured interview	3 (M=2)	-	-	2-14 Relapsed=1
Christensen and Elmeland, 2015 (216)	Psychology	Denmark	AA (11), Natural recovery (NR) (31)	Qualitative, Semi-structured interview	42 (M=26)	45	-	2-10(AA) 2-24(NR)
Dalgarno, 2018 (217)	Philosophy	Australia	Natural recovery, AA	Qualitative, Autobiographies	7	NA	Aboriginal	-
Dunlop and Tracy, 2013 (218)	Psychology	Canada	AA	Qualitative, Structured interview and questionnaire	132 (M=58)	54, 38	White=99	0.3-4
Dunlop and Tracy, 2013 (219)	Psychology	Canada	AA	Qualitative, Autobiographies	46 (M=23)	22-82	White =34 Indigenous=6 Other=6	0.3-39
Garland et al., 2012 (220)	Social Work	USA	Mindfulness-Oriented Recovery Enhancement	Qualitative, Semi-structured interview	18 (M=14)	40	White =7 Black=11	-
Gubi and Marsden-Hughes, 2013 (221)	Counselling	UK	AA	Qualitative, Semi-structured interview	8 (M=4)	51-84	White =8	17-48

Lead Author			Methods		Participants			
Study ID	**Academic discipline**	**Country**	**Setting of recovery**	**Study design, Data collection**	**Sample size** (Male)	**Age** (years)[e]	**Ethnicity**	**Length of sobriety** (years)
Haarni and Hautamäki, 2010 (222)	Sociology	Finland	No specific treatment setting[b]	Qualitative, Semi-structured interview	31 (M=15)	60-75	-	Current and ex-consumer
Hanninen and Koski-Jannes, 1999 (223)	Social Psychology	Finland	Natural recovery, Therapeutic and self-help groups, AA, Psychiatrist consultation	Qualitative, Story writing by participants in 3rd person	51 (M=22)	-	-	-
Inman and Kornegay, 2004 (224)	Social Work	USA	Psychology clinics, medical rehabilitation groups, AA, Self-motivation	Qualitative, Semi-structured interview	5 (M=5)	52-75	-	6-25(n=3) still drinking (n=1) Controlled drinking (n=1)
Jones, 2013 (225)	Sports Psychology	UK	Community alcohol services, AA, Sporting chance clinic	Qualitative, Open-ended interview	1 (M=1)	30's	White	Sober
Laitman and Lederman, 2008 (226)	Substance abuse	USA	Rutgers college recovery support program	Qualitative, Un-specified	1 (M=0)	19	-	Sober
Laville, 2006 (227)	Community research	UK	Psychiatric unit, AKABA[c]	Qualitative, Self-narrative	1 (M=1)	45	Black	Sober
Lederman and Menegatos, 2011 (94)	Social sciences	USA	AA	Qualitative, Open-ended questionnaire	178 (M=86)	19-75	White =171	
Liezille Jacobs*, 2015 (228)	Public Health	South Africa	AA	Qualitative, Narrative interview	10 (M=0)	30-62	-	>0.6
Mellor et al., 2021 (194)	Substance Misuse	Australia	Natural recovery	Qualitative, Semi-structured interview	12 (M=5)	30-70	-	No alcohol in 12 months (n=6)

Lead Author			Methods		Participants			
Study ID	**Academic discipline**	**Country**	**Setting of recovery**	**Study design, Data collection**	**Sample size** (Male)	**Age** (years)[e]	**Ethnicity**	**Length of sobriety** (years)
Mohatt et al., 2008 (229)	Psychology	USA	Natural recovery (38%), AA (33%), Combination of AA and other treatment programmes (29%)	Qualitative, Semi-structured interview	57 (M=26)	26-72	Alaskan Native	>5
Newton, 2007 (230)	Adult liver transplant	USA	Liver transplant services	Mixed Methods, Unstructured interview	76[f] (M=39)	-	-	Relapsed=4
Opačić, 2019 (231)	Social Work	Croatia	Alcohol treatment services (*n*=6), Natural recovery (*n*=3)	Qualitative, Unstructured interview	9 (M=7)	46-73	-	2-15
Paris and Bradley, 2001 (232)	Psychology of recovery	USA	Natural recovery (2), AA (1)	Qualitative, Unstructured interview	3 (M=0)	21-52	-	6-26
Punzi and Tidefors, 2014 (233)	Psychology	Sweden	Alcohol residential care unit	Qualitative, Semi-structured interview	5 (M=4)	50-60	-	0.8-several
Robbins, 2015 (234)	Nursing	USA	Alcohol treatment services	Mixed methods, Semi-structured interview	21 (M=0)	37-67	White =15 Hispanic=6	2
Rowan and Butler, 2014 (235)	Social Work	USA	Natural recovery, AA, Alanon, ACOA[d]	Qualitative, Semi-structured interview	20 (M=0)	50-70	White =19 B=1	1-32
Sawer et al., 2020 (236)	Psychology	UK	AA	Qualitative, Semi-structured interview	8 (M=5)	27-74	-	1.9-35
Stott and Priest, 2018 (93)	Clinical Psychology	UK	Substance misuse services, Specialist mental health services	Qualitative, Unstructured interview	10 (M=6)	30-69	White =9 Black=1	Abstinent(n=7), active (n=3)
Strobbe and Kurtz, 2012(237)	Psychiatry	USA	AA	Qualitative, Stories from AA "big book"	24 (M=14)	17-75	-	Sober

Lead Author			Methods				Participants	
Study ID	**Academic discipline**	**Country**	**Setting of recovery**	**Study design, Data collection**	**Sample size** (Male)	**Age** (years)[e]	**Ethnicity**	**Length of sobriety** (years)
Suprina, 2006 (238)	Psychology	USA	AA	Mixed methods, BASIS-A Questionnaire, and Interview	10 (M=10)	33-63	White =8 Black=1 Latin=1	3-25
Vaughn and Long, 1999 (239)	Education	USA	AA	Qualitative, Semi-structured interview	7 (M=5)	22-32	White =7	5-15
Weegmann and Piwowoz-Hjort, 2009 (240)	Psychology	UK, Sweden	AA	Qualitative, Semi-structured interview	9 (M=4)	40-75	White=9	9-23
Zakrzewski and Hector, 2004 (241)	Psychology	USA	AA	Qualitative, Non-directive interviews	7 (M=7)	32-65	-	1-25

[a]Natural recovery (recovery outside the treatment setting,): The authors specified recovery outside the treatment setting where; i) participant did not have formal alcohol treatment in an institution, organisation or by a person with an objective to relive alcohol problem. Or ii) No participation in substance abuse treatment or self-help groups 2 years prior to achieving abstinence or iii) Fewer than 9 sessions with AA or temperance society (194, 214, 216)
[b]No specific treatment settings: the author did not specify settings
[c]AKABA- Outreach support services for black men with mental health problems and substance misuse, run by Kush Supported Housing and Outreach services (98 Stoke Newington High Street, London, N167NY)
[d]ACOA-Adult children of alcoholics
[e]Age in years is given as a range or mean
[f]Of all participants 18 had a liver transplant for alcohol-related liver disease

5.3.1 Participants

A total of 1055 participants were recruited across all included studies. The age range was 17-82 years, 52.1% (*n*=550) of participants identified as male, 46.4% (n=490) as female and 1.4% as gender unspecified (n=15). Eight studies only included participants of a single gender. Only 16 studies accounting for 563 participants provided ethnicity details, 74.8% (*n*=421) of participants in these studies were white. Participants were recruited from various treatment settings; 12 studies solely recruited participants (41.9%, *n*=442) known to AA, of these participants 49.3% (*n*=218) were male. The length of sobriety of participants ranged from a few months to over three decades. Three studies (93, 222, 224) included both active and abstinent drinkers, in one study (194) half of the participants had consumed alcohol in the past 12 months and two studies (215, 230) included participants who relapsed after a period of sobriety (Table 5-1).

5.3.2 Quality assessment of included studies

Of the 32 studies, seven (21.9%) were rated high quality, 19 (59.4%) medium and six (18.8%) low quality (Table 5-2).

5.3.3 Conceptual framework

Eight dimensions (genre, identity, recovery setting, drinking trajectory, drinking behaviours and traits, stages, spirituality and religion, and recovery experience) were derived and arranged in three superordinate categories: form, structure, and content. Each dimension had several types and subtypes, as specified in Table 5-3.

Table 5-2. Risk of bias and Quality of included studies

Stud ID	Study quality	Was there a clear statement of the aims of the research?	Is a qualitative methodology appropriate?	Was the research design appropriate to address the aims of the research?	Was the recruitment strategy appropriate to the aims of the research?	Was the data collected in a way that addressed the research issue?	Has the relationship between researcher and participants been adequately considered?
Best et al.(2016)	Low	Yes	N/A	Yes	Yes	Yes	No
Burman et al. (1997)	Medium	Yes	Yes	Yes	Yes	Yes	No
Cain et al. (1991)	Low	Yes	Yes	Poorly defined data analysis	Yes	Yes	No
Christensen and Elmeland. (2015)	Medium	Yes	Yes	Yes	Yes	Yes	No
Dalgarno et al.(2018)	Medium	Yes	Yes	Yes	Yes	Yes	No
Dunlop and Tracy.(2013)	High	Yes	Yes	Yes	Yes	Yes	Yes
Dunlop and Tracy.(2013)	High	Yes	Yes	Yes	Yes	Yes	Yes
Garland et al.(2012)	Medium	Yes	Yes	Yes	Yes	Yes	No
Gubi and Marsden-Hughes.(2013)	Medium	Yes	Yes	Yes	Yes	Yes	No
Haarni and Hautamäki. (2010)	Medium	Yes	Yes	Yes	Yes	Yes	No
Hanninen and Koski-Jannes.(1999)	Medium	Yes	Yes	Yes	Yes	Yes	No
Inman and Kornegay.(2004)	Medium	Yes	Yes	Yes	Yes	Yes	No
Jones et al.(2013)	Medium	Yes	Yes	Yes	Yes	Yes	No

Stud ID	Study quality	Was there a clear statement of the aims of the research?	Is a qualitative methodology appropriate?	Was the research design appropriate to address the aims of the research?	Was the recruitment strategy appropriate to the aims of the research?	Was the data collected in a way that addressed the research issue?	Has the relationship between researcher and participants been adequately considered?
Laitman and Lederman.(2008)	Low	Yes	Yes	Yes	Yes	Can't tell	No
Laville et al. (2006)	Low	No	Yes	Yes	Yes	Yes	N/A
Lederman and Menegatos.(2011)	Medium	Yes	Yes	Yes	Yes	Yes	No
Liezille Jacobs. (2015)	Medium	Yes	Yes	Yes	Yes	Yes	No
Mohatt et al.(2008)	Low	Yes	No	Yes	Yes	Yes	No
Mohatt et al.(2008)	Medium	Yes	Yes	Yes	Yes	Yes	No
Newton et al.(2007)	Medium	Yes	Yes	Yes	Yes	Yes	No
Opačić et al. (2019)	High	Yes	Yes	Yes	Yes	Yes	Yes
Paris and Bradley.(2001)	High	Yes	Yes	Yes	Yes	Yes	Yes
Punzi and Tidefors. (2014)	Medium	Yes	Yes	Yes	YEs	Yes	No
Robbins et al. (2015)	Medium	Yes	Yes	Yes	Yes	Yes	No
Rowan and Butler. (2014)	High	Yes	Yes	Yes	Yes	Yes	Yes
Sawer et al. (2020)	Medium	Yes	Yes	Yes	Yes	Yes	No
Stott and Priest. (2018)	Medium	Yes	Yes	Yes	Yes	Yes	No
Strobbe and Kurtz.(2012)	Low	Yes	Yes	Yes	Yes	Can't tell	No
Suprina et al. (2006)	Medium	Yes	Yes	Yes	Yes	Yes	No

Stud ID	Study quality	Was there a clear statement of the aims of the research?	Is a qualitative methodology appropriate?	Was the research design appropriate to address the aims of the research?	Was the recruitment strategy appropriate to the aims of the research?	Was the data collected in a way that addressed the research issue?	Has the relationship between researcher and participants been adequately considered?
Vaughn and Long. (1999)	Medium	Yes	Yes	Yes	Yes	No	No
Weegmann and Piwowoz-Hjort.(2009)	Medium	Yes	Yes	Yes	Yes	Yes	No
Zakrzewski and Hector. (2004)	High	Yes	Yes	Yes	Yes	Yes	Yes

Table 5-3. Dimensions of alcohol recovery stories

Superordinate category	Reference	Dimensions	Types			
Form	(93, 94, 217, 218, 222-224, 226, 228, 229, 234-236, 238, 239, 241)	**Genre**	Drama	Redemption	Drinking tale	Identity tale
	(94, 195, 214-217, 221, 224, 232, 234, 236, 237, 239, 240)	**Identity**	Renewal	Construction	Formation	
	(93, 94, 194, 195, 214-241)	**Recovery setting (positioning)**	Recovery within treatment	Recovery outside treatment		
Structure	(195, 222)	**Drinking trajectory**	Upward	Fluctuating	Steady	Downward
	(215, 221, 231)	**Drinking behaviours and traits**	Non-alcoholic	Alcoholic	Personality traits	
	(93, 195, 215, 220, 221, 224, 228, 229, 231, 235, 237, 240, 241)	**Stages (sequence)**	Origin of difficulty	Episode of Change	Recovery	Ongoing struggle

Superordinate category	Reference	Dimensions	Types	
Content	(214, 215, 217, 232, 234, 235, 237-241)	**Spirituality and religion**	Religion versus spirituality	Belonging
	(214, 227, 230, 237)	**Recovery experience**	Positive	Negative

5.3.3.1 Genre

Four genres from 13 studies were identified: **Drama; Redemption; Drinking tale and Identity tale** (Table 5-4) (3, 242).

5.3.3.1.1 Drama

Drama has three subtypes. *Melodrama*: narratives that are high in emotional content and present exaggerated characters and exciting events. *Comedy theatre:* narratives with humorous elements, which often use dramatic irony to induce laughter. *Quest:* narratives that take recipients on a journey in search of something (such as a successful recovery).

5.3.3.1.2 Redemption

Redemption has two subtypes. *Redemptive narratives:* describe stories that are centred on the idea of self-redemption, a phenomenon used to describe positive personal change after a negative experience (218). Redemptive narratives were often shared by narrators who were in long-term recovery from alcohol misuse, and who perceived they had benefited from their adversities (243). They showed elements of difficult experience, positive self-transformation, greater improvement in general health, and a high chance of sustained sobriety. *Non-redemptive narratives*: had a short-term recovery, lacked positive experience, had less improvement in general health, and increased risk of relapse to drinking (218).

5.3.3.1.3 Drinking Tale

Drinking tale describes how sharing a narrative impacts the narrators themselves (244). Sharing life stories helped the narrator's recovery in five different ways; by being reminded of their painful past, reinforcing their own recovery, losing their sense of uniqueness, facilitating and improving their relationship with themselves, and eventually helping others (94).

5.3.3.1.4 Identity Tale

Identity tale comprised narratives which foregrounded characteristics in relation to their alcohol use and social context (e.g., narrator's age, gender, sexual orientation, and ethnicity). Some research specifically sought the narratives of marginalised people such as Indigenous Australians and Alaskans. Drinking behaviour and recovery varied by life stage. Associated characteristics expounded through subgroup analysis.

5.3.3.2 Identity

Identity as a dimension involves self transformation. This is a multi-stage process and distinct from the 'identity tale' which by comparison emphasizes social, cultural, and demographic aspects of recovery. Fourteen publications discussed the importance of identity in the context of alcohol recovery. The concept of identity acquisition is a cornerstone of recovery in AA, where a person who has problems with alcohol accepts "alcoholism" as a disease and identifies as an "alcoholic" (215). This concept of identity acquisition is not generally used in recovery outside formal treatment settings (194, 214).

The concept of identity transformation was characteristic of these narratives., Within this dimension, we identified the following stages - **identity renewal**, **identity construction**, and **identity formation** (Table 5-4).

5.3.3.2.1 Identity renewal

During this first stage, the individual lacks a specific identity, nor is effort expended in forming one, a phenomenon described in the psychological literature as "identity diffusion" (245). Alcohol misuse causes a personal and social crisis and the person experiences fear, guilt, and shame. Participants spoke of recuperating and rebounding from "rock bottom".

5.3.3.2.2 Identity construction

The ensuing stage comprises of self-nurturing where a person arrives at a point where they begin to look for help, share their situation with others and 'surrender' to the process of recovery from alcohol misuse (237, 239, 240). The individual goes through cognitive restructuring, whereby one starts giving up on destructive thoughts, believing in the self, committing to change and attaining a new identity (214).

5.3.3.2.3 Identity formation

In the final stage, a person accepts their renewed identity as a self-aware "alcoholic". What followed in the narratives was an affinity and group membership, adapting to their emerging new role. The narratives characterised reconstructing social identity and mending relationships and generating the capacity to help others (215, 223, 232).

5.3.3.3 Recovery setting

In the recovery setting type, two subtypes were identified **recovery within treatment** and **recovery outside treatment** (Table 5-3). Recovery within treatment describes the experiences of a participant who was formally treated by an institution, clinicians, alcohol support workers, an organisation, or a person for alcohol misuse. Recovery

outside treatment describes the experiences of a participant who had minimal or no formal input from an institution, clinicians, alcohol support workers, organisation, or a person for alcohol misuse *(194, 214, 216)*.

5.3.3.3.1 Recovery within treatment

Recovery within treatment has the following subtypes. *AA narrative:* was most common for recovery within a formal treatment system, the core of an AA narrative was hitting rock bottom, sharing a story, spirituality, and acceptance of the new identity as an ”alcoholic” (215, 216, 223, 224, 234). *Dual diagnosis:* has narratives of *alcohol misuse and mental health*, *alcohol misuse and diabetes, and polydrug misuse* (93, 224).

Alcohol misuse and mental health have the following narratives. *Dominant cultural narrative:* participants were more inclined to accept a diagnosis of a mental health problem but were resistant to the label of an “alcoholic”. *Community and family narratives:* participants described recovery as an ongoing process involving significant others and achieving recovery through a sense of belonging, mutual aid, and sharing experiences. In both contexts, mental health services played a pivotal role in the recovery processes (93).

Alcohol misuse and diabetes: In these narratives, all participants believed in the genetic inheritance of diabetes but not of “alcoholism”. Participants often confused symptoms of alcohol withdrawal with hypoglycaemia which resulted in erratic eating and drinking habits. The involvement of specialist diabetic services and alcohol support groups improved participant knowledge and facilitated recovery (224).

Polydrug misuse: has narratives of participants who suffered childhood trauma, a strict code of keeping family secrets and denying negative feelings, resulting in multiple substances addiction. Therapeutic and self-help groups played an important role in the recovery of people with these experiences (224).

5.3.3.3.2 Recovery outside a treatment

Recovery outside treatment has the following subtypes. *Natural recovery:* narratives were less homogenous than those within the treatment setting. They included internal and external influences and did not feature significant involvement of others. Participants who described natural recovery tended to disagree with labelling and did not believe sharing stories helped recovery (214, 216). Cognitive restructuring and positive recovery capital played a key role in natural recovery (195, 214). *Emancipation narratives:* described identity development through making changes in

life and liberation from oppressive circumstances. *Discovery narratives:* in these narratives participants identified themselves as being different and developed their identity by consciously expanding experiences including art and the use of psychedelic drugs such as LSD. *Mastery narratives:* in these narratives' participants felt social pressure to demonstrate mastery over things like winning fights and/or drinking more, alcohol misuse was seen as irrational behaviour, with recovery involving an increased awareness of a drinking problem. *Coping narratives:* described a lifelong struggle, difficult personal circumstances, and the use of diagnostic labels to help recovery (194).

5.3.3.4 Drinking trajectory

The drinking trajectory describes the impact of ageing on drinking habits and comprises four types (Table 5-4) (195, 222).

5.3.3.4.1 Upward drinking career

Upward drinking career describes the increase of alcohol intake in adulthood and had two further *subtypes mildly* upward and *sharply upward*. In the *mildly upward career* alcohol was part of social life and slowly increased with age. The *sharply upward drinking* trajectory was found to be common in women, with drinking becoming part of the person's lifestyle in the latter part of their working years.

5.3.3.4.2 Fluctuating drinking career

Fluctuating drinking career describes drinking patterns which varied with time and life circumstances. Those with fluctuating drinking careers were aware of heavy episodic alcohol intake, and although they had reflected on it, they were not specifically concerned about it as this was all part of their past now (222).

5.3.3.4.3 Steady drinking career

A steady drinking career describes drinking habits which remained the same throughout a person's life span despite increasing age and changes happening in life. The drinking was moderate to scant, no particular attention was paid to drinking due to a lack of change in the volume of alcohol consumed (222).

5.3.3.4.4 Downward drinking career

A downward drinking career describes a decline in alcohol consumption as the person got older. This was either *mildly downward*, where change was slow, or *steeply downward*, where change was rapid (222). Alcohol careers can include the late onset of alcohol dependence (often after specific triggers such as bereavement or

retirement) with resolution shortly thereafter (195). Dunlop et al. (2013) showed age positively correlates with improved self-esteem, general health, and authentic pride and negatively with aggression which in turn increases the chances of recovery from alcohol misuse (219).

5.3.3.5 Drinking behaviours and traits

5.3.3.5.1 Non-alcoholic drinking

The non-alcoholic drinking type comprises narratives of participants who were drinking actively but in a controlled manner.

5.3.3.5.2 Non-alcoholic non-drinking

The non-alcoholic non-drinking type comprises narratives of participants who completely abstained from alcohol. In the *alcoholic drinking* type participants were active alcoholics. In the *alcohol non-drinking* type, the participants were either non-drinking alcoholics or recovering alcoholics (215, 222).

5.3.3.5.3 Personality traits

In *personality traits* type antisocial, passive, prosocial, grandiose, and dishonest were commonly associated with alcohol misuse (221, 231).

5.3.3.6 Stages (sequence)

The commonly used alcohol recovery model has the following stages: the **origin of the difficulty, episode of change, attainment of recovery, and ongoing struggle** (Table 5-4) (93, 221, 229).

In narratives describing the sequence of alcohol misuse, the common triggers of alcohol use were social and cultural difficulties, norms and pressures, childhood abuse, mental health problems, a lack of belonging and numbing the pain (226, 238, 239). As drinking progressed, physical, mental health, and social problems attributable to alcohol consumption developed, whereby the person sought to escape from fear and shame. Turning points described by participants ranged from no specific event to near-death experiences, embarrassment, spiritual experiences, a sense of loss, death of a family member, loss of a friend by suicide, and physical and mental health decline (235, 241). On one occasion a person described a phase of rejection and denial, but an eventual acknowledgement of the problem was followed by help-seeking behaviours or natural recovery, culminating in sobriety. Ongoing struggle describes the efforts made by the individual to maintain their sobriety and recovery

(221). By participating in meaningful activities, adopting a new identity, and creating positive recovery capital, the narrators of these stories felt they were more likely to achieve long term sobriety (195).

5.3.3.7 Spirituality and religion

A lack of sense of belonging was a common theme that resonated across numerous recovery stories, particularly in stories from more marginalised communities such as Indigenous Americans and Australians and those in the LGBTQ+ community (217, 229, 235, 238). Spirituality and belief in a higher power were a cornerstone for recovery in the AA model (215, 224). Participants described **religion** as dogmatic, ritualistic, biased against sexual orientation and identity, and had strict codes of moral behaviour, while **spirituality** as more individualistic, open, inclusive, and flexible (238). Lack of belonging and social isolation triggered alcohol use, and support groups such as AA provided an opportunity for spiritual reconnection as well as a chance to attain a sense of belonging and sobriety (232, 235, 237, 238).

5.3.3.8 Recovery experience

Recovery experience narratives were positive, negative or both (Table 5-4).

5.3.3.8.1 Positive recovery experiences

Positive recovery experiences were ego ideal for participants and improved their self-pride, empowerment, trust, and relationships. They found lost opportunities, felt more integrated into society, were happy to be alive, and enjoyed new hobbies and activities.

5.3.3.8.2 Negative recovery experiences

Negative recovery occurs when the cost of giving up alcohol is considerable. Narratives that displayed negative recovery experiences were characterised by a craving for alcohol, feeling the pressure of intense self-discipline, losing drinking friends and social contacts, inadequate coping skills, and concomitant mental health illness. The *narratives of liver transplant recipients* were dominated by a concept of “life-altering” events and particularly offered the themes of financial and job-related issues and the impact of other comorbidities (214, 230).

Table 5-4. Description of types and subtypes of alcohol recovery stories dimensions

Genre			
Drama	*Redemption*	*Drinking tale*	*Identity tale*
Melodrama	Redemptive	Painful past	Stages of life
Comedy theatre	Non-redemptive	Reinforcement	Sex
Quest		Loss of uniqueness	Sexual orientation
		Relationship with oneself	Marginalised societies
		Helping others	
Identity			
Renewal	*Construction*	*Formation*	
Motivation to change	Self-nurturing	Perceived Life change	
Emotional response	Beyond self	Adaptation	
Shame and crises	Cognitive restructuring	Acceptance	
Identity diffusion	Admittance and surrender	Reconstructing relationships	
		Delivering back	
Recovery setting (positioning)			
Recovery within treatment setting		*Recovery outside treatment setting*	
AA narratives		Self-changer or natural recovery	
Dual diagnosis narratives		Personal growth story	
Polydrug abuse narratives		Emancipation narrative	
		Discovery narratives	
		Mastery narratives	
		Coping narratives	
Drinking trajectory			
Upward	*Fluctuating*	*Steady*	*Downward*
Mildly upward drinking careers	Suspended drinking career		Mildly downward drinking career
Sharply upward drinking career			Steeper downward drinking career
Drinking behaviours			
Non-alcoholic		*Alcoholic*	*Alcohol impact*
Drinking	Nondrinking	Uncontrolled drinking	Antisocial

Controlled	Abstainer	Active alcoholic	Passive
Normal drinker	Nondrinking alcoholics		Prosocial
Recovering alcoholic	Recovered alcoholics		Grandiose
			Dishonest
Stages (sequence) (can be non-linear)			
Origin of difficulty	*Episode of Change*	*Recovery*	*Ongoing struggle*
Start of drinking	Blame and escape	Acknowledging problem	Being sober
Negative effect	Identification of problem	Surrender	Maintaining sobriety
Drinking progress	Alcoholic regression	Acceptance	Maintaining recovery
Problems	Rejection and denial	Help	
Drinking worsen	Turning points	Become sober	
Spirituality and religion			
spirituality versus Religion		*Community Belonging*	
Religion	**Spirituality**	Lack of belonging	
Community	Individual	A search for belonging	
Bound	Limitless	Attain belonging	
Dogmatic and ritualistic	Flexible and transformative		
Exclusive	Inclusive		
Recovery experience			
Positive		*Negative*	
Ego ideal		Craving	
Self-pride		Intense self-discipline	
Empowerment		Loss of drinking friends and social contacts	
Improved relationships		Intrusive disturbing memories	
Improved trust in family		Inadequate coping skills to face reality	
Reintegration into society		Depression, anxiety	
Lost opportunities found		Loneliness	
Happy to be alive		Work and financial issues	
Enjoy doing thing		Impact of comorbidities	
		Life stinks	

5.3.4 Subgroup analysis

5.3.4.1 Age

Along the dimension of age, young people's drinking habits and activities often involved peer pressure whilst socialising with friends, such as taking part in drinking games in college and as part of social status, whereas the drinking habits of older individuals related to later life experiences and challenges (222, 226). Thus, demonstrating the importance of social and cultural influences on drinking behaviours, which may influence recovery (3, 242).

5.3.4.2 Gender

Five studies reported the narratives of female participants only, these studies emphasized identity renewal and the affective response of shame as characteristics of the recovery narrative (226, 228, 232, 234, 235). Shame is a social and regulatory emotion that invokes self-awareness and self-other obligations (228, 235); we also found that females use shame as an impetus to build relationships through the help of networks. This was a common affective response that contributed to coping when stepping out of addiction and into a new identity. There was a heavy reliance on social networks, which was present in all narratives apart from Christensen and Elmeland. (2015) where participants used new hobbies and activities for self-renewal. Studies with male only participants showed no distinct characteristics in the sample except the study using shame as the impetus described above (216).

5.3.4.3 Sexual orientation

In the studies with participants identifying themselves as LGBTQ+, we note that spiritual awakening was more commonly sought rather than religious affiliation (235, 238). Alcohol use was a lifestyle choice recognised by participants from the LGBTQ+ community. Building a new identity through recovery programs and networks enabled recovery and the formation of new productive relationships outside of alcohol use (235, 238).

5.3.4.4 Marginalised communities

Analysis of studies discussing the experiences of Indigenous Australian and Alaskan people’s recovery (217, 229) showed although they experienced similar stages of recovery, they tended to have more emphasis on elements of stereotyping, alienation, marginalisation, inequality, low wages, and the impact of sudden gaining of citizenship

status and money. The recovery process was unpredictable and messy (217), and participants achieved recovery both within and outside treatment settings.

5.3.4.5 Alcohol and mental health

Analysis of studies discussing dual diagnosis of alcohol misuse and mental health problems showed participants often suffered from negative self-perceptions, including low self-esteem, lack of love from others, lack of desire to belong, anger, and shame (93, 214, 218, 221, 223, 225, 232, 237, 239). Mental health problems often acted as a trigger to drink harmfully (239). Common mental health problems reported were anxiety, depression, obsessive-compulsive disorders, post-traumatic disorders (mostly due to difficult childhoods), attention-seeking behaviours, eating disorders, and emotional instability (93, 218, 221, 223, 225, 239). Facilitators to recovery were integrated support from mental health and substance misuse services, a flexible and trustworthy relationship with care providers, individualised treatment pathways, and easy to understand step-by-step support. Whereas barriers to recovery were undiagnosed or unrecognised mental health problems, inadequate support from mental health services, underfunded services, and punitive response to alcohol misuse (93). Participants who had negative recovery experiences reported ongoing mental health difficulties comprised of anxiety, depression, and intrusive or disturbing memories. This in turn impacted the longevity of sobriety (214).

5.3.4.6 Medium and high-quality studies:

On performing subgroup analysis including twenty-six medium and high-quality studies most dimension types were present in the framework apart from the narratives of college drinking, indigenous Australians, and redemption.

5.4 Discussion

5.4.1 Summary of key findings

The current review identified a rich source of existing literature that describes alcohol recovery narratives and summarises their characteristics. Included studies were multi-disciplinary and summarised the alcohol recovery experiences of over a thousand participants spanning 30 years of research. Narratives analysed included studies belonging to people from a variety of social and demographic orientations. Although this sample was not entirely diverse in terms of ethnic distribution, the review does include studies which voiced the recovery experience of more marginalised communities such as Alaskans and indigenous Australians (217, 229).

5.4.2 Dimensions and existing evidence

The review collated a diverse source of multidimensional narratives using conceptual similarities and differences into eight dimensions with each its own specific types and subtypes. Dimensions identified were genre, identity, recovery setting, drinking trajectories, drinking behaviours and traits, stages, spirituality and religion, and recovery experience.

The notion of *Genre* as a dimension describes overarching styles of narrating alcohol recovery narratives. The genres we identified characterize recovery narratives in four ways. These are drama, redemption, drinking tale and identity tale, which in different ways demonstrate a progression of an emotional self, actively constructing an identity to aid in stepping out of addictive lifestyle practices contributing to the recovery process.

The *Identity* as a dimension describes self-transformation in a multistage process. In this regards the stages of identity construction were representative of reviewed narratives of alcohol recovery. The individuals grow through identity renewal, identity construction and identity formation to often find sustainable recovery, sometimes finding themselves in a role to help others struggling with addiction (246). The motivation to reinvent the self by the construction of a new identity is a behavioural pattern associated with addiction (247). The stages observed uses narratives to demonstrate the argument that recovery is largely driven by a personal and effective evaluation of the self, leaving behind one identity in pursuit of another (195). That is, the individual returns, when used in the narrative, to a mode of evaluation regarding

how bad things are (current identity) and how reachable and better things could be (renewed identity within the new group) (248).

Recovery setting as a dimension describes two types of alcohol recovery narratives recovery within treatment setting and recovery outside treatment setting. Participants recovered from alcohol misuse both within and outside formal treatment settings, however, the majority of included studies described achieving recovery through AA or participants who interacted with more than one service and tried numerous recovery strategies (249). In review, 41% of participant narratives were from people who were known to AA. A Cochrane review found AA and other 12-Step programmes were superior to other clinical interventions at continuous abstinence from alcohol both in the short and long term. However, the author acknowledges that those who do not see improvements in AA after a certain period should be offered a different approach (250). Narratives from people who had followed the AA model in our review used similar types of language e.g., rock bottom. Those who rejected formal treatment of this kind and opted for natural recovery described not being able to relate to the language and concepts used in AA. Our work may help better understand the characteristics of those who find AA works for them, and those who do not, which would reduce uptake of multiple treatment modalities and feelings of frustration.

Drinking trajectory as a dimension describes the impact of ageing on drinking habits. In this context, one can reflect both prospectively by anticipating future impact, or retrospect from ones past experience. Furthermore, the narrator can display a tendency to account for their narrated experience in terms of change in social and personal circumstances. This suggests that recovery narratives involve the socio-economic and highly personalised experience of ageing as a catalyst in piecing together the old identity one revisits, now, in narrating recovery retrospectively.

Drinking behaviours and traits as a dimension describe drinking habits and personality traits. This personality trait may support addictive behaviours, perhaps due to factors such as peer pressure, or companionship drinking to maintain social acceptance (251). In terms of recovery, it was important to recognise the significant role these traits played. Particularly in so far as these can be informative in designing interventions to mitigate high-risk addictive behaviours.

Sequence as a dimension organises the stages of alcohol recovery. The review demonstrated the dynamic nature of recovery as a nonlinear- and non-dichotomous process, which supports previous work in the area (249). In narratives describing the sequence of alcohol misuse, the common triggers of alcohol use were social and

cultural difficulties, norms and pressures, childhood abuse, mental health problems, a lack of belonging and numbing the pain (226, 238, 239). In particular, the subtype ongoing struggle was important for giving voice to some peoples continued daily efforts to recover. The most frequent turning points were, seeking help, changing from negative to positive social connections, self-realisation, and seeking a new identity (195).

Spirituality and religion as a dimension describe the role of religion and spirituality in alcohol recovery. The ideology of spirituality and belief in a higher power was common among AA narratives and was central in providing directions to recovery (215, 224). The LGBTQ+ community in particular voiced that religion has a strict code of conduct and was less tolerant of varied sexual practices whereas spirituality was more open and less regulated (238).

Recovery experience as a dimension describes participants' experience of recovery as positive or negative. In actual life experience, one would have experienced a confluence of both tendencies. Congruent thoughts and beliefs can impact the individuals' anticipations and personal estimates of negative or positive outcomes associated with addiction. Recognising the positive and negative impact of recovery can help to pre-emptively build networks, which can support and maintain sobriety.

5.4.3 Subgroups

The work highlighted the diversity in participants' narratives based on multiple factors such as age, gender, sexual orientation, marginalised communities, and mental health. All dimensions were present in most subgroups. *Shame* was a prominent theme for female narrators, *lack of sense of belonging* and *spirituality* were prominent for LGBTQ+ narrators, and *alienation* and *inequality* were prominent for indigenous narrators.

5.4.4 Strengths and limitations

I followed a robust three stage process to synthesise the results. I first created a preliminary conceptual framework based on initial findings, the preliminary framework was then reviewed by a multidisciplinary team with expertise in qualitative work, and finally, I tested the robustness of the framework by sub-group analysis. The work was supervised by a multidisciplinary team with diverse experiences including members with prior experience in creating conceptual frameworks describing mental health recovery narratives. This enabled me to have a rich discussion with the rest of the

team and to give careful consideration while choosing terms to describe alcohol misuse and the social context of participants including sexual orientation.

The following limitations of the review were noted. First, the result of the review may not be generalised to low-income countries, and non-Caucasian populations as all the included studies were conducted in high-income countries with a white predominant population. Detailed ethnic distribution was missing in most studies add the search strategy was restricted to the English language. Second, the author's personal viewpoints and experiences might have influenced the data interpretations, to minimise this, a three-stage approach was followed for data synthesis.

5.4.5 Implications

The conceptual framework developed in the current chapter provides researchers, practitioners, policymakers, and other stakeholders with an accessible resource to build future research and practice. Concepts and their relations proposed by the framework facilitated alcohol recovery video stories (ARVS) recording which were later used as part of the KLIFAD study interventions.

5.4.5.1 For research and practice

The review contributes an understanding of narratives in relation to both structured support and unsupported natural journeys of recovery; an area that remains poorly developed and understood in research (252) and I recommend should be expanded. The review assimilates diverse types of narratives recognised in the literature such as emancipation, discovery and mastery, and contributes to the distinction of unstructured recovery narratives as cognitively loaded (i.e. mental effort in restructuring beliefs and coping with associated emotions), involving meaningful activity like art and psychedelic drugs, and with less involvement and support from others (194, 246). The review finds evidence through narratives of recovery from alcohol, for the notion of recovery is motivated by push factors (hitting rock bottom, shame, identity loss, alienation) and pull factors (the good life, the social relationships one wants to develop and starts to enjoy) (253). This dynamic applied to individuals from a range of social orientations, actively seeking renewal of identity.

I found that the path to recovery involved some higher order (religious/spiritual) system of thought and practice toward what is more broadly recognised in addiction research as the recoveree "developing a sense of future"(254). Driven emotionally with hope and positive feelings, individuals found forming or mending relationships with significant others helped their recovery. Through meaningful activity, they

acquired goals and acquired safety and confidence, often in a program that offered a social support network. I note that amongst individuals who were part of the LGBTQ+ community, recovery from alcohol misuse was particularly aided by a sense of belonging to groups. Latent mental health problems were described as acting as a trigger in some narratives, and narratives describing dual diagnoses provided information about forms of mental health intervention that helped (including effective services) and did not help (including pejorative treatment of alcohol use).

5.4.5.2 For thesis studies

Recovery stories have long been proven as an effective measure for mental health disorders (97, 255). Lately, the recovery narrative, as a form of intervention is becoming more popular among drug and alcohol treatment settings with an increasing number of services embracing it (256). I aimed to produce alcohol recovery video stories that have the maximum beneficial impact on the alcohol use of KLIFAD trial participants (e.g. the video contributes to the person substantially reducing or ceasing their alcohol use). The framework produced characterised alcohol recovery narratives which provided strong conceptual grounds to develop the guide for recording future alcohol recovery narratives and supported their use as part of KLIFAD intervention.

Once a person shares their lived experience as a narrative it can be processed in different ways by recipients (researcher, care provider, and patient) a phenomenon described as polysemy by Bruner (1986) (257). This in turn can introduce further complexity, that might affect the intended use of narratives. Having a standardised framework based guide enabled me to ensure the recovery narratives collected were inclusive of different dimensions including recovery within and outside treatment settings. This, in turn, helped to maximise the intended beneficial effects for trial participants. The evidence supports that a clear understanding of the characteristics of alcohol misuse recovery narratives could help to optimise the use of these narratives in clinical practice and maximise their positive impact (258).

5.5 Conclusions

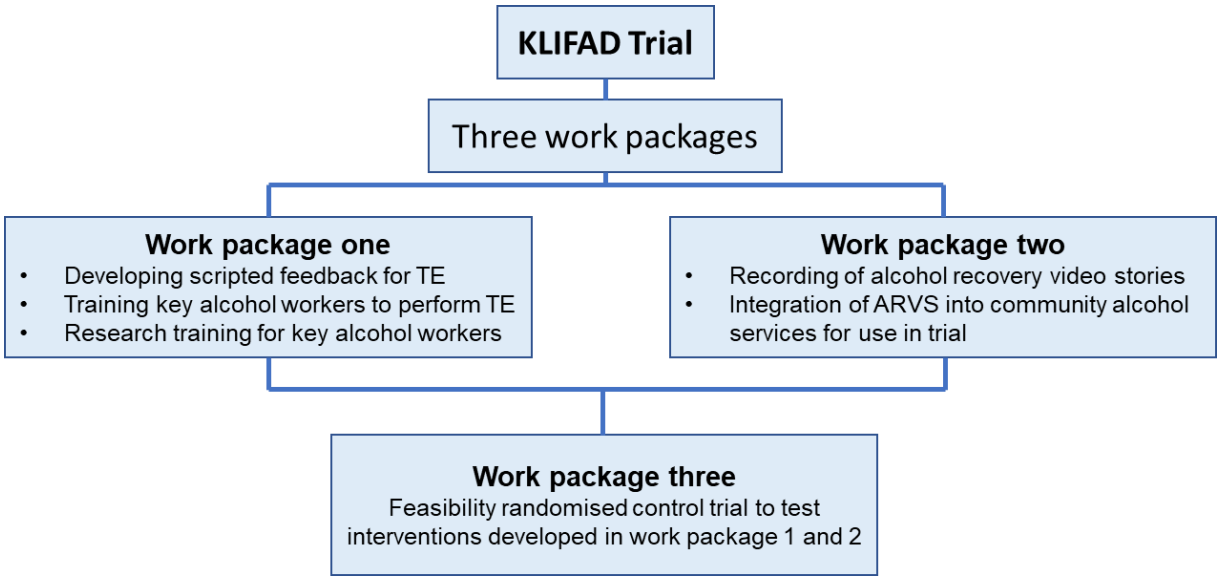
The role of narratives in alcohol recovery is only partially understood (237, 259). In this context, our review provides characteristics of alcohol recovery narratives, with implications for both research and healthcare practice. We recommend research focus on collecting narratives from people in low income countries, those who have recovered outside of mainstream services or those who have used services other than AA, and more ethnic diversity in studies.

Chapter 6. KLIFAD: overview and developmental methodology

KLIFAD (**K**nowledge of **LI**ver **F**ibrosis **A**ffects **D**rinking) is a parallel design feasibility RCT. Ethical approval was obtained from the West of Scotland Research Ethics Service (WoSRES) (20/WS/0179). Written informed consent was obtained from all participants. The work presented in KLIFAD has informed the conduct of a clinical trial (ISRCTN 16922410, prospectively registered on 26/01/2021). The trial protocol was published prospectively (156).

This was a single-centre trial conducted at three alcohol treatment services including Wellbeing Hub (WH) community alcohol services, Edwin House (EH) a community inpatient alcohol detox unit, both hosted by Nottingham Recovery Network (NRN), and primary care substance misuse clinic run by Windmill GP practice. The KLIFAD trial consisted of three work packages (Figure 6-1).

Figure 6-1. Flow chart for KLIFAD work packages



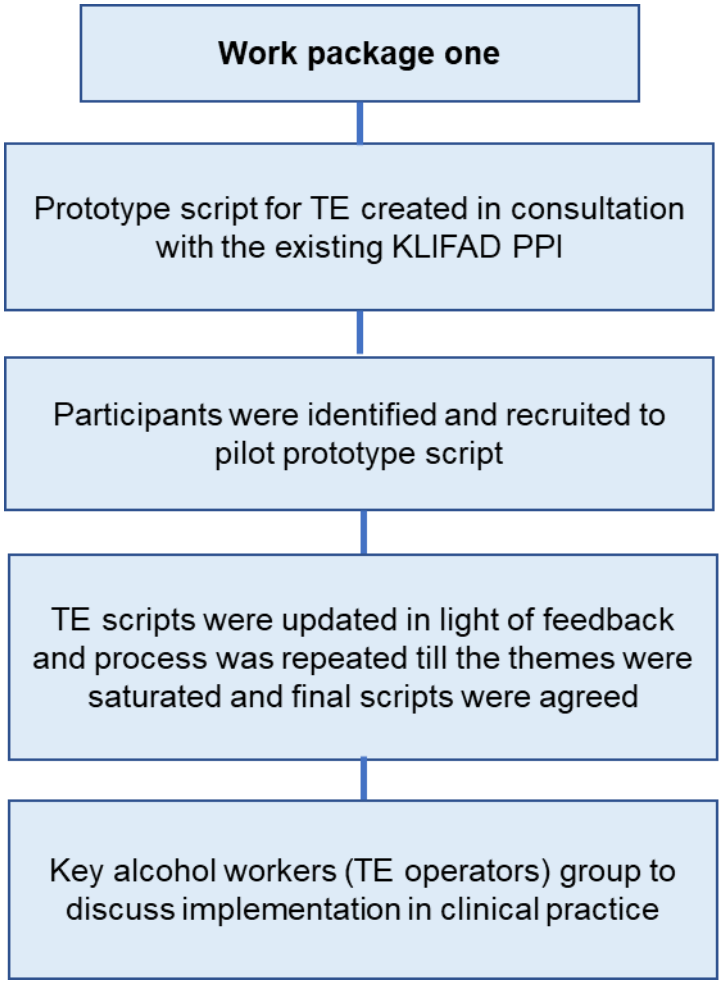
6.1 Work Package one (WP1)

WP1 aimed to design a standardised script framework for transient elastography operators to deliver liver disease-specific advice to participants having transient elastography as part of the feasibility RCT (WP3).

Transient elastography was performed by using FibroScan, an ultrasound technology developed by Echosens, France, which non-invasively assesses liver stiffness. A

prototype script for transient elastography was created in consultation with the existing KLIFAD Patient Public Involvement (PPI) group covering three ranges of transient elastography scores, normal ≤7 Kilopascal (kPa), intermediate fibrosis 8-14 kPa and advanced fibrosis ≥15 kPa. The flow chart for WP1 is in Figure 6-2.

Figure 6-2. Flow chart KLIFAD WP 1



We then organised separate focus groups for participants and transient elastography operators to collect feedback on the prototype scripts. The participants' focus group allowed us to investigate the key messages to be included in the scripted feedback, and how best to present the transient elastography results (e.g., graphically, in the text). The transient elastography operators' focus group specifically discussed implementation in clinical practice.

Following Krueger's (1988) focus group guide, each focus group aimed to include five to eight participants and last for a maximum of two hours (260). Due to Covid-19 restrictions at the time, the focus group were organised virtually. A topic guide was

used. We arranged one focus group for participants and one focus group for transient elastography operators. Examples of questions included:

a) If you were a participant in the trial, would the script make sense to you?
b) Are there any parts of the script that you do not understand, and if so, why?
c) What is the best way to present the results of the FibroScan (e.g., graphically, in the text)?

Participants of age ≥ 18 years, with alcohol as primary substance misuse, and who had transient elastography in past were included. Participants with primary substance misuse other than alcohol or who lacked the capacity to confirm consent were excluded. Eligible participants were identified through existing patient forums at all three recruitment settings, the KLIFAD PPI group, by offering information to patients self-presenting to any of the trial treatment settings, snowball methods, Black, Asian and minority ethnicity and Framework PPI groups.

The focus group meetings were recorded and transcribed verbatim by an independent sponsor-approved transcriber. After the first participant focus group the scripts were edited considering feedback and a second focus group was then held to review iterated scripts. The final scripts were sent via email to participants of focus groups for final thoughts. We then organised a transient elastography operator focus group of key alcohol workers working at any of the recruitment settings who are willing to give informed consent, to discuss any specific implementation issues. A sample scripted feedback for transient Elastography demonstrating advanced liver fibrosis is given in Script 1.

Script 1: Example scripted feedback for advanced liver fibrosis

Advanced (fibrosis) Fibroscan information for patients

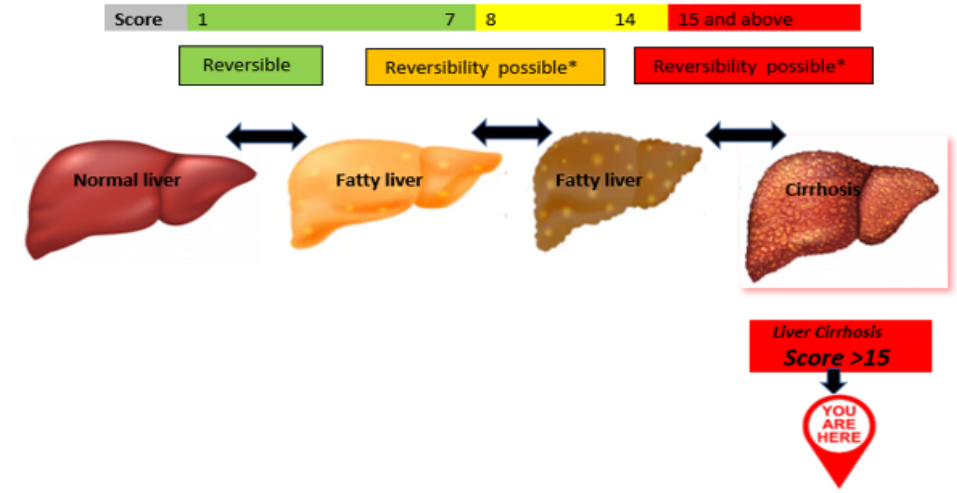
Title of the Study: Does knowledge of liver fibrosis affect high-risk drinking behaviour (KLIFAD)? A feasibility randomised controlled trial.

Thank you for volunteering to have a Fibroscan today.

Interpretation of results

Fibrosis is the medical term for the scarring of the liver. Fibroscan is a device that measures this scarring by estimating the stiffness of the liver. The stiffness is measured in units called Kilopascal or kPa. The score below gives an estimate of your liver fibrosis.

Your scan result was: kPa



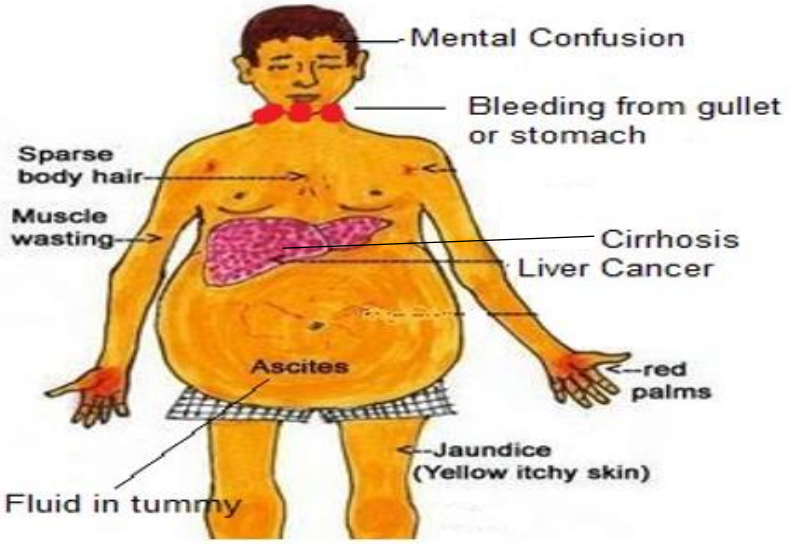
Your liver **stiffness score is high.** With score in this range, we expect to see **advanced liver scarring/Cirrhosis**

What risk is there to my health?

Alcohol is one of the main causes of cirrhosis. If you continue to drink at the current level and do not abstain from alcohol, you have more than **30% (1 person in 3)** chance of dying within **5 years.** Once you develop complications, the **risk of death within 5 years is as high as 65% (2 person in 3)**.

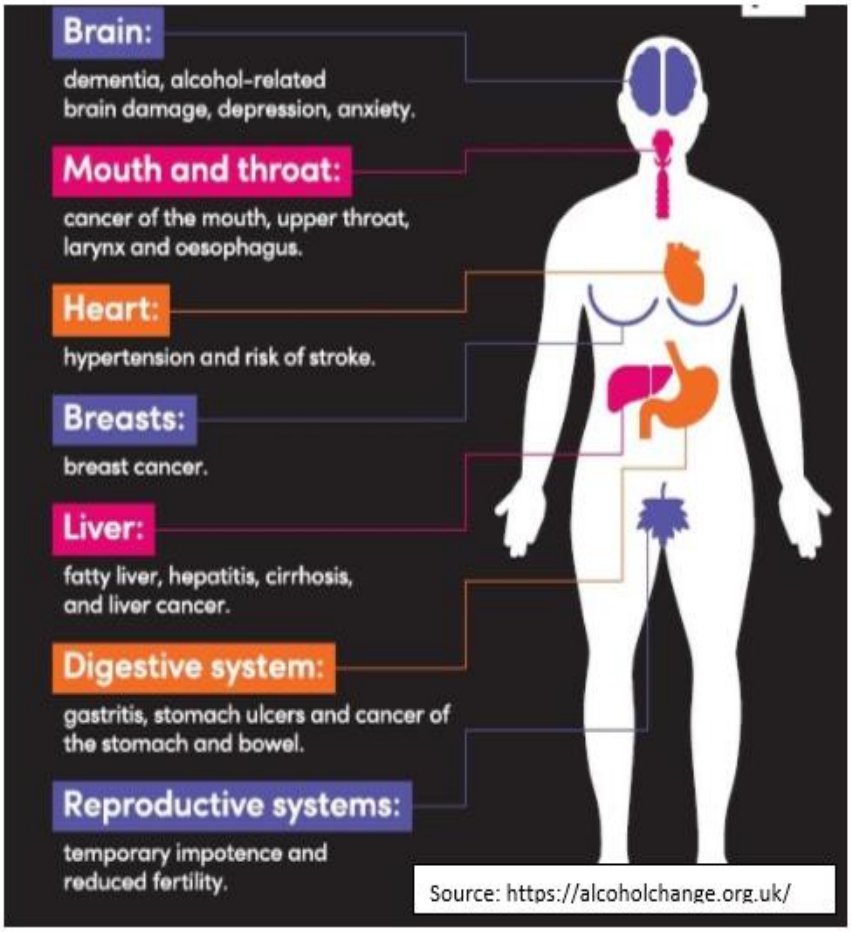
It is very important that you should stop drinking alcohol completely. **If you can stop drinking alcohol, your risk of future liver problems is significantly reduced.** If you continue to drink heavily then you are at risk of serious complications, such as liver failure as shown in next image. Liver failure has a huge impact on people, affecting their ability to live independently and increasing their risk of early death.

Liver disease complications



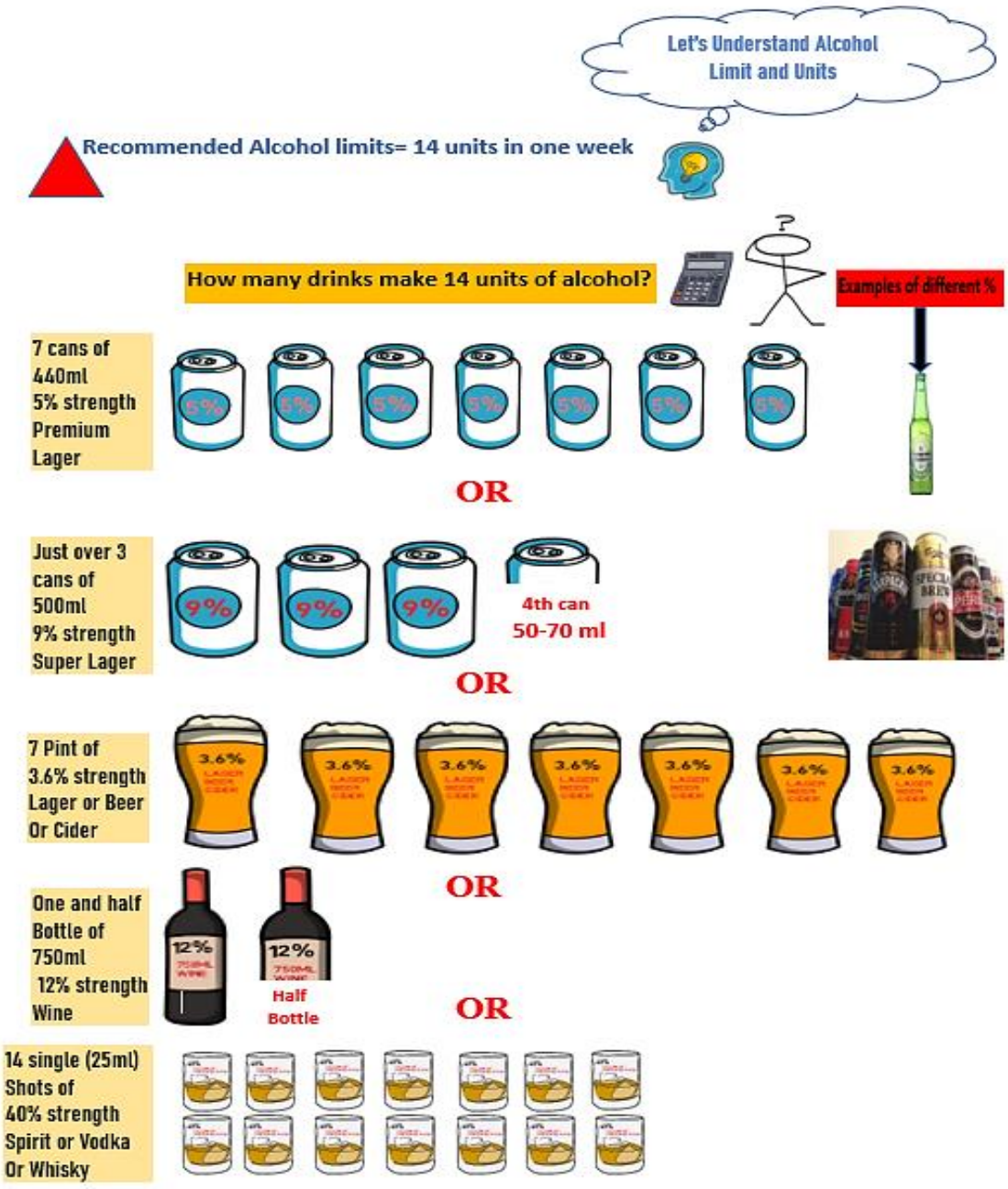
Other potential health problems

Drinking excessively can also impact your health in lots of other ways. The picture below shows other **long-term risks of drinking excess alcohol:**

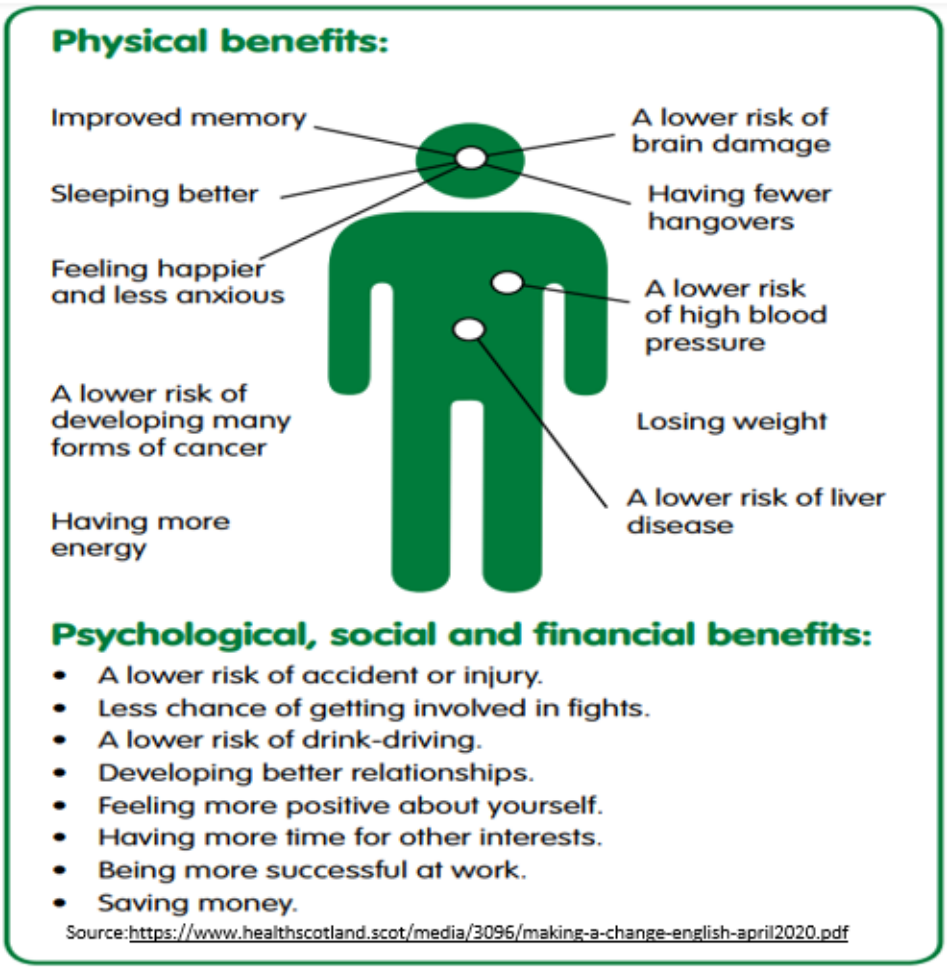


Advice

With liver damage is at this stage there is still a possibility of reversibility. Our advice is to stop drinking alcohol permanently as this will help your liver to function well and prevent further damage and future complications. For some people, **it may be dangerous to stop drinking suddenly**, so we advise gradually reducing the amount you drink and discussing this with your key alcohol worker or GP. We will also recommend that your GP refers you to the Nottingham University Hospital Liver team for further advice.



Benefits of reducing or stopping alcohol



Links for more information on alcohol misuse and ways to find support

If you are interested to read more on how alcohol can affect your health and what help is available please follow these links for more information

NHS alcohol misuse guide
https://www.nhs.uk/conditions/alcohol-misuse/risks/

Patient.info Alcohol Dependence and Problem Drinking
https://patient.info/healthy-living/alcohol-and-liver-disease/alcoholism-and-problem-drinking

NHS Alcohol support
https://www.nhs.uk/live-well/alcohol-support/

Alcohol Change UK- Get help now
https://alcoholchange.org.uk/help-and-support/get-help-now

6.2 Work Package Two (WP2)

WP2 aimed to create a video library of ARVS from people with a history of alcohol use disorder (AUD). Receiving mental health recovery stories can provide benefits to some people experiencing mental health distress (97, 255, 261), and the effectiveness of mental health recovery stories as an intervention to increase the quality of life has been examined in clinical trials (262). However, equivalent evidence is not available for the impact of ARVS. So that we can explore the impact of stories of recovery from AUD.

The detailed methods describing WP2 along with results are provided in chapter seven titled “Validation of conceptual framework describing alcohol recovery narratives”.

6.3 Work Package 3 (WP3)- Feasibility RCT

In WP3 a feasibility RCT of parallel groups (one-to-one) was conducted to compare usual care (assessment and entry into an alcohol reduction programme which does not include information on liver disease severity) to usual care plus feedback from transient elastography and ARVS.

Based on Bowen et al (2009)’s guide for feasibility studies (263) following objectives were set for feasibility RCT.

1. **Test:** the intervention (FibroScan plus feedback and ARVS) in a feasibility randomised control trial.
2. **Acceptability**: of the feasibility of randomised control trial-related procedures and interventions among patients and healthcare workers.
3. **Feasibility outcomes**: to establish recruitment rate, consent rate, dropout rate, and completion rate for accurate sample size calculation for future large-scale RCT.
4. **Refine**: the eligibility and randomisation criteria for a future large-scale RCT.
5. **Implementation and practicality:** to assess the ability of community alcohol services to deliver the intervention, and training and support needs for community alcohol services keyworkers for delivering the intervention.
6. **Adaptation:** of KLIFAD trial interventions, FibroScan feedback, and ARVS format and access as per suggestions from participants and key alcohol workers
7. **Extent of efficacy**: to test the extent of efficacy of KLIFAD interventions

This study is reported as Chapter eight titled “KLIFAD RCT”.

Chapter 7. Validation of conceptual framework describing alcohol recovery narratives

7.1 Rationale and Overview

To facilitate the understanding of complex health-related problems, a common practice in health research has been the development of conceptual frameworks presenting networks of linked concepts which serve to explain the phenomenon (264). This in turn can enable the refinement of individual concepts and the framework as a whole (265). The process of developing conceptual frameworks is led by clearly articulated and strong concepts (266). Health-related conceptual frameworks can be influential. For example, the CHIME framework (connectedness; hope and optimism about the future; identity; meaning in life; empowerment) on mental health recovery processes has influenced policy, research, and practice internationally. A recent example of conceptual frameworks specifically describing the characteristics of recovery narratives include those focused on mental health (267), childhood trauma (268), and social isolation (269).

In the previous chapter, I proposed a conceptual framework characterising the alcohol recovery narrative through a systematic review and narrative synthesis (270). The proposed alcohol recovery narrative conceptual framework (ARNCF) assimilated all published work on the characteristics of recovery narratives but was not tested in a contemporary cohort. Prior research has demonstrated the value of validating conceptual frameworks produced through systematic reviews by analysing the new datasets not used in the development of the conceptual framework (258, 271). Validation studies can extend and modify existing conceptual frameworks, making them more robust, and hence extending their value to policy, practice, and research. Validating a framework can involve applying it as a coding framework to new data (258), and hence validation studies can develop practical knowledge on the use of a conceptual framework to understand the content of qualitative data.

In this chapter, I aim to validate the ARNCF by applying it to alcohol misuse recovery narratives generated through semi-structured interviews. The objectives are (a) to assess the relevance of existing dimensions and types, (b) to identify any needed additional dimensions and types, (c) to validate and extend the pre-existing subgroups of ARNCF (d) to gain a preliminary understanding of the types of knowledge that can be developed by applying the framework to narratives.

7.2 Methods

The study was conducted as part of the KLIFAD feasibility randomised control trial (156). Ethical approval was obtained from the West of Scotland Research Ethics Service (WoSRES), REC reference: 20/WS/0179. Written informed consent was obtained from all participants. The work presented in this paper has informed the conduct of a clinical trial (ISRCTN 16922410, prospectively registered on 26/01/2021). The preliminary typology of characteristics of alcohol recovery narratives was based on the published systematic review (270).

Alcohol misuse recovery was defined as “A deeply personal, unique process of change, a way of living a satisfying, hopeful and contributing life even with limitations caused by illness [and] a process involving the development of new meaning or purpose in one’s life” (255, 272).

7.2.1 Participants

The following eligibility criteria for participants selection were applied

7.2.1.1 Inclusion Criteria

The participants fulfilling the following criteria were included: (a) a person of age 18 with a history of alcohol misuse, (b) is certain in their belief to have experienced recovery from alcohol misuse or has been identified as having experienced recovery by the study team against definitions above, (c) can give informed consent, (d) has previously received one or more transient elastography, (e) can recall and are willing to share with the research team their first FibroScan score, or can identify an approximate value for their score.

7.2.1.2 Exclusion Criteria

The participants who had a primary substance misuse other than alcohol or lacked first-hand experience of recovery such as family members were excluded.

7.2.2 Recruitment

Participants were purposively identified based on age, gender, ethnicity, and liver stiffness measures (273). They were recruited through existing patient forums at recruitment settings, by offering information to patients self-presenting to any of the trial treatment settings, and by snowball methods. A maximum variation sample on

liver stiffness was sought, covering self-reported Transient elastography scores indicating normal, intermediate, and advanced liver stiffness (274). For other dimensions, convenience sampling methods were applied.

7.2.3 Procedure

7.2.3.1 Variables collected

Data on the following variable was collected on a case report form at the start of the face-to-face interviews: age, gender, ethnicity, peak alcohol intake, living arrangement, occupation, current drinking status, length of sobriety, and liver stiffness measure (LSM). Based on LSM participants were divided into three groups: normal LSM (≤7 kilopascals), intermediate LSM (8-14 kilopascals), and advanced LSM in the range of cirrhosis (≥15 kilopascals). If participants disclosed the name of a specific person, institution, or place in the interview they were removed to keep the anonymity of data.

7.2.3.2 Qualitative semi-structured interviews

The qualitative semi-structured interviews were conducted by the lead researcher (MS). Each participant took part in a 30-60 minute interview conducted in a clinical setting or at the participant's usual place of living. A topic guide was drafted in consultation with the patient and public involvement (PPI) group who had personal experience of alcohol recovery. Following accepted practice in narrative inquiry research the initial part of the topic guide comprised open-ended questions to elicit alcohol recovery narratives, with minimal or no interruption from the researcher (258, 275). The participants were asked to narrate their alcohol recovery story over time with a beginning, middle, current situation, and future planning (258, 276). A sample interview guide is given in the supporting material (

Table 7-1). All interviews were video recorded, transcribed and pseudonymised.

Table 7-1. Sample interview guide alcohol recovery video interviews

What was life for you before you started using alcohol?
What triggered you to drink harmfully?
What was your social setup like?
How much you were drinking at peak?
What does recovery mean to you?
What gives you hope?

What makes you feel well?

What has helped your recovery?

What was your first step on your recovery journey?

What helped you take this step?

What works for you and why?

What activities have helped you?

How do you feel when you are doing them?

What has helped during times of hardship?

At what point did you realise that you needed support?

Where did you find the support? Was this challenging?

Who has supported you during your recovery journey?

What were the barriers to recovery?

How did you overcome them?

What has been unhelpful or missing in your recovery?

What have you learned about recovery?

Do you have any techniques that have been helpful when you are feeling down?

What sort of lessons would you like to pass on to others?

If you could give one thing to assist someone's recovery what would that be?

What has helped you to build resilience?

What would you tell someone who feels they won't recover?

How did you deal with changes to your recovery journey?

7.2.3.3 Principles to guide narrative collections

The following principles were adapted from a Scottish Recovery Network guide to facilitate narrative collection (277)

Control: Participants should always be in control of the process. Their story should not be altered or adapted. They should be able to decide what is shared, how it is shared and when it is shared.

Support: Participants should be given the time and resources they need to think through their story and to decide what they want to share.

Respect: Everyone's lived experience and recovery journey are different. The experiences of video participants should be respected.

Wellbeing: Sharing stories is an empowering experience but it can feel emotional and challenging at times. The well-being of the participants should always be at the centre of our considerations and be given as much time as they need to feel comfortable to

proceed. A participant has the right to withdraw if they feel that they are unable to start or continue

Responsibility: The participant sharing their story is ultimately responsible for deciding what they want to share, when and with whom.

7.2.3.4 Role of researcher

The role of the researcher was to support the participant in describing what their recovery from excessive alcohol use has meant to them and to facilitate producing authentic accounts. The researcher also checked with the interview participants about whether receiving transient elastography has had an impact on the participant's recovery (either positive or negative).

7.2.4 Analysis

The transcribed interviews were uploaded to NVivo version 12 (QSR International). Where possible the language used by participants was preserved while maintaining the clarity of analysis. Where the terms "alcoholic" or "alcoholism" were used by the participants to describe alcohol misuse, these have been retained.

All interviews were independently coded by two researchers (MS and UT), and the overall process was supervised by another researcher (SRE) with expertise in qualitative research.

A two stage narrative inquiry approach was used to analyse the narratives (275). The narrative inquiry as an approach focuses on to analyse of stories, autobiographies, and life experiences to understand how participants construct stories and narratives from their personal experiences (278). In narrative inquiry, stories are collected to explore one's experiences as lived and told, the recovery stories have a dual layer of interpretation (279). First, the narrator interprets and analyses their own recovery journey, and then the researchers explore the construction of their narratives (279).

The two stage deductive and inductive analysis consisted of the following steps : (a) organisation of data, (b) obtaining the general sense of narratives, (c) coding of narratives, (d) identifications of themes and subthemes, and (e) data interpretation and compilation of results (280).

Through stages d and e, the author also attended to the contents of coded transcript fragments and used this material to develop narrative descriptions of phenomena relevant to alcohol misuse recovery processes. These are summarised in the results section.

7.2.4.1 First stage

In the first stage, narratives were analysed deductively, using dimensions and types from the preliminary alcohol recovery narratives conceptual framework (ARNCF) as codes (Table 7-2) (270). This was to assess the fit of the existing alcohol recovery narratives conceptual framework (ARNCF) to the data.

Table 7-2. Alcohol recovery narratives conceptual framework (ARNCF)

Dimensions	**Types**			
Genre	Drama	Redemption	Drinking tale	Identity tale
Identity	Renewal	Construction	Formation	
Recovery setting (positioning)	Recovery within treatment	Recovery outside treatment		
Drinking trajectory	Upward	Fluctuating	Steady	Downward
Drinking behaviours and traits	Non-alcoholic	Alcoholic	Personality traits	
Stages (sequence)	Origin of difficulty	Episode of Change	Recovery	Ongoing struggle
Spirituality and religion	Religion versus spirituality	Belonging		
Recovery experience	Positive	Negative		

7.2.4.2 Second stage

In the second stage, the interview material not covered by the existing conceptual framework was inductively categorised into new codes. These codes were later classified as either new dimensions or types; thereby extending the alcohol recovery narratives conceptual framework (ARNCF).

7.2.5 Subgroup analysis

To explore the impact of participants' shared characteristics on ARNCF a subgroup analysis was conducted. The subgroups were adopted in priori from the previously published systematic review (270) and were further supplemented based on the initial

two-stage analysis and themes. The primary data were analysed for the following subgroups: (a) gender, (b) history of homelessness, and (c) mental health. Themes were insufficient for subgroup analysis based on sexual orientation. The two-stage analysis process was repeated to assess the validity of ARNCF for individual subgroups. We further conducted vote counting for individual categories in subgroups for the most frequently occurred codes.

7.3 Results

Eleven participants were recruited. Mean age was 56.0 years (SD +/- 9.9 years), six (54.5%) participants identified themselves as male and five (45.5%) as female. Ten identified as white whereas one participant identified with a minority ethnicity. Median alcohol intake of the whole cohort around their peak was 190 (range 105-300) units per week. The length of sobriety ranged from three years to over ten years. The median LSM was 14.3 (range 3.6-27) kilopascal (kPa). In three participants LSM was within in normal range (≤ 7 kPa), four participants had intermediate LSM (8-14 kPa), and four participants had advanced LSM in the range of cirrhosis (≥15 kPa). Two participants had a history of homelessness, five were unemployed, four were working, and two were retired. Only a single participant had engaged with Alcohol Anonymous (AA).

7.3.1 Comprehensiveness of alcohol recovery narratives framework (ARNCF)

The recently developed ARNCF comprised of eight dimensions: genre, identity, recovery setting, drinking trajectories, drinking behaviours and traits, stages, spirituality and religion, and recovery experience.

Eight dimensions were present in all narratives (Table 7-3). The type *spirituality versus religion* was not identified in any narratives, six participants expanded on *belonging*. There were no narratives from the LGBTQ+ community.

Table 7-3. Comprehensiveness of alcohol recovery narratives framework (ARNCF)

Participant	**Dimensions**							
ID	**Genre**	**Identity**	**Recovery setting**	**Drinking trajectory**	**Drinking behaviours and traits**	**Stages (sequence)**	**Spirituality and religion**	**Recovery experience**
P1	Yes	Yes	Yes	Yes	Yes	Yes		Yes
P2	Yes	Yes	Yes	Yes	Yes	Yes		Yes
P3	Yes	Yes	Yes	Yes	Yes	Yes		Yes
P4	Yes	Yes	Yes	Yes	Yes	Yes		Yes
P5	Yes	Yes	Yes	Yes	Yes	Yes		Yes
P6	Yes	Yes	Yes	Yes	Yes	Yes		Yes
P7	Yes	Yes	Yes	Yes	Yes	Yes		Yes
P8	Yes	Yes	Yes	Yes	Yes	Yes		Yes
P9	Yes	Yes	Yes	Yes	Yes	Yes		Yes
P10	Yes	Yes	Yes	Yes	Yes	Yes		Yes
P11	Yes		Yes	Yes	Yes	Yes		Yes

7.3.1.1 Genre.

All four types (drama, redemption, drinking tale, identity tale) were present in the narratives. The *drama* type had three subtypes. There is *Comedy theatre* where participants shared funny encounters they had during their recovery journey, *Quest* where one went on ventures to find recovery and start a new life, and in *melodrama* subtype narrators shared stories which were high in emotional content. Most participants apart from the two had redemptive narratives. In the *drinking tale* type the subtype's painful past, reinforcement, loss of uniqueness, relationship with oneself and helping others were present in all narratives. In the *identity tale* type the subtypes, “stages of life”, “sex”, and “marginalised societies” were present, whereas “sexual orientation” was not identified. The illustrative examples from participants' interviews are given in Table 7-4.

Table 7-4. Illustrative examples for Genre

	Quotes from narratives
Drama	
Comedy Theatre	I still learn stuff every day about alcohol, how to hide it, how to disguise your drinking and stuff like that. And it’s pretty funny some of it, like ‘oh I wish I’d thought of that’ you know?
Quest	‘That’s when we disappeared for three-four years, we went our own way and I said to ‘A’ I said ‘right, it’s me, you and Turbo, we’re going to sort this out in our head’ and then further down the line we decided to try and help people through things like this
Melodrama	‘The checking, I get anxious, I get thoughts, I’ve got negative thoughts going on in my head. I think I-I, you know, I get that silly side all the time, but I just get really worked up and wound up by things' ‘I think what a lot of it is, is people keep telling how talented, I get told that I taught Paul Smith everything he knows
Redemption	
Redemptive	I’ve got to be careful right through now, erm, I was perhaps fairly fortunate'. 'It was hard, it was hard. Erm, I didn’t want to die of liver disease, I don’t know if you’ve ever seen anyone, it’s not nice. I’ve got 5 children, I couldn’t. I thought I cannot, if that’s going to happen to me, I cannot have any of my family around me, I don’t want them to see me like that, yellow, bloated, horrible, I thought ‘I can’t do that’. And erm, I don’t want to die like that, it’s not nice, it’s slow, lingering, there’s nothing nice about it.
Non-redemptive	Well, I think sometimes there bloody is, the problem has been the problem, the other people’s problem that thinks I’ve got a problem, you know what I mean
Drinking tale	
	Find someone you trust and talk to them about it, don’t let them talk to you, you talk to them about it, because the last thing an alcoholic needs is somebody talking at them, they need to just take a step back, get them in a scenario where they will talk and let them talk because I think you’ll find, what within minutes they’ll come out with reasons why they actually drink a lot, and once they’ve said it, they’ve more or less been truthful to themselves, whereas if they weren’t given the opportunity to talk to somebody, they’ll carry on drinking

Painful past	'My husband divorced, and I got myself into a very bad relationship which was based on drink and that is when my drinking got serious'. 'My dad died, and I just went through a really big bad patch when I was on holiday and started drinking more and more and it just had a big effect on me, and it's just changed my life'. 'I think erm, my friend who committed suicide but rang me up before he did it, that was the killer for me in terms of drinking, that was just like, I couldn't cope, I really couldn't cope with that '.
Reinforcement	I was perhaps fairly fortunate in that erm, it was a, it wasn't a close friend but I played bowls with him, and he was diagnosed just maybe six months before me but he didn't stop drinking and he's not with us anymore and he used to give advice as well, he'd say 'whatever they say to you H, just do it', so I've tried to do that so support from that friend as well.
Loss of uniqueness	I'm just a regular person that likes Coro and Eastenders and things like that, erm, but also that regular person that's lost a lot.
Improved relation with oneself	I'm quite an intelligent person as well and erm, I just it just got hold of me
Helping other	Yeah, it does, honestly, it's been the hardest time of my life and I've got another chance now, and I'm going to make the most of it, and if I can help anybody, anybody, I will, I will, I feel for all of them out there, I really do, it's really cruel.
Identity tale	Erm, I don't really have much to do with men anymore, I try to keep that, you know, that's, I think my upbringing and the men in my life have been my main triggers erm.

7.3.1.2 Identity

During their recovery journeys, participants went through different stages of identity transformation including *identity renewal*, *identity construction* and *identity formation*. Participants shared emotions of guilt, shame and hitting rock bottom. They went through cognitive restructuring to construct a new identity.

> 'I just got to that real rock bottom that somehow, I just managed to stop (P2)'.

> 'Completely different, yeah, I have acceptance of myself today. I can't believe, I can't believe how the difference in myself, of my thinking, of who I am. In fact, even before I started drinking even you know err as a child up to my drinking, I am a different person, yeah (P2)'.

> 'Those friends that I met, voluntarily we set up an extra group and just people, I still see those people once a week every week now, three years on (P11)'.

Eventually, the participants adapted to their new roles and reconstructed their social relationships. The multiple stages of identity transformation involve a shift in

perspective, that may be sustained through positively reinforcing cues such as social processing of emotions, change in recovery capital, and self-nurturing. This shift in perspective eventually leads to a change from addictive to non-addictive behaviour.

7.3.1.3 Recovery setting

Most of the participants apart from one (P11) had *recovery within treatment settings*. The most common institutions participants formally interacted with included community alcohol services, community alcohol detox units, primary care substance misuse clinics, Alcoholics Anonymous, mental health services, and secondary care hospitals. The participants described their interaction within treatment settings as positive and supportive towards recovery.

> 'I went into that place in ….., and it was good, it was structured (P6)'.

> 'I decided to, through the help of my GP and my liver specialist, I sought out a local group and I volunteered myself (P8)'.

The participant who achieved *recovery outside treatment setting* (P11) particularly did not like group therapy and people telling them to stop drinking or change their behaviour. They disagreed with labelling and believed though they were drinking more than recommended they were still in control.

> 'I would read about it, I mean I always read what I could about being an alcoholic and how it creeps up on you and everything and about recovery and the twelve steps and sitting with a group of people saying, 'I'm an alcoholic' and I thought it's not for me, I don't want that. I actually ended up not saying anything cos I thought well I'm going to have to stop some of these people in order to say, 'I have a fairly normal life, I just drink too much bloody alcohol and I want help stopping it', but this isn't helping me I'm afraid, so that was the end of that. I never had that breakthrough; I could certainly never sit in a group and say, 'I'm an alcoholic (P10)'.

The person shared the natural recovery which is briefly described here. The natural recovery appears to exhibit an internal locus of control, whereby, the tendency to give control away to agents in the recovery setting may require the building of either trust over time with others, or a self-driven attempt to come full circle with one's addiction. This involves processing shame in some cases.

7.3.1.4 Drinking trajectory

In the drinking trajectory as a dimension, participants exhibited *upward*, *downward*, and *fluctuating* trajectories, whilst the *steady* drinking trajectory type was absent. Nine participants demonstrated a *slow* upward trajectory whereas two had a *sharp* upward trajectory. The participant further alluded to factors which supplemented different types of trajectories. Specifically, in the context of how ageing relates to drinking habits and the ensuing impact on addiction, participants displayed a tendency to account for their narrated experiences in terms of change in social and personal circumstances. This suggests that recovery narratives involve the socio-economic and highly personalised experience of ageing as a catalyst in piecing together the old identity one revisits, now, in narrating recovery retrospectively. The participants talked about the impact of retirement, change in social responsibilities, and surplus income supplementing increases in alcohol intake. Whereas a decline in physical health, enhanced family support and a change in social capital supported a reduction in alcohol consumption.

> 'I'd got my normal money going in, mortgage being paid, normal things being looked after and then this bonus money, so of course, the amount that I was drinking went up quite steadily (P7)'

> 'I'd started to drink a little more heavily I was what now is called an assistant head in a secondary school (P5)'

7.3.1.5 Drinking behaviours and traits

At the time of the interviews, seven participants were abstinent, three had significantly reduced alcohol intake and one participant was drinking in a controlled manner in line with the latest recommendations from the department of health. In relation to ARNCF, the following '*personality traits'* were present, passive, prosocial, anti-social, and dishonest. The grandiose trait was not observed.

In the context of reviewed narratives, 'prosocial' and 'passive' personality traits supported addictive behaviours. Participants began drinking due to peer pressure or in the form of companionship drinking largely in order to maintain social acceptance. On the other hand, a passive trait made participants vulnerable to abuse, exploitation, and manipulative practices by others, particularly where spousal relationships were involved. At the same time once, one became dependent on alcohol it promoted dishonesty and anti-social tendencies such as stealing, getting into a conflict, lying and self-harm.

'I used to be the, go to the pub on the way home from work, five o clock, couple of pints, you know with the mates and that kind of thing (P1)'

'I took me to a part in a very dangerous, dark time where I was considering taking my own life, laid on tram tracks, stole from shops, stole bottles of wine (P9)'.

7.3.1.6 Stages (sequence)

Most participants described recovery as a non-linear process, which involved dealing with setbacks such as relapse, adversities, social pressure, and multiple interactions with alcohol treatment services. Common triggers for alcohol misuse were, companionship drinking, occupational stressors, psychological trauma such as childhood abuse or toxic relationships, loss, grief due to the death of a family member or friend, mental health issues, and having surplus income or time. Participants described feelings of rejection, denial, acceptance, acknowledgement of the problem, and surrender eventually leading to a successful recovery. The most frequent turning points were, seeking help, having a near-death experience, being informed of having liver disease, changing from negative to positive social connections, self-realisation, and observing others having physical diseases due to alcohol. The illustrative examples from participant interviews are given in Table 7-5.

Table 7-5. Illustrative examples for stages

	Quotes from narratives
Origin of difficulty	
Start of drinking	I got divorced and then it just went, it spiralled downhill from then on. I think the killer for me was one of my friends rang me up, told me that he loved me and then committed suicide. And the first time I drank in the morning was at his funeral, that was the start
Negative effect	I thought it could kill the pain but [sighs] the pain I was suffering, but no
Drinking progress	We did have a lot of fun to be fair, but it just got a bit more and more and more
Problems	I lost my license; I lost my job
Drinking worsen	I would get a box of, I don't know, ten, the fridge packs, and a first that would last a couple of nights, then it would last a night, so you'd need to get a bigger box and a bigger box
Episode of Change	
Blame and escape	But we were very honest with the doctor about how much we were drinking, and he never said 'you need to stop that'

Identification of problem	It was just my friend, she picked us up cos you know your just collapsing and you're not able to do anything and you're getting all worked up and I thought 'ohh I'm fine' and she said 'not you're not, you're not looking after yourself
Alcoholic regression	It just gradually stopped, gradually
Rejection and denial	I think the thing that I could never be about alcohol and as I say right up this minute is I've never been honest about it, I always denied that I had a problem because in my head I didn't believe I had a problem
Turning points	I went to see my GP and they thought I needed help and that's when I got counselling and got support to just realise, I've got an issue
Recovery	
Acknowledging problem	It meant that I'd got severe damage to my liver and that I had to be careful.
Surrender	I'll be honest, when I gave up, obviously 'A' gave up and her liver failed, and she had that pain, but I made the decision to give up and I'll be honest and truthful
Acceptance	I think I drank all my emotions; I never had any acceptance of myself and erm, that's different today, I've worked, I've just worked through all that
Help	I think it's admitting that you needed help and to grab that help was a big thing for me, especially because I'd, I'd had such a long sobriety before.
Become sober	I had that done in the March and then I actually stopped drinking in the April. So, and I've been three years sober now
Ongoing struggle	
Being sober	I'm just, a small path, small path, I'm hoping that somehow it gets better. But it wasn't as easy as that.
Maintaining sobriety	I've told all my friends, relatives, everyone that I've given up drinking, so I have no social pressure and I avoid any social occasions where I'm on my own, so I'm not tempted individually to have a drink
Maintaining recovery	My friend had come up to visit me and I just had to be strong and just, I just decided, once you got through being detoxed, I just carried on, however hard that was, which it was, it was very hard to do, but err I managed to pull myself back up with help of other people of course

7.3.1.7 Recovery experience

Participants had a combination of *positive* and *negative* recovery experiences. The *positive* type was predominant across the narratives. The commonly recurring positive recovery experiences were empowerment, improved relationship, and family trust,

finding lost opportunities, enjoying doing things, and improved mental health. Participants revised their roles to better reintegrate into society and felt happy to be alive. On the other hand, they still experience wandering thoughts from their painful past, lost friends, and financial burdens. The associated physical and mental health comorbidities such as fibromyalgia, anxiety, and depression made life harder.

7.3.1.8 spirituality and religion

S*pirituality versus religion* as a type was not identified in the narratives. Participants did talk about a sense of belonging. *Belonging* as a type represented the adaptive feelings participants exhibited across key events to do with reintegration into society. In the *belonging* type, participants further shared experiencing a lack of belonging, a search for belonging and attaining belonging.

7.3.2 Subgroup analysis

7.3.2.1 Gender

Of all included participants six identified themselves as male and five as female. The females were younger with a mean age of 51.2 years (SD +/- 3.9) compared to males with a mean age of 59.9 years (SD +/- 10.6). The female participants displayed a tendency to consume a higher quantity of alcohol (units per week) at peak compared to males (mean 236.0, SD +/- 55.9 vs 164.1, SD +/- 36.6). Furthermore, on average females had higher liver stiffness measures (mean 15.2 kilopascals, SD +/- 8.6 vs 10.7 kilopascals, SD +/- 5.3). Female narrators sometimes included acknowledgements of the impact of harmful relationships with men as a trigger for alcohol misuse. Moreover, females expressed the feeling of drinking behind closed doors to avoid social stigma and shame.

> ‘Like most of my problems in my life have been bad choices in men. I don’t really have much to do with men anymore (female)’

> ‘I was never, I was a drinker behind closed doors, I was never a pub drinker or going out. I always used to do it in secret (female)’

> ‘I thought all the things I knew that I shouldn’t be thinking I just thought I could just control it, and I couldn’t. I think a lot of shame around that as well (female)’

7.3.2.2 Homelessness and alcohol recovery

Two participants had personal experiences of homelessness. Both shared history of a painful past, and a lack of sense of belonging making them vulnerable to addictive and anti-social behaviours.

> 'I've been taken to hospital that many times, I've been arrested that many times, erm, I'd been in fights, I'd had black eyes, I was, I've been sectioned. It took me to a part in a very dangerous, dark time where I was considering taking my own life, erm, tried numerous occasions, laid on tram tracks, stole from shops, stole bottles of wine, and obviously when I was homeless(P3).'

Recovery was only made possible within a treatment setting by a multiagency integrated healthcare approach involving mental health, community alcohol, and social care services. As part of recovery, they went through a significant identity shift from a non-functional person to a more functional and integrated member of society. Therefore, they found the path to recovery was hard but achievable within a holistic framework.

> 'I had that many fallbacks when I went through this process, it's not easy, I'm not going to say it's easy, nobody who has ever been in my position will ever say it's easy, cos it's not, it's not (P4).'

7.3.2.3 Alcohol and mental health

Alcohol misuse and mental health problems were common themes across all of the narratives. The analysis confirmed participants suffered from low personal self-esteem, cognitive dissonance, lack of love from others and a sense of belonging, denial, rejection, and shame. Mental health could be the cause or consequence of alcohol addiction.

> 'I was very anxious, very anxious. I think on the outside I always looked confident, so I always had that anxiety and fear and I always used to. I think what it did looking back, it gave me confidence that I never had to be, you know, to be in those, I think socially I was quite awkward as well, so it gave me that ability to be more confident, yeah (P2).'

Participants used alcohol as medication to numb the physical or psychological pain, suppress anxiety, and look more confident by surpassing internal conflict and insecurity.

> 'I just feel what happened to me could really happen to anybody. It's that alcohol is the best painkiller, is the best reliever of stress and anxiety that's out there (P3).'

Common mental health problems reported by participants were anxiety, depression, post-traumatic stress disorder often associated with childhood trauma or abusive relationship, obsessive-compulsive disorder, antisocial behaviours, lack of self-confidence, emotional instability, feeling on edge, and suicidal thoughts. The affective disorders were most prevalent across the group, influenced their construal of inter-personal reality driving, and acted as a driver for alcohol addiction. Although participants narrated that input from mental health services was useful both in obtaining and maintaining recovery, they were put off by long waiting times and felt let down by the system.

> 'They promised from a personal point of view, they said, 'you get clean and stay sober for say six months, we'll give you' and I have this in writing actually, he gave me therapy/counselling that I need, and he said, 'and you will have earned it'. Erm so I'm sober nearly three years and I'm still waiting, yeah, still waiting, so yeah, the system, I feel let down a bit by the system (P11).'

7.3.3 Refinement of alcohol recovery narratives framework (ARNCF)

Following due consideration, refinements were made to three dimensions; recovery settings, drinking trajectory, and drinking behaviour and traits. Based on themes identified across the interviews a new dimension of the *alcohol environment* was added (Table 7-6).

Table 7-6. Refinement of alcohol recovery narratives conceptual framework

Dimensions	Types
Recovery setting (positioning)	Recovery within treatment
Pre-existing subtypes	AA Narratives Dual diagnosis narratives Polydrug abuse narratives
New subtypes	Post hospitalisation narratives

	Post non-invasive tests (NITs) for liver disease narratives	
Drinking trajectory	Triggers for an upward trajectory Retirement Kids living independently Surplus income Surplus time	Turning points Decline in physical health Supporting partner
Drinking behaviours and traits	Personality traits	
Pre-existing subtypes	Antisocial Prosocial Passive Dishonest	
Missing subtype	Grandiose	
New subtype	Avoidance behaviour	
Alcohol environment	Policy and practice Affordability Availability Exposure and advertisement Constrained service Opportunistic testing Impact of pandemic	Social dynamics Acceptability Impact of pandemic

The recovery settings dimension originally represented the mode of recovery either within or out of formal treatment settings (former termed 'natural recovery'). In the type *recovery within treatment settings*, there were three subtypes, two further subtypes evolved through analysis of narratives, these were termed *post-hospitalisation narratives* and *post-non-invasive tests (NITs) for liver disease narratives*. Hospitalisation and interaction with medical healthcare providers facilitated the recovery.

> 'You know I'm lying in that hospital bed in the liver unit absolutely scared stiff and I didn't know why apart from reading the thing 'liver unit'. So, during that night, it was praying and also realism and truth, I was there in bed that night and I was facing the truth. My consultant, I said to him I said 'what is it? What else can I do to get my liver better?' he says, 'you're okay, well you're not okay but' he says, 'because you've taken the problem away from your liver, you should be okay (P3).'

Moreover, additional non-invasive tests (NITs) for liver disease conducted in primary or secondary care supported change. Participants said that knowledge of liver disease obtained by having a test such as transient elastography supplemented change in their drinking behaviour. In certain cases, participants preferred to have

follow-up tests. Here results appeared to induce feelings of reward in those who anticipated improvements based on the changes they had made since treatment began. At the same time, a low stiffness score was reassuring.

> 'So started at 27, 29, 27, the next time I went back it was 24, that was six months later. Six months later 19, so there's my motivation again 'ohh it's working, not drinking, my liver's getting better, it's getting softer (P8).'

> 'I think it would have knocked me more the other way if it had been bad, definitely, because I knew what I was doing, even though I couldn't stop. I think it, yes it would of, it would have had a different impact on me (P1).'

The *drinking trajectory* as a dimension describes the impact of ageing on drinking but lacks the details of the associated changes in socioeconomic circumstances. We observed that during the process of ageing the following factors acted as a trigger to increase alcohol consumption; retirement, kids starting living independently and having surplus income and time. Whereas a decline in physical health, a supporting partner acted as the turning point.

> 'But eventually erm after I retired, I got depressed, I had nothing to do, it was horrible, and of course, you're thinking about drinking (P5).'

> 'I'd got my normal money going in, mortgage being paid, normal things being looked after and then this bonus money, so of course, the amount that I was drinking went up quite steadily (P7)'

The *drinking behaviour and traits* as a dimension represent antecedents or consequences of alcohol misuse. We identified a new subtype which we have labelled *avoidance behaviour* related to alcohol misuse. Participants possessing this trait find it difficult to manage others and found alcohol as the route to escape from responsibilities.

> 'I knew it right from being a child that I couldn't control other people, and I didn't want to control other people, so internally I had a big conflict that each time I moved on I felt like I was moving away from the bit that I liked (P7).'

The current study provides information on ‘homelessness and alcohol misuse’ which hitherto remains absent in the previously proposed framework. In these participants, recovery was only possible by an integrated multiagency approach due to the complexity of associated social and mental health issues.

7.3.3.1 New dimension

Alcohol environment as a dimension comprises of following types, *policy and practice*, and *social dynamics*. The policy and practice iteratively inform each other wherein the former relates to the generation of ideas followed by the latter, which typically covers implementation concerns. Here, it describes the impact of alcohol-related policies on addictive behaviours and subsequent recovery. *Social dynamic* as a type indicates the impact of change in social practice over time. Based on emerging themes the following sub-types were found, affordability, acceptability, availability, exposure and advertisement, constrained services, pandemic, and role of opportunistic testing for early detection of liver disease in populations at risk.

Affordability describes the buying capacity of a person to afford alcohol. One can consume more alcohol if purchasing power is increased or otherwise can turn to cheap alternatives if purchasing power decreases. *Acceptability* describes the social acceptance of different drinking behaviours, specifically, our participants found that certain factors within a culture supported detrimental levels of alcohol consumption to the extent that was experienced as a normal behaviour validated by others. *Availability* describes the ease of access to alcohol. Our participants narrated that over the years alcohol has become easier to access due to policies such as changes in supermarket alcohol licensing and seasonal deals, allowing alcohol sales outside pubs with extended hours of business, and the adjacent propensity of drinking at home. *Exposure and advertisement* describe how alcohol has been promoted through multimedia, at times ambiguously labelled, or often lacking details concerning the harmful impact of alcohol on health. *Constrained services* describe the pressure on health services to deal with alcohol misuse and associated mental health problems in a timely manner, which can result in reduced trust among service users. The *Pandemic* describes the impact of the Coronavirus outbreak and imposed social restrictions on drinking behaviours. Participants described their alcohol consumption as increasing during the pandemic. *Early detection of liver disease* describes the impact of having non-invasive tests for liver disease and knowing the results. Participants narrated that by knowing the results of transient elastography supported

them to change addictive behaviour. The illustrative examples for policy and practice as a dimension are given in Table 7-7

Table 7-7. Illustrative examples for policy and practice

	Quotes from narratives
Affordability	I started work and one of the things that changed about drinking was that up to the 70s basically, if you wanted to drink you went to a pub, if you wanted to buy a bottle of beer to drink at home, you went to the pub and you bought it and it cost a lot of money. So, drinking at home wasn't really very much of an option. While money was a bit tighter but also you could buy cheap alcohol in the supermarket
Acceptability	It's a big part of our culture. English, British culture. I've had numerous discussions with my partner about this and erm, Britain as a country and as a society has, I think a very unhealthy attitude to alcohol.
Availability	The other problem is it's so readily available. It got to the point where you go into the supermarkets, they're on offer, so I would get a box.
Exposure and advertisement	I think people don't take a blind bit of notice and I think also on the packaging I mean the unit thing is, you look on a packet of cigarettes and it's the whole packet. But there's no advert with the poor, sad alcohol-dependent grandad, brother, uncle, sister, auntie
Constrained services	And I've been in touch and on the books with the mental health system for years, and they agreed that I have issues and need some help with them. Erm, but they wouldn't touch me because I was drinking, they said it was a dangerous road to go down,
Pandemic	During the lockdown, I wasn't, but I used to go to car boots and things, so I'd have somewhere to go, say a Wednesday, Saturday, Sunday, but I won't go near the motor if I've been drinking
Early detection of liver disease	It wasn't until the FibroScan that I realised how much damage I had actually done and how little time I had left, so check it out, kids

7.4 Discussion

7.4.1 Summary of key findings

The study validated and extended the preliminary alcohol recovery narrative conceptual framework (ARNCF) (270). All conceptual dimensions were present in collected narratives, with three of these dimensions extended by adding types and subtypes. A new dimension of the *Alcohol environment* was added to the framework. Which functions to discern and identify broader policy level as well as nested individual level factors driving various patterns of alcohol misuse. The included participants were predominantly white but represented diverse socioeconomic backgrounds including a history of homelessness, unemployment, varying degrees of severity of alcohol use disorder, and the stage of liver disease. Most participants apart from one achieved recovery within treatment settings. The most common institution participants interacted with was community alcohol services. The participant who achieved recovery outside treatment settings disliked labelling and group therapy. During the recovery, participants went through cognitive restructuring to build a new identity. Most participants described recovery as a non-linear process comprising multiple interactions with health services, relapses and struggles before eventually attaining recovery.

The triggers for drinking harmfully were very diverse and included companionship drinking, occupational stressors, psychological trauma such as childhood abuse or toxic relationships, loss, grief due to the death of a family member or friend, mental health issues, and having surplus income or time. In addition, I identified avoidance behaviour as a strong trigger for alcohol misuse. Whereas common turning points were seeking help, having a near-death experience, being informed of having liver disease, changing from negative to positive social connections, self-realisation, and observing others having physical diseases due to alcohol.

The female participants were younger than the male, of note, they consumed more alcohol at peak and had higher liver stiffness measures. As proposed in the original ARCF I observed social stigma and shame were common across female participants. The co-existing mental health issues were a recurring theme. Anxiety, depression, PTSD, emotional instability, OCD, and antisocial behaviour were common mental health problems.

7.4.2 Strengths and limitations

I adopted the pre-existing robust two stage methodology to analyse and synthesise the evidence which increases the validity of the refined framework (258). The included participants represented varying socioeconomic backgrounds, the severity of alcohol consumption, and the stage of liver disease. The study explored the novel idea of implementing opportunistic screening of liver disease in the population at risk by non-invasive tests (146) and found that not only does it facilitate early identification of liver disease it can supplement a change in high-risk drinking behaviours.

I included narratives of people who experienced homelessness associated with alcohol misuse and mental health issues. According to Public Health England 2021 report, there were over 274,000 homeless people in England (281). Homelessness could be a cause or consequence of addictive behaviours (282). The current study provides insight into the recovery dynamics of people with a history of homelessness, specifically, the cases suggest that homelessness increases vulnerability to addictive behaviours and chances of recovery are higher in structured recovery programmes. People with a history of homelessness are often underserved in healthcare research (283, 284). Dame Carol Black's 2020 independent review concerning illicit drug prevention, treatment, and recovery reported almost a quarter of people engaging with drug and alcohol services have severe housing problems and worryingly this was often associated with higher morbidity (285). In this context, the current study provides insight into the complex interaction of addiction, mental health problems and social issues associated with homelessness and could provide a framework for designing interventions to effectively address addictive behaviours in this group.

The limitations of the study include a lack of ethnic diversity, only a single participant was from a minority ethnicity group. This may be due to the majority coming in contact with alcohol and health care services are predominantly identified as belonging to the white ethnic background (16). The current study only recruited participants from the UK, interviews were conducted in the English language and none of the included narrators was from the LBBTQ^{+} group. The other point of consideration is that the mean age of the cohort was 56 years old which could potentially have an impact on the drinking trajectory. In this respect, a pool of younger participants may provide novel drinking trajectories and corresponding behaviours.

Religion versus spirituality as a type was not identified from these interviews. This in large may have been due to the under-representation of narratives from participants who experienced recovery within an AA setting. Spirituality in the AA setting functions

to instil a sense or belief in a higher power, so one may surrender to ground reality upon hitting rock bottom and acknowledging the need for a transformation (286). In this sense, spirituality and religion may have been a catalyst to recovery in the AA model (270). Participants did share experiences of belonging. Due to distinct and divergent behaviours across the cases with regard to the sense of belonging, there is potential for further exploration to determine any dimensionality in this regard.

7.4.3 Other evidence

The conceptual frameworks facilitate the understanding of complex health issues by characterising and breaking them into types and sub-types. Recent examples of the conceptual frameworks include the CHIME framework (connectedness; hope and optimism about the future; identity; meaning in life; empowerment), a framework describing mental health recovery narratives, childhood trauma, and social isolation (267, 287).

In the new dimension, *Alcohol environment,* participants shared their thoughts on common factors at the policy and practice level contributing to an increase in harmful alcohol consumption. Globalisation, ease of access, advertising, and increased buying capacity have facilitated a sharp rise in alcohol use (288). The fifth report of the Lancet commission on liver disease showed evidence of rising alcohol consumption and associated liver disease in the United Kingdom (289). The commission highlights an urgent need to change regulations concerning alcohol. The recommendations included the implementation of minimum unit pricing, increase funding for alcohol treatment services and close monitoring of advertisement and labelling of alcohol (289).

The dual diagnosis of alcohol use disorder and mental health issues is a recurring theme and is often related to poor outcomes (290). The chronic underfunding of drug and alcohol services in the UK and the lack of provision of integrated health care services including mental health services has only contributed to a soaring number of alcohol-related harm. A recent AUDIT of drug and alcohol services in Scotland, in 2020 showed funding cuts were related to increased drug-related deaths specifically among people from lower socioeconomic backgrounds (291).

In people exhibiting avoidance behaviour, social processing of emotions in self and others can impact a change in behaviour to promote drinking (292). Social cues one finds hard to cope with and may attempt to avoid initially, induce negative feelings, these may be processed through social interactions (processing) that enable the

individual to continue down a path of drinking (293). The pathological avoidance behaviour can also induce a variety of mental health problems such as anxiety, depression, and post-traumatic stress disorder (PTSD), the management involves the removal of trigger sources and cognitive restructuring (294). Actively addressing mental issues at both policy and practice level promote the longevity of sobriety (295).

7.4.4 Implications

The refined framework enhances understanding of recovery from alcohol addiction. Multiple dimensions and types were present across the narratives. The findings demonstrated that recovery from alcohol misuse followed a non-linear path and often required a multiagency approach. This supports the evidence from the original systematic review stating that there are multiple constituent dimensions with associated types and subtypes of alcohol recovery narratives (270). Furthermore, it highlights the need for an integrated healthcare model to effectively mitigate rising alcohol-related harm (296, 297).

The conceptual framework describes the characteristics of recovery narratives. It can be used to develop material which supports clinicians in comprehending the subtleties of the recovery journey described by patients during consultations, enhancing the clinician-patient relationship and opening communication channels. In turn, this might enable clinicians to make the most effective choices about treatment, by taking into account the complex influences sustaining alcohol misuse. The validated framework can provide structure for future research, policy making, and the development of personalised interventions for alcohol misuse.

7.5 Conclusion

The study validated the preliminary alcohol recovery narrative conceptual framework (ARNCF) and confirmed that alcohol recovery narratives are composed of multiple dimensions each with distinct types and sub-types. The findings demonstrate that recovery from alcohol follows a non-linear path and is often achieved through interactions with multiple services. Consequently, the study highlights the need for an integrated healthcare model involving a multiagency approach to effectively mitigate rising alcohol-related harm, holistically. The validated ARNCF can provide an enhanced approach to inform narrative-based research, policy, practice, and intervention development in the field of drug and alcohol addiction.

Chapter 8. KLIFAD: RCT

8.1 Rationale and Overview

Alcohol is an avoidable cause of liver disease if preventive measures are taken at an appropriate time (298). In 2020, Dame Carol Black conducted an independent review concerning drug and alcohol prevention, treatment, and recovery (285). In this context, the review specifically highlighted the unmet needs of this community and emphasizes that a greater focus is required on prevention. Systematic targeting of the risk factors for liver disease such as hazardous alcohol intake, high BMI, and type 2 diabetes in the community enhance the detection rate of significant liver disease and create a window of opportunities for effective measures such as behavioural interventions (60).

The data from Nottingham community alcohol services showed by opportunistic non-invasive testing of otherwise asymptomatic high-risk individuals 38% had raised liver stiffness measure (LSM), and of them, one in ten was in the cirrhotic range (299). At six months follow-up, the group with raised liver stiffness reduced alcohol intake by a median of 75.0 units per week compared to 25.0 units per week in the group with normal liver stiffness. This may imply the added behavioural impact of receiving feedback based on NITs for liver disease. A recent prospective study from Denmark recruited participants from the general population at risk of ARLD or non-alcoholic fatty liver disease (NAFLD). Participants had transient elastography, enhanced liver fibrosis (ELF) tests, and the FIB-4 score calculated. Participants subsequently received advice based on the results of their screening tests and were recommended lifestyle changes to treat or avoid liver disease (300). The screening was associated with a reduction in alcohol consumption, an increase in healthy eating, and weight loss of more than 3 kg after six months. The changes were more marked in people with a positive screening test. Due to methodological limitations of these studies such as observational design and lack of a control group, it is difficult to distinguish with certainty whether the desired effect was due to the participant's prior motivation, an invitation for the screening test, receiving the advice based on the of the test result, or due to combination of these factors.

In chapter 5 I presented findings from my systematic review with meta-analysis and demonstrated that providing feedback to individuals based on markers of liver injury could be an effective way to reduce harmful alcohol intake (62). One of the limitations of included studies was that no group received biofeedback without brief advice. A sensitivity analysis comparing biofeedback plus brief advice with a range of

alternatives showed a non-significant reduction in self-report alcohol intake and a significant reduction in GGT in the intervention group compared to the control group.

Recovery narratives have been used by healthcare practitioners as an intervention to support patients' recovery from physical and mental health problems (200, 301). Sharing illness narratives can also help patients to make informed choices on the selection of a specific treatment and can improve their compliance with it (201). The act of sharing alcohol narratives has been an important component of the AA 12-step programme (94). The use of recovery narratives is well established in mental health but relatively under explored in drug and alcohol services specifically in the UK (97, 98). Peer support from people who have recovered from alcohol misuse could be beneficial in modifying high-risk drinking behaviour (99).

In this chapter, I aim to present RCT (KLIFAD WP 3) evaluating the feasibility of integrating scripted feedback based on transient elastography results and alcohol recovery video stories as behavioural interventions in addition to usual care in community alcohol services.

8.2 Methods

8.2.1 Study population

Participants were recruited at three sites, Wellbeing Hub, Edwin House, and the primary care substance misuse clinic. Two of these sites Wellbeing Hub and Edwin House are run by Nottingham Recovery Network.

Wellbeing Hub is a Nottingham city centre based drug and alcohol service, in addition to drug and alcohol, the services also provide support for mental health, housing and employment. The majority of individuals self-present to these services, and a minority get referred by general practitioners (GP) or hospital based physicians and alcohol care teams.

Edwin House is a community based rehabilitation and detox facility for adults of age 18 years and over who experience physical and mental health problems due to drug and alcohol use disorder.

The primary care substance misuse clinic is run by Windmill GP surgery. The clinic is run on a self-referral basis. Individuals with drug and alcohol addiction are initially screened by one of the GP for suitability to the substance misuse clinic. Once in the

clinic, the individuals are attended by drug and alcohol support workers and GP with a special interest in drug and alcohol use disorder.

8.2.1.1 Eligibility criteria

The following eligibility criteria were applied (Table 8-1)

Table 8-1. KLIFAD eligibility criteria WP3 feasibility RCT

Work-package-3 the randomisation phase	
Inclusion criteria	Exclusion criteria
A person of age ≥18 years	Other primary substance misuses even where alcohol is a factor
The primary problem of alcohol misuse	Lacks the capacity to confirm consent
	Referrals from driving offences and student referrals[a]
	Out-of-area clients at Edwin house[b]
	Participants unable to comply with study procedures

[a]As these individuals are essentially not self-presenting, may have different motivations and have lower overall levels of alcohol use and so are at substantially lower risk of having liver disease

[b]In whom we cannot obtain follow-up data due to lack of follow-up availability

8.2.2 Sampling

8.2.2.1 Sample size

After a discussion with the community alcohol services data manager and considering variation in the number of patients presenting per week, we aimed to approach 40 eligible participants per month. Assuming a 50% consent rate we anticipated randomising 20 participants per month (10 per month per arm) for a recruitment period of six months. With an estimated sample size of 120, we were able to calculate a dropout rate of 80% within a 95% confidence interval of +/-7.1%. Assuming a non-differential follow-rate of 80%, this target sample size should provide follow-up outcome data on a minimum of 48 participants in each of the two arms.

8.2.2.2 Randomisation

The participants were individually allocated on a one-to-one ratio using minimisation with a probabilistic element. The minimisation variables were age, gender, ethnicity, and severity of alcohol misuse based on the Severity of Alcohol Dependence Questionnaire (SADQ) score. To minimise selection bias an online randomisation tool

(REDCap cloud) was used and the randomisation was externally performed by a data manager from Nottingham Recovery Network not directly involved in the study process. The REDCap cloud is a subscription (paid) based digital database developed by Vanderbilt University. In addition to other functions, it is also used for randomisation in clinical trials. Locally at Nottingham, the REDCap cloud is hosted and supported by Nottingham University Hospitals. Due to the nature of interventions, it was not possible to blind the participants or key alcohol workers

8.2.3 Intervention delivery

The usual care (control group) was compared to the usual care plus feedback based on LSM and watching ARVS (intervention group)

8.2.3.1 Intervention Group

Participants randomised to the intervention arm in addition to receiving usual care had liver stiffness measured by transient elastography, followed by feedback based on liver stiffness measure (LSM) results, and watched ARVS immediately after receiving the results. The ARVS were made available at services should a participant wish to watch them later. The participants were provided with a catalogue of ARVS with brief information (gender, peak alcohol intake, LSM) about the narrator and were given the liberty to choose to watch one or more ARVS of their choice.

8.2.3.2 Control group

Participants randomised to the control arm continued with standard treatment (usual care) provided at the three treatment settings. The participants in this arm were offered transient elastography at 6 months.

As part of standard treatment, the recruitment settings provide different types of interventions to participants in line with the National Drug Treatment Monitoring System Dataset (NDTMS) and Public health England (PHE) guidelines (302). Existing treatment programmes can run for up to 12 weeks.

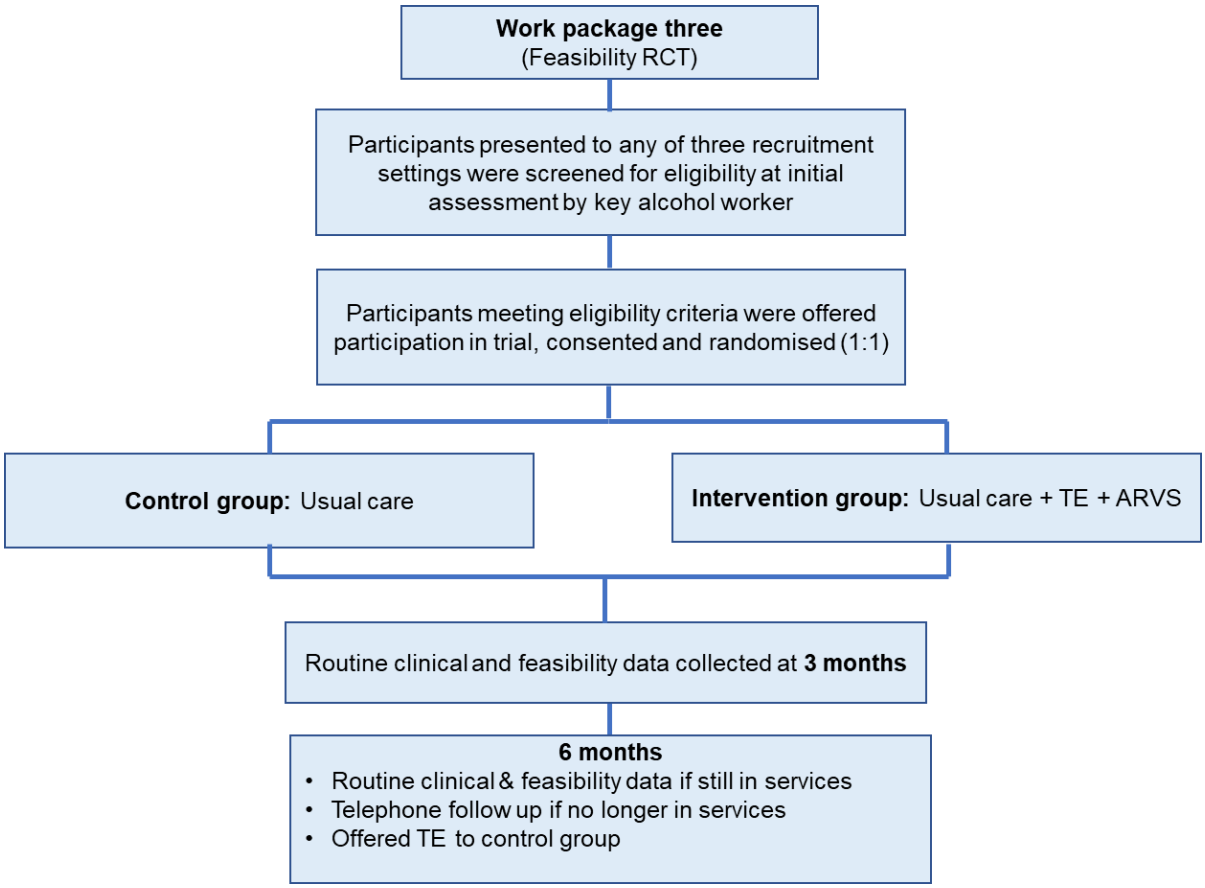
For adult drug and alcohol services, there are three main categories of standard intervention (usual care) delivered by the NRN:

a) Psychological: This includes motivational interventions, family and social network interventions, and cognitive and behavioural based relapse prevention interventions (substance misuse specific).
b) Recovery Support: This includes 12-step work and counselling.

c) Pharmacological: This involves prescribing medication for drug and/or alcohol relapse prevention support. For example, naltrexone, acamprosate, disulfiram as part of alcohol or opioid relapse prevention therapy and Chlordiazepoxide for acute alcohol withdrawal.

Specific treatment programmes are started after an initial assessment and based on the participant's needs. The duration of contact with services varies, most participants stay with services for 12 weeks, some get discharged early, and a few stay longer than six months. The flow chart for WP3 is given in Figure 8-1.

Figure 8-1. Flow chart WP3 feasibility RCT



8.2.3.3 Schedule of visits

8.2.3.3.1 Screening

All participants present to community alcohol services had initial screening by key alcohol workers. Participants were offered KLIFAD trial information, and their eligibility was assessed. Participants who met the eligibility criteria were offered participation in the KLIFAD trial, informed consent was taken, and randomisation was carried out.

8.2.3.3.2 Baseline

The baseline visit was the day when the participant started standard treatment at any recruitment setting. Participants in both arms had an initial detailed assessment as part of their standard care. This included the collection of baseline demographic and clinical data (e.g., age, gender, ethnicity). Participants randomised to the control arm continued with usual care while participants randomised to the intervention arm in addition to receiving usual care were given a further appointment to have transient elastography followed by standardised script feedback with ARVS watched immediately after receiving liver stiffness measure (LSM) results.

8.2.3.3.3 Three months

This visit was part of usual care, no research specific activity was carried out. The research data was extracted from routinely collected data at three treatment settings.

8.2.3.3.4 Six months

This was a telephone consultation or in-person appointment by the research team for participants no longer in treatment services. The research admin support worker unaware of group allocation contacted patients and arranged to follow-up call or face-to-face appointment with the researcher (MS or HK) blinded to randomisation. Each participant was contacted on a minimum of three separate occasions at least two days apart. Participants in the control arm were offered a FibroScan after the completion of outcomes. The six-month follow-up is specifically to cover those who were lost to follow-up at NRN from the treatment programme. A detailed schedule of the visits is given in Table 8-2

Table 8-2. Work package 3 (feasibility RCT) schedule of visits and variables for data

Study Activity	Baseline visit	3[a] Months	6[b] months
Control group			
Date & Time	Yes	Yes	Yes
Baseline consent	Yes	-	-
Fibroscan + Feedback	-	-	Yes
Watching video stories	-	-	Yes
Qualitative interview	-	-	Yes
Demographics	Yes	-	-
AUDIT score	Yes	Yes	Yes
SADQ score	Yes	Yes	Yes
Self-reported alcohol intake[c]	Yes	Yes	Yes
Breath alcohol test	Yes	Yes	Yes
Substance misuse other than alcohol	Yes	Yes	Yes
Data on feasibility outcomes	Yes	Yes	Yes
Intervention group			

Date & Time	Yes	Yes	Yes
Baseline consent	Yes	-	-
Fibroscan + Feedback	Yes	-	-
Watching video stories	Yes	-	-
Qualitative interview	-	-	Yes
Demographics	Yes	-	-
AUDIT score	Yes	Yes	Yes
SADQ score	Yes	Yes	Yes
Self-reported alcohol intake	Yes	Yes	Yes
Breath alcohol test	Yes	Yes	Yes
Substance misuse other than alcohol	Yes	Yes	Yes
Data on feasibility outcomes	Yes	Yes	Yes

(Alcohol Use Disorder Identification Test- AUDIT, Severity of alcohol dependence questionnaire-SADQ)
[a]3-months visit: this will be a routine visit no trial-specific procedure will be carried out
[b]6 -months visit: will be a telephone consultation and/or if possible/required in person. The participant in the control group will be offered a Fibroscan at 6 months if they attend it will be an in-person appointment
[c]Self-reported alcohol intake in grams and units per week

At Baseline, three and six months, the following data were collected (Table 8-2)

a) Demographics (including address, email address and contact number). This was archived and kept separate from the main database.
b) Alcohol Use Disorder Identification Test (AUDIT) scores.
c) The severity of Alcohol Dependence Questionnaire (SADQ) scores.
d) Self-reported alcohol intake (gram and unit per week).
e) Substance misuse other than alcohol.
f) Data on feasibility outcomes (e.g., screening rate, recruitment rate, retention rate).

All the above measurements are part of routine outcome data collected by all three recruitment settings, apart from the six-month data collected for those who are no longer in a treatment programme at six months. All three services included in this trial record all of the above outcomes as part of the 12-week programme standard data set and report these to commissioners. Follow-up data were obtained at every attendance and includes the above dataset breath alcohol testing.

8.2.4 Outcomes

The outcomes were designed to assess the feasibility and acceptability of the KLIFAD intervention and research processes to help inform a future large-scale RCT. The following outcomes are reported:

a) Recruitment rate.
b) Retention rate.
c) Consent rate.
d) Acceptability of the intervention (FibroScan and ARVS).
e) The willingness of participants to be randomised to trial arms.

f) Acceptability of the intervention to patients.
g) Participant adherence.
h) Feasibility of outcome measures.

These feasibility outcomes will enable the trial team to:

a) Determine the best primary endpoint for the future definitive trial.
b) Provide sample size estimates for the future definitive trial.
c) Record ARVS which will contribute to the video library used in a later large-scale RCT.

8.2.5 Statistical and data analysis plan

The analyses of the quantitative data were in line with Consolidated Standards of Reporting Trials (CONSORT) guidelines for pilot and feasibility trials (303). Sekhon et al's (2017) framework for acceptability testing was used (304).

As per consort reporting guidelines and to reflect the true effect of KLIFAD intervention intention-to-treat and per-protocol analyses were conducted (305, 306). In per-protocol analysis participants with missing data, who lost to follow-up, or who did not receive allocated intervention were excluded. As per protocol, a complete case analysis was conducted no data imputation was performed.

Data were summarised using frequency (%), mean (SD) or median (IQR) depending on the distribution of the data. The correlation between normally distributed quantitative variables was assessed by parametric tests (Pearson's correlation coefficient, T-test, ANOVA test) and non-normally distributed by non-parametric tests (Spearman's correlation coefficient, Mann-Whitney U test). Categorical variables were analysed by the Chi-Squared test/fisher's exact test, with results reported as absolute and relative frequencies ± 95% confidence interval. Summary measures are presented along with their 95% confidence intervals whenever appropriate. The results of the data analysis are presented using appropriate tables and graphs.

The trial was not powered to investigate statistical significance between the two arms. The results of the feasibility variables are presented by categories of different variables (age, gender, ethnicity, severity of alcohol misuse).

8.2.6 Ethical considerations

8.2.6.1 Ethical approval

The trial received favourable ethical approval from the West of Scotland Research Ethics Service (WoSRES) on 20th January 2021, REC reference: 20/WS/0179. ISRCTN16922410. The work presented in this paper has informed the conduct of a clinical trial (ISRCTN 16922410, prospectively registered on 26/01/2021). The trial protocol was published prospectively (156).

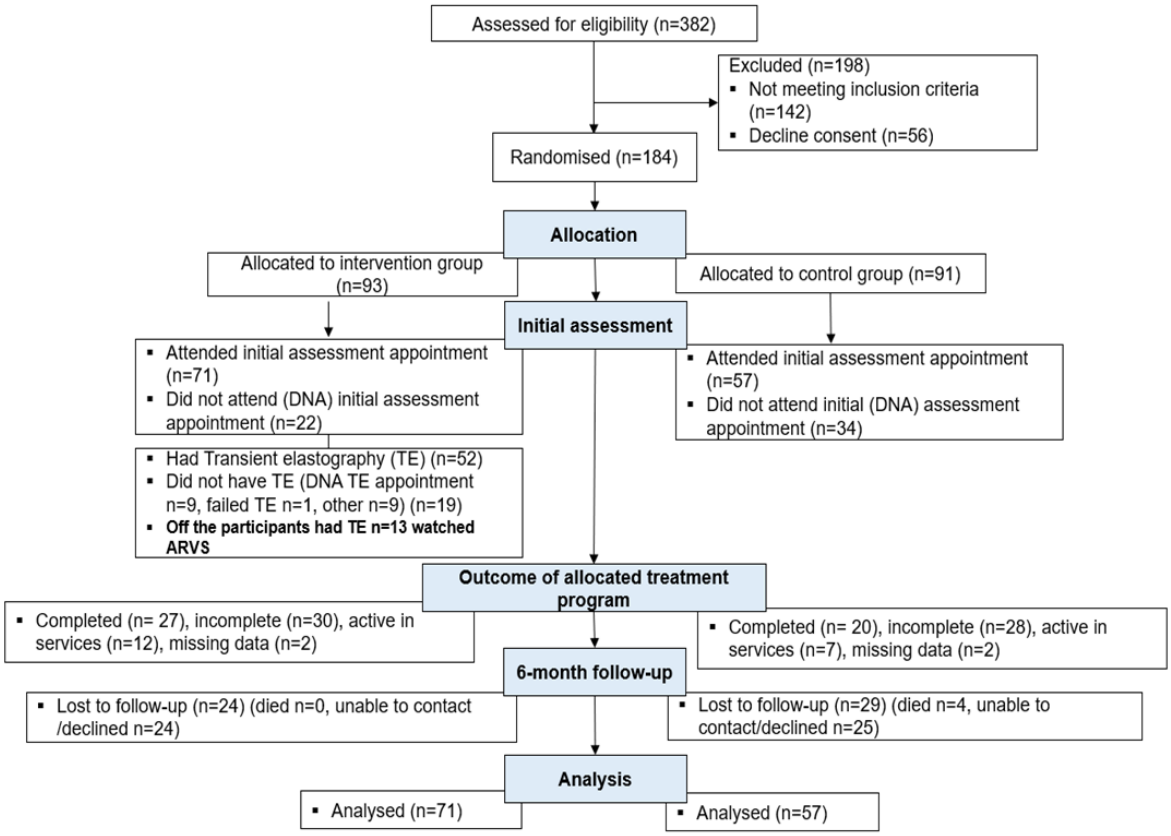
8.2.6.2 Ongoing care

It is anticipated that a small number of people will be identified who have previously unknown cirrhosis and so would be at risk of complications of liver disease. This will be mitigated by offering onward referral to hepatology outpatient for all participants with a liver stiffness measure ≥15 Kilopascal(kPa). This will be via contact with the participant's GP and would follow the current NUHT Nottinghamshire adult liver disease stratification pathway for referral (307). Some risk mitigations will be through the feedback included in this trial which covers cirrhosis.

8.3 Results

A total of 382 individuals were assessed for eligibility in three recruitment settings. Of them, 184 patients were randomised (intervention group n=93, control group n=91). Of randomised patients, 128 (intervention group n=71, control group=57) attended post-randomisation baseline appointments and were included. The follow-up rate at 6 months for the control group was 49.1% (n=28/57) and 66.1% for the intervention group (n=38/71). The detailed breakdown of enrolment and follow-up is provided in the consort flow diagram (Figure 8-2).

Figure 8-2. Consort flow diagram



8.3.1 Baseline characteristics of the study population

The mean age was 43.9 years (SD=11.9), and the majority identified as male (*n*=94, 73.4%), white (*n*=106, 82.8%), and heterosexual (*n*=115, 89.8%). Median self-reported alcohol intake at baseline was 28 days (range 1-28) per month and 26 units (range 2-73) per day. On the AUDIT assessment, 92.8% (n=116) had possible alcohol dependence, on SADQ, 54.3% (*n*=69) had severe alcohol dependence. Over a quarter were using substances other than alcohol (*n*=25, 27.35), 22.8% (*n*=29) had a

co-existing disability, 75.8% (*n*=97) had mental health diagnosis and 39.5% (*n*=49) were employed. The baseline characteristics of the study population are given in Table 8-3

Table 8-3. Baseline characteristics of participants

	Control group (n=57)	Intervention group (n=71)	p	Total (n=128)
Age (mean)	43.6 +/- 10.6	44.4 +/- 12.9	0.719[a]	43.9 +/- 11.9
Gender			0.389	
Male	44 (77.2)	50 (70.4)		94 (73.4)
Female	13 (22.8)	21 (29.6)		34 (26.6)
Sexuality			0.999	
Heterosexual	52 (91.2)	63 (90.0)		115 (90.6)
LGBTQ+	5 (8.8)	7 (10.0)		12 (9.4)
Missing	0	1		1
Religion			0.911	
None	40 (70.2)	47 (67.1)		87 (68.5)
Christian	12 (21.1)	17 (24.3)		29 (22.8)
Other	5 (8.8)	6 (8.6)		11 (8.7)
Missing	0	1		
Ethnic Origin			0.641	
White	46 (80.7)	60 (84.5)		106 (82.8)
Minority	11 (19.3)	11 (15.5)		22 (17.2)
Disability			0.400	
Yes	15 (26.8)	14 (20.0)		29 (22.8)
None	41 (73.2)	56 (80.0)		97 (76.4)
Missing/Not stated	1	1		1
Mental Health			0.837	
Yes	44 (77.2)	53 (74.7)		97 (75.8)
None	13 (22.8)	18 (25.3)		31 (24.2)
Housing problem			0.999	
Yes	8 (14.0)	10 (14.1)		18 (14.1)
No	49 (86.0)	61 (85.9)		110 (85.9)
Employment Status			0.382	
Employed	20 (35.1)	29 (40.8)		49 (39.5)
Unemployed	12 (21.1)	15 (21.1)		27 (21.8)
Long term sick or disable	20 (35.1)	18 (25.4)		38 (30.6)
Student	1 (1.8)	5 (7.0)		6 (4.8)
Retired	1 (1.8)	3 (4.2)		4 (3.2)
Other/Not Stated	3 (5.3)	1 (1.4)		4
Substance use other than alcohol			0.815	
Yes	15 (26.3)	20 (28.2)		35 (27.3)
No	42 (73.7)	51 (71.8)		72.7
Drinking Days (month[c])				
	23.3 +/- 7.8	22.6 +/- 7.8	0.627[a]	22.9 +/- 7.8

Daily alcohol intake				
Daily (units)	28 (3-73)	24 (2-71)	0.429[b]	26 (2-73)
AUDIT score (median)				
	32 (12-40)	31 (12-40)	0.462[b]	32 (12-40)
AUDIT category			0.712	
Hazardous (8-15)	2 (3.6)	1 (1.4)		3 (2.4)
Harmful (16-19)	3 (5.4)	3 (4.3)		6 (4.8)
Possible dependence (≥20)	51 (91.1)	65 (94.2)		116 (92.8)
Missing/Not stated	1	2		3
SADQ SCORE			0.975	
Non-dependent (0-7)	4 (7.0)	4 (5.7)		8 (6.3)
Mild dependence (8-15)	7 (12.3)	9 (12.9)		16 (12.6)
Moderate dependence (16-30)	16 (28.1)	18 (25.7)		34 (26.8)
Severe Dependence (31-60)	30 (52.6)	40 (56.7)		69 (54.3)
Missing/Not stated		1		1
Liver stiffness measure (kPA)				
Low (≤ 7 Kpa)		41 (78.8)		
Intermediate (8-14 kPa)		4 (7.7)		
Advanced (≥ 15 kPa)		7 (13.5)		

Mean (SD), median (range), number (%)

[a]Parametric tests, [b]non-parametric tests, [c]per four weeks

8.3.2 Liver stiffness measure

Of the 52 participants who had transient elastography, 21.2% (*n*=11) had raised LSM (≥8 kilopascals) (Table 8-3). Of the participants who had transient elastography 25.0% (n=13) watched ARVS. Length of appointment and not being able to access ARVS at home were the most common reason for not accessing the videos.

8.3.3 Intervention versus control group

At baseline, there were no significant differences in mean age, median drinking days per month, daily self-reported alcohol intake, and distributions for gender, sexual orientation, religion, ethnic origin, disability, mental health, housing problems, employment status, substance use other than alcohol, AUDIT categories, and SADQ categories between the intervention and control groups (Table 8-3).

8.3.4 Completion of the allocated treatment program at services

Intention to treat analysis: The mean duration of engagement with services for the intervention group was 159.0 days (SD=10.6.4) and for the control group was 150.4 days (SD=100.2) (mean difference 8.6 days SD=18.4). In the control group, 35.1% (n=20) completed the allocated treatment program by either reducing alcohol intake

or stopping drinking, 15.8% (n=9) dropped out, 26.3% (n=15) delined treatment, and 7.0% died (n=4). Whereas in the intervention group, 42.3% (n=30) completed the allocated treatment program by either reducing alcohol intake or stopping drinking, 14.1% (n=10) dropped out, and 28.2% (n=20) delined treatment There was no reported death in the intervention group. In the intervention group, 16.9% (n=12) were still active in service at the end of the trial (stopped drinking n=5, 7.0%, reduced alcohol intake n=7, 9.9%). In the control group 12.3% (n=7) were still active in service at the end of the trial (stopped drinking n=4, 7.0%, reduced alcohol intake n=1, 1.8%, increased alcohol intake n=2, 3.5%) (Table 8-4).

Per-protocol analysis: The mean duration of engagement with services for the participants who had transient elastography was 180.1 days (SD=107.1) and the follow-up rate at 6 months was 73.1% (n=38/52). In the control group, 36.4% (n=20) completed the allocated treatment program by either reducing alcohol intake or stopping drinking, 16.4% (n=9) dropped out, 27.3% (n=15) delined treatment, and 7.8% (n=4) died (n=4). In the intervention group, n=52 had transient elastography, of these 48.0% (n=24) completed the allocated treatment program by either reducing alcohol intake or stopping drinking, 8.0% (n=4) dropped out, and 22.0% (n=11) delined treatment. In the intervention group, 22.0% (n=11) were still active in service at the end of the trial (stopped drinking n=5, 10.0%, reduced alcohol intake n=6, 12.0%). In the control group 12.7% (n=7) were still active in service at the end of the trial (stopped drinking n=4, 7.3%, reduced alcohol intake n=1, 1.8%, increased alcohol intake n=2, 3.6%) (Table 8-4).

Table 8-4. Completion of the allocated treatment program at services

Table 2: Completion of the allocated treatment program at services

Intention to treat analysis	**Control group (n=57)**	**Intervention group (n=71)**
Incomplete died	4 (7.0)[a]	0 (0.0)
Incomplete dropped out	9 (15.8)	10 (14.1)
Incomplete declined	15 (26.3)	20 (28.2)
Completed alcohol free	9 (15.8)	14 (19.7)
Completed occasional alcohol user	11 (19.3)	13 (18.3)
Active in services alcohol free	4 (7.0)	5 (7.0)
Active in service occasional alcohol user	1 (1.8)	7 (9.9)
Active in service increased alcohol intake	2 (3.5)	0 (0.0)
Missing	2 (3.5)	2 (2.8)

Per-protocol analysis[b]	Control group (n=51)	Intervention group (n=41)
Incomplete died	4 (7.3)	0
Incomplete dropped out	9 (16.4)	4 (8.0)
Incomplete declined	15 (27.3)	11 (22.0)
Completed alcohol free	9 (16.4)	13 (26.0)
Completed occasional alcohol user	11 (20.0)	11 (22.0)
Active in services alcohol free	4 (7.3)	5 (10.0)
Active in service occasional alcohol user	1 (1.8)	6 (12.0)
Active in service increased alcohol intake	2 (3.6)	0
Missing	2	2
Subgroup analysis (watched ARVS)	**Yes (n=13)**	
Incomplete dropped out	1 (9.1)	
Incomplete declined	3 (27.3)	
Completed alcohol free	2 (18.2)	
Completed occasional alcohol user	2 (18.2)	
Active in services alcohol free	0	
Active in service occasional alcohol user	3 (27.3)	
Missing	2	

Data are in number (%), (ARVS-alcohol recovery video stories)

[a]Deaths were unrelated to study procedures/interventions

[b]Participants with missing data and who did not have transient elastography were excluded

Alcohol free: participants stopped drinking alcohol

Occasional alcohol user: participants reported a reduction in alcohol intake

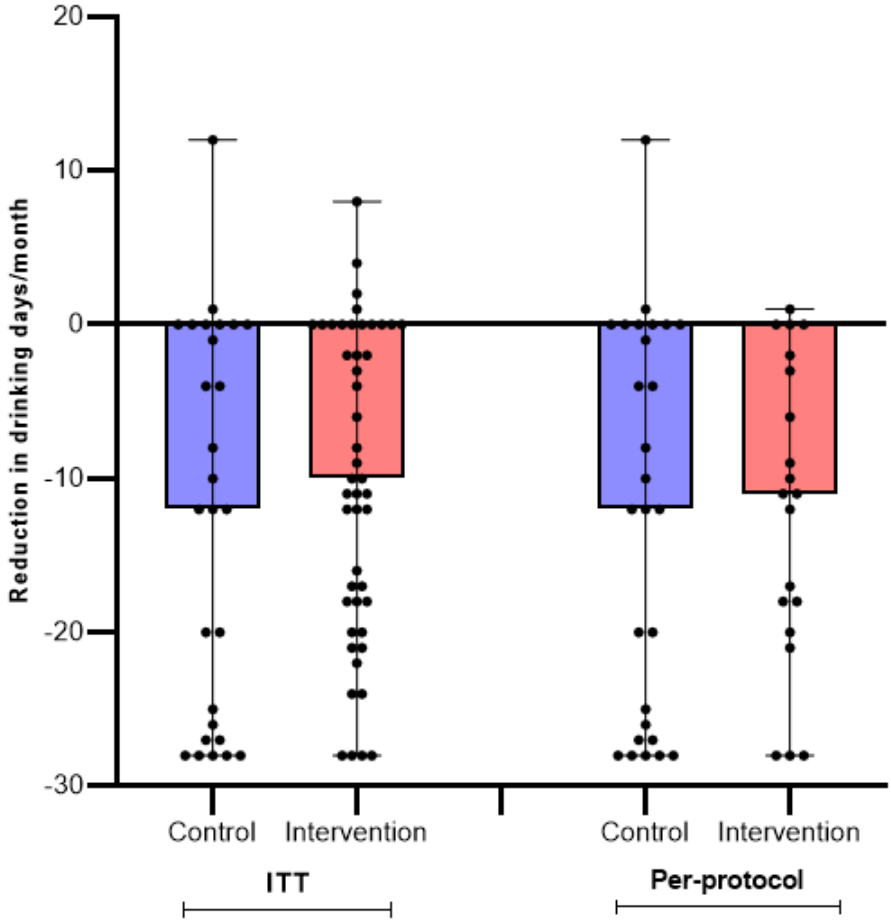
8.3.5 Self-reported alcohol

8.3.5.1 Reduction in drinking days per month

Intention to treat analysis: median reduction in drinking days by the control group was -12.0 (range 12.0, -28.0) days per month compared to -10.0 (range 8.0, -28.0) days per month in the intervention group (Figure 8-3).

Per-protocol analysis: median reduction in drinking days by the control group was -12.0 (range 12.0, -28.0) days per month compared to -11.0 (range 1.0, -28.0) days per month in the intervention group (Figure 8-3).

Figure 8-3. Median reduction in drinking days per month

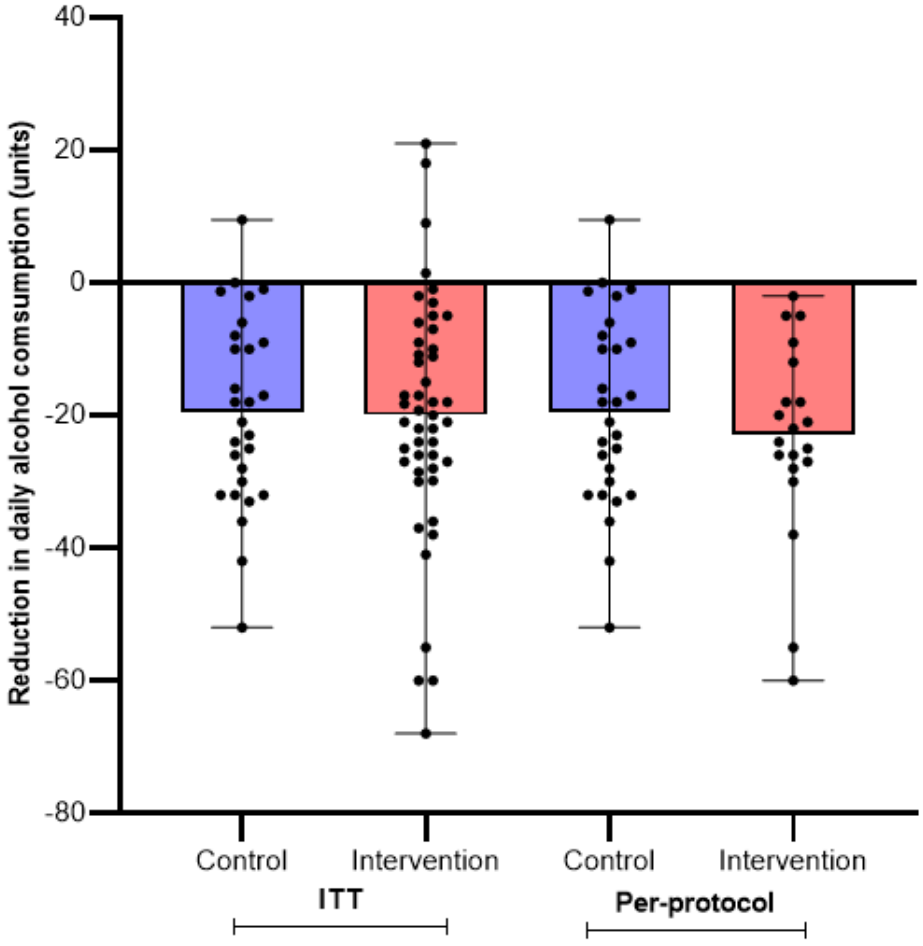


8.3.5.2 Reduction in daily alcohol consumption (units)

Intention to treat analysis: median reduction in daily alcohol consumption by the control group was -19.5 (range 9.5, -52.0) units per day compared to -20.0 (range 21.0, -68.0) units per day in the intervention group (Figure 8-4).

Per-protocol analysis: median reduction in daily alcohol consumption by the control group was -19.5 (range 9.5, -52.0) units per day compared to -23.0 (range -2.0, -60.0) units per day in the intervention group (Figure 8-4).

Figure 8-4. Median (range) reduction in daily consumption of alcohol (units)



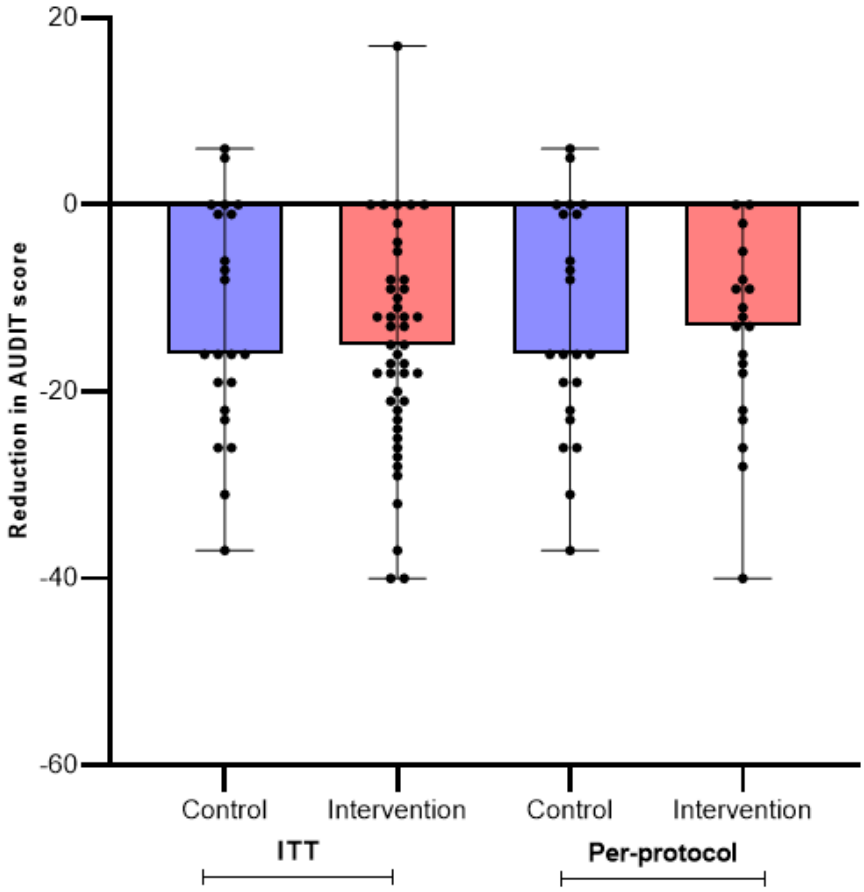
8.3.6 Alcohol use disorder identification test (AUDIT)

8.3.6.1 Change in AUDIT score

Intention to treat analysis: the control group had a median reduction of -16.0 (range 6.0, -37.0) in AUDIT score compared to -15.0 (range 17.0, -40.0) in the intervention group. Two participants in the control group and one in the intervention group had an increase in AUDIT score (Figure 8-5).

Per-protocol analysis: the control group had a median reduction of -16.0 (range 6.0, -37.0) in AUDIT score compared to -13.0 (range 0.0, -40.0) in the intervention group. Two participants in the control group and none in the intervention group had an increase in AUDIT score (Figure 8-5).

Figure 8-5. Median reduction in AUDIT score



8.3.6.2 Change in the AUDIT category

Based on the AUDIT score at baseline 88.9% (n=24) in the control group and 94.6% (n=35) in the intervention had possible alcohol dependence, and no participant was in the low-risk category. At 6 months 35.7% (n=10) in the control group and 36.8% (n=14) in the intervention group had possible alcohol dependence. Moreover, 25.0% (n=7) and 28.9% (n=11) in control and intervention respectively had AUDIT scores consistent with no alcohol use disorder (Table 8-5).

Table 8-5. Change in AUDIT Category at 6 months[a]

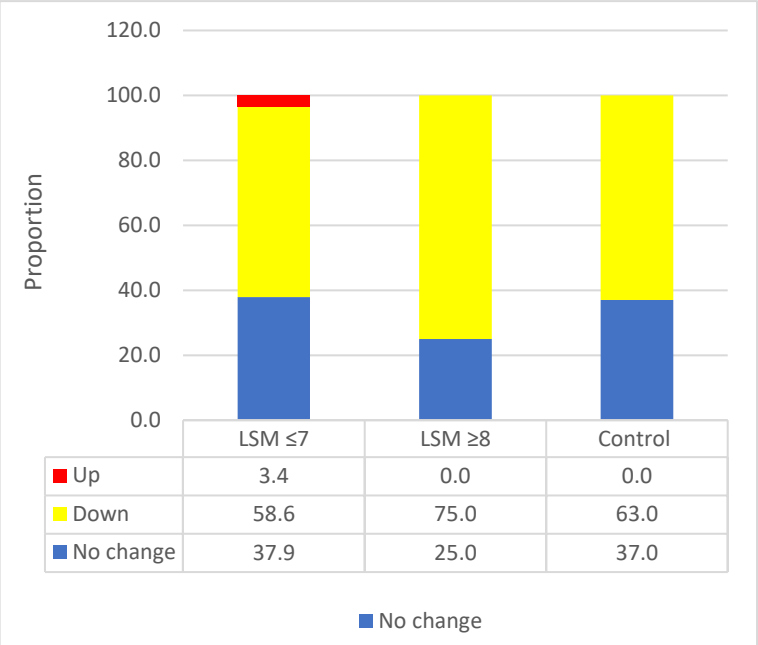
	Baseline[b]	
AUDIT category	Control group (n=28)	Intervention group (n=38)
Low risk (0-7)	0	0 (0.0)
Hazardous (8-15)	1 (3.7)	0 (0.0)
Harmful (16-19)	2 (7.4)	2 (5.4)
Possible dependence (≥20)	24 (88.9)	35 (94.6)
Missing/Not stated	1	1
	6 months	
Low risk (0-7)	7 (25.0)	11 (28.9)
Hazardous (8-15)	9 (32.1)	10 (26.3)
Harmful (16-19)	2 (7.1)	3 (7.9)
Possible dependence (≥20)	10 (35.7)	14 (36.8)
Missing/Not stated	0	0

[a]Per-protocol analysis including participants who had transient elastography
[b]Baseline characteristics of participants still in follow-up at 6 months

8.3.6.2.1 Increase or reduction in AUDIT category based on TE results

At end of the 6-month follow-up period, 58.6% (n=17) of participants with normal LSM, 75.0% (n=6) with raised LSM, and 63.0% (n=17) in the control group reduced the AUDIT at least by one category. Only one participant with normal LSM demonstrated an increase in the AUDIT category (Figure 8-6)

Figure 8-6. Change in AUDIT category at end of 6 months follow-up period (LSM- liver stiffness measure)



8.3.7 Subgroup analysis: Participants watched alcohol-recovery video stories

Of the participants (n=52) who had transient elastography (TE) 13 watched alcohol recovery video stories. The mean age of these participants was 43.7 years (SD +/- 15.5), 69.2% (n=9) were male, and 23.1% (n=3) had raised liver stiffness measure. The mean duration of engagement with services for these participants was 174.1 days (SD=97.89).

Among the participants who watched ARVS the outcome data on the allocated treatment program was available in n=11, of them 9.1% (n=1) dropped out of alcohol services, 27.3% (n=3) declined the treatment program, 45.5% (n=5) completed the allocated treatment program and stopped drinking, 18.2% (n=2) allocated treatment program and reduced alcohol intake (Table 8-4). Median self-reported alcohol intake at baseline was 28 days (range 3-28) per month and 20 units (range 12-37) per day. The median AUDIT score at baseline was 29 (range 12-40) and the SADQ score was 19 (range 0-60). At 6 months, the median, drinking days were 4 days (range 0-28) per month, daily alcohol consumption was 6 units (range 0-7) per day, and the AUDIT score was 18 (range 2-27).

8.3.8 Summary of key findings

The study demonstrated that the integration of non-invasive testing of liver stiffness by transient elastography into community alcohol services is feasible. Of the eligible individuals, 77% gave informed consent, 65% completed the allocated 12-week treatment program, and 59% attended the six-month trial specific follow-up.

This intervention detected a significant, previously unknown, burden of liver disease. In this asymptomatic but high-risk group, we show that one in five had a raised liver stiffness measure, and of particular concern one in seven of them were in the cirrhotic range. The community burden of undiagnosed liver disease, especially in a high-risk population is an ongoing concern among the liver community (308). The population based studies using non-invasive tests for liver disease report around 5% of the general population and 18-27% of the at-risk population have undetected significant liver fibrosis (309). The integration of non-invasive testing for liver disease into community alcohol services provides a unique opportunity for early detection of liver disease in an otherwise high-risk asymptomatic population. The National Institute for Health and Care Excellence (NICE) guidelines state adults with high levels of alcohol dependency should be assessed and offered intensive structured community-based interventions (with or without medical therapy) as these provide the best chance of achieving and maintaining abstinence from alcohol (25).

While not powered to show a statistical difference in key indicators of behaviour change related to alcohol intake, there were very promising trends shown in our study. Intervention compared to the control group had a longer duration of engagement with services (mean difference 8.6 days SD=18.4), was more likely to complete the allocated treatment program (38.0%-vs-35.1%), stop drinking (19.7%-vs-15.8%), and reduce AUDIT category (57.8%-vs-53.2%). At six months, the intervention group reduced their self-reported alcohol intake by 23 units per day compared to 19.5 units in the control group and 28.9% in the intervention group were free of AUD compared to 25.0% in the control group based on AUDIT. Participants who received transient elastography were more likely to attend further assessment appointments, stay in services, and complete the allocated treatment program. Reassuringly a normal liver stiffness result did not provide false reassurance to participants with no evidence of an increase in self-reported alcohol consumption or AUDIT category.

8.3.9 Strengths and limitations

This is the first randomised control trial to demonstrate the feasibility of the addition of feedback based on liver stiffness measures into community alcohol services. Alcohol treatment services are an ideal setting for early diagnosis of ARLD and interventions to prevent further physical harm. There is a large burden of undiagnosed liver disease in the community. By integrating non-invasive liver stiffness testing into these services, it creates an opportunity to change the natural history of disease progression in high-risk individuals (9).

This study does have limitations. The patient sample may not be representative of all harmful drinkers. Most individuals who attend the community alcohol services have self-presented and often have high levels of dependency; this is likely to have introduced selection bias. Due to the nature of the intervention, it was not possible to blind the participant to the intervention. The other limitations include the study conducted at a single centre with a predominantly white ethnic distribution. The study was to demonstrate the feasibility, the future RCT aims to be more inclusive to overcome these limitations.

Transient elastography was performed on participants without any prior specific preparation, factors such as non-fasting status, and active drinking might have impacted the liver stiffness measure (310). Moreover, factors such as a high coefficient of variation, and LSM confounders (BMI >28 kg/m^2, liver inflammation, operator experience, cholestasis, and liver congestion) limit its use as a surveillance tool for liver fibrosis (311). In the current study, LSM was used as a component complex intervention to supplement change in high-risk drinking behaviour.

Only a quarter of participants watched the alcohol recovery video stories (ARVS). These participants showed a reduction in drinking days, daily alcohol consumption and in AUDIT score. Based on preliminary analysis of semi-structured interviews and feedback from key alcohol workers the length of the appointment and restricted access to ARVS only at recruitment services were the most common reasons for not watching ARVS. Studies from mental health settings have demonstrated that mental health recovery narratives can be integrated into web-based interventions (312), learning from this we plan to revisit the strategy of sharing the ARVS because there is evidence from other studies that the addition of recovery stories helps mental health illness and addiction recovery (97, 98). The addition of recovery stories helps one's mental health illness and addiction recovery (97, 98). Peer support from people who have recovered from alcohol misuse had been proven beneficial in modifying high-

risk drinking behaviour(99). Recovery narratives have also been used by healthcare practitioners as an intervention to support patients' recovery from physical and mental health problems (200, 301). For example, recovery narratives have been used in stroke rehabilitation, where they can help patients to reorient their identity toward the possibility of recovery post-stroke (200). Sharing illness narratives can also help patients to make informed choices on the selection of a specific treatment and can improve compliance (201).

8.3.10 Other evidence

The recruitment and retention rates were higher than what was previously demonstrated in primary care-based studies screening for chronic liver disease (313) and were similar to evidence investigating behavioural intervention in smoking cessation (314) and diabetes (84, 85). The current study also demonstrates that TE acceptable intervention for patients presenting to community alcohol services, which is consistent with previously reported evidence exploring the acceptability of TE to screen for CLD in a UK primary care setting (315).

The alcohol harm paradox is a well-known phenomenon, an observation that shows younger people from lower socioeconomic status (SES) tend to experience greater alcohol-related harm than those from higher socioeconomic status. This is despite the people from lower SES report drinking the same or less on average than those from higher SES (316, 317). The study highlights ethnic, gender and age-related disparities, where alcohol-related liver disease stereotypically is associated with white middle-aged men (318-320). This in turn can disadvantage the wider at-risk groups this could be due to a lack of mutual engagement in health care and research.

The integration of non-invasive testing (NITs) for liver disease into community alcohol services provides a unique opportunity for early detection of liver disease in an otherwise high-risk asymptomatic population. A recent systematic review suggested providing feedback to patients based on markers of liver injury is an effective way to reduce harmful alcohol intake (62). Similar findings have been reported in smoking cessation studies investigating the impact of advice based on test results demonstrating the severity of lung damage (83). A prospective observational study from Scotland involving individuals who self-identified themselves as harmful drinkers and presented to community alcohol services demonstrated that the provision of transient elastography was associated with subsequent high uptake both in nurse lead and specialist liver clinics (180). The lack of negative effect on participants who had normal LSM partly alleviates the ongoing concern raised regarding the risks of

non-invasive test-based feedback methods potentially providing false reassurance leading to unintended negative consequences such as exacerbating pre-existing addictive behaviours (63).

Self-motivation has been widely shown to be an independent factor in behavioural change, and self-motivated people are more likely to sustain long-term recovery from substance misuse (321). Self-presentation was the most common source of referral in our study, as per the transtheoretical model of health behaviour change they have been more likely to engage with health promotion programmes (322). As noted in the VALID study, if patients are motivated to attend then there can be high uptake of services as shown by the ≥95 % intervention uptake (323). The evidence supports that this patient subset should be the focus of action-oriented behavioural intervention programmes including in managing alcohol use disorder (322).

8.3.11 Implications

The study has demonstrated the successful feasibility of conducting a randomised control trial to test the effectiveness of advice based on non-invasive tests for liver disease compared to usual care. The finding support integration of transient elastography into community alcohol services both for early diagnosis of liver disease and to supplement the desired behaviour change. A significant proportion of individuals attending community alcohol services have clinically significant liver disease. In the community systematic targeting of the risk factors for liver disease (hazardous alcohol intake and type 2 diabetes) significantly enhance the detection rates of disease (60). By integrating non-invasive liver stiffness testing into these services, it creates an opportunity to change the natural history of disease progression in high-risk individuals (9). Early detection of liver disease followed by targeted interventions is a logical and effective way to reduce the risk of late presentation of liver disease and to minimise alcohol-related harm. Screening patients with novel biomarkers to demonstrate significant physical damage can have an additional benefit to just detecting disease and can supplement subsequent decision making towards a healthier lifestyle (81, 144, 324, 325).

8.4 Conclusion

Integration of transient elastography in addition to usual care in community alcohol services is feasible. It can supplement the change in high-risk drinking behaviour, improve compliance with allocated treatment programs at services, and increase trial specific follow-up rates. One in five patients presenting to these services has a raised

liver stiffness measure (LSM) at opportunistic screening. Normal liver stiffness results do not provide false reassurance. Dual diagnosis of alcohol use disorder and mental health was observed in over two third of trial participants.

Chapter 9. Discussion of thesis

9.1 Main findings of the thesis

The focus of my thesis was to explore the epidemiology of alcohol use disorder in secondary care settings and determine the feasibility of future RCT investigating the effectiveness of advice based on non-invasive tests for liver disease along with alcohol recovery video stories (ARVS) in community alcohol services as behavioural interventions in addition to usual care in changing high-risk drinking behaviours.

In chapter 3 I began by assessing the overall prevalence of alcohol use disorder (AUD) in secondary care settings and found that 16.5% of hospitalised patients had a concomitant AUD based on AUDIT-C assessment. Over two third of patients with AUD were white, males in their 50s. Those with AUD compared to no AUD were more likely to be younger, admitted through the emergency, and cared for by surgical specialities predominantly general surgery and trauma & orthopaedics. Although there was an overall reduction in the number of admissions during the pandemic, a significantly higher proportion during the pandemic compared to pre-pandemic were alcohol dependent and had associated mental and behavioural disorders. Covid-19 positive patients with concomitant AUD died as an inpatient at a significantly younger age.

In chapter 4 I presented a systematic review and meta-analysis comparing intervention-based advice to routine care and demonstrated that intervention-based advice was associated with a greater reduction (36%) in self-report alcohol intake compared to routine care (7%). A similar pattern was observed for the reduction in GGT in the intervention group compared to the control. Moreover, intervention-based advice compared to routine care resulted in a greater reduction in length of hospital stay, sickness absence, physician's visits, and long-term mortality.

In chapter 5 based on a systematic review and narrative synthesis, I proposed a conceptual framework characterising alcohol recovery narratives that exist in literature. Eight principle narrative dimensions were identified (genre, identity, recovery setting, drinking trajectory, drinking behaviours, stages, spirituality and religion, and recovery experience) each with types and subtypes. All dimensions were present in most subgroups. *Shame* was a prominent theme for female narrators, *lack of sense of belonging* and *spirituality* were prominent for LGBTQ+ narrators, and *alienation* and *inequality* were prominent for indigenous narrators. Spirituality in this context functions to instil a sense or belief in a higher power, so one may surrender

to ground reality upon hitting rock bottom and acknowledging the need for a transformation (286).

In chapter 6 I validated the alcohol recovery narratives conceptual framework (ARNCF) by applying it to semi-structured video-recorded interviews conducted as part of KLIFAD WP 2 featuring alcohol recovery stories. All conceptual framework dimensions were present in collected narratives, with three of these dimensions extended by adding types and subtypes. *Religion versus spirituality* as a type was not identified in these interviews. A new dimension of the *Alcohol environment* was added.

In chapter 7 I provided an overview of the KLIFAD work package (wp) one and two. Finally, in chapter 8 I presented the results of KLIFAD WP 3. Over 76% of eligible participants agreed to be part of the trial, gave informed consent, and were randomised. Once randomised 70% of participants attended the initial assessment. Of the participants who attended the initial assessment, 65% were still in services at three months and 59% at six-month follow-up. The majority of included participants were white, male, and in the fourth decade of life. Over 90% were alcohol dependent, a quarter reported using substances other than alcohol, 23% had a co-existing disability and 76% had mental health issues. Of participants who had transient elastography, 21% had raised liver stiffness measure (LSM), and one in seven had LSM in the range of cirrhosis. Provision of NITs (LSM) based advice in addition to usual care was associated greater reduction in self-reported alcohol intake and AUDIT category at six months. A quarter of the participants watched the alcohol recovery video stories (ARVS). These participants showed a clear reduction in drinking days, daily alcohol consumption and AUDIT score. Moreover, the intervention group compared to the control were more likely to attend initial assessment appointments, and complete the allocated treatment program. Reassuringly a normal liver stiffness measure did not provide carte blanche for drinking.

9.2 Challenges and Reflections

As a clinical research fellow, I also provide out-of-hour cover (1:10) for acute gastroenterology emergencies. During the Covid-19 pandemic, I had a temporary interruption and have to suspend my PhD (1st of April 2020 to 31st of August 2020) to provide emergency medical cover as a contingency measure for qualified healthcare professionals. Nottingham Recovery Network (NRN) had to close its community alcohol services during the initial wave of the Covid-19 pandemic. NRN later opened limited services at Wellbeing Hub (community day care unit) and Edwin house (community alcohol detox unit) but the community alcohol clinic run by NRN remained

closed during the study period. This resulted in a delay in starting the KLIFAD trial and looking for an additional setting to replace the NRN community alcohol clinics. I approached the director of Windmill GP surgery as they run a substance misuse clinic in parallel to routine services. The GP surgery management was very appreciative of the idea and after minor amendments, I was able to add the substance misuse clinic as an additional site for study recruitment. I found that a GP surgery offers a group of patients different from specialist Drug and alcohol services. Including primary care added more inclusivity to the trial. On reflection, I should have thought of including primary care as one of the recruitment sites from the start.

There is significant heterogeneity in the language used to describe harmful alcohol intake. The choice of words describing alcohol use is critically important as some of these terms such as alcoholic, and alcoholic liver disease have associated stigma (326). The evidence shows stigma has a significant contribution to negative health outcomes and can act as a barrier to recovery (326, 327). After careful thinking and discussion with supervisors, I adopted alcohol misuse to describe excess alcohol intake, harmful alcohol intake, drinking problems, alcohol dependence, and alcohol use disorder. Down the line, I had further discussions with an addiction psychiatrist and read the literature describing the term alcohol misuse as pejorative for example on occasion it can be just replaced with alcohol use when talking about alcohol consumption. In this context, I found DSM 5 terminology alcohol use disorder was more elaborative and provides a better understanding of the level of harm related to alcohol (328, 329). Moreover, Kelly et al. (2009) showed when highly trained mental health professionals were exposed to two commonly used terms “substance abuser” vs “having a substance use disorder”, they triggered different systematic judgments perpetuating stigmatising attitudes (327). Taking this into account for thesis purposes I use the term alcohol use disorder to describe excess alcohol intake, harmful alcohol intake, drinking problems, alcohol dependence, and alcohol misuse.

The standard AUDIT score asks an individual about their alcohol consumption over the last one year (330). As part of the KLIFAD trial, I was planning to collect follow-up data at three and six months. I realised the standard AUDIT score will not be the true representative of change at three and six months. I did a literature search to identify if researchers have faced a similar issue with AUDIT in past and if so, how they dealt with it. The researchers have previously compared 30-day AUDIT with 12-month AUDIT and reported both AUDIT scales had good discriminatory properties to differentiate between risk groups of alcohol use disorder (331). Another study compared psychometric properties of 3-month and 6-month AUDIT for different cut-

off points (low risk 0-7, hazardous 8-15, harmful 16-19, possible dependence ≥20) for alcohol use disorder and found that standard cut-off points were optimal for both 3 months and 6-month AUDIT scales (332). After a discussion with my PhD supervisors (JRM and SDR), I adopted a 3-month AUDIT scale for three months follow-up and a 6-month AUDIT scale for six months follow-up.

I planned to include alcohol recovery stories as part of interventions in the KLIFAD trial, there remains an ongoing debate in contemporary literature concerning the optimal definition of recovery (195). Some researchers focus on recovery as a relatively objective phenomenon, that can be empirically measured across various domains of functioning. Whilst others see recovery as a purely subjective phenomenon that is heterogeneous and reveals underlying idiosyncrasies of the recovery process (195). In some definitions sustained abstinence from alcohol is a key component of recovery (333), whereas in others the recovery from AUD is defined as a process of change through which individuals improve their health and wellness, live a self-directed life, and strive to reach their full potential (334). In view of this ongoing debate and to improve the understanding of complex healthcare phenomena of alcohol recovery I conducted a systematic review characterising alcohol recovery narratives. Based on the review of the literature I adopted the following definition of recovery for my thesis “a deeply personal, unique process of change, a way of living a satisfying, hopeful and contributing life even with limitations caused by illness [and] a process involving the development of new meaning or purpose in one’s life” (255, 272). I found this definition was broader and gave me flexibility for including the participants for video interviews reflective of the true struggle most people with AUD face in real life. This improved the originality and authenticity of collected videos which in turn has been shown to impact the intended effect on the behaviour of a person watching these videos (335).

Finally, the alcohol recovery video stories (ARVS) were shown to participants on handheld devices only available at recruitment sites. Participants find it hard to watch ARVS due to limited availability and long length of appointments. After initial feedback we let participants watch ARVS at any of their follow-up appointments with community alcohol services. In view of final feedback from key alcohol workers from recruitment sites and from trial participants, I aim to make videos available through an online website or platform. Apart from making ARVS accessible from home, this will allow me to collect details like the number of times each participant accessed a specific ARVS, the most popular ARVS, and the average length of time participants spent on ARVS.

9.3 Implications

9.3.1 For clinical practice

The thesis has many implications for clinical practice.

Firstly, I demonstrated alcohol use disorder is highly prevalent among hospitalised patients. I further described the shared high-risk characteristics of patients with AUD including the most common mode of admission and in-patient specialities of care. The finding from chapter 3 describing the epidemiology of AUD was submitted to Nottingham University Hospital's clinical governance department. The changes were made in the structure of the alcohol care team with a particular focus on the provision of alcohol services at the front door in the Accident & Emergency department and extending the services across seven days a week. The findings were also presented at a departmental meeting and efforts have been since made to take surgical colleagues on board to facilitate the provision of alcohol identification and brief advice (AIBA). I presented a strong case that universal alcohol screening of hospitalised patients should be adopted nationwide as it enhances the pickup rate of AUD and creates a window of opportunity to intervene.

Alcohol services provide community treatment for people self-identifying as at risk for alcohol-related harm including physical disease, currently screening for physical disease and interventions which can link to ongoing medical care are not widely available in these services (299, 336). There is a large burden of undiagnosed clinically significant liver disease in an at-risk population such as in community alcohol services. I demonstrated it is feasible to integrate non-invasive testing of liver disease into community alcohol services and facilitate early diagnosis of liver disease. At the same time, it also creates a unique window of opportunity for healthcare professionals to provide holistic intervention leading to change in the natural history of liver disease in these at-risk individuals. In community alcohol services where the majority of attendees have a severe spectrum of alcohol dependence, the NICE recommend these individuals should be offered an intensive structured community-based intervention (with or without medical therapy) as these provide the best chance of achieving and maintaining abstinence from alcohol (25).

In addition to facilitating early diagnosis of liver disease, non-invasive tests (NITs) can play an additional role as biofeedback to supplement change in high-risk drinking behaviour. I demonstrated that NITs based advice was associated with a greater reduction in self-reported alcohol intake and change in the AUDIT category. This

builds the case for the addition of NITs based biofeedback to usual care while providing advice to the individual with alcohol use disorder. Similar changes in alcohol consumption in response to NITs of liver disease have been previously reported in patients with hazardous alcohol consumption in primary and secondary care but not in community alcohol services (144-146). This change in alcohol consumption is backed up by previous evidence that providing personalised healthcare communications has been shown to enhance the motivation to overcome addictive behaviour (86, 87). For hazardous and harmful alcohol users, providing feedback based on a simple liver fibrosis test prompts a reduction in alcohol consumption for both with and without evidence of liver damage (88).

People with drug and alcohol addiction often suffer from social stigma and stereotyping, this could be due to inadequate knowledge, awareness and negative attitudes toward patients with AUD (100). This biased attitude of healthcare professionals toward drug and alcohol addiction, in turn, impacts the level of care these patients received and is related to poorer outcomes (337). There is an urgent need for a reference shift away from negative attitudes toward addiction both within the community and among healthcare professionals. In this context, the alcohol recovery video stories (ARVS) can be used to educate the public and healthcare providers to facilitate this reference shift. This in part can help to dampen the perception that people with AUD are hard to treat and most of them are destined to have poor outcomes. Moreover, a clear understanding of the characteristics of alcohol recovery narratives could optimise the use of these narratives in clinical practice and maximise their positive impact (258). Given that narratives play a substantial part in health communication (for example as part of routine consultations with clinicians, where clinicians frequently seek to understand the phenomenology of illness as part of the process of selecting appropriate treatments) then such frameworks might have a substantial influence on clinical practice.

9.3.2 For research

The data describing the impact of the Covid-19 pandemic on alcohol use disorder in secondary care was well received both nationally and internationally. I was invited to present at the European Society for Biomedical Research 0n Alcoholism (ESBRA) annual conference in 2021, the abstract was selected among the best abstracts and was part of the European Association for the Study of the Liver (EASL) media release for the virtual annual conference 2021.

There are three commonly available non-invasive tests for liver fibrosis with a substantial evidence base for their clinical use. Transient elastography (TE) is a modified form of ultrasound and two blood tests enhanced liver fibrosis (ELF) test and the Southampton Traffic Light Test (STLT) and each has its own advantages and disadvantages.

The Southampton Traffic Light Test (STLT) has not been widely adopted or externally validated outside the single centre nor does it has been approved by FDA (338). Whereas both TE and ELF tests have been extensively validated and have shown high diagnostic accuracy for fibrosis staging in liver disease including in alcohol-related liver disease (339-342). The feasibility of the integration of non-invasive tests into community pathways for early detection of liver disease has been well demonstrated (299, 307). Liver stiffness measurement by TE can be influenced by factors such as non-fasting status, active drinking BMI >28 kg/m^2, liver inflammation, operator experience, cholestasis, and liver congestion (310). Moreover, TE has a high coefficient of variation compared to the ELF test which limits its use as a surveillance tool for liver fibrosis (311, 343). Both TE and ELF have high acceptability and have been shown to be cost-effective in screening for liver fibrosis in community settings (344-346). Although the feasibility of using non-invasive tests as biofeedback to impact drinking behaviours has been demonstrated (88, 156) and there is good evidence that these technologies can identify liver disease with good accuracy. There is however no evidence currently as to which may work best in a community alcohol services setting and will require further research.

Based on KLIFAD feasibility RCT results I am planning to apply for definitive RCT to test the effectiveness of NITs based advice with and without alcohol recovery video stories in community alcohol services. The most common criticism I received is regarding the risks of NITs based feedback methods potentially providing false reassurance leading to unintended negative consequences such as exacerbating pre-existing addictive behaviours (63). This has been a source of anxiety among the wider research funders. In KLIFAD I have demonstrated that a normal liver stiffness measure was associated with negative outcomes. I hope this will help to address this long-standing concern among the research community and facilitate future funding applications and implementation of this approach into clinical practice.

Alcohol use disorder and alcohol recovery are complex health conditions with associated mental health and social issues (347). To improve the understanding of complex health phenomena researchers often proposed frameworks presenting

networks of linked concepts which serve to explain the phenomenon (264). For example, the CHIME framework on mental health recovery processes (connectedness; hope and optimism about the future; identity; meaning in life; empowerment), conceptual frameworks describing mental health recovery narratives, childhood trauma, and social isolation (267-269). To enhance the understanding of alcohol recovery I have proposed a conceptual framework characterising alcohol recovery narratives (270). The conceptual framework breakdown alcohol recovery narratives into dimensions each with its own types and sub-types. The framework has given me an in-depth understanding of recovery from AUD and provided conceptual ground to design alcohol recovery video stories (ARVS) used as part of the intervention in the KLIFAD trial. I realised that recovery from AUD follows a non-linear path and requires a holistic approach. This helped me to pay particular attention while developing ARVS to make them as close to real life as possible.

Natural recovery was another concept I came across while defining the characteristics of alcohol recovery narratives (348). The natural recovery appears to exhibit an internal locus of control, whereby, the tendency to give control away to agents in the recovery setting may require the building of either trust over a time period with others, or a self-driven attempt to come full circle with one's addiction (348). One of the biggest concerns in the hepatology community is that over half of the liver patients present with end-stage liver disease at a stage when the scope of any medical or behavioural intervention is minimal (9, 20, 41). This also demonstrates that only a minority of individuals with AUD are likely to come in contact with treatment settings such as community alcohol services. The BBC 2 documentary “Drinkers Like Me” featuring Adrian Chiles impactfully demonstrated how an ordinary person can drink more than recommended without even realising it causes harm. This highlight the importance of improving the awareness among public and promoting natural recovery. The evidence to describe natural recovery is relatively scant and will require concerted effort from research community to conduct more research defining key characteristics of this mode of recovery.

9.4 Patient and Public Involvement (PPI)

The National Institute for Health and Care Research (NIHR) strongly advocate for active engagement of PPI in research and defined PPI as "research being carried out with or by members of the public rather than to, or about or for them" (p 6) (349). Among many, these are a few examples of PPI contributions, they make research more relevant to participants, make research design acceptable, improve the quality

of participant information and make it easy to understand, improve the participant experience, and facilitate dissemination of results.

Patients recognise the necessity for better ways of helping people reduce their alcohol consumption. The James Lind Alliance has worked with the British Society for Gastroenterology to prioritise research around ARLD. The top priority agreed upon jointly by patients, carers and health professionals is to address the question “What are the most effective ways to help people with alcohol-related liver disease stop drinking?”

The NIHR Nottingham Biomedical Research Centre GI/Liver PPI group provided considerable input to the Lind Alliance process with focus groups working on these key top ten questions. As part of the KLIFAD feasibility study, I have successfully established a dedicated PPI group including members of the public who have lived experience of alcohol misuse and alcohol-related liver disease. The PPI coordinator and a member of the public are co-applicants in this proposal. The PPI co-applicants have extensive experience in public involvement in research and have been co-ordinating the PPI group.

There are several key areas of PPI input for the KLIFAD trial in all work packages. In WP 1 and WP 2 PPI groups actively help with participant recruitment. The PPI group has helped to design the participant's feedback after receiving the liver stiffness test, in this particular example the transient elastography. They expressed concerns that participants with alcohol use disorder frequently have a reading problem and in certain cases dyslexia, it was ensured that the feedback has a fine balance of written text and pictures to facilitate recipient understanding. Moreover, the PPI group was closely involved in the development of alcohol recovery stories.

The PPI group felt strongly that everyone with alcohol misuse should be offered an opportunity to have non-invasive testing for liver disease (transient elastography) followed by personalised feedback. Hence as part of the KLIFAD trial, I offered transient elastography to participants in the control group at 6 months from recruitment. The PPI group recommended having a multidisciplinary partnership specifically involving mental health specialists to develop effective interventions. The PPI group also helped to identify research-oriented members of the public to expand the pre-existing PPI pool.

9.5 Overall conclusion of the thesis

The prevalence of alcohol use disorder (AUD) in secondary care is higher than previously reported. Alcohol assessment by AUDIT-C is an effective tool to screen for AUD among hospitalised patients. Universal alcohol screening provides a unique opportunity for early detection of AUD in a hospital setting followed by intervention to effectively mitigate future risk of harm. During the Covid-19 pandemic, a significantly higher proportion of hospitalised patients had alcohol dependence and associated mental health disorders. AUD in Covid-19 patients increased the risk of dying at a younger age compared to Covid-19 patients with no AUD.

The alcohol recovery narrative conceptual framework (ARNCF) provides the characteristics of alcohol recovery narratives, which facilitates an in-depth understanding of alcohol recovery. The review shows alcohol recovery is a non-linear process and often requires a multidisciplinary integrated approach to maintain long-term sobriety. Experience of recovery can be positive or negative, in actual life, one would have experienced a confluence of both tendencies. Congruent thoughts and beliefs can impact the individual's anticipations and personal estimates of negative or positive outcomes associated with addiction. Recognising the positive and negative impact of recovery can help to pre-emptively build networks, which can support and maintain sobriety.

I demonstrated that the integration of transient elastography into community alcohol services is feasible. Transient elastography can be used to stratify clinically significant liver disease. It significantly enhances the pick-up rate of undiagnosed liver disease among high-risk alcohol users and provides a unique opportunity for early targeted interventions. It can stimulate change in drinking behaviour and can be used as part of biofeedback to high-risk drinkers.

Appendix 1. Adjusted multivariable logistic regression analysis for AUD risk groups

	Increase risk	p	High risk	p	Dependent	p
Age group (years)						
18-29	1		1		1	
30-39	0.97 (0.83-1.15)	0.755	1.24 (0.98-1.56)	0.078	2.35 (1.61-3.42)	<0.001
40-49	1.26 (1.07-1.49)	0.006	1.44 (1.13-1.84)	<0.001	3.43 (2.34-5.02)	<0.001
50-59	1.51 (1.26-1.79)	<0.001	1.95 (1.51-2.52)	<0.001	4.19 (2.88-6.29)	<0.001
60-69	1.59 (1.31-1.95)	<0.001	1.76 (1.31-2.40)	0.003	3.82 (2.41-6.04)	<0.001
>70	1.37 (1.08-1.74)	0.008	1.36 (0.96-1.93)	0.073	3.27 (1.94-5.54)	<0.001
Sex						
Female	0.65 (0.61-0.69)	<0.001	0.57 (0.52-0.63)	<0.001	0.60 (0.53-0.69)	<0.001
Male	1		1		1	
Ethnicity						
MINORITY ETHNICITY	0.68 (0.59-0.78)	<0.001	0.65 (0.53-0.79)	<0.001	0.67 (0.51-0.89)	0.006
White	1		1		1	
IMD quintiles						
1 (most deprived)	0.81 (0.73-0.89)	<0.001	0.97 (0.84 (1.12)	0.724	1.21 (0.98-1.50)	0.073
2	0.84 (0.75-0.93)	0.001	0.93 (0.79-1.08)	0.341	1.16 (0.92-1.46)	0.199
3	0.86 (0.77-0.95)	0.004	0.92 (0.78-1.07)	0.282	1.03 (0.81-1.32)	0.797
4	0.94 (0.85-1.04)	0.279	0.96 (0.82-1.13)	0.660	1.04 (0.81-1.33)	0.739
5 (least deprived)	1		1		1	
Civil status						
Not in a relationship[a]	1.05 (0.97-1.13)	0.256	1.14 (1.02-1.28)	0.025	1.37 (1.16-1.61)	<0.001
In a relationship[b]	1		1		1	
Mode of admission						
Emergency	1.04 (0.96-1.11)	0.330	1.17 (1.06-1.30)	0.003	1.38 (1.17-1.61)	<0.01
Other	1				1	
Speciality						

	Increase risk	p	High risk	p	Dependent	p
Medicine	0.85 (0.79-0.91)	<0.001	0.89 (0.79-0.98)	0.027	1.16 (0.99-1.35)	0.066
Surgery	1		1		1	
Length of Stay (days)						
	0.99 (0.98-0.99)	<0.01	1.00 (0.99-1.03)	0.477	1.00 (0.99-1.01)	0.404
Number of admissions						
	0.98 (0.97-0.99)	<0.01	0.98 (0.97-1.00)	0.042	0.98 (0.96-1.01)	0.146

Odds ratio (95% CI), Low risk group was set as reference category

[a] Not in a relationship includes married, in a civil partnership or in long term relationship

[b] In a relationship includes single, divorced, separated, dissolved civil partnership, widowed, or surviving civil partner

p for full adjusted multivariable logistic regression analysis

Appendix 2.Covid-19 negative vs Covid-19 positive subgroups in pandemic cohort

	Covid-19 negative (n=19604)	**Covid-19 positive (n=994)**	***p***
All admissions	25893 (94.7%)	1456 (5.3%)	
Individuals	19604 (95.2%)	994 (4.8%)	
Male	9624 (49.1%)	536 (53.9%)	0.003
Age years (SD)	63.0 (20.0)	69.0 (18.0)	<0.001
Ethnicity			<0.001
White	14134 (91.0%)	711 (86.1%)	
Minority ethnicity	1402 (9.0%)	115 (13.9%)	
Unknown	4068	168	
IMD Quantiles			0.043
1 (most deprived)	4530 (23.2%)	221 (22.5%)	
2	3376 (17.3%)	137 (14.0%)	
3	3281 (16.8%)	164 (16.7%)	
4	3456 (17.7%)	183 (18.7%)	
5 (least deprived)	4924 (25.2%)	276 (28.1%)	
Missing data	37	13	
Civil status			<0.001
In a relationship[a]	10218 (62.9%)	598 (70.7%)	
Not in a relationship[b]	6028 (37.1%)	248 (29.3%)	
Unknown	3358	148	
Mode of admission			<0.001
Emergency	12564 (64.1%)	826 (83.1%)	
Other	7040 (35.9%)	168 (16.9%)	
Speciality			<0.001
Medicine	11000 (57.9%)	880 (89.2%)	
Surgery	8000 (42.1%)	106 (10.8%)	
Other or unknown	604	8	
Length of Stay (days)	4 (1-174)	7 (1-147)	<0.001

	Covid-19 negative (n=19604)	**Covid-19 positive (n=994)**	***p***
Number of readmissions	1 (1-13)	1 (1-8)	<0.001
Inpatient death	1498 (7.6%)	265 (26.6%)	<0.001
Age at death	76 (13.6)	78 (11.9)	0.011
IMD Quantiles for inpatient death			0.258
1 (most deprived)	271 (18.15)	57 (21.5%)	
2	244 (16.35)	35 (13.2%)	
3	262 (17.55)	46 (17.4%)	
4	279 (18.6%)	56 (21.1%)	
5 (least deprived)	439 (29.3%)	65 (24.5%)	
Missing data	3	6	

Data are number (%), mean (SD) or median (range), [a] In a relationship includes married, in a civil partnership or in long term relationship, [b] Not in a relationship includes single, divorced, separated, dissolved civil partnership, widowed, or surviving civil partner

Appendix 3. Data abstraction table chapter 4

Eligibility			
Study characteristics	**Question**	**Outcome**	**Location in text**
Eligibility	**Inclusion criteria**	**Met/Not met**	
	Exclusion criteria	**Met/Not met**	
Decision	**Include**	**Yes/No**	
	Exclude	**Yes/No**	
Reason for exclusion	free text		
Methods			
Study ID			
Study title			
author name			
author email			
Study aim			
Study design			
Recruitment			
Study start date			
Study end date			
Duration of follow up			
Country			
Setting	Community	Yes/No	
	Hospital	Yes/No	
Ethical approval		Yes/No	
Statistical analysis			
Participants			
Age	mean (SD)		

Gender			
Ethnicity			
Number screened			
Number recruited			
Number retained			
Drop out			
Self-report alcohol intake	gram/week		
Alcohol scores			
Other substance			
Advise	Intervention based	Yes/No	
	Non-intervention based	Yes/No	
Subgroups			
LFTs			
Any other outcome			
Limitation and Mitigation strategy			
Limitations			
Strengths			
Explanations			
Conclusion			
Author conclusion			
any other information			
Note			
Eligibility			
Study characteristics	Question	Outcome	Location in text
Study ID			

Appendix 4. Sample search strategy chapter 5

	Search terms
1	exp Alcoholics/
2	exp alcoholism/
3	exp alcohol-related disorders/
4	exp Alcohol Drinking/
5	exp Alcohol Abstinence/
6	exp Liver Diseases, Alcoholic/
7	exp alcoholic intoxication/
8	exp alcohol-induced disorders/
9	("alcohol*misuse" or "alcohol dependen*" or "alcohol mis use" or "alcohol abuse").ti,ab.
10	("Alcohol use disorder*" or "alcohol abstinen*" or "alcohol cessation" or "reduce drinking").ti,ab.
11	("alcoholic*" or "alcoholism" or "binge drink*" or "heavy drink*" or "underage drink*" or "underage drink*" or "alcohol drink*" or "alcohol use").ti,ab.
12	(Cirrhosis or cirrhotic or liverADJ4alcohol*).ti,ab.
13	exp Narration/
14	exp Narrative Therapy/
15	exp personal narrative/
16	("Recovery Story" or "Recovery Stories" or "recovery narrative*" or "lived experience*").ti,ab.
17	(narrat* or story or stories or storytelling or telling or tale* or restory* or "counter-narrative*" or disnarrat* or memoir* or testimon* or biograph* or autobiograph* or "auto-biograph*" or autoethnograph* or "auto-ethnograph*" or photovoice).ti,ab.

Appendix 5. PRISMA checklist (2009), for systematic review chapter 5

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	Yes #1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	Yes #3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	Yes #5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	Yes #5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	Yes #6
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	Yes #6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	Yes #6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Yes #6
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	Yes #6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	Yes #6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	Yes #7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	Yes #6

Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	Yes
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	Yes #7
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	Yes #10
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	Yes
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Yes #7
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Yes # table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Yes #10, figure 4
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Yes #7-10
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Yes
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Yes
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Yes #8
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	Yes #10
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	Yes #12
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	Yes #12
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	Yes #2

Appendix 6. Data extraction form chapter 6

Eligibility	Inclusion criteria Exclusion criteria	Met/Not met Met/Not met
Decision	Include Exclude	Yes/No Yes/No
Reason for exclusion	free text	
Methods		
Study reference Publication source Country of researchers Academic discipline Methodology Data collection Analytical approach	 Quantitative Qualitative Mixed	
Narratives		
Format of narrative Pre-existing or new Number of narrators Sex Condition (research named) How narratives named by the researcher How recovery narratives defined Structure of narratives Characteristics of Narratives Types identified Definition of types Any other explanation		

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