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Comorbidities and medications of patients with chronic hepatitis C under specialist care in the UK

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Designing services with the capacity and expertise to meet the needs of the chronic hepatitis C (CHC) population in the era of direct acting antivirals (DAAs), and widening access to such treatments, requires detailed understanding of the characteristics and healthcare needs of the existing patient population. In this retrospective analysis of data from the National HCV Research UK Biobank between March 2012 and October 2014, the characteristics of the CHC population currently under specialist care in the UK were evaluated—with specific focus upon use of medications, adverse lifestyle choices, and comorbidities. Demographic data, risk factors for CHC acquisition, HCV genotype, liver disease status, lifestyle factors, comorbidities, and medication classes were collected. Data were analyzed by history of injecting drug use (IDU), age, and severity of liver disease. A total of 6278 patients (70.5% white; median age, 52 years) from 59 UK specialist centres were included; 59.1% of patients had acquired HCV through IDU. The prevalence of adverse lifestyle factors was significantly lower in non-IDU compared with previous IDU or recent IDU patients. Depression was common in the previous (50.8%) and recent IDU (68.1%) groups, compared with 27.6% in non-IDU patients. Cirrhosis was common (23.6%), and prevalence increased with age. We describe a heterogeneous, polymorbid, and aging population of CHC patients in secondary care, and demonstrate underrepresentation of injecting drug users within the current system. The implications of this present significant challenges to physicians and healthcare commissioners in designing services which are fit for purpose inthe DAA era.

KEYWORDS
chronic hepatitis C, direct-acting antivirals, drug-drug interaction, hepatitis c virus, injecting drug use

1 | BACKGROUND

Chronic hepatitis C (CHC) is estimated to affect approximately 130-150 million people worldwide, causing around 500 000 liver-related deaths per year.[1] In 2013/2014, approximately 214 000 individuals had CHC in the UK. Between 1996 and 2012, deaths from end-stage liver disease or hepatocellular carcinoma where hepatitis C was mentioned on the death certificate more than tripled in the UK.[2] In 2012 in the UK, approximately

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3% of patients diagnosed with CHC received CHC treatment, a figure which is thought to be lower among people who inject drugs (PWID).[3]

In the UK, 90% of individuals infected with hepatitis C virus (HCV) are thought to have acquired the infection through injecting drug use (IDU), and approximately 50% of PWID are estimated to have CHC.[4] Data from Public Health England demonstrate that rapid upscaling of treatment with new therapies is required if further rises in severe CHC-related disease are to be prevented.[5]

The introduction of interferon-free direct-acting antivirals (DAAs) has changed the CHC treatment paradigm.[6,7] Compared to interferon-based regimens, treatment with DAAs is more efficacious, better tolerated, and of shorter duration.[8] While there was previously no available therapy for CHC with advanced liver disease, recent data show effectiveness of DAA therapy in this population: in an observational cohort study of 467 patients in the UK, of whom 409 had decompensated cirrhosis, DAA therapy led to viral clearance in 81.6% of patients.[9] Sustained virological response was associated with improvements in liver function within 6 months compared with an untreated, matched control group.

Studies suggest that, compared with individuals without HCV infection, patients with CHC have a higher burden of comorbidities (such as psychiatric disorders, co-infection with hepatitis B and/or HIV, atherosclerosis, and chronic kidney disease) in addition to a high prevalence of adverse lifestyle choices such as alcohol and substance abuse.[10,11] Such factors may pose challenges to effective treatment, particularly for patients who have acquired HCV through IDU.[12,13] Almost all current DAAs are associated with risks of drug-drug interactions (DDIs), although these differ substantially between agents.[6]

Unlike in HIV, where there is a live national dataset for all patients enrolled in treatment (The HIV and AIDS Reporting System; https://www.gov.uk/guidance/hiv-surveillance-systems), very little is known about the make-up of the UK CHC patient population currently in secondary care—for whom services and treatments will need to be designed and appropriately prioritized in the DAA era. The absence of such information leaves vital clinical, commissioning, and public health questions unanswered. These include how clinical services should be structured to address the specific healthcare needs of the population requiring treatment, the extent of the future resource requirement, the expertise required to provide such care (both in terms of disease management and in laboratory services), and the associated cost implications of this. From a public health perspective, it is unclear whether the population currently enrolled in secondary care services, and therefore those to whom DAAs will be available, reflect the wider UK HCV population and, if not, how efforts to provide more equitable access to care should be focused. Understanding the characteristics and wider health needs of the UK CHC population currently in secondary care, and how this reflects wider population estimates, is essential in this regard. Furthermore, an appreciation of the factors specifically affecting PWID is vital in widening access to care in this already disadvantaged group.

The aim of this study was to use patient data from the National HCV Research UK Biobank to describe the demographics of patients currently under specialist hepatology care in the UK who are likely to be eligible for DAA treatment over the next 5 years, and investigate the prevalence of comorbidities, adverse lifestyle factors, and use of medications with potential DDIs involving DAAs. This is with a view to estimating clinical need, informing future service design, and directing public health interventions. The characteristics of patients who acquired HCV through IDU and non-IDU transmission routes were also compared.

2 | PATIENTS AND METHODS

This was a retrospective analysis of patient data from centres enrolled in the National HCV Research UK Biobank (http://hcvresearchuk.org). HCV Research UK is a national cohort of over 10 000 patients with HCV infection recruited from 59 secondary care clinics across England, Scotland, and Wales. Eligibility criteria for enrolment in the database were attendance at a secondary care clinic for management of chronic HCV infection and ability to give informed consent.

Inclusion criteria in this analysis were CHC patients enrolled in HCV Research UK from 2012 onwards, aged over 18 years, infected with any HCV genotype, viraemic at enrolment, and not receiving a course of CHC treatment at enrolment. Excluded patients included those who had cleared CHC or were on treatment. This represents the population who will be currently under consideration for DAA treatment within the UK.

Data from March 2012 to October 2014 were collected from fixed text data fields which comprised demographic data; risk factors for CHC acquisition (collected hierarchically in the following order: IDU, blood/blood product transfusion, born abroad, sexual partner with HCV, perinatal exposure, other [mostly exposure through tattoo needles, body piercing, other needle exposure]); HCV genotype; liver disease status; lifestyle factors (tobacco smoking, cannabis use, and alcohol use); comorbidities (renal failure requiring dialysis, diabetes, cancer, depression [defined as a positive answer to any of the following queries: ever diagnosed with clinical depression, ever treated for depression, ever admitted to hospital for depression, ever attempted suicide], HIV co-infection, bleeding disorder, and cryoglobulinaemia); and history of medication with classes of medications with known DDI potential to DAAs (antidiabetics, antidepressants, antiretrovirals, hypnotics, opiate substitution therapy, steroids, other immunosuppressives, statins). Antidepressants, opioids, and hypnotics were grouped collectively as psychotropic agents. For patients who had acquired HCV through IDU, patients were further categorized according to drug use at the time of enrolment. Patients who had injected within the last 6 months or who were requiring opioid replacement therapy at the time of enrolment were classified as "recent IDU." Patients who had acquired CHC through previous intravenous drug use, but who had not injected within the last 6 months and were currently not requiring opioid replacement therapy were classified as "previous IDU."

Logistic regression was used to determine differences in lifestyle factors, comorbidities, and medication use according to the method of HCV acquisition. Non-IDU patients were used as the reference group, with odds ratios and 95% confidence intervals determined for the previous IDU and recent IDU groups separately. Odds ratios over 1 relate to a higher likelihood of the lifestyle factor/comorbidity/medication in the previous or current IDU group than in the reference non-IDU group.

Univariable logistic regression was performed initially, then odds ratios were adjusted for age to account for differences between acquisition routes. Where indicated, proportions were age-standardized by direct standardization, using the non-IDU group as the reference. Statistical analysis was carried out using Stata 13.1 (StatCorp, Austin, TX).

3 | RESULTS

A total of 6278 patients with CHC from 59 UK specialist centres were included in the analysis. Patient demographics are shown in Table 1. Over two-thirds (70.5%) of patients were male, and 85% were white. Overall, 58% of patients were aged 50 years or above; median age was 52 (interquartile range 43-59) years. Overall, 59.1% of patients had acquired CHC through IDU (Fig. S1). The median age of patients who acquired HCV through IDU was 50 years (interquartile range 42-56) compared with 55 years (interquartile range 46-62) in non-IDU patients. The mean age of the IDU group was significantly lower than the non-IDU group (49.2 vs 54.0, $P < 0.0001$). In total, 50% of patients were infected with HCV genotype 1, and 33.7% were infected with genotype 3. The distribution of patients by genotype was broadly similar in IDU and non-IDU acquisition groups.

The severity of liver disease at enrolment was recorded by the treating clinician and classified as non-cirrhotic, cirrhosis, or decompensated cirrhosis. The overall prevalence of cirrhosis (compensated and decompensated) was 23.6% across the whole cohort, a figure that was not significantly different between etiological groups. The prevalence of cirrhosis rose sharply with age, with 36.6% of those over 60 years of age having cirrhosis or decompensated cirrhosis.

Table 2 shows the prevalence of adverse lifestyle factors. After adjusting for age, the prevalence of all adverse lifestyle factors were significantly higher in patients with previous and recent IDU compared with non-IDU patients. The prevalence of all adverse lifestyle factors other than current alcohol use were significantly higher in patients with recent IDU compared with non-IDU patients.

Table 3 shows prevalence of comorbidities. The most common comorbidities were depression (26.1%), diabetes (11.3%), and malignancy (not including hepatocellular carcinoma [HCC]) (5.0%). HIV co-infection was present in 5.0% of patients. Compared with patients who had not acquired HCV through IDU (after adjusting for age), depression was significantly more common among patients with previous or recent IDU, while diabetes and renal failure were significantly less common. After age adjustment, malignancy and HIV were significantly less common among patients with recent IDU compared with non-IDU (1.5% and 4.1% vs 6.7% and 5.5%, respectively).

Figure 1 shows that the prevalence of diabetes, malignancy, and renal failure increased with age, reaching 22.9%, 18.1%, and 2.2%,

TABLE 1 Patient demographics

	n (%)		
	Total, N = 6278	**HCV acquired via IDU, N = 3714**	**HCV acquired via route other than IDU, N = 2564**
Male	4424 (70.5)	2815 (75.8)	1527 (62.2)
White	5315 (84.7)	3550 (95.6)	1674 (68.2)
Median age (IQR), years	52 (43-59)	50 (42-56)	55 (46-62)
Age, years			
18-29	165 (2.6)	92 (2.5)	71 (2.9)
30-39	861 (13.7)	564 (15.2)	283 (11.5)
40-49	1613 (25.7)	1149 (31.0)	446 (18.2)
50-59	2156 (34.3)	1296 (34.9)	823 (33.5)
60-69	1176 (18.7)	574 (15.5)	574 (23.4)
≥70	294 (4.7)	32 (0.9)	254 (10.3)
Unknown	13 (0.2)	7 (0.2)	5 (0.2)
Genotype			
1	3141 (50.0)	1908 (51.4)	1184 (48.2)
2	250 (4.0)	147 (3.96)	99 (4.03)
3	2115 (33.7)	1291 (34.8)	792 (32.3)
4	225 (3.6)	58 (1.6)	163 (6.6)
5	15 (0.2)	1 (0.03)	13 (0.53)
6	8 (0.1)	3 (0.08)	3 (0.12)
Other	23 (0.37)	19 (0.51)	4 (0.16)
Unknown	501 (8.0)	287 (7.73)	198 (8.06)

IDU, injecting drug use; IQR, interquartile range; HCV, hepatitis C virus.

TABLE 2 Alcohol consumption, current tobacco, and cannabis use, by IDU status (non-IDU, previous IDU, and recent IDU)

Lifestyle factors	Non-IDU (ref), n = 2456 n (%)	Previous IDU, n = 2256 n (%)	Unadj. OR (95%CI)	Age-adj. OR (95%CI)	Recent IDU, n = 1458 n %	Unadj. OR (95%CI)	Age-adj. OR (95%CI)
Current alcohol use	843 (34.3)	1036 (45.9)	1.6 (1.4, 1.8)	1.6 (1.4, 1.8)	594 (40.7)	1.3 (1.1, 1.5)	1.2 (1.0, 1.4)
History of high alcohol consumption	496 (20.2)	1165 (51.6)	4.0 (3.5, 4.5)	4.0 (3.6, 4.6)	696 (47.7)	3.4 (3.0, 3.9)	3.6 (3.1, 4.2)
Current smoking	741 (30.2)	1356 (60.1)	3.4 (3.1, 3.9)	3.4 (3.0, 3.8)	1281 (87.9)	16.5 (13.8, 19.8)	12.8 (10.7, 15.4)
Current cannabis use	223 (9.1)	640 (28.4)	3.9 (3.3, 4.6)	3.8 (3.2, 4.5)	667 (45.7)	8.3 (7.0, 9.8)	7.4 (6.2, 8.8)

CI, confidence interval; IDU, injecting drug use; OR, odds ratio. The non-IDU group was used as the reference group when calculating the unadjusted (unadj.) and age-adjusted (age-adj.) ORs.

respectively in patients aged 60 years and above. Depression was the only pathology that became less common with advancing age.

Overall, the most common medications with DDI potential were psychotropic agents (antidepressants, opioids, and hypnotics) (38.6%), antidiabetics (9.3%), immunosuppressants (6.1%), statins (4.9%), and antiretrovirals (4.9%). Table 4 shows the prevalence of prescribed medications. Compared with the non-IDU group, the use of psychotropic agents was significantly more common in previous and recent IDU groups. Among patients with current IDU, 48% were prescribed antidepressants and/or hypnotic combined, of which 80% were antidepressants alone. Use of antidiabetics was significantly lower in previous IDU and recent IDU patients compared with non-IDU patients. Use of immunosuppressants, antiretrovirals, and statins was significantly lower in patients with recent IDU versus non-IDU. The relatively high proportion of patients on immunosuppressants, particularly in the non-IDU group, may be reflective of the proportion of the cohort who had

undergone orthotopic liver transplantation (OLT). 5.2% of the cohort (9.3% of non-IDU group, 4.3% of previous IDU group, 0.2% of recent IDU group) were recorded as having undergone OLT prior to treatment. OLT was recorded as a free text field (as opposed to a compulsory fixed text field), so these figures may represent an underestimate.

Figure 2 shows the prevalence of medication use by age. Use of antidiabetics, immunosuppressants, and statins increased with age (18.8%, 12.7%, and 11.7%, respectively, in patients over 60 years of age). Use of psychotropic medication demonstrated the opposite trend with frequency of use decreasing with age.

Supplementary Table S1 shows the frequencies of common co-medications relating to stage of liver disease. The increased rates of antidiabetic medications among cirrhotic patients may reflect the significance of diabetes as a risk factor for the development of cirrhosis. Immunosuppressant usage is likely to reflect rates of liver transplantation, with increased use in patients with non-cirrhotic

TABLE 3 Prevalence of comorbidities by IDU status (non-IDU, previous IDU, and recent IDU)

Comorbidities	Non-IDU (ref) n = 2456 n (%)	Previous IDU, n = 2256 n (%)	Unadj. OR (95%CI)	Age-adj. OR (95%CI)	Recent IDU, n = 1458 n (%)	Unadj. OR (95%CI)	Age-adj. OR (95%CI)
History of depression	679 (27.6)	1145 (50.8)	2.3 (2.0, 2.6)	2.3 (2.0, 2.6)	993 (68.1)	3.4 (2.9, 3.9)	3.4 (2.9, 3.9)
Diabetes	437 (17.8)	208 (9.2)	0.5 (0.4, 0.6)	0.6 (0.5, 0.7)	51 (3.5)	0.2 (0.1, 0.2)	0.3 (0.2, 0.4)
Malignancy (not including HCC)	176 (6.7)	118 (5.23)	0.7 (0.6, 0.9)	0.9 (0.7, 1.1)	22 (1.5)	0.2 (0.1, 0.3)	0.4 (0.2, 0.6)
HIV	135 (5.5)	109 (4.8)	0.9 (0.7, 1.1)	0.8 (0.6, 1.1)	60 (4.1)	0.7 (0.5, 1.0)	0.6 (0.4, 0.8)
Renal failure	58 (2.4)	15 (0.7)	0.3 (0.2, 0.5)	0.3 (0.2, 0.5)	6 (0.4)	0.2 (0.1, 0.4)	0.2 (0.1, 0.5)

CI, confidence interval; HCC, hepatocellular carcinoma; HIV, human immunodeficiency virus; IDU, injecting drug use; OR, odds ratio. The non-IDU group was used as the reference group when calculating the unadjusted and age-adjusted ORs.
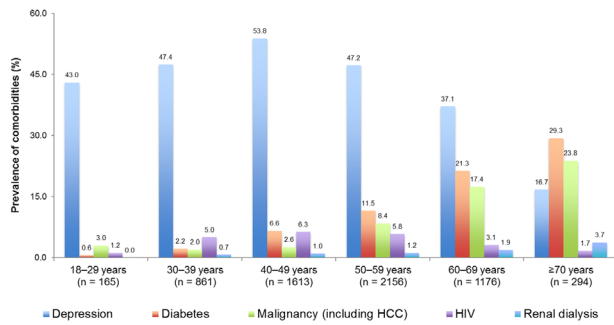
FIGURE 1 Prevalence of comorbidities by age group. HCC, hepatocellular carcinoma; HIV, human immunodeficiency virus

grafts, and smaller numbers of patients with concomitant graft cirrhosis requiring ongoing immunosuppression.

4 | DISCUSSION

This study represents the first description of patterns of non-HCV comorbidities, co-medications with DDI potential, and lifestyle factors in patients with CHC who are or will be eligible for DAA treatment in the UK.

Comorbidities were common in the overall cohort, particularly depression (26.1%), diabetes (11.3%), and non-hepatic malignancy (5.0%). Use of medications with potential DDIs involving DAAs were also widespread, with psychotropic medications (38.6%), antidiabetics (9.3%), immunosuppressants (6.1%), statins (4.9%), and antiretrovirals (4.9%) being the most commonly recorded agents.

In this cohort, 59.1% of patients had acquired HCV through IDU, and 23% were recent injectors. In the UK it is estimated 90% of individuals infected with HCV are thought to have acquired the infection through IDU and approximately 50% of PWID have CHC.[4] As such the number of PWID in this cohort appears disproportionately low, indicating it is likely that PWID are significantly under-represented in secondary care. This may reflect inequity in access to

treatment for these patients under the traditional service model.[3] Although NICE guidelines were changed in 2004 to include current injectors,[14] there is evidence that some hospitals still use this as a criterion for exclusion from treatment.[3]

Aside from the ethical responsibility to deliver services which equate to need—there are further public health benefits of focussing service delivery strategies around this group. A recent modelling analysis by Martin et al[15] suggested that the treatment of active injectors is an effective measure for decreasing HCV infection in a community by reducing the pool of patients capable of passing the infection onto others.

At present access to DAA treatment within the NHS is dependent upon enrolment in a secondary care clinic, and our results demonstrate this model of care is unlikely to be fit for purpose in providing appropriate access to the IDU community. The Scottish Hepatitis C Action Plan, which specifically targets PWID and ensures those infected receive rapid and optimal treatment, is an example of how service design could be revisited in order to redress this inequity. Initiatives ranged from the introduction of testing in specialist drug services through finger-prick blood sampling by non-clinical staff, to the setting of government targets to ensure rapid scale-up of antiviral therapy.[16]

In addition to the problems with accessing PWID, our data demonstrates this population may be particularly challenging to treat, given the levels of comorbidities and use of medications with potential DDIs. Prevalence of hazardous lifestyle factors, such as smoking, alcohol abuse, and cannabis use, were significantly higher in previous and recent IDU patients compared with the non-IDU group. Mental illness was extremely common in the IDU cohorts, reflected by the high prevalence of depression and use of psychotropic medication (the latter may be an indicator of additional, uncaptured, recreational drug use).

Conversely, age adjusted use of other medication classes by current injectors was significantly lower compared with non-IDU patients (Table 4), a trend that was mirrored when looking at prevalence of physical comorbidities. Whereas differences observed in psychiatric co-morbidity were largely expected, the opposite trend

TABLE 4 Prevalence of medication with DDI potential by IDU status (non-IDU, previous IDU, and recent IDU)

Medications	Non-IDU (ref) n = 2456 n (%)	Previous IDU, n = 2256 n (%)	Unadj. OR (95%CI)	Age-adj. OR (95%CI)	Recent IDU, n = 1458 n %	Unadj. OR (95%CI)	Age-adj. OR (95%CI)
Psychotropics[a]	420 (17.1)	635 (28.1)	1.9 (1.6, 2.2)	1.9 (1.6, 2.2)	1343 (92.1)	56.2[b] (45.3, 69.8)	55.9[b] (44.7, 69.9)
Antidiabetics	375 (15.3)	157 (7.0)	0.4 (0.3, 0.5)	0.5 (0.4, 0.6)	40 (2.7)	0.2 (0.1, 0.2)	0.3 (0.2, 0.4)
Immuno-suppressants	217 (8.8)	136 (6.0)	0.7 (0.5, 0.8)	0.8 (0.6, 1.0)	15 (1.0)	0.1 (0.1, 0.2)	0.2 (0.1, 0.3)
Antiretrovirals	130 (5.4)	110 (4.9)	0.9 (0.7, 1.2)	0.9 (0.7, 1.1)	59 (4.0)	0.7 (0.5, 1.0)	0.7 (0.5, 0.9)
Statins	165 (6.7)	96 (4.3)	0.7 (0.5, 0.9)	0.9 (0.7, 1.2)	39 (2.7)	0.3 (0.2, 0.4)	0.6 (0.4, 0.9)

CI, confidence interval; DDI, drug-drug interaction; IDU, injecting drug user; OR, odds ratio. The non-IDU group was used as the reference group when calculating the unadjusted (unadj.) and age-adjusted (age-adj.) ORs.
[a]Psychotropics include antidepressants, opioids, and hypnotics.
[b]Definition of recent IDU included those on opioid substitution therapy. Opioids were also classified as a psychotropic agent in this calculation, partly accounting for high odds ratio here. Odds ratios removing opioids from definition of psychotropic agents: Unadjusted: Previous IDU: 2.0 (CI 1.8-2.3) Recent IDU: 4.8 (CI 4.2-5.6) Age adjusted: Previous IDU: 2.0 (CI 1.8-2.3) Recent IDU: 4.9 (CI 4.2-5.7).
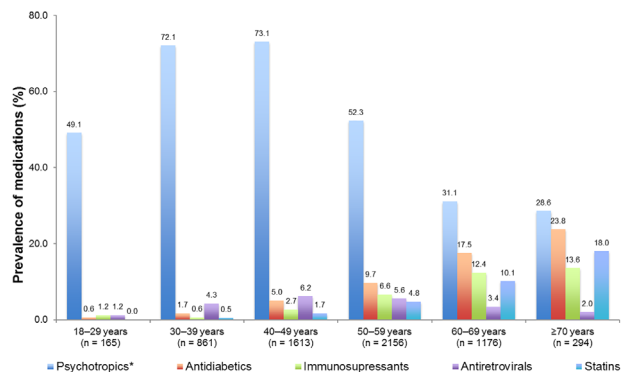
FIGURE 2 Prevalence of medication by age group.
*Psychotropics include antidepressants, opioids, and hypnotics

with physical co-morbidity was unexpected. Several possible explanations for this exist, the first relating to potential differences in health seeking behaviors between the groups. Data were recorded at the point of enrolment in secondary care. Given the commonly circuitous and limited access to healthcare amongst IDU communities described above, it is plausible that the physical co-morbidities would have been under-diagnosed or reported at the point of enrolment, and as such not captured in the data. Characteristics (in terms of social support, access to healthcare, etc) of PWID enrolled in secondary care may be different to an otherwise matched population not enrolled in secondary care. Given the under-representation of PWID in this secondary care cohort, it is unlikely that reported levels of co-morbidity accurately reflect those of the wider IDU HCV population. Conversely, characteristics of the non-IDU group are likely to be more representative. IDU groups were significantly younger, and therefore less likely to have age related co-morbidities, such as type 2 diabetes and hypercholesterolaemia. Statistical adjustment for age was undertaken, with rates of comorbidity significantly lower following adjustment, but not before. While we consider this adjusted comparison more appropriate, it assumes a linear effect of increasing age which has the potential to overstate differences. Recorded OLT was significantly more common within the non-IDU group (9.3% non-IDU vs 2.7%—IDU overall). Metabolic syndrome increases dramatically following OLT,[17] and the substantially higher rates of OLT amongst non-IDU patients may have contributed to the higher rates of statin and anti-diabetic use in this group. It is likely that complications from cirrhosis are commonly replaced by complications of the metabolic syndrome among patients who undergo OLT prior to treatment—a factor which impacts disproportionately on the non-IDU group in this analysis.

In the current study population, 23.6% of patients in this cohort had cirrhosis. Although advanced liver disease in patients with CHC has previously been a barrier to effective CHC treatment, the safety and clinical efficacy of DAAs in patients with decompensated cirrhosis has been widely demonstrated.[9] Patients with advanced liver disease nonetheless represent a vulnerable group who are likely to require more prolonged and complex treatments, will be more susceptible to adverse events, and in whom the potential effects of DDI may be more severe. Rates of cirrhosis increased sharply with age. The proportion of patients commencing treatment with cirrhosis is therefore also likely to

increase in line with the projected increases in age of the CHC population under treatment over the next decade. This has service design implications beyond HCV treatment itself, in that expertise in the management of decompensated cirrhosis will need to be integrated within service design—an important point of consideration, particularly in areas where HCV treatment is co-ordinated by infectious disease physicians as opposed to hepatologists, or when considering the allocation of specialist physician time when designing nurse, or community centred services.

The results of our study concur with the high rates of comorbidities and use of medications with DDI potential to DAAs reported among patients with CHC in studies conducted in predominantly specialist settings in the USA[18,19] and Germany.[20] Our study complements a recent analysis of patients with CHC seen in UK primary care.[21] In this study over two-thirds of patients received medication with a potential DDI to at least one DAA, but less than 1% of patients received medications with contraindications to all four DAAs studied. High levels of comorbidity were also reported, with similar age-related trends as observed in the current study. Both studies concur that patients with CHC in the UK have high levels of non-HCV comorbidity and polypharmacy.

The data used for this analysis were obtained from an opt-in database: only those data added by clinicians were available, and clinical notes were not accessible, creating a risk of information bias. While the cohort analyzed in this study may not be reflective of the CHC population as a whole, we consider it representative of CHC patients attending UK secondary care, owing to the wide geographic range covered and the types of clinics that participated. Indeed, in the largest centres, 100% of patients were recruited. Lastly our analysis only includes data from patients within secondary care services. A comparison with untreated hepatitis C patients outside of secondary care services may better highlight gaps in current access to treatment. Furthermore, this may better describe the demographics of the IDU population, and provide further insight into how strategies to improve access should be targeted.

Our study demonstrates that the current population of patients with CHC seen in UK secondary care constitutes a complex and heterogeneous group at high risk of disease-drug and drug-drug interactions, both of which can have damaging consequences for the patient and limit effectiveness of therapy. We demonstrate that PWID are currently under-represented in secondary care clinics, and that this group is disproportionately affected by concomitant burdens of adverse lifestyle factors and mental illness, both of which may further limit effectiveness of treatment.

Upscaling CHC treatment and widening of access to care has the potential to reduce population prevalence and ultimately deaths from CHC-related end-stage liver disease. For this to be achieved, current service models will need be re-evaluated, taking into account the current inequitable access to PWID, and the necessary physician expertise required to manage this complex and comorbid population. Careful consideration of the clinical and cost implications will be required by providers and payors.

CONFLICTS OF INTEREST

William Irving has participated in advisory committees or review panels for Novartis, MSD, Janssen Cilag and Bristol Myers Squibb; received grant/research support from GSK, Pfizer, Janssen Cilag, Gilead Sciences; and received speaking and teaching fees from Janssen Cilag and Roche. Benjamin Hudson and Alex J. Walker have nothing to disclose.

AUTHORS' CONTRIBUTIONS

WLI contributed in study concept and design. BH contributed in analysis and interpretation of data. BH, AJW, WLI contributed in critical revision of the manuscript and AJW contributed in statistical analysis.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.