ALCOHOL RESEARCH UK

Liver Disease Risk Factors in Patients Treated for Alcohol and Drug Dependence

Katherine I. Morley, Michael T. Lynskey, Giulia Toti, Pia Singh, Nicola J. Kalk, Carol-Ann Getty, Lindsey A. Hines, Stephanie Fincham-Campbell

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AUTHOR DETAILS

Dr Katherine I. Morley[1,2] (katherine.morley@kcl.ac.uk)
Prof Michael T. Lynskey[1] (michael.lynskey@kcl.ac.uk)
Dr Giulia Toti[1,3*] (gtoti@uh.edu)
Ms Pia Singh[1*] (pia.singh@live.com)
Dr Nicola J. Kalk[1] (nicola.kalk@kcl.ac.uk)
Ms Carol-Ann Getty[1] (carol-ann.getty@kcl.ac.uk)
Dr Lindsey A. Hines[1,4*] (lindsey.a.hines@kcl.ac.uk)
Ms Stephanie Fincham-Campbell[1] (Stephanie.fincham-cambell@kcl.ac.uk)

[1]National Addiction Centre, King's College London Institute of Psychiatry, Psychology, and Neuroscience, 4 Windsor Walk, Denmark Hill, London SE5 8BB, United Kingdom.
[2] Melbourne School of Population and Global Health, 235 Bouverie St, Carlton VIC 3053, Australia.
[3] University of Houston Department of Computer Science, Philip Guthrie Hoffman Hall, 3551 Cullen Blvd., Houston, TX 77204-3010, USA.
[4] Centre for Adolescent Health, Royal Children's Hospital, 50 Flemington Road, VIC 3052, Australia.
[*] Indicates author was affiliated to King's College London when working on this project; current institution provided where available.

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EXECUTIVE SUMMARY

Overall there were substantial percentages of CDATS patients with one or more risk factors for liver disease, many of which are modifiable. Over half of patients have a record of engaging in hazardous alcohol use, and approximately a quarter have injected drugs, with a similar percentage having hepatitis C.

Although the percentage of clients with liver disease risk factors appeared to be higher based on self-reported questionnaire data, particularly for hepatitis C and mental health, much of this is likely to be due to the limitations of the available electronic medical record data.

Clinical staff view the major obstacles to treatment for liver disease risk factors as low client prioritisation of overall health and lack of understanding about the consequences of viral infections and alcohol use. Clinical support tools focused on improving risk communication could enhance treatment interest and uptake.

However, staff also highlighted clients' unstable living situations and poor mental health as obstacles to treatment for liver disease risk factors. This is particularly concerning given the large percentage of patients who reported unstable living situations (approximately 30-40%), and mental health problems (between 10% and 65%). Supporting clients to organise stable housing and access mental health treatment may also indirectly improve treatment for liver disease risk factors.

LIST OF ABBREVIATIONS

BRC	Biomedical Research Centre
CDLS	Clinical Data Linkage Service
CDATS	Community Drug and Alcohol Treatment Services
CRIS	Clinical Record Interactive Search
EHR	Electronic Health Record
ePJS	Electronic Patient Journal System
HES	Hospital Episode Statistics
ICD-10	International Classification of Disease version 10
ONS	Office of National Statistics
PWID	People Who Inject Drugs
SUD	Substance Use Disorder
SLaM	South London and Maudsley NHS Foundation Trust

INTRODUCTION

Background

The UK liver disease mortality rate has increased 400% since 1970, making it the third largest cause of premature mortality (Williams et al. 2014). The major causes of advanced liver disease in the UK are alcoholic cirrhosis and chronic viral hepatitis (Tsochatzis et al. 2014; Edeghere et al. 2015). People with substance use disorders (SUDs) have greater alcohol consumption, and hepatitis B and hepatitis C infection than the general population, making them important targets for liver disease prevention. Over 35% of people treated for SUDs are treated for alcohol use, and at least 25% treated for illicit drug use also drink heavily (Public Health England 2014; Gossop et al. 2003). Estimated hepatitis B and C exposure is 32% and 50.5% respectively in people who inject drugs (PWID) in the UK, with this group accounting for most new hepatitis C infections (Nelson et al. 2011; Bennett et al. 2015).

Prevention and early intervention are effective in stabilising liver disease progression and reducing morbidity, mortality, and the need for transplantation. Achieving sustained virologic response in hepatitis C treatment is associated with regression of liver fibrosis and cirrhosis, substantially reduced risk of hepatocellular carcinoma and mortality, and 13-fold lower subsequent medical costs (Tsochatzis et al. 2014; Smith-Palmer et al. 2015). Reduction in the use of tobacco, alcohol, and cannabis is also beneficial; even in non-alcoholic liver disease, moderate use of alcohol more than doubles the risk of cirrhosis, while tobacco and cannabis use both worsen the progression of fibrosis (Tsochatzis et al. 2014). However, treatment levels for hepatitis B and hepatitis C infection, and secondary alcohol misuse, are low especially amongst SUD patients which has led to calls for tools to help clinicians identify high-risk patients and target treatment (Staiger et al. 2013; Williams et al. 2014; Bennett et al. 2015; Tsochatzis et al. 2014; Smith-Palmer et al. 2015).

Study Aims and Objectives

The aim of this project was to characterise the current clinical landscape regarding detection and treatment of liver disease risk factors in individuals undergoing treatment for alcohol and/or drug dependence, using a combination of electronic medical record data and data directly collected from staff and clients. It addressed the following research questions:

1. What is the percentage of addiction services clients who have known risk factors for liver disease?
2. How do self-reports of risk factors compare to what is included in clinical records?
3. What are the attitudes of clinical staff and clients to interventions for liver disease risk factors?

METHODS

Selection of Risk Factors for Liver Disease

Risk factors for liver disease were identified from the literature and discussions with clinical colleagues who work with clients in treatment for drug and alcohol dependence. We selected a range of individual-level risk factors, with a focus on relevance to treatment and potential for modification:

- Sociodemographics
  - Country of birth
  - Living situation
  - Time in prison
- Substance use
  - Hazard alcohol use
  - Illicit drug use
- Physical health
  - Diabetes
  - Blood-borne viruses: hepatitis A, B, and C and HIV/AIDS
- Risk behaviours
  - Injecting drugs, sharing injecting equipment, high-risk sexual behaviour
- Mental health
  - Psychotic illnesses
  - Anxiety and depression

This selection guided the focus of the information that was extracted from the medical record data, and the design of the client and staff surveys.

Electronic Health Record Data

Data Source

The South London and Maudsley NHS Foundation Trust (SLaM) BRC Case Register was set up in 2008 as a novel data resource derived directly from the routine EHR data from a large mental healthcare provider which provides comprehensive mental health services to a geographic catchment of over 1.2 million residents in south London, as well as some regional/national specialist services. The Case Register currently contains records for over 250,000 patients and includes both structured data and clinical notes. Clinical records have been electronic across all SLaM services since April 2006, using the bespoke electronic Patient Journey System (ePJS). The Clinical Record Interactive Search (CRIS) application was developed to anonymise and structure data from ePJS, making it available for research use. The Case Register and CRIS application have been described in depth in multiple publications (Stewart et al. 2009; Perera et al. 2016).

Additionally, SLaM has established the Clinical Data Linkage Service (CDLS) as a trusted third party safe haven to enable safe and secure data processing services (linkage, and/or storage, and/or extraction) on distinct data sets for secondary

research use, which enables CRIS data to be linked to other external data sources (Stewart et al. 2009; Perera et al. 2016). One of the available data linkages were relevant to this project: Hospital Episode Statistics (HES). HES data are compiled from all NHS Trusts in England (both acute and mental health services), including statistical abstracts of records of all inpatient episodes, as well as outpatient and emergency care.

Study Design

The complex longitudinal nature of EHR data lends itself to the use of a range of study designs. For this project, we were interested in the percentage of patients with liver disease risk factors at commencement of CDATS treatment. We defined this as the first time an individual engaged with a SLaM CDATS within the timeframe covered by CRIS (from January 1st, 2007 to our census date of May 4th, 2017).

However, resolving this index date is not straightforward as referral to a DATS will create a record in the SLaM EHR system if the patient is accepted for treatment, even if the patient referred does not subsequently make contact with clinical staff. Consequently, as the type and outcome of appointments is also recorded in case register, we defined the index date as the first face-to-face appointment with a CDATS that an accepted patient attended.

Ideally, all the information collected for each patient would occur at initial contact, but there are many reasons why this may not happen in clinical practice. Following the framework of other EHR-based studies (e.g. (Jordan et al. 2017; Rapsomaniki et al. 2014)), we used information recorded within a time window around the index date to generate baseline measurements. We conducted a series of initial database searches to determine the best trade-off between the size of the time window and data completeness and determined that a window of one year prior to the index date, and 28 days after the index date was optimal for these patients.

All adult patients (aged 16 years and above) who engaged with a SLaM CDATS on a face-to-face basis within the study timeframe were considered eligible for cohort inclusion. We excluded those patients for whom no drug or alcohol use information was recorded within the baseline time window due to uncertainty regarding whether these patients were being treated for a SUD (approximately 1% of otherwise eligible patients). No other exclusion criteria were applied.

Risk Factors and Phenotype Algorithm Development

We initially focused on extracting risk factor variables from the CRIS data as the data linkage process used to combine CRIS data with those from HES can only be conducted once. When data linkage is complete, the BRC identification number used in CRIS is replaced with a new randomly generated ID, so no further data from CRIS can be added to the cohort. Once the finalised CRIS data set was linked to relevant data from HES, a final round of data integration was completed for variables where additional information was extracted from HES.

The CRIS system is complex as the ePJS is used by many different clinical services with different medical records needs. Consequently, information relevant to the definition of a single variable may be recorded in multiple database tables and free-text documents (e.g. clinical notes, referral letters). To combine data from these sources in the most efficient way, we took a staged approach to variable definition. We first considered available structured data, and then considered use of natural language processing (NLP) data for variables where structured fields (e.g. diagnoses recorded using structured code systems such as ICD-10) did not yield sufficient data. For each variable, we used the following overall approach to identify the data available and how data from different sources could be integrated:

1. *Identify sources of structured information*: Data sources were identified via discussions with clinical and informatics colleagues, and examination of database table structure.
2. *Examine content of each structured information source*: Using a test cohort of patients meeting the basic inclusion criteria we examined how frequently the relevant database fields were populated with non-null values (within the cohort entry time window).
3. *Consider NLP data sources*: For variables where structured fields were not well populated, we considered the use of NLP to extract data from clinical notes and other documents. If relevant NLP algorithms for use with CRIS data already existed, we applied these to the test cohort to determine whether sufficient data could be extracted from available documents for this patient population. If no algorithm existed, the decision regarding whether to develop a *de novo* NLP algorithm was made based how frequently the relevant information was likely to be included in text documents and how critical the variable was to the planned analyses. Further details of NLP approaches are provided in Appendix 1.
4. *Integrate structured and unstructured data*: For those variable where data was extracted from more than one source, EHR phenotype algorithms were developed to define the strategy used to integrate and reconcile these data.

The phenotype algorithms developed for extracting these data are a research output in their own right, but as the focus of this project is the data they are used to extract, details of the algorithms developed are only provided in Appendix 4 for the interested reader, rather than in the main Results section.

Ethical Approval

The SLaM BRC CRIS system has ethical and s251 approval. Ethical approval is therefore not required for individual projects, but the CRIS Oversight Committee reviews all proposed research; Dr Morley received approval from the Committee for this project in June 2016.

Data Analysis

Standard descriptive statistics (mean, variance, percentages, counts) were used to summarise the risk factor information extracted from the medical record data. All analyses were conducted using the R Statistical Software.

Client Survey

Study Design

This was a mixed-methods pilot study involving quantitative and optional qualitative interviews with SLaM Community Drug and Alcohol Treatment Services (CDATS) clients, and linkage of the quantitative interview data to medical records and national mortality data. It involved three components outlined below: a quantitative structured interview, a qualitative semi-structured interview, and permission for access to participants' NHS records.

In the structured interview, clients were asked about previous diagnoses with liver disease or related conditions, risk factors, and treatment for any diagnosed conditions. The interview questionnaire includes the Alcohol Use Disorders Identification Test Alcohol Consumption questions (AUDIT-C) (Bush et al. 1998), Mini-International Neuropsychiatric Interview (Sheehan et al. 1998), and items from the Treatment Outcomes Profile (TOP) (Marsden et al. 2008), the Blood Borne Virus Transmission Risk Assessment Questionnaire (Stoové et al. 2008), the HIV Risk-taking Behaviour Scale (Darke et al. 1991; Rash et al. 2016), and the Australian Needle and Syringe Program Survey (Wand et al. 2012). Although participants could complete the questionnaire themselves, we have found that when working with this patient population, structured interviews result in better quality data (i.e. internally consistent, less missing data). The structured interview form is provided in Appendix 2.

Based on the quantitative interview, participants who reported being diagnosed with one of the following conditions and not receiving/seeking treatment were invited to discuss this further in a semi-structured interview: alcohol dependence, diabetes, hepatitis A, B, or C, HIV/AIDS, liver disease. It was audio recorded and transcribed for analysis.

Participants were asked for permission to link their *quantitative* interview data to their electronic medical record data held by SLaM, and to medical record data held in the Hospital Episode Statistics (HES) database, and to mortality data held by the Office of National Statistics (ONS), linked via NHS number.

Participation in the *qualitative* interview and data linkage were optional (see Figure 1 for detailed outline of procedures). All participants were reimbursed £20 for their time regardless of whether they consented to optional components to avoid coercion. The reimbursement amount was determined in consultation with the SLaM Addictions Service User Research Group (SURG; www.kcl.ac.uk/ioppn/depts/addictions/research/SURG/index.aspx).

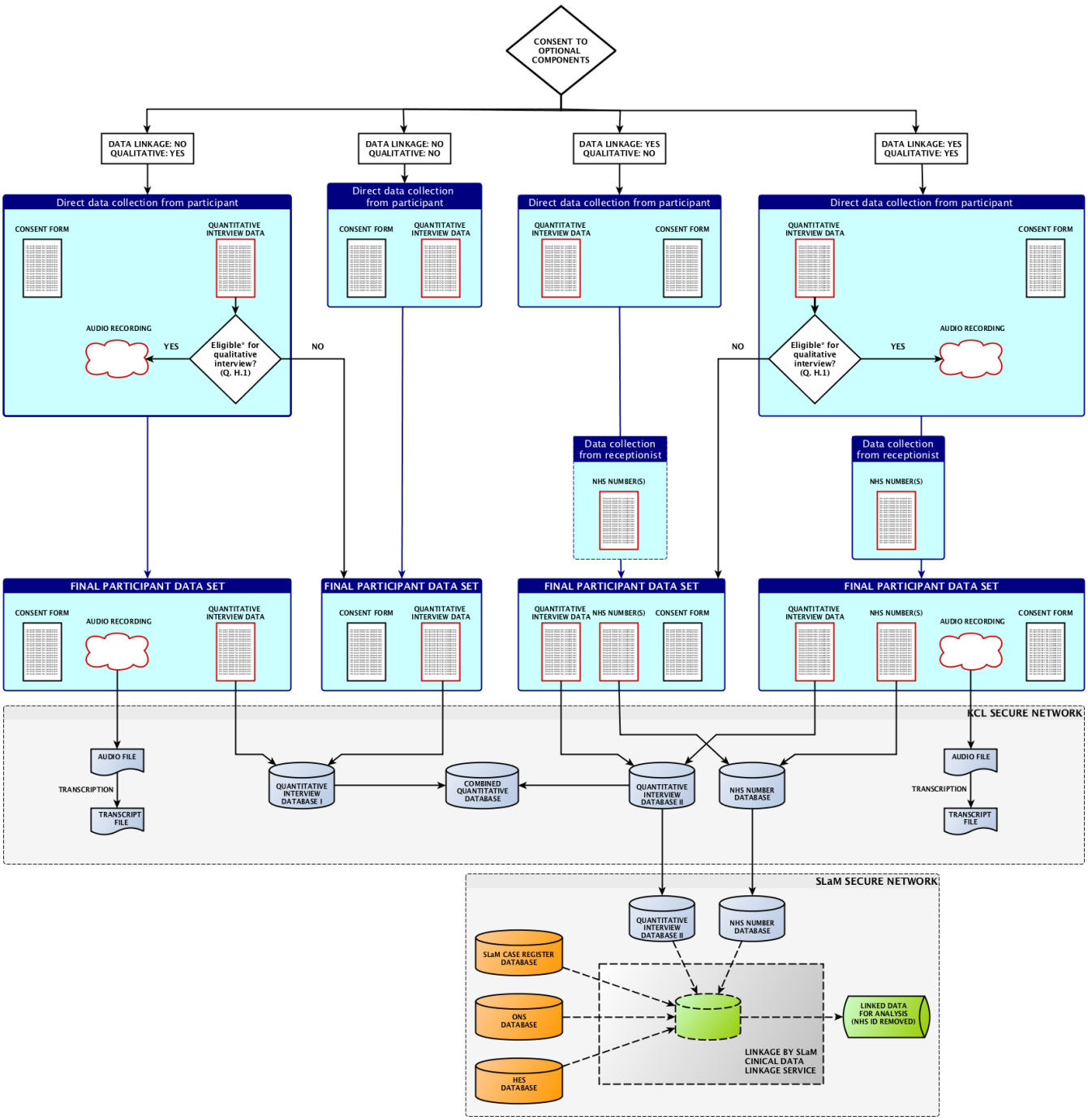

Figure 1: Diagram of data management and linkage of participant data. Participants will be eligible to take part in the qualitative interview if they report being diagnosed with, but not treated for, the following conditions: alcohol dependence, diabetes, hepatitis A, B, or C, or liver disease. Dashed lines indicate temporary links used to create final anonymised, linked, data set. Audio recording (qualitative interview) data is not linked to other data, nor is the consent form. All data collection items will be securely stored; those outlined in red will be securely destroyed at the conclusion of the pilot study.

Sample Recruitment

As this was a pilot feasibility study that was not dependent upon the sample being representative, we used a convenience sample. Participants were recruited from two SLaM Addiction Services clinics: Lambeth Drug and Alcohol Liaison and Assessment Service, and Wandsworth Drug and Alcohol Service.

Before recruiting participants, the Chief Investigator attended staff meetings at each SLaM Addiction Services Clinic to present an overview of the study and request that clinic staff tell their clients about the study and how to contact research staff if they wish to be involved. The research team then liaised with the managers from each clinic to identify the days/times when it would be most suitable for research staff to recruit clients from their clinic.

Potential participants were identified and referred by clinical staff to the research team member present at the clinic, who determined whether clients are eligible for the study before proceeding further. Clients were eligible for participation if they were currently receiving treatment for any substance use disorder, and were adults aged 16 years and over. Clients were excluded if they had insufficient written and/or spoken English to provide informed consent and participate in the study, or were intoxicated at the time of obtaining informed consent and/or conducting the interview.

Ethical Approval

This study was given a favourable opinion by the East of England – Cambridge Central Research Ethics Committee (17/EE/0193) on the 5th of June 2017, and NHS Health Research Authority Approval on the 25th of July 2017. South London and Maudsley NHS Trust Research and Development approval (R&D2017/063) was granted on the 14th of August 2017.

Data Analysis

Questionnaire responses were double-entered into custom-designed databases and stored securely on a restricted-access server. Standard descriptive statistics (mean, variance, percentages, counts) were used to calculate the percentage of potential participants who agreed to participate in the study, and to summarise the risk factor information contained in the quantitative interview data. All analyses were conducted using the R Statistical Software.

The aim of the qualitative analysis of interview transcripts is to identify patterns of meaning relating to barriers to treatment for liver disease and associated risk factors, some of which may not have been previously considered in the literature. Thematic analysis is currently underway. This method of qualitative analysis is designed to answer questions relating to people's experiences, or people's views and perceptions (Braun & Clarke 2014; Braun & Clarke 2006). It is undertaken using iterative

categorisation, which permits the use of both deductive (coding and theme development directed by existing concepts or ideas) and inductive (coding and theme development directed by the content of the data) approaches (Neale 2016). Iterative categorisation does not require specialist software and can be conducted using a standard word processing package.

Staff Survey

Study Design and Participant Recruitment

Anonymous questionnaire surveys of clinical staff were administered in three SLaM CDATS. The aim of this study was to investigate support for, and barriers to, treatment for liver disease and associated risk factors (viral infections, heavy alcohol consumption, safe sex and injecting practices) in addiction services. The questionnaire items were informed by:

1. UK Department of Health guidelines on clinical management of drug misuse and dependence;
2. NICE Clinical Guidelines for alcohol-use disorders, type-2 diabetes, hepatitis B;
3. British HIV Association guidelines for treatment of HIV positive adults;
4. Royal College of Physicians guidelines on management of hepatitis C.

The full questionnaire can be found in Appendix 3 and includes collection of information on:

1. resources for educating/treating clients for liver disease and associated risk factors;
2. which conditions should be addressed during treatment;
3. client interest in treatment;
4. obstacles to treatment.

Strategies for participant recruitment were devised via discussion with Clinical Leads at each site to minimise disruption to normal clinical practice and maximise participation. Participants at two sites were recruited by a member of the research team presenting an overview of the study prior to a staff meeting and distributing the surveys to staff in attendance. Staff could return the questionnaire to the research team member at that time, or at another time of their choosing using a stamped envelope with the Chief Investigators postal address provided by the research team. At the third site, the Clinical Lead emailed the questionnaire to clinical staff who printed the forms and then either returned them to the Chief Investigator via post, or via email through the Clinical Lead. All clinical staff were eligible to participate; there were no exclusion criteria.

Ethical Approval

The study was classified as a clinical audit and approved by the local SLaM NHS Foundation Trust Audit Committee in November 2016.

Data Analysis

Questionnaire responses were double-entered into custom-designed databases and stored securely on a restricted-access server. Standard descriptive statistics (mean, variance, percentages, counts) were used to summarise the risk factor information extracted from the medical record data. All analyses were conducted using the R Statistical Software.

RESULTS

Electronic Health Record Data

Sample Characteristics

A total of 18,848 patients met our eligibility criteria. The majority (70.0%) were male (see Table 1) and the average age was 39.7 years (standard deviation 11 years, minimum of 16 and maximum of 88). Based on self-reported ethnicity, 76.4% were White, 13.2% Black, and 3.4% Asian. Almost a third (28.2%) had an unstable housing situation. It was not possible to extract any data on time spent in prison.

Table 1: Sociodemographic characteristics of electronic health record data sample

Category	Value	N	Percent
Gender	Female	5652	30
	Male	13195	70
	Not Known	1	0
Ethnicity	Asian	634	3.4
	Black	2492	13.2
	Mixed	548	2.9
	Other	521	2.8
	Unknown	256	1.4
	White	14397	76.4
Housing status	Stable	12979	68.9
	Unknown	547	2.9
	Unstable	5322	28.2

Just over half the sample (51.9%) had a diagnosis of alcohol dependence or a record of problematic alcohol use. Opiates were the most commonly used drug with 39.8% of the sample meeting our criteria for use. The next most commonly used substance was cocaine or crack cocaine (35.6%), followed by cannabis (22.5%), methadone or buprenorphine (7.0%), and benzodiazepines (1.1%).

Liver Disease and Clinical Risk factors

A total of 751 patients (4% of total sample) had a liver disease diagnosis recorded at the time of CDATS contact. Only 2% of patients had a diagnosis recorded for any type of diabetes.

Data on hepatitis A were insufficient to generate diagnoses. For the majority of the sample, patient status for HIV, hepatitis B, and hepatitis C were missing (95.9%, 87%, and 83.9% respectively). Where data were available, 30.0% were HIV positive, 6.6% were HBV positive, and 25.2% were HCV positive.

Of the total sample, 65.4% had never injected drugs while 10.3% had previously injected and 13.6% reported currently injecting drugs. Of those individuals who reported use of heroin and/or cocaine/crack, 24.7% reported currently injecting and 17.2% reported injecting in the past. Sharing equipment was not common; only 20.8% of patients who reported current or previous injecting also reported sharing equipment. Only 5.1% of the cohort reported engaging in high-risk sexual behaviour, although this information was unknown for just over a quarter of patients.

Following previous research using CRIS data (Chang et al. 2010), we defined the diagnosis of a serious mental illness (SMI) as a record of schizophrenia, schizoaffective disorders, or bipolar affective disorder. Just over 7% of patients had a SMI diagnosis recorded, with the majority being a psychosis-related diagnosis (89.8%). A diagnosis of anxiety or depression was recorded for 11.8% of patients.

Client Survey

Sample Characteristics

A total of 103 clients from two CDATS participated in the study. Due to the fact that recruitment to the study occurred via a gatekeeper (clinical staff) the participation rate cannot be calculated, but 100% of clients who made contact with research staff agreed to participate. Of these, 93% (n = 96) consented to linkage of their research questionnaire data to their electronic medical record data.

Participants were predominantly male (78.6%), born in the UK (68%), and heterosexual (91.3%; see Table 2). The majority (69%) had spent time in prison, although only 17.5% of the sample had done so in the past year. A large proportion of participants were in rental accommodation (40.8%) or living with friends or relatives (15.5%), but many were homeless (28.2%; n = 29) or in unstable living situations (15.5%).

Table 2: Sociodemographic characteristics of client survey sample

Category	Value	N	Percent
Gender	Female	22	21.4
	Male	81	78.6
Country of birth	Non-UK	33	32
	UK	70	68
Sexual orientation	Bisexual	5	4.9
	Heterosexual	94	91.3

	Homosexual	4	3.9
Time in prison	No	32	31.1
	Yes, but not in the past year	53	51.5
	Yes, in past year	18	17.5
Accommodation	Hostel	6	5.8
	Hotel or bed and breakfast	1	1
	Living with friends/relatives	16	15.5
	No fixed abode	29	28.2
	Other	9	8.7
	Rented (LHA)	29	28.2
	Rented (private)	13	12.6

Participants were predominantly receiving treatment for heroin use (68.9%; n = 71), but large proportions were receiving treatment for alcohol use (34%; n = 35), and crack cocaine use (30.1%; n = 31).

Liver Disease and Associated Clinical Risk Factors

A comparison of the percentage of clients with liver disease and associated risk factors in the self-report questionnaire data and EHR data described previously is shown in Table 3. Note that missing data has a different meaning for EHR data as a diagnosis code is usually only recorded to indicate confirmation that a condition is present; a code is not generally recorded to indicate the *absence* of a condition. Thus data for most conditions will be missing for most patients by default and does not necessarily indicate poor data quality (as would be the case for a traditional epidemiological survey).

Table 3: Comparison of results from electronic health record data and questionnaire data for clients

Condition or risk factor	**Values**	**EHR data (N = 18,848)**	**Questionnaire data (N = 103)**
Liver disease	Yes	4%	24.3%
	No	-	71%
	Missing	96%	3.9%
Hazardous alcohol use	Yes	52%	56.3%
	No	-	43.7%
	Missing	48%	0%
Diabetes	Yes	2%	3.9%
	No	0%	95.1%

	Missing	98%	1%
Hepatitis A	Yes	0%	1%
	No	0%	96%
	Missing	100%	2%
Hepatitis B	Yes	1%	2%
	No	12%	95%
	Missing	87%	2%
Hepatitis C	Yes	4%	25%
	No	12%	70%
	Missing	84%	4%
HIV/AIDS	Yes	1%	4%
	No	3%	95%
	Missing	96%	1%
Injecting drugs	Currently	14%	20%
	Previously	10%	29%
	Never	65%	51%
	Missing	11%	0%
Sharing injecting equipment	Not sharing	84%	82%
	Sharing	5%	18%
	Missing	11%	0%
High-risk sexual behaviour	Yes	5%	17%
	No	69%	83%
	Missing	26%	0%
Serious mental illness	Yes	7%	13%
	No	-	87%
	Missing	93%	0%
Anxiety and/or depression	Yes	12%	66%
	No	-	34%
	Missing	88%	0%

For many conditions the results from the two samples are similar, but they differ for liver disease itself and some key risk factors. Liver disease diagnoses were recorded for 4% of the EHR sample, but 24.3% of questionnaire participants reported a liver disease diagnosis. This is similar to the results for hepatitis C; 4% of the EHR sample had a record of the condition, compared to 25% of the questionnaire sample. Questionnaire participants were also more likely to report having been diagnosed with mental health conditions, with 13% reporting a SMI (compared to 7% in the EHR data), and 66% reporting anxiety and/or depression (compared to 12% of the EHR sample).

Treatment for Liver Disease and Associated Risk Factors

In the majority of cases, clients who had been diagnosed with liver disease or associated risk factors reported receiving treatment. Of the 25 participants who reported a liver disease diagnosis, 32% had received treatment and 20% had not (the remainder were unsure). The percentages receiving treatment for risk factors were: 76% for alcohol dependence, 100% for diabetes, 100% for hepatitis A, 50% for hepatitis B, 58% for hepatitis C, and 75% for HIV/AIDS. Note that the percentages for diabetes, hepatitis B and C and based on small diagnosis numbers (4, 2 and 4 participants respectively).

Patients who had not received treatment were invited to participate in a semi-structured qualitative interview to explore this further. Analysis of these data is ongoing but preliminary results suggest that: (i) patients not receiving treatment for alcohol dependence is due to patient refusal rather than lack of clinical support; (ii) lack of treatment for hepatitis C and liver disease is due to difficulties in accessing treatment via the NHS, particularly long waiting times, rather than lack of support from CDATS staff.

Staff Survey

Sample Characteristics

A total of 50 clinical staff from three sites participated in the survey. Participation rates for the two sites where data were physically collected were 69% and 100%. The participation rate for the site where data where questionnaires were distributed electronically is unknown. The sample was 56% female with an average age of 43.4 years (s.d. = 9.4 years). On average, participants had 11.6 years of clinical experience (s.d. = 7.5 years). Participants were mainly Drug Recovery Workers (38%) or Registered Nurses (26%), with the remaining participants including Psychologists, Psychiatrists, and Support Staff.

Resources and Training for Addressing Liver Disease Risk Factors

The majority of participants felt they had access to sufficient access to resources to support for clients in regard to alcohol dependence (84%), hepatitis B (86%), hepatitis C (86%), HIV (82%), safe sex practices (78%), and needle exchange (92%). Fewer participants felt there were adequate resources for addressing liver disease, with only 66% reporting sufficient resources, 18% reporting insufficient resources, and 16% unsure or not responding to the question. Just over a quarter of the sample (28%) had participated in further training regarding liver disease, but 56% reported that they had not been given an opportunity for further training.

Addressing Risk Factors During Alcohol/Drug Treatment

Participants reported that alcohol use, liver disease, HIV/AIDS, and hepatitis C were all considered a high priority for addressing during alcohol/drug treatment (Figure 2). However, responses were more mixed for diabetes, and hepatitis A and B.

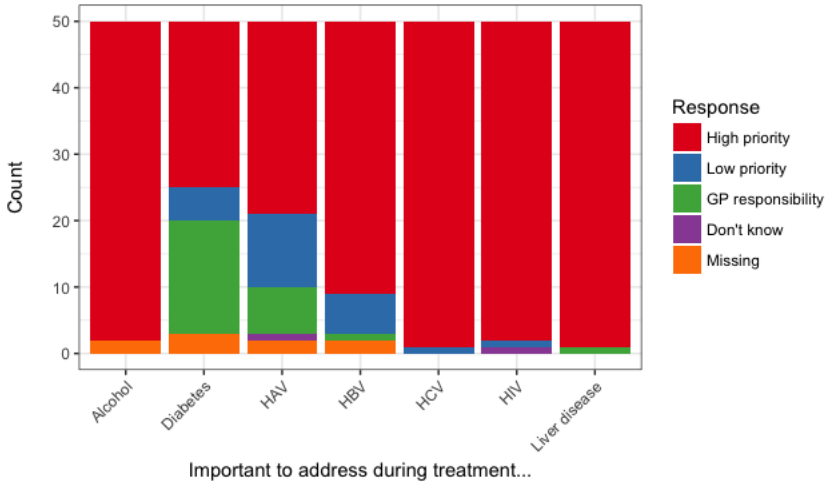

Figure 2: Staff priority for addressing liver disease and associated risk factors during alcohol/drug treatment

Perception of *client* interest in addressing these factors during treatment was similar to staff importance (see Figure 3), although the results suggest that clients view liver disease as less of a priority than clinical staff.

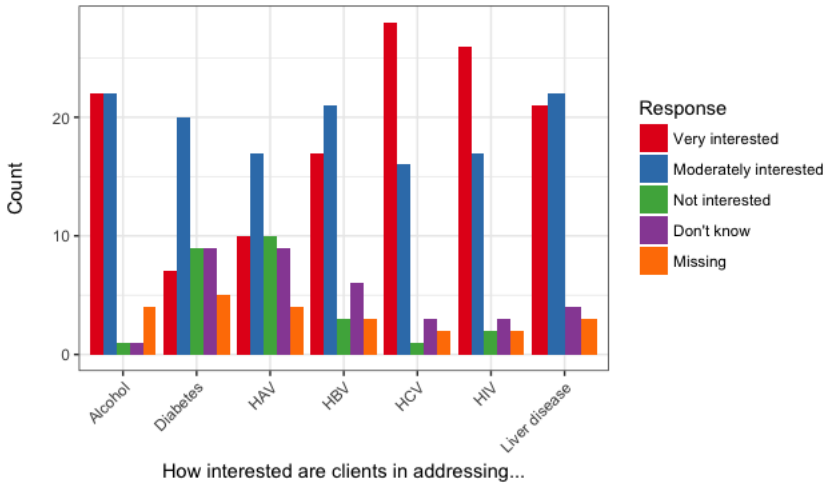

Figure 3: Perceived client interest in addressing liver disease and associated risk factors during alcohol/drug treatment

Obstacles to Treatment for Liver Disease and Associated Risk Factors

Participants viewed the biggest obstacles to treatment for liver disease and associated risk factors for clients as their low personal health priorities (72%), their underappreciation of the health consequences of heavy alcohol use (68%), and their lack of understanding of viral hepatitis and its health consequences (62%). Practical difficulties and fear of stigma or discrimination were less likely to be viewed as obstacles (52% and 46% respectively).

From a clinical perspective, the three most frequently endorsed obstacles to treatment were: clients failing to engage with treatment (80%), clients' unstable living arrangements (70%), and client mental health (60%). Uncertainty over duty of care and lack of client abstinence were less frequently viewed as obstacles (14% and 46% respectively).

DISCUSSION

Presence of Liver Disease and Associated Risk Factors

Overall there were substantial percentages of CDATS patients with one or more risk factors for liver disease, many of which are modifiable. Over half of patients have a record of engaging in hazardous alcohol use, and approximately a quarter have injected drugs, with a similar percentage having hepatitis C.

Comparison of Electronic Health Record and Self-Reported Data

Liver Disease

The percentage of patients with a diagnosis of liver disease varied substantially between the two CDATS patient samples; 4% of the EHR sample were diagnosed with liver disease compared to 24% of the questionnaire sample. There are multiple possible reasons for this. The first is the definition of liver disease. For the EHR data we focused on serious liver conditions i.e. Stage 2 (fibrosis, cirrhosis, hepatocellular carcinoma etc.) and Stage 3 (liver failure). However, most of the patients interviewed were unsure about the type of liver disease they had been diagnosed with, and it is likely that many of them had been diagnosed with Stage 1 conditions such as alcoholic liver disease. Second, patients may have been warned that their alcohol use and/or hepatitis C infection was having an impact on their liver function, and confused this receiving a formal diagnosis of liver disease. Third, the EHR data is limited in terms of timeframe and location, and patients may have referenced diagnoses that occurred outside our timeframe, or outside the NHS (England) system.

Sociodemographic Risk Factors

A large proportion of both samples were in unstable housing; 28.2% of the EHR sample and 43.7% of the questionnaire sample. The difference between the two samples may be due to bias in the sampling strategy and reimbursement for the questionnaire sample. Recruitment had to occur via a gatekeeper, so we do not know who refused contact with the research time; those in unstable housing situations may have been more likely to participate due to the participant payment offered. However, most clients interviewed were unaware they would be compensated for their time until it was explained to them as part of the consent process. A comparison of country of birth and time in prison between the EHR and questionnaire samples was not possible as this information was not accessible from the EHR database.

Clinical Risk Factors

The percentages of participants with clinical risk factors for liver disease were similar between the EHR and questionnaire samples for the majority of factors, but there were striking differences for hepatitis C and mental health conditions. For hepatitis C, 4% of the EHR sample had a record of the condition, compared to 25% of the questionnaire sample. However, this difference is primarily due to how blood test

results are recorded in ePJS. Blood test results are returned to clinical staff as an image file, rather than a text file, and these are not currently accessible via the research EHR interface (CRIS). Although there are text-based ePJS fields that blood test results can be entered into (and thus accessed for research), in practice, given the time-pressures faced by clinical staff, this is rarely done as from the clinic-facing side of the system this would be an unnecessary duplication of information.

There was also a substantial difference in the percentage of participants reporting anxiety and/or depression diagnoses. This was reported by 66% of the questionnaire sample, but diagnoses were only recorded for 12% of the EHR sample. One partial explanation may be that some participants were reporting on having feelings of anxiety or depression, rather than receiving clinical diagnosis, although 78% of those who reported depression also reported receiving clinical treatment (e.g. cognitive behavioural therapy and/or antidepressant medication). The major cause of the difference is likely to be the absence of primary care data for the SLaM EHR resource, as many of these diagnoses and associated treatment are likely to have been made by a GP. Linkage between the GP databases for the SLaM catchment is underway, but not yet complete.

Attitudes to Interventions for Risk Factors for Liver Disease

Clinical perspectives on patient obstacles to treatment for liver disease risk factors related to low client priorities regarding overall health and lack of understanding about the consequences of viral infections and alcohol use, with the consequence that clients did not engage with specialist treatment. This suggests a possible role for tools focused on improving risk communication and patient education, and thus increasing treatment interest and uptake.

However, staff also highlighted unstable living situations and poor mental health as obstacles to treatment for liver disease risk factors. This is particularly concerning given the large percentage of patients who reported unstable living situations (approximately 30-40%), and mental health problems (between 10 and 65%). This suggests that supporting clients to organise stable housing and access mental health treatment (either medication or psychological therapy) may also indirectly improve treatment of liver disease risk factors.

Assessment of Pilot Study

In practical terms, the original objectives of this study were to:

(i) extract and analyse EHR data on liver disease risk factors from SLaM CDATS clients;
(ii) collect and analyse questionnaire data from 250 SLaM CDATS clients;
(iii) link and analyse questionnaire data from SLaM CDATS clients to their EHR data;
(iv) collect and analyse questionnaire data from 50 SLaM CDATS clinical staff members.

Objectives (i) and (ii) were successfully completed. Objective (iii) was only partially completed, in that only 103 clients were recruited. This was due to a number of factors. First, the SLaM Service User Research Group that we discussed the project with advised on increasing our proposed participant reimbursement from £15 to £20, which reduced the number of participants we could recruit with available funds to 200. Second, ethical and regulatory approvals took eight months, which was approximately double the time anticipated based on previous applications. Third, in consequence of the delay two members of the research team (one 100% FTE, one 60% FTE) who were planning to undertake data collection left the project before data collection started (one took parental leave, and the other was awarded a travel fellowship).

This problem was partially solved by employing two casual Research Assistants to help the Principle Investigator undertake data collection (using discretionary funds held by the Principle Investigator). We were able to recruit 103 participants with only 15 days of data collection; were more time and more funds for staff available, we would have reached our revised goal of 200 participants. Due to the delayed start of data collection, we have not completed objective (iv), but linkage will be completed within the next two months.

Overall, the pilot of this study has been successful in developing a viable study protocol, and demonstrating the feasibility of recruiting CDATS patients. It has also demonstrated the acceptability of linking self-reported questionnaire data to EHR data to CDATS clients, with 93% of participants consenting to this.

NEXT STEPS

The immediate next steps for this research are to complete the data linkage and analyses and prepare the results for publication in a scientific journal. Once published, this article will be sent to Alcohol Research UK.

The medium-term next steps relate to both funding and further research. The results of this study, and the protocol itself, will form the basis of a grant application to undertake this research on a larger scale and in different patient populations in which understanding alcohol and drug use is clinically important (e.g. in emergency psychiatric care admissions). The data set linking client self-report questionnaire and medical record data will also be valuable for the further development of algorithms for reliably extracting information from EHR data sources.

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APPENDIX 1 – NATURAL LANGUAGE PROCESSING

Information Extraction

Two Information Extraction (IE) tools are currently available for use with CRIS: *TextHunter* and *SemEHR*. *TextHunter* has been used over a number of years to develop applications for extracting information on a range of psychiatric diagnoses and symptoms, as well as substance use and physical health conditions (for summary see (Perera et al. 2016). Output from existing *TextHunter* applications was used in the development of some variables, but as no new applications were developed for this cohort we do not describe *TextHunter* in detail here. Full details can be found in (Jackson et al. 2014).

The *SemEHR* IE tool has only recently become available for use with CRIS data. We used it to develop applications for extracting data on hepatitis C virus (HCV) infection and diagnosis of liver disease (LD). Briefly, *SemEHR* uses a NLP pipeline dedicated to annotating UMLS (Unified Medical Language System) concepts to identify mentions of a wide range of biomedical concepts in clinical notes, including terms from SNOMED CT, ICD-10, LOINC, and Drug Ontology. Each concept mention is also associated with 4-dimensional context information - negated, historical, hypothetical and experiencer. A patient-centric data model is then constructed to represent and associate three types of entities - Patient, Concept Mention and Clinical Note. Based on the model, a semantic search index is constructed to realise google-style searching for all entities and their associations. Most importantly, SemEHR incorporates semantic associations (from biomedical ontologies) between concepts (e.g. Steatohepatitis is a liver condition; Ribavirin is a drug for treating Hepatitis C), which are utilised in all types of searches SemEHR provides. Full details are available in (Wu et al. 2018).

Development of Patient-level Classifiers

The IE applications developed for this project recognise and classify individual mentions of a concept in available text, but do not produce an assessment at patient level. For example, a patient who is HCV positive is likely to have many mentions of HCV-related concepts in her clinical notes. However, not all of these mentions will necessarily indicate that the patient is HCV positive; some may refer to previous negative test results, or the HCV status of a relative or partner. The user must then develop a strategy for using the collection of results to produce an assessment at patient level. For each phenotype for which IE application data were available, we explored rule-based and statistical learning approaches to producing patient-level classifications.

APPENDIX 2 – CLIENT QUESTIONNAIRE

QUANTITATIVE INTERVIEWER-ADMINSTERED QUESTIONNAIRE

ASTERISK STUDY ID: _____ **CLINIC:** _____

A. SOCIODEMOGRAPHIC INFORMATION

A.1. AGE ☐☐ **A.2. GENDER** ☐ Male ☐ Female ☐ Transgender

A.3. COUNTRY OF BIRTH _____

A.4. SEXUAL ORIENTATION

☐ Heterosexual ☐ Homosexual ☐ Bisexual ☐ Prefer not to say

A.5. PRISON

Have you ever been in prison?

☐ No ☐ Yes, in the past year ☐ Yes, but not in the past year ☐ Don't know

A.6. CURRENT ACCOMMODATION

Where are you currently living?

☐ Owner occupied ☐ Rented (LHA) ☐ Rented (private) ☐ Living with friends/relatives

☐ Hostel ☐ No fixed abode ☐ Hotel or Bed & breakfast ☐ Other (specify): _____

A.7. HEIGHT **A.8. WEIGHT**

_____ cm _____ kg

A.9. GP VISITS IN THE LAST YEAR

For any reason, not just substance use

☐ None ☐ 1-2 times ☐ 3-6 times ☐ More than 6 times

SECTION A COMPLETE – TURN TO SECTION B (**PAGE 2**) FOR **ALL PARTICIPANTS**

B. SUBSTANCE USE TREATMENT

B.1. TIME IN TREATMENT

In total, how many years/months have you been in treatment for substance use in the UK?

_____ years _____ months

B.2. TREATMENT SUBSTANCES

What are the main substances you are receiving treatment for at the moment?

Multiple options possible; Use list to prompt if needed.

☐ Tobacco	☐ Heroin	☐ Crack
☐ Cannabis	☐ Morphine	☐ Cocaine
☐ Synthetic cannabinoids (e.g. spice, black mamba)	☐ Codeine	☐ Amphetamines
☐ Benzodiazepines	☐ **Alcohol** ***IF YES ASK B.3.***	☐ Other (specify): _____

B.3. EFFECT OF ALCOHOL DETOXIFICATION

How did your mood change after alcohol detoxification?

Could be community or residential. Use list to prompt. ONE ANSWER ONLY

☐ Haven't had detox.	☐ Improved mood	☐ Worsened mood
☐ No change	☐ Don't know	

B.4. TYPES OF TREATMENT RECEIVED

What type of treatment do you receive?

Multiple options possible; Use list to prompt if needed.

☐ Keyworking	☐ Group work	☐ Informal/open access	☐ Mutual aid support
☐ **OST: methadone** ***IF YES ASK B.5.***	☐ **OST: buprenorphine** ***IF YES ASK B.5.***	☐ Other pharmacotherapy (specify): _____	☐ Other (specify): _____

B.5. EFFECT OF OPIOID SUBSTITUTION TREATMENT

Did/does opioid substitution treatment affect your mood?

Use list to prompt; ONE ANSWER ONLY

☐ Improved mood a lot	☐ Improved mood a little	☐ No change
☐ Worsened mood a little	☐ Worsened mood a lot	☐ Don't know

SECTION B COMPLETE – TURN TO SECTION C (**PAGE 3**) FOR **ALL PARTICIPANTS**

C. SUBSTANCE USE

C.1. SUBSTANCE USE IN PREVIOUS 28 DAYS

Thinking back over the past 28 days, how many days did you use the following drugs each week?

Substance	Week 4	Week 3	Week 2	Week 1	Average per day
Alcohol	0-7	0-7	0-7	0-7	units
Tobacco *Include ready-made, hand-rolled, cannabis joints with tobacco, pipe, shisha, etc.*	0-7	0-7	0-7	0-7	
Cannabis	0-7	0-7	0-7	0-7	g
Synthetic cannabis	0-7	0-7	0-7	0-7	g
Heroin or non-prescribed opioid substitutes *(Methadone or buprenorphine)*	0-7	0-7	0-7	0-7	g
Morphine	0-7	0-7	0-7	0-7	tablets
Codeine	0-7	0-7	0-7	0-7	tablets
Crack	0-7	0-7	0-7	0-7	g
Cocaine	0-7	0-7	0-7	0-7	g
Amphetamines	0-7	0-7	0-7	0-7	g
Benzodiazepines	0-7	0-7	0-7	0-7	g
Other (specify):	0-7	0-7	0-7	0-7	g

C.2. HAZARDOUS ALCOHOL USE [AUDIT-C]

C.2.a. *How often do you have a drink containing alcohol?*

☐ Never ☐ Monthly or less ☐ 2-4 times per month ☐ 2-3 times per week ☐ 4+ times per week

C.2.b. *How many units of alcohol do you drink on a typical day when you are drinking?*

1 unit is equivalent to a third of a pint of beer, half a glass of wine, a 25mL single shot of whiskey

☐ 1-2 units ☐ 3-4 units ☐ 5-6 units ☐ 7-9 units ☐ 10+ units

C.2.c. *How often have you had 6 or more units (if female) or 8 or more units (if male), on a single occasion in the last year?*

Prompt: (if female) that's 3 glasses of wine or two pints of beer; (if male) that's 4 glasses of wine or 3 pints of beer

☐ Never ☐ Less than monthly ☐ Monthly ☐ Weekly ☐ Daily or almost daily

SECTION C COMPLETE – TURN TO SECTION D (**PAGE 4**) FOR **ALL PARTICIPANTS**

D. MENTAL HEALTH AND TREATMENT

D.1. PSYCHIATRIC DIAGNOSES

Have you ever been diagnosed or treated for the following conditions?

Multiple options possible.

☐ Schizophrenia	☐ Generalised anxiety disorder	☐ Conduct disorder	☐ Antisocial personality disorder
☐ Bipolar disorder	☐ Social phobia	☐ Compulsive disorder	☐ Attention deficit hyperactivity (ADHD)
☐ Other psychotic illness	☐ Agoraphobia	☐ Post-traumatic stress (PTSD)	☐ Borderline personality disorder
☐ Eating disorder	☐ Panic attack	☐ **Depression** ***IF YES ASK D.2.***	☐ Other (specify): _____

D.2. TREATMENTS FOR DEPRESSION

What treatments did you receive for depression?

☐ Anti-depressant medication	☐ Cognitive behavioural therapy (CBT)	☐ No treatment	☐ Other (specify): _____

D.3. SUICIDE

Have you ever attempted suicide?

☐ No	☐ Yes	☐ Prefer not to say

D.4. DEPRESSED MOOD

D.4.a. *Have you ever been consistently depressed, nearly every day, most of the day AND stopped enjoying most things, for at least two weeks?*

☐ **Yes** ***ASK D.4.b.***	☐ No ***Skip to Section E.***

D.4.b. *During that period, did you have problems with the following?*

Multiple options possible.

☐ Sleep	☐ Appetite	☐ Feeling guilty	☐ Problems concentrating
☐ Wishing you were dead			

SECTION D COMPLETE – TURN TO SECTION E (**PAGE 5**) FOR **ALL PARTICIPANTS**

E. SEXUAL RISK BEHAVIOUR

E.1. NUMBER OF PARTNERS

How many people, including clients, have you had sex with in the last month?

☐ More than 10 people	☐ 6-10 people	☐ 3-5 people
☐ 2 people	☐ 1 person	☐ **None**

IF NONE, SKIP TO SECTION F (PAGE 6), ELSE CONTINUE

E.2. CONDOM USE (REGULAR PARTNERS)

How often have you used condoms when having sex with your regular partner(s) in the last month?

☐ No regular partners OR no penetrative sex	☐ Every time	☐ Often
☐ Sometimes	☐ Rarely	☐ Never

E.3. CONDOM USE (CASUAL PARTNERS)

How often have you used condoms when you had sex with casual partners in the last month?

☐ No casual partners OR no penetrative sex	☐ Every time	☐ Often
☐ Sometimes	☐ Rarely	☐ Never

E.4. TRANSACTIONAL SEX

How often have you used condoms if/when you have been paid, or you have paid, for sex with money or drugs in the last month?

☐ No paid sex OR no penetrative sex	☐ Every time	☐ Often
☐ Sometimes	☐ Rarely	☐ Never

E.5. ANAL SEX

How many times did you have anal sex in the last month?

☐ No times	☐ One time	☐ Two times
☐ 3-5 times	☐ 6-10 times	☐ More than 10 times

SECTION E COMPLETE – TURN TO SECTION F (**PAGE 6**) FOR **ALL PARTICIPANTS**

F. INJECTING RISK BEHAVIOUR

F.1. LIFETIME INJECTING DRUG USE

Have you ever injected drugs?

☐ Yes ☐ **No**

IF NO, SKIP TO SECTION G (PAGE 7), ELSE CONTINUE

F.2. DURATION OF INJECTING DRUG USE

For how long have you been, or were you, injecting drugs?

_____ years _____ months

F.3. PAST MONTH USE

How often have you injected drugs in the past month?

☐ Daily (or more) ☐ Less than daily ☐ Not in last month

F.4. LAST DRUG INJECTED

What was the last drug you injected?

☐ Amphetamine or methamphetamine ☐ Heroin ☐ Cocaine

☐ Methadone ☐ Morphine ☐ Buprenorphine

☐ Other (specify): _____

F.5. NEEDLE SHARING

When you inject/ed drugs, how often do/did you inject with another person's used needle or syringe?

☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Every time

F.6. EQUIPMENT SHARING

When you inject/ed drugs, how often do/did you inject using another person's spoon, filter, or water?

☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Every time

F.7. CLEANING EQUIPMENT

When you have shared a needle, syringe, or other equipment, how often did you rinse it with a combination of full-strength bleach and water (i.e. the 2x2x2 method) before you used it?

☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Every time

SECTION F CONTINUES OVER PAGE (PAGE 7)

F. INJECTING RISK BEHAVIOUR (CONTINUED)

F.8. INJECTING SITE

When you inject/ed drugs, where do/did you usually inject?

☐ Arms ☐ Hands ☐ Feet ☐ Neck

☐ Groin ☐ Other (specify): _____

F.9. INJECTING-RELATED INJURIES AND DISEASES

Have you ever had any of the following injecting-related injuries, diseases, or problems?

Use list to prompt; multiple answers possible.

☐ Problems finding a vein

☐ Injection site infection for more than one week

☐ Septicaemia (blood poisoning; a serious bloodstream infection)

☐ Thrombosis (a clot in your vein)

☐ Prominent scarring/bruising

☐ Leg aneurysm

☐ Swelling of hands or feet after injecting

☐ Endocarditis (heart valve inflammation)

☐ Venuous ulcers (leg ulcers)

☐ Abscess

SECTION F COMPLETE – TURN TO SECTION G (**PAGE 8**) FOR **ALL PARTICIPANTS**

G. HEPATITIS

G.1. HEALTH INFORMATION AWARENESS

Are you aware of health information about hepatitis (i.e. prevention and treatment measures)?

☐ Yes, I have read leaflets at the clinic ☐ Yes, I have been given information by clinic staff ☐ No

G.2. HEPATITIS TESTING

Have you ever been tested for hepatitis A, B, or C?

☐ Yes, hepatitis A ☐ Yes, hepatitis B ☐ Yes, hepatitis C

☐ I was offered testing but refused ☐ Don't know ☐ No

G.3. HEPATITIS VACCINATION

Have you had a hepatitis A or hepatitis B vaccination?

☐ **No** ☐ Hepatitis A (complete) ☐ Hepatitis A (incomplete) ☐ Hepatitis A (unsure)

☐ **Don't know** ☐ Hepatitis B (complete) ☐ Hepatitis B (incomplete) ☐ Hepatitis B (unsure)

IF NO OR DON'T KNOW, SKIP TO SECTION H (PAGE 8), ELSE CONTINUE

G.4. VACCINATION TIMING

When did you have the vaccine/s

☐ Within the last 12 months ☐ 1-5 years ago ☐ 6-10 years ago ☐ Don't remember

G.5. BOOSTER VACCINATION

Have you had a booster vaccine since then?

☐ **Yes** ☐ No ☐ Don't know

IF YES, SKIP TO SECTION H (PAGE 9), ELSE CONTINUE

G.6. BOOSTER VACCINATION OFFERED

Have you been offered a booster vaccine?

☐ Yes ☐ No ☐ Don't know

SECTION G COMPLETE – TURN TO SECTION H (**PAGE 9**) FOR **ALL PARTICIPANTS**

H. LIVER DISEASE AND ASSOCIATED RISK FACTORS

H.1. PREVIOUS DIAGNOSES AND TREATMENT

Have you ever been diagnosed with, or treated for, the following:

	DIAGNOSED			TREATED		
	Yes	No	Don't know	Yes	No	Don't know
Alcohol dependence						
Diabetes						
Hepatitis A						
Hepatitis B						
Hepatitis C						
HIV/AIDS						
Liver disease						

Ask H.2.

H.2. TYPE OF LIVER DISEASE

What type of liver disease were you diagnosed with?

- ☐ Non-alcoholic fatty liver disease
- ☐ Alcohol-related liver disease
- ☐ Liver fibrosis
- ☐ Liver cirrhosis
- ☐ Liver cancer
- ☐ Don't know

H.3. LIVER FUNCTION TEST

Have you ever had, or been advised to have, blood tests to check how your liver is working?

- ☐ No
- ☐ Yes, at Drug and Alcohol Service
- ☐ Yes, at GP
- ☐ Yes, other (specify): _____
- ☐ Don't know

QUANTITATIVE INTERVIEW COMPLETE

IF PARTICIPANT SAID "YES" TO DIAGNOSIS OF CONDITION IN H.1. BUT "NO" TO TREATMENT, INVITE THEM TO PARTICIPATE IN QUALITATIVE INTERVIEW

IF PARTICIPANT REFUSES, OR IS NOT ELIGIBLE, THANK THEM FOR PARTICIPATING, ASK IF THEY HAVE ANY FURTHER QUESTIONS, AND PROVIDE REIMBURSEMENT

APPENDIX 3 – STAFF QUESTIONNAIRE

APPEAL FOR STAFF OPINIONS ON AVAILABLE NHS RESOURCES FOR TREATMENT OF LIVER DISEASE AND LIVER DISEASE RISK FACTORS IN ADDICTION SERVICES CLIENTS

Age (years): ***Gender:*** *Male* *Female* ***Clinic:_____***

Length of work experience with addiction clients: *years* *months*

1. Please select the professional group you are from *(tick only one box)*

- Admin and support
- Assistant Psychologist
- Consultant Clinical Psychologist
- Training Grade Doctor
- Trainee Psychologist
- Consultant Psychiatrist/Physician
- Non-training Grade Doctor
- Social worker
- Occupational Therapist
- Registered Nurse
- Drug Worker/Recovery Worker
- Manager
- Other (please specify):_____

2. Do you feel adequate resources are available in order to educate service users or provide services for the following? *(please tick as appropriate)*

	Yes	No	Don't know
Alcohol consumption (in drug-dependent clients)			
Hepatitis B			
Hepatitis C			
HIV			
Safer-sex practices			
Syringe exchange service			
Liver disease			

3. Have you been given opportunities for further or specialist training about liver disease?
(please tick only one box)

- Yes, I have taken part in a training course
- Yes, but I have not had the time to take part yet
- Yes, but I have not taken part as it is not relevant to my role
- Yes, but I have not taken part as the training required out of pocket expenses
- No, I have not been given an opportunity for training about liver disease
- Other (please specify):_____

4. Which, if any, of these conditions do you feel it is important to address during drug and alcohol treatment? *(please tick as appropriate)*

	High priority	Low priority	Responsibility of GP	Don't know
Alcohol consumption in drug-dependent clients				
Diabetes				
Hepatitis A				
Hepatitis B				
Hepatitis C				
HIV				
Liver disease				

5. How interested do you think service users are in addressing the following conditions? *(please tick as appropriate)*

	Very interested	Moderately interested	Not interested	Don't know
Alcohol consumption in drug-dependent clients				
Diabetes				
Hepatitis A				
Hepatitis B				
Hepatitis C				
HIV				
Liver disease				

6. What do you think are the biggest obstacles in the treatment of liver disease and associated risk factors from a service user perspective? *(tick all that apply)*

- ☐ Clients' low priority to personal health problems
- ☐ Clients' lack of understanding of hepatitis and its associated health consequences
- ☐ Clients' underappreciation of the health consequences of heavy alcohol consumption
- ☐ Practical difficulties in attending specialist clinics
- ☐ Fear of stigma/discrimination in primary care and/or specialist clinics
- ☐ Other (please specify):_____

7. What do you think are the most important obstacles to treatment of liver disease and risk factors from a clinical perspective? *(tick all that apply)*

- ☐ Service users refusing, or failing to turn up for, specialist referral appointments
- ☐ Homelessness or unstable living arrangements in service users
- ☐ Mental health problems in service users
- ☐ Other (please specify): _____
- ☐ Lack of liver doctors providing outreach clinics or scanning facilities in drug and alcohol services
- ☐ Uncertainty about duty of care between drug and alcohol services and primary care
- ☐ Lack of abstinence from alcohol/drugs in service users

8. What do you think are the percentages of clients who are vaccinated against hepatitis A and B in your service? *(please tick as appropriate)*

	0-20%	21-40%	41-60%	61-80%	81-100%	Not sure
Hepatitis A						
Hepatitis B						
Hepatitis A and B						

9. What do you think is the percentage of clients who are aware of hepatitis B and C treatments in your clinic?

☐ 0-20% ☐ 21-40% ☐ 41-60% ☐ 61-80% ☐ 81-100% ☐ Not sure

10. The Addictions Department at King's College London conducts research within SLaM drug and alcohol services on a regular basis. Have you been part of or involved in the recent PRAISe study?

☐ Yes ☐ No ☐ Don't know

11. Do you have any further comments about the treatment of liver disease and liver disease risk factors? *(please use the space provided)*

APPENDIX 4 – PHENOTYPE ALGORITHMS

Socio-demographics

Gender and ethnicity were readily available and required no further processing. Age at first face-to-face contact was computed using the cleaned date of birth (year and month of birth, but not the day). Whether a patient has previously spent time in prison is not routinely recorded in any structured fields. Patient living situation and employment status involved the integration of structured data from multiple sources. Patients were considered to be in an unstable living situation if there were data in the structured record reporting: participant housing status as homeless or unstable; a housing problem; or urgent need for accommodation. Patients with no records indicating an unstable living situation *and* a report confirming a stable living situation or no housing problem were categorised as being in a stable living situation. All other patients were treated as having missing data.

Alcohol and Drug Use

Information on substance was available from a wide range of sources and covers a broad range of substances, but we focused on those illicit drugs that are reported relatively frequently in these clients (Simonavicius et al. 2018) namely: opiates (including opioid analgesics), cocaine (including crack cocaine), and cannabis. We also included methadone and buprenorphine use, and benzodiazepine use. For alcohol and illicit drugs there were multiple sources of information that included ICD-10 diagnosis codes and keyword; those used are shown in the table below:

Substance	**Keywords**	**ICD-10 codes**
Alcohol	Alcohol	F10*
Opiate	Heroin, Other Opiates, Dihydrocodeine, Fentanyl, Physeptone, Opium, Codeine	F11*
Cocaine	Cocaine, Cocaine Hydrochloride, Crack Cocaine	F14*
Cannabis	Cannabis, Cannabis Herbal (Skunk)	F12*
Methadone or Buprenorphine	Methadone, Buprenorphine	
Benzodiazepam	Benzodiazepam, Diazepam, Alprazolam	

We treated the recording of an ICD-10 diagnosis relating to a substance, or listing of a substance keyword in fields relating to current use, as an indication of use.

Liver Disease

As few diagnoses of liver disease were identified based on structured fields in CRIS, we developed an IE tool for clinical notes using *SemEHR*. We used terms relating to liver diseases that could be at least partially causes by alcohol and/or drug abuse, with the exception of viral hepatitis as this would have created an overlap with the hepatitis C tool. As the tool only provided one source of information (presence or absence of a relevant term), a simple rule-based phenotype was used with the presence of at least one term considered sufficient for a diagnosis. We combined this information with liver disease diagnoses recorded using ICD-10 codes in HES data: K70.2, K70.3, K70.4, K71.7, K72.1, K72.9, K74.0, K74.1, K74.2, K74.6, K76.6.

Mental Health

Following previous research using CRIS data (Chang et al. 2010), we defined the diagnosis of a serious mental illness (SMI) as a record of schizophrenia, schizoaffective disorders, or bipolar affective disorder during the time window. Data were extracted as ICD-10 codes from the CRIS Diagnosis table and HES inpatient and outpatient diagnoses (F20, F25, and F31 respectively), and via keyword searches of the Diagnosis IE tool output. We defined the diagnosis of anxiety and/or depression as a record of depressive episode, recurrent depressive disorder, phobic anxiety disorders, or other anxiety disorders. ICD-10 codes F32, F33, F40, and F41 were used respectively, in addition to keyword searches of the Diagnosis IE tool output.

Diabetes

We applied an existing IE application for diabetes as no diabetes diagnoses were recorded in structured fields, but CRIS records contained insufficient information to generate diagnoses. Thus only diagnoses from HES, using ICD-10 codes, were included: E10*, E11*, E12*, E13*, E14*.

Risk Behaviours

Information on injecting drug use and sexual-risk taking is not well-recorded in HES, so this information was only drawn from CRIS using assessment forms specifically designed for addiction services: Treatment Outcomes Profile (Marsden et al. 2008), and clinical risk assessment tools.

Blood-borne Viruses

As few diagnoses of hepatitis C were identified based on structured fields in CRIS, we developed an IE tool for clinical notes using *SemEHR*. We used terms relating to

diagnosis of hepatitis C, and also terms for drug combinations used primarily for treatment of hepatitis C. For more information see (Wu et al. 2018). For HIV/AIDS we used an existing *TextHunter* IE tool which focused on HIV/AIDS diagnoses and medication used to treat the condition. The output for the IE tools was combined with relevant ICD-10 codes recorded in HES data: B15*, B16*, B17.0, B17.1, B18.0, B18.1, B18.2, B20*, B21*, B22*, B23*, B24*.