Public Health England

Protecting and improving the nation's health

Hepatitis C treatment monitoring in England

Content, completeness and preliminary findings from the Hepatitis C patient registry and treatment outcome system

About Public Health England

Public Health England exists to protect and improve the nation's health and wellbeing, and reduce health inequalities. We do this through world-leading science, knowledge and intelligence, advocacy, partnerships and the delivery of specialist public health services. We are an executive agency of the Department of Health and Social Care, and a distinct delivery organisation with operational autonomy. We provide government, local government, the NHS, Parliament, industry and the public with evidence-based professional, scientific and delivery expertise and support.

Public Health England
Wellington House, 133-155 Waterloo Road, London SE1 8UG
Tel: 020 7654 8000
www.gov.uk/phe
Twitter: @PHE_uk; Facebook: www.facebook.com/PublicHealthEngland

Prepared by: Helen Harris, Annastella Costella and Sema Mandal.
Contributors: Daniel Bradshaw, Derrick Crook, Ross Harris, Peter Huskinson, Rosanna O'Connor, Nick Phin, and William Irving.
Acknowledgements: Our thanks also go to Graham Foster, Mike Gent, Rachel Halford, and Jon White for their input and review of the report, and to the clinicians and Operational Delivery Network staff who have contributed and entered data into the NHS England Hepatitis C patient registry and treatment outcome system.

Suggested Citation: Harris HE, Costella A, Mandal S and contributors. Hepatitis C treatment monitoring in England: Content, completeness and preliminary findings from the Hepatitis C patient registry and treatment outcome system. November 2018. Public Health England, London.

For queries relating to this document, please contact Helen Harris (helen.harris@phe.gov.uk)

Published November 2019
PHE publications gateway number: 2018621

PHE supports the UN Sustainable Development Goals

Corporate member of Plain English Campaign
Committed to clearer communication
339

Contents

List of abbreviations

CQUIN	Commissioning for Quality and Innovation
DAA	Direct Acting Antiviral
ESLD	End-stage liver disease
GHSS	Global Health Sector Strategy
GUM	Genitourinary Medicine
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
MDT	Multi-disciplinary team
MSM	Men who have sex with men
ODN	Operational Delivery Network
OST	Opioid substitution treatment
PDS	Patient Demographic Service
PWID	People who inject drugs
SVR	Sustained Viral Response
SVR12	Sustained Viral Response 12 weeks post treatment completion
WHO	World Health Organization

Executive summary

The World Health Organization (WHO) estimates that in 2015, 71 million people were living with chronic hepatitis C virus (HCV) infection worldwide, and that nearly 400,000 people died from cirrhosis or hepatocellular carcinoma caused by HCV infection.[1] Closer to home, modelling suggests that there were around 145,000 chronic infections in England in 2015, the majority of which were acquired via injecting drug use.[2],[3]

In May 2016, the World Health Assembly endorsed the Global Health Sector Strategy (GHSS) on viral hepatitis.[4] This strategy proposes to eliminate viral hepatitis as a major public health threat by 2030.[4] In addition to prevention of infection, elimination requires 90% of those already infected to be diagnosed and 80% of those diagnosed to be treated.[4] To reach these targets in England, more infected individuals need to be diagnosed and access curative treatments.

Improvements in treatment over recent years, mean that therapies can now be more easily and safely rolled out into community and outreach settings where more of the infected population can access them. As well as reducing morbidity and mortality in the short and medium term,[5] modelling suggests that an additional 'prevention benefit' may be possible when treatment reaches those who are actively transmitting the virus.[6],[7]

Knowing the numbers accessing treatment and its outcome, at both national and local levels, is key for monitoring the progress of elimination. In the past, various methods have been used to estimate numbers accessing HCV treatment in England, including estimating numbers from data on HCV drug sales and prescribing,[8],[3] using serial patterns of HCV testing in surveillance data to determine treatment rates.[9],[3] Most recently, numbers accessing treatment have been based on NHS England commissioning data, using clinician intention to treat and invoicing.[3]

In the absence of any existing HCV treatment database with national coverage, comprehensive data for key public health variables, or the ability for comprehensive linkage to existing national datasets, a national treatment monitoring dataset was agreed, and the Hepatitis C patient registry and treatment outcome system was established to capture these data for patients.

The first data download from the NHS England Hepatitis C patient registry and treatment outcome system were passed to Public Health England on 30 April 2018. The main analysis presented here focuses on those patients with a treatment episode in the Register (24,592 people in total), most of whom were treated in the financial years 2015/16-2017/18. For these 24,592 individuals, sociodemographic, infection and clinical characteristics are described, along with information on the outcome of

treatment and completeness of data within the Register. The outcome of subsequent treatment is described for the 196 patients with two treatment episodes in the Register. The characteristics of the 7,816 people entered into the Register but not yet treated are also described and compared to those who have already accessed treatment.
The creation of the Hepatitis C patient registry and treatment outcome system is a significant milestone in the monitoring of HCV elimination in England.

Although there was some duplication of information and variation between Operational Delivery Networks (ODNs), overall, data completeness exceeded 90% for many key variables, including age, sex, HCV genotype, source of referral, previous treatment, disease stage, as well as expected duration, date and setting of treatment. Where levels of data completeness were sub-optimal (ethnicity 89%, country of birth 71%, injecting route of transmission 61%, and likely route of transmission 54% complete, for example), available data still represent a significant improvement on that previously available in England. Commissioning for Quality and Innovation (CQUIN) incentives put in place by NHS England[10] should support further improvements in data quality.

Amongst those in whom it was possible to establish the outcome of treatment, 95% achieved a sustained viral response (SVR), 12 weeks after completing treatment (SVR12). Univariable analyses suggest that those who failed to achieve an SVR12 were significantly more likely to be male, older, Black/African/Caribbean/Black British, infected with non-1 genotypes, to have cirrhosis, to have been treated previously, to have hepatocellular carcinoma (HCC), to have been assigned a longer estimated treatment duration but received a shorter actual treatment duration, or to have alcohol reported as a likely contributing factor, but they did not differ significantly from those achieving SVR12 by country of birth, injecting route of transmission, year of first diagnosis, likely route of transmission, source of referral, post-transplant status, HIV status, renal failure status, or setting of treatment. Further multivariable analyses of these data are planned and will be reported elsewhere. Amongst those having a subsequent course of treatment, 87% achieved SVR12 following previous treatment failure or re-infection.

It is reassuring to see that treatment is reaching some of the key risk groups, with 11% of those treated being of Asian ethnicity and 29% born outside the UK. Seventy percent of those treated reported injecting drug use as their likely risk for acquiring HCV and 16% of those treated were reported to have either currently or recently injected drugs. While most referrals came from primary care (44%), just 16% came directly from drug services or prisons, which likely represents an improvement on earlier years, but needs to be improved if we are to reach those who are actively transmitting the virus.
Amongst those with a treatment episode in the Register, disease stage data were available in 96% of cases, and showed that around one third (32%) had cirrhosis prior to treatment. Fifty eight percent had no, or only mild, fibrosis prior to treatment, which suggests that many treatment services have largely completed treating patients known to them who have severe HCV-related disease.

Registry data suggest that the vast majority of treatment continues to take place within secondary care, with just 13% of treatments undertaken in drug services, prisons or other outreach settings. As with HCV testing services, it will be important to strive to improve the numbers accessing treatment locally, including within drug services, prisons and via primary care.

Univariable analyses suggest that patients in the Register yet to be treated, tended to be significantly younger, of white ethnicity, and UK born, when compared to those who have already accessed treatment. They were significantly more likely to have currently, or recently, injected drugs, or to have acquired their infections via sex between men.

Patients yet to be treated were also more likely to come from drug, prison, Genitourinary Medicine (GUM) and GP services rather than from secondary care settings and were far less likely to have undergone any previous treatment for their HCV. Those yet to be treated were significantly more likely to have mild/moderate liver disease, than those with a treatment episode in the Register. While further multivariable analyses are required, these early data suggest that people who inject drugs (PWID) and men who have sex with men (MSM) with relatively more recent infection are starting to be identified via local and outreach services.

In addition to those patients in the register yet to be treated, it is recognised that there are tens of thousands of people with previously diagnosed HCV infection who are not in contact with treatment services. A national patient re-engagement exercise was launched in September 2018 by PHE and NHS England, to help find and treat those people who were diagnosed with hepatitis C in the past and who may not have been treated. Treatment uptake resulting from the national re-engagement exercise will be monitored by recording referrals from this source in the Hepatitis C patient registry and treatment outcome system, and via linkage of patient lists to the Register database.

Data already available in the Register have helped us to better understand the socio-demographic, infection and clinical characteristics of people in England who have been diagnosed with chronic HCV infection and have accessed treatment services. These data will be invaluable for targeting allocation of resources for finding and treating patients, improving equity of access to treatment, modelling the future burden of HCV-related disease, and monitoring the progress of elimination, in England.

As more data become available, and data completeness improves, our progress eliminating hepatitis C as a major public health threat will be better tracked and interventions more easily identified. Linking these data to other data, like laboratory diagnoses of HCV infection, sentinel surveillance of HCV testing, cancer registry, hospital episode and death data will help inform the cascade of care for people with HCV infection in England.

Background

Hepatitis C is a blood borne virus (HCV) that is often asymptomatic, and symptoms may not appear until the liver is severely damaged. As a consequence, many individuals with chronic HCV infection remain undiagnosed and fail to access treatment. These individuals can then present late with complications of HCV-related end-stage liver disease and cancer, which have poor survival rates.

The World Health Organization (WHO) estimates that in 2015, 71 million people were living with chronic HCV infection worldwide, and that nearly 400,000 people died from cirrhosis or hepatocellular carcinoma caused by HCV infection.[1] Closer to home, modelling suggests that there were around 145,000 chronic infections in England in 2015, the majority of which were acquired via injecting drug use.[2],[3]

In May 2016, the World Health Assembly endorsed the Global Health Sector Strategy (GHSS) on viral hepatitis.[4] This strategy proposes to eliminate viral hepatitis as a major public health threat by 2030, and this is defined as a 90% reduction in incidence of viral hepatitis infection and a 65% reduction in mortality.[4] Elimination of viral hepatitis as a major public health threat requires 90% of those infected to be diagnosed and 80% of those diagnosed to be treated.[4] To reach these elimination targets in England, there are a number of key interventions that will help us to reduce transmission of HCV, and the morbidity and mortality that results; these include raising awareness, harm reduction measures in people who inject drugs (PWID) - like optimal access to clean injecting equipment via needle and syringe programmes and to opioid substitution treatment - as well as improved access to HCV testing and treatment.[3]

The availability of new direct acting antiviral (DAA) drugs in England,[11],[12],[13],[14], [15],[16] has transformed our ability to tackle HCV infection as these new DAA drugs offer a fast and effective cure to the vast majority who receive them, without many of the complications associated with previous treatments.[5],[17] These improvements mean that therapy can be safely rolled out into community and outreach settings where access can be easier. As well as reducing morbidity and mortality in the short and medium term[5], modelling suggests that an additional ‘prevention benefit’ may be possible when treatment reaches those who are actively transmitting the virus.[6],[7]

Improving access to treatment is therefore key if we are to meet our obligations to eliminate hepatitis C as a major public health threat by 2030.[4] Monitoring access and uptake of treatment is essential to inform prevention and control strategies and to track our progress against WHO elimination targets (see appendix 1).

Introduction

Our progress in meeting the GHSS elimination targets[4] is reported annually in Public Health England's (PHE) *Hepatitis C in England* report.[3] In the 2018 report, it was concluded that elimination goals to reduce HCV-related morbidity and mortality should be within our reach provided current improvements in numbers accessing treatment could be sustained in future years.[3]

Our ability to sustain the current increase in numbers accessing treatment is limited by our capacity to find and treat those who remain undiagnosed, and to help those who are diagnosed but untreated to engage with local services; only then will we be able to build on the current fall in avoidable HCV-related deaths that has been observed in recent years.[3] The England report also highlighted the importance of making preliminary assessments of the equity, access, uptake and impact of treatment on the future burden of HCV-related disease in England.[3]

In the past, various methods have been used to estimate numbers accessing HCV treatment in England. In 2007-2011, estimates were made using data on HCV drug sales and prescribing;[8],[3] in 2012-14, serial patterns of HCV testing in surveillance data were used to determine treatment rates.[9],[3] Since 2015, numbers accessing treatment have been based on NHS England commissioning data, based on clinician intention to treat and invoicing, rather than patient level treatment registry data.[3]

In the absence of any existing HCV treatment database with: (i) national coverage, (ii) comprehensive data for key public health variables, and (iii) the ability to link to existing national datasets, PHE worked with NHS England, clinicians, and other stakeholders to develop a national treatment monitoring dataset. Arden and Greater East Midlands (GEM) Commissioning Support Unit were subsequently commissioned by NHS England to produce the Hepatitis C patient registry and treatment outcome system to capture these data for patients (see Appendix 2). Following system rollout in May/June 2017, NHS HCV Operational Delivery Networks (ODN) throughout England have been inputting data into the system, supported by the Commissioning for Quality and Innovation (CQUIN) framework, which supports improvements in the quality of services and the creation of new, improved patterns of care.[18]

This report summarises the content and completeness of data contained within the Hepatitis C patient registry and treatment outcome system at the end of April 2018, enabling a preliminary assessment of HCV treatment and its monitoring in England.

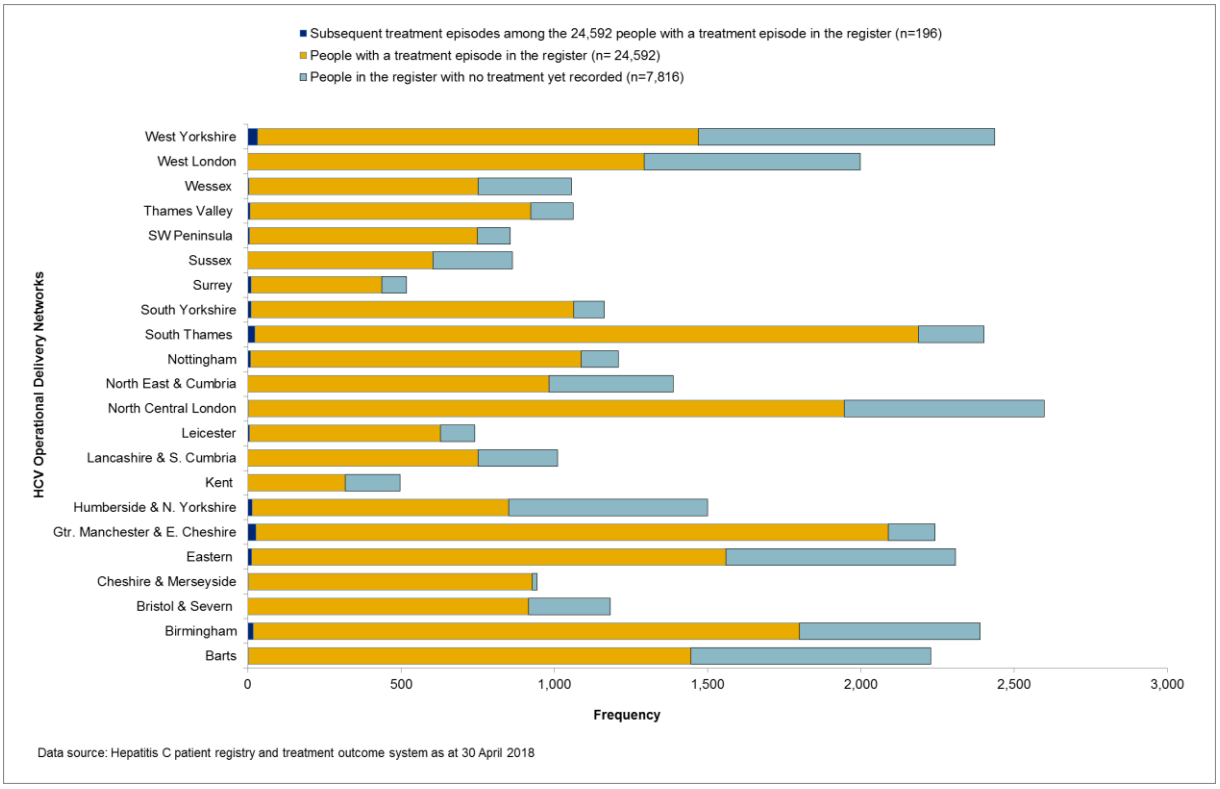
Sample

The first data download from the NHS England Hepatitis C patient registry and treatment outcome system were passed to PHE on 30 April 2018 (see information governance detail in Appendix 3). The dataset contained 33,455 records, of which 851 were excluded as they represented duplicate records (127 were duplicate treatment episodes; 724 were people with a treatment episode who appeared again just as a registry entry, or who had no treatment episodes but appeared in the register more than once). The remaining 32,604 records were for: 7,816 people who had no treatment, 24,396 people who had just one treatment episode in the database, and 196 people who had two treatment episodes in the database (Figure 1).

Analysis

The main analysis focuses on those patients with a treatment episode in the Register (24,592 people in total; yellow bars, Figure 1), most of whom were treated in the financial years 2015/16-2017/18, including 24,396 treatments from those patients with just one treatment episode in the Register and the 196 'first' treatments from those 196 patients with two treatment episodes recorded in the Register. These 24,592 patients came from 109 providers within 22 ODNs throughout England (Figure 1).

Figure 1. Distribution of patient treatment episodes, and patients yet to be treated, in the Hepatitis C patient registry and treatment outcome system, by ODN.



For these 24,592 individuals, sociodemographic, infection and clinical characteristics are described, along with information on the outcome of treatment and completeness of data within the Register. The outcome of subsequent treatment is described for those 196 patients with two treatment episodes in the Register (dark blue bars, Figure 1). The characteristics of the 7,816 people entered into the Register but not yet treated (light blue bars, Figure 1), are also described and compared to those who have already accessed treatment.

Socio-demographic characteristics

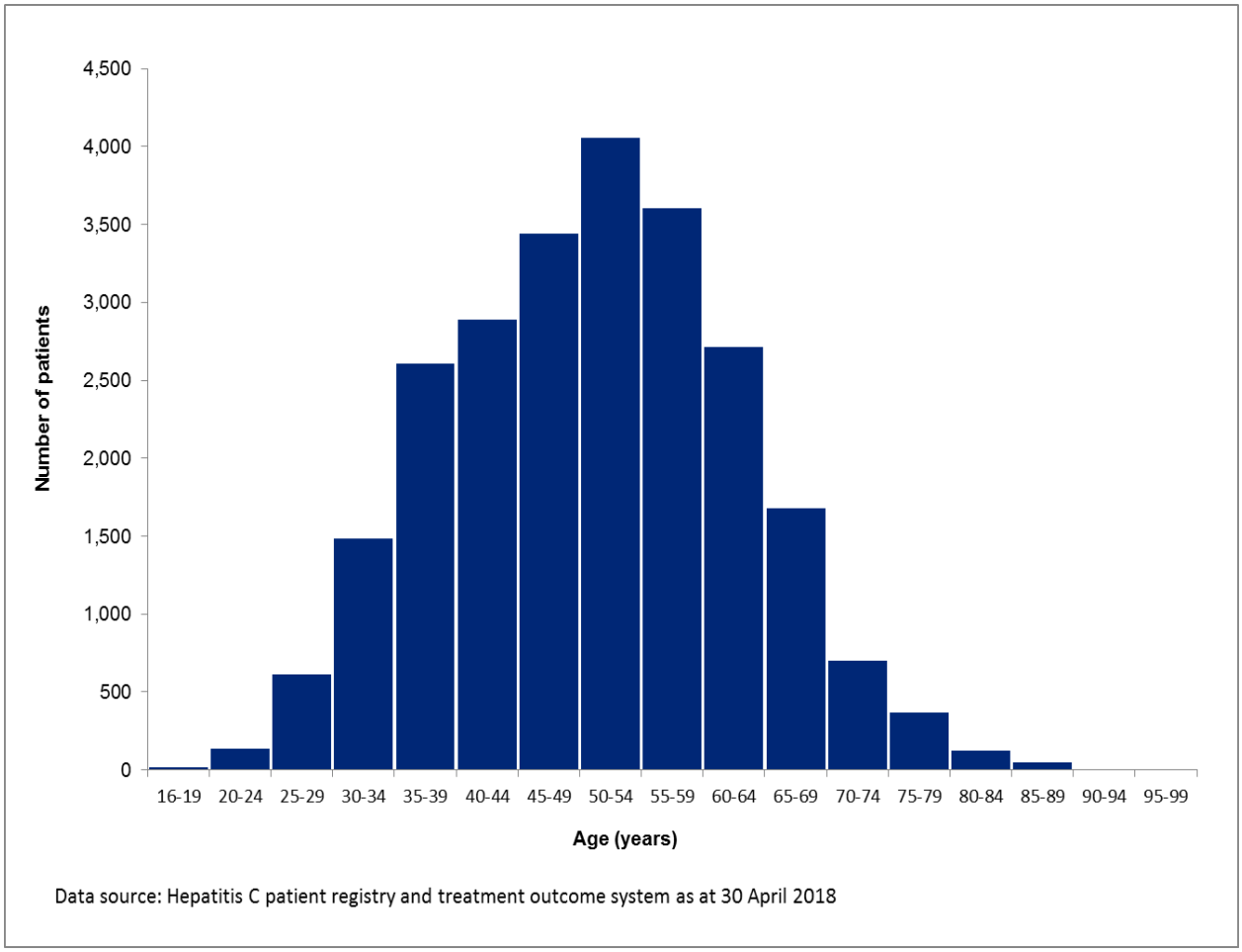
The socio-demographic characteristics of the 24,592 patients with a treatment episode in the Register are summarised in Table 1.

Table 1. Sociodemographic characteristics of patients with a treatment episode in Hepatitis C patient registry and treatment outcome system (n= 24,592).

Variable		Proportion of sample with data for that variable (%)
Age (Mean ± SD, years)	50.6 ± 11.8	99.5
Sex (% male)	70.3	98.7
Ethnicity (%)		89.0
White	79.1	
Asian/Asian British	10.6	
Black/African/Caribbean/Black British	4.6	
Mixed/Multiple Groups	1.0	
Other	4.7	
Country of Birth (%)		71.3
UK	70.9	
Non-UK	29.1	
Postcode		22.4
Data source: Hepatitis C patient registry and treatment outcome system as at 30 April 2018		

After excluding those recoded as having age greater than 100 (n=1) or less than 16 (n=35, nearly all of whom had dates of birth making them under the age of 3), the mean age of patients was 51 years (Table 1, Figure 2). Nearly all of the patients (98.7%) had their sex recorded and 70% were male (Table1). Data completeness was relatively lower for ethnicity (89.0%) and country of birth (71.3%), with most patients classified as White (79.1%) or Asian/Asian British (10.6%), and around 70% of all patients were UK born (Table 1). Of the 5,095 patients recorded as being born outside the UK, 24% were born in Pakistan, 10% in Poland, 6% in Lithuania, 5% in Portugal, 5% in Romania, 5% in Latvia and 5% were born in Italy. Postcode was missing for 78% of patients (Table 1) and invalid in a proportion of those for whom it was reported.

Figure 2. Age distribution of patients with a treatment episode in the Hepatitis C patient registry and treatment outcome system.



Infection details

Infection details for the 24,592 patients with a treatment episode in the Register are summarised in Table 2.

After excluding those with a first diagnosis date in the future or prior to 1990 (n= 488), the mean date of first diagnosis of HCV was reported to be 2011 (Table 2, Figure 3), with around half (52.8%) of infections having been first diagnosed in 2013 or earlier, and one quarter (24.8%) having a first diagnosis after 2015. The spike in numbers infected in 1990, 2000 and 2010 (Figure 3) suggests some estimates are crude or subject to recall bias.

Table 2. HCV infection details for patients with a treatment episode in the Hepatitis C patient registry and treatment outcome system (n= 24,592).

Variable		Proportion of sample with data for that variable (%)
Year of first diagnosis (Mean ± SD, years)	2011 ± 6.31	65.4
HCV Genotype (%)		98.9
1	54.3	
2	4.3	
3	36.1	
4	4.8	
5	0.1	
6	0.2	
Mixed	0.1	
Other	0.1	
Injecting route of transmission (%)		60.6
Current/recent PWID (injected in past 3 years)	16.2	
Past PWID	46.3	
Never PWID	37.4	
Likely route of transmission (%)		54.3
Mother to child	0.8	
Non-occupational contact with blood in a healthcare setting (e.g. via transfusion, receipt of blood products or use of inadequately sterilised medical equipment)	12.0	
Occupational exposure	0.6	
Other blood exposure e.g. tattoo	5.0	
PWID	69.7	
Sex between men	4.5	
Sex between men and women	2.0	
Other	5.5	
Data source: Hepatitis C patient registry and treatment outcome system as at 30 April 2018		

Most infections in the Register were genotype 1 (54.3%, Table 2), the majority of these being subtype 1a (66.6% of all genotype 1 infection; Figure 4); over one third (36.1%) were genotype 3, around a quarter of which (24.0%) were reported to be subtype 3a (Figure 4).

Information on injecting status was provided for 61% of the sample, and showed 16.2% to be people who had currently/recently injected drugs (injected in the last 3 years), 37.4% were recorded as never having injected drugs, while most (46.3%) were reported to be people who had injected drugs in the past but were no longer injecting (Table 2). The distribution of injecting status amongst those accessing treatment, varied considerably by ODN (Figure 5), and it is encouraging to see a significant proportion of people who currently/recently injected drugs accessing treatment in a number of ODNs in the North (Figure 5). Where route of transmission was known (54.3%), the majority acquired their infection via injecting drug use (69.7%) or via non-occupational contact with blood in a healthcare setting (12.0%), although other routes were reported (Table 2).

Figure 3. Year of first diagnosis for patients with a treatment episode in the Hepatitis C patient registry and treatment outcome system.

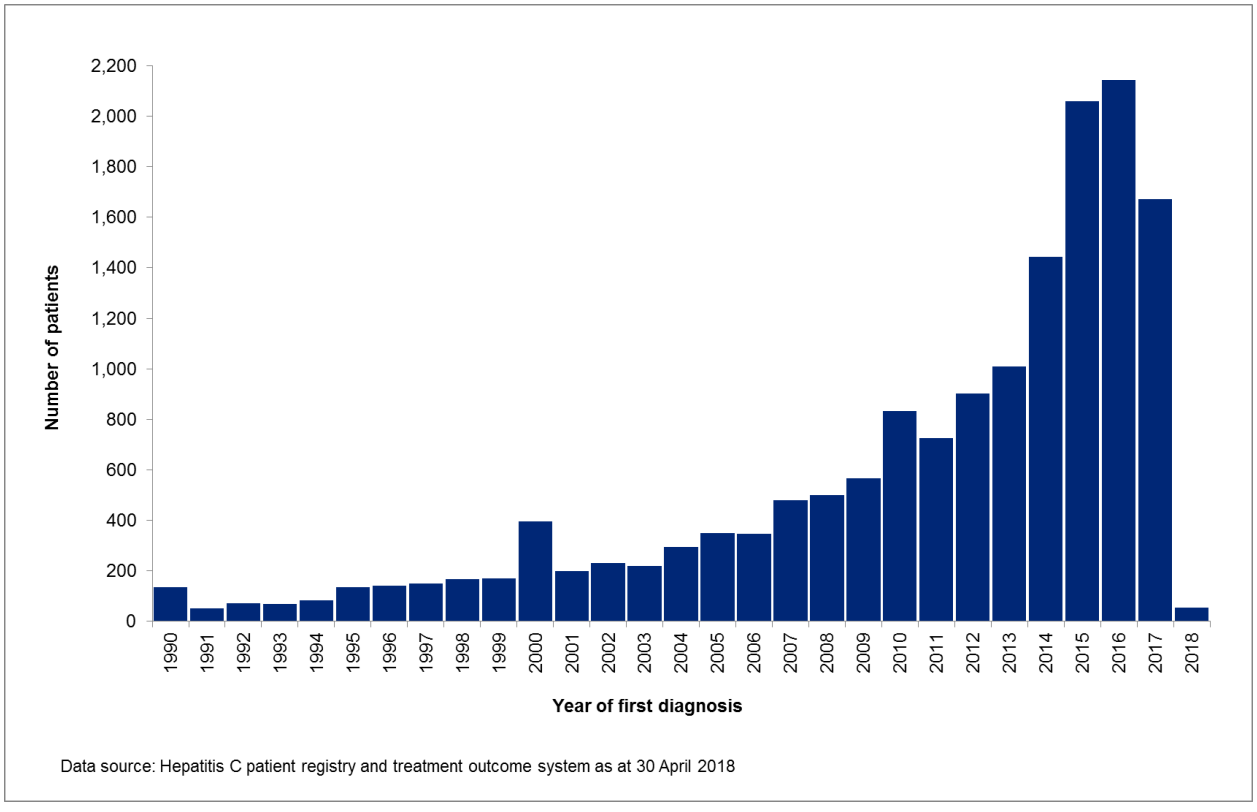
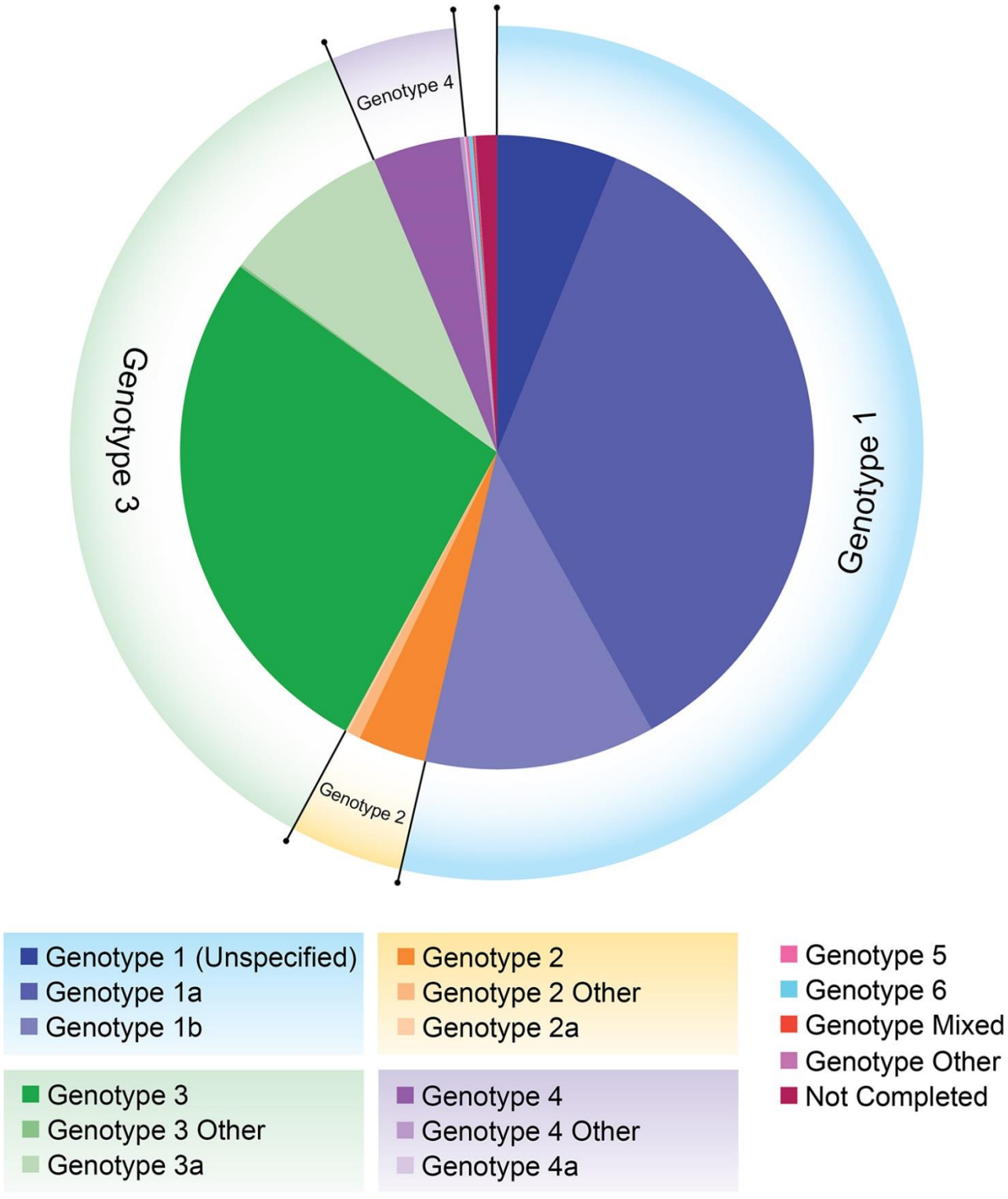
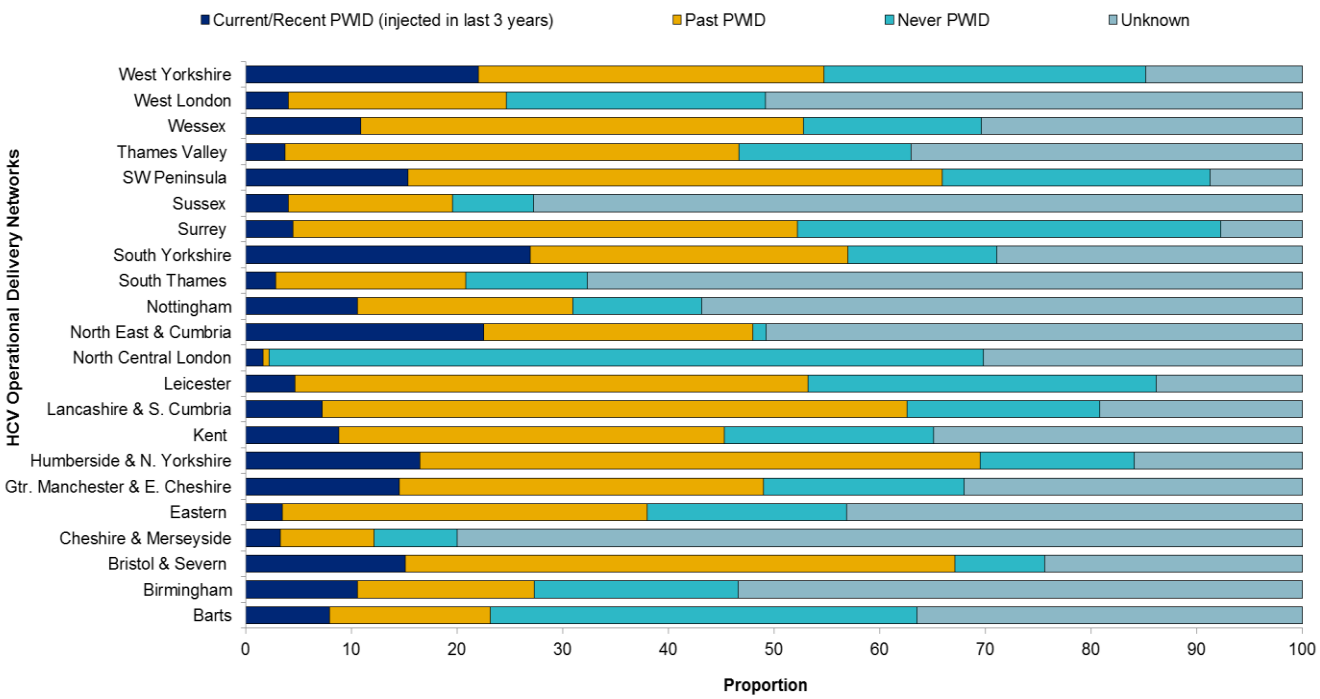


Figure 4. HCV genotype distribution for patients with a treatment episode in the Hepatitis C patient registry and treatment outcome system.



Data source: Hepatitis C patient registry and treatment outcome system as at 30 April 2018

Figure 5. Injecting route of transmission for patients with a treatment episode in the Hepatitis C patient registry and treatment outcome system, by ODN (n= 24,592).



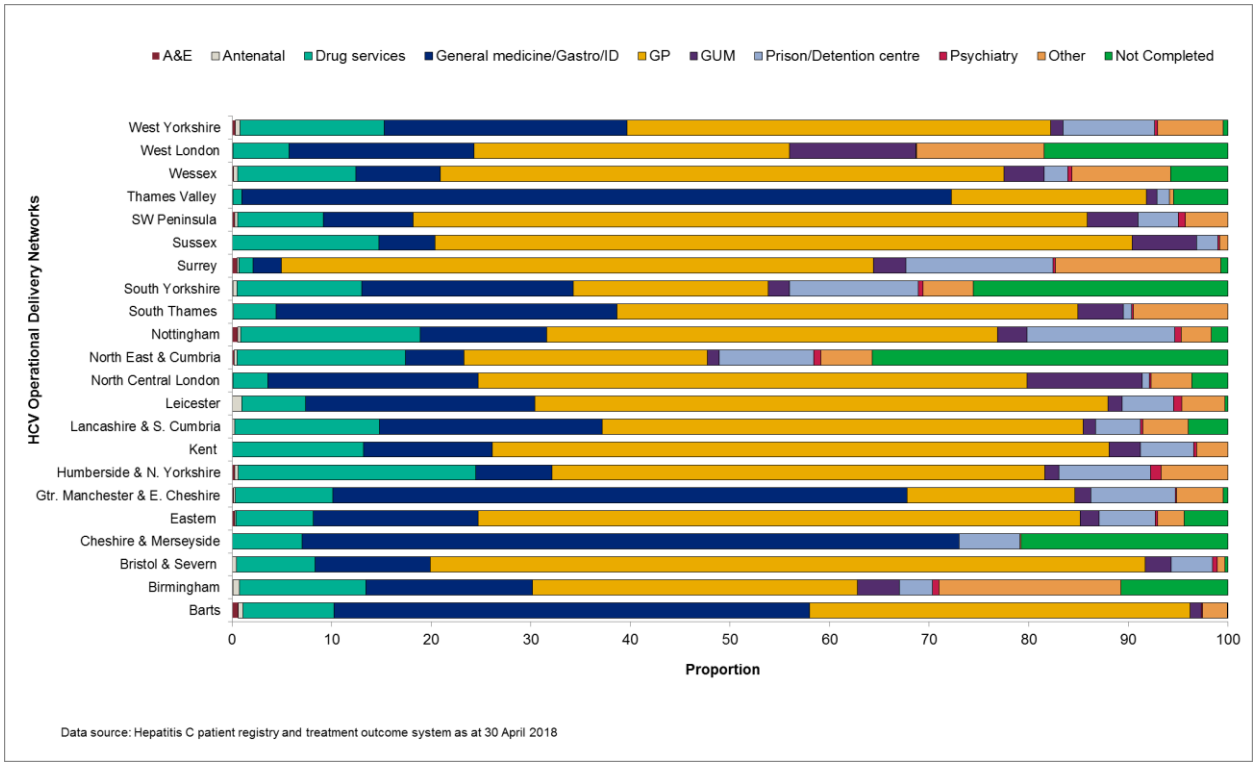
Data source: Hepatitis C patient registry and treatment outcome system as at 30 April 2018

Clinical details

Clinical details for the 24,592 patients with a treatment episode in the Register are summarised in Table 3.

Most patients were referred from primary care (44.3%), with 28.4% coming from General Medicine, Gastroenterology, or Infectious Diseases; 15.9% from drug services (10.4%) and prisons (5.5%); and 4.0% via Genitourinary Medicine (GUM) services (Table 3). Referrals from other sources were relatively rare, making up less than 10% of the overall total (Table 3). The distribution of referral sources amongst those accessing treatment, varied by ODN (Figure 6), and it is encouraging to see a significant proportion of people from drug services and prisons accessing treatment in a number of ODNs (e.g. Humberside and N. Yorkshire, and Nottingham; Figure 6).

Figure 6. Source of referral for patients with a treatment episode in the Hepatitis C patient registry and treatment outcome system, by ODN (n= 24,592).



Previous treatment was reported for a quarter (25.0%) of patients; 22% reported previous treatment with interferon/pegylated interferon (with or without ribavirin), 3.5% reported pegylated interferon (with or without ribavirin) plus a protease inhibitor, and 1.4% reported previous treatment with an all-oral interferon-free regimen (some reported having more than one of these previous treatments; Table 3).

Table 3. Clinical details for patients with a treatment episode in the Hepatitis C patient registry and treatment outcome system (n=24,592).

Variable		Proportion of sample with data for that variable (%)
Source of referral (%)		93.7
A&E	0.2	
Antenatal	0.3	
Drug Services	10.4	
General Medicine, Infectious Diseases and Gastroenterology	28.4	
GP	44.3	
GUM	4.0	
Prison/Detention	5.5	
Psychiatry	0.4	
Other	6.5	
Previous treatment with interferon/pegylated interferon (+/-ribavirin) (%)	22	Not known*
Previous treatment with pegylated interferon (+/- ribavirin) and protease inhibitor (%)	3.5	Not known*
Previous treatment with all oral, interferon-free regimen (%)	1.4	Not known*
Disease stage (%)		96.4
No fibrosis	31.6	
Mild fibrosis (Metavir F1/F2 or equivalent)	25.9	
Moderate fibrosis (Metavir F3 or equivalent)	10.4	
Compensated cirrhosis	28.2	
Compensated cirrhosis with past decompensation	1.2	
Decompensated cirrhosis	2.7	
Fibroscan (%, kPa)**		80.7
< 2.5	7.7	
2.5 to ≤ 10 (Mild/Moderate fibrosis)	60.4	
10 to < 13 (F3, Advanced fibrosis)	10.0	
≥ 13 (F4, Cirrhosis)	22.0	
Post-transplant (%)	1.6	Not known*
Hepatocellular carcinoma (%)	5.2	Not known*
HIV (%)	7.2	Not known*
Renal failure (eGFR<30 or dialysis; %)	1	Not known*
Alcohol felt to be a contributor to liver disease (%)	15.1	Not known*
Expected duration (weeks) of treatment agreed at MDT (%)		98.0
<8	0.2	
8	16.7	
12	72.5	
16	6.6	
24	4.0	
>24	0.0	
Other durations (potential errors)	0.0	
Enrolled in HCV Research UK (%)[19]	7.4	Not known*
Data source: Hepatitis C patient registry and treatment outcome system as at 30 April 2018		

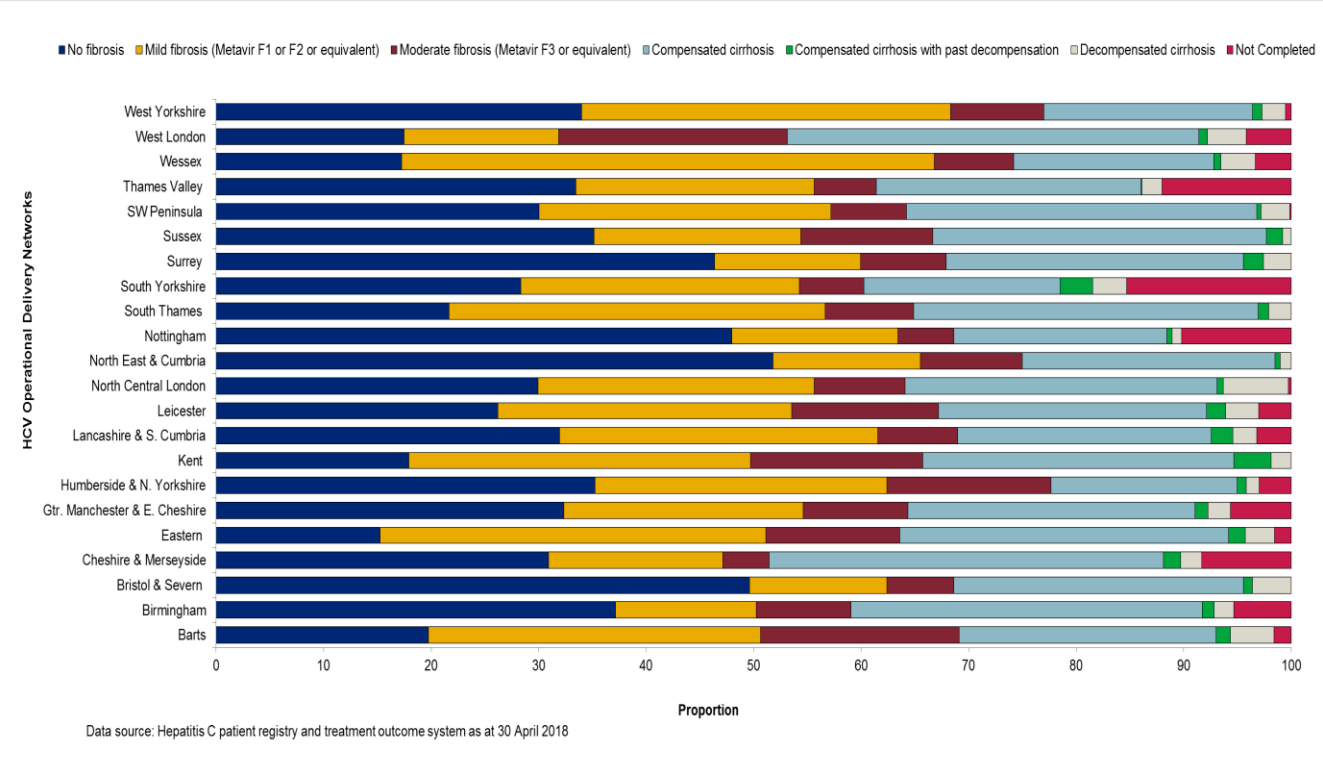
* Data completeness is not known as this field in the Register defaults to 'no' unless 'yes' is selected; as such it is not possible to distinguish between missing data and those without these conditions

** Classified according to EASL Recommendations on treatment of Hepatitis C, 2018 (20)

In 15.1% of patients, alcohol was reported to be a contributor to the individual's liver disease, 7.2% were reported to be co-infected with HIV and 1.0% were reported to be in renal failure (Table 3). However, it was not possible to determine where data were missing for these variables, as these fields default to 'no' in the Register unless 'yes' is selected, making it impossible to distinguish between missing data and those without these conditions.

The field 'disease stage,' which was well completed (96.4% complete), suggested that around one third of patients (32.1%) had cirrhosis prior to treatment (Table 3), some of which was decompensated (2.7% of those with cirrhosis) or had past decompensation (1.2% of those with cirrhosis). Over half of all patients (57.5%) treated had either no evidence of fibrosis prior to treatment (31.6%) or had only mild fibrosis (25.9%). The distribution of disease stage at treatment varied by ODN (Figure 7). Given that patients with severe disease were initially prioritised,(21) it is clear that all ODNs are now treating a significant proportion of people with no, or only mild, fibrosis (Figure 7). Fibroscan results were recorded for only around 80% of the sample (Table 3), and 22% of these people had scores indicative of cirrhosis.[20]

Figure 7. Disease stage of patients with a treatment episode in the Hepatitis C patient registry and treatment outcome system, by ODN (n= 24,592).



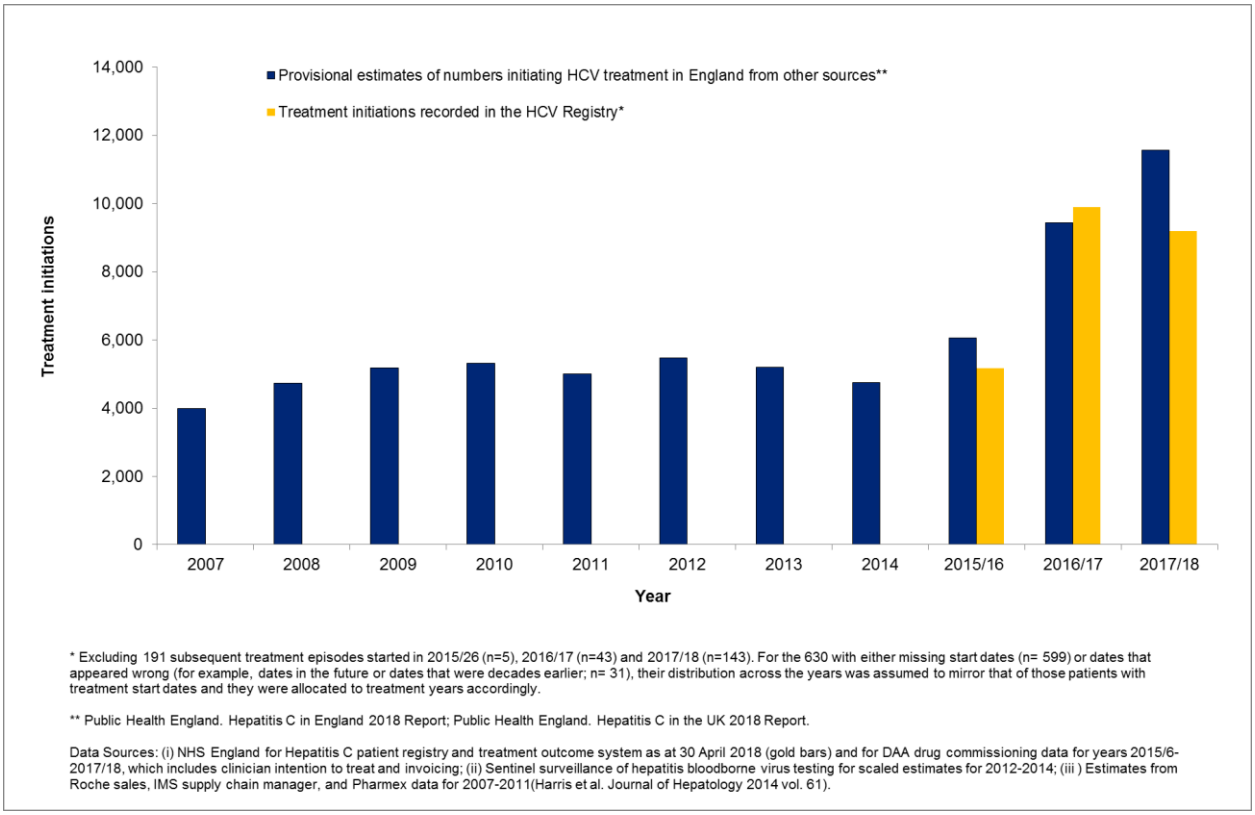
Of the 24,592 patients, 1.6% were reported to be post-transplant and 5.2% diagnosed with hepatocellular carcinoma (HCC) but, as for other presence/absence variables in the Register, it was not possible to determine the completeness of these data.

Treatment and outcome

Treatment details for the 24,592 patients with a treatment episode in the Register are summarised in Table 4.

Of the 24,592 patients with a treatment episode in the Register, 23,993 had treatment start dates (97.6%). For the 630 with either missing start dates (n= 599) or dates that appeared wrong (for example, dates in the future or dates that were decades earlier; n= 31), their distribution across the years was assumed to mirror that of those patients with treatment start dates, and they were allocated to treatment years accordingly. The distribution of treatment initiations from Registry data for financial years 2015/16-2017/18 is shown in Figure 8, and compared to previously published provisional estimates of numbers initiating HCV treatment in England.[22],[3]

Figure 8. Treatment initiations in the Hepatitis C patient registry and treatment outcome system compared to provisional estimates of numbers initiating HCV treatment in England, 2007- 2017/2018 from other sources.[22], [3]



In 2015/16, 22% less treatment episodes were recorded in the Register than were estimated to have taken place using Direct Acting Antiviral (DAA) drug commissioning data, based on clinician intention to treat and invoicing, even after including the small number of subsequent treatments that some patients had in that year (Figure 8). This could be due to underreporting or be because data collected prior to the Register 'go-

live' date, are yet to be fully uploaded. It is also possible that those with missing treatment start dates were more likely to be from earlier years. In 2016/17, after including subsequent treatments that also took place in 2016/17, Registry data suggest that 5% more treatment took place than estimates based on commissioning data suggest (Figure 8). This could be partially explained by commissioning data only including treatments with DAA drugs, and in 2016/17, Registry data suggest that 224 patients were treated with interferon (and/or Ribavirin) alone; this would reduce the difference between the two data sources to 3%. Again, some of the difference could be explained by those with missing treatment start dates being more likely to be from these years. In 2017/18, far fewer treatment episodes were recorded in the Register than were estimated to have taken place using DAA drug commissioning data (Figure 8).

This could simply be because data are not always entered in real-time, leading to a lag between treatment starting and details being entered into the Register. At multidisciplinary team meetings prior to starting therapy, nearly 90% were **allocated** to receive 12 weeks of treatment (72.5%) or 8 weeks (16.7%) of treatment (Table 3) and similar numbers actually **underwent** these durations of treatment (73.6% and 13.7% respectively; Table 4), although data were more often missing for actual duration of treatment (26% compared to 2%; Tables 3 & 4). In those for whom both estimated and actual durations of treatment were available (n=17,911; 73% of the sample), 91% completed the planned duration of treatment, 6.4% completed less treatment than planned and 2.6% underwent longer treatment than planned.

The vast majority of patients (88%) were treated in secondary care, with the remainder receiving treatment in either drugs services (5.7%), prisons (5.1%) or elsewhere (1.8%; Table 4). Again, this varied by ODN, with some notable exceptions, like Nottingham and Sussex, treating a significant minority of patients in drug services (Figure 9).

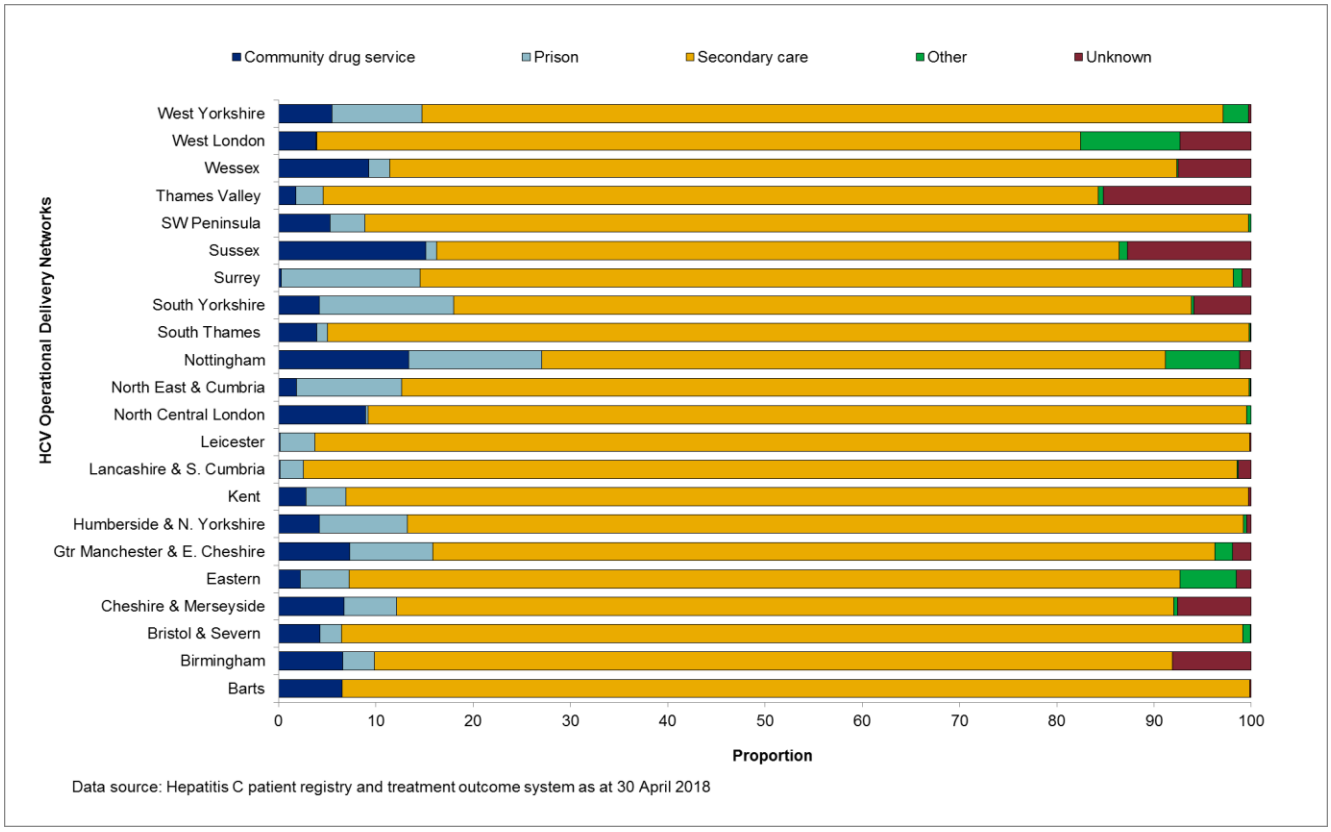
Table 4 Treatment and outcome for patients with a treatment episode in the Hepatitis C patient registry and treatment outcome system (n= 24,592).

Variable		Proportion of sample with data for that variable (%)
Setting of treatment (%)		97.0
Community drug service	5.7	
Prison	5.1	
Secondary care	87.5	
Other	1.8	
Treatment start date (financial years, %)		97.6
2014/15	0.5	
2015/16	21.0	
2016/17	40.2	
2017/18	37.4	
2018/19 (April 2018 only)	0.9	
Other years**	0.1	
Drug(s) used in treatment (%)		Not known*
Elbasvir/Grazoprevir	13.8	
Sofosbuvir/Velpatasvir	14.0	
Sofosbuvir	36.0	
Ledipasvir	20.3	
Daclatasvir	6.6	
Paritaprevir/Ombitasvir	23.5	
Dasabuvir	21.1	
Ribavirin	51.7	
Pegylated interferon	8.6	
Simeprevir	0.7	
NHS funded trial drug	0.5	
Non-NHS funded trail drug	0.6	
Glecaprevir/Pibrentasvir (Early Access to Medicines Scheme)	1.3	
Glecaprevir/Pibrentasvir (Non-Early Access to Medicines Scheme)	8.5	
Treatment outcome (%)		76.0
SVR 12 (HCV RNA negative 12 week after completion of treatment	84.5	
Relapse (HCV RNA negative during treatment but became HCVRNA positive in the post treatment period	3.0	
Breakthrough (HCV RNA negative during treatment but became HCV RNA positive again during treatment)	0.4	
Non-response (Remained HCV RNA positive)	0.8	
Lost to follow-up (Did not attend 12/24 week post-treatment follow-up appointments)	7.6	
Died before treatment started	0.0	
Died after treatment initiation but before 12/24 week testing to establish outcome)	0.8	
Other	2.8	
Actual duration (weeks) of treatment (%)		74.2
<8	2.6	
8	13.7	
12	73.6	
16	5.0	
24	3.8	
>24	0.1	
Other durations (potential errors**)	1.2	
Data source: Hepatitis C patient registry and treatment outcome system as at 30 April 2018		

* Data completeness is not known as this field in the Register defaults to 'no' unless 'yes' is selected; as such it is not possible to distinguish between missing data and those without these conditions.

**Likely to be errors, for example, reported as dates in the future or dates decades earlier.

Figure 9. Treatment setting of patients with a treatment episode in the Hepatitis C patient registry and treatment outcome system, by ODN (n= 24,592).



Amongst those in whom it was possible to determine the outcome of treatment (n= 16,571; Table 4), 95.2% achieved an SVR12 (0.5% breakthrough, 3.4% relapse and 0.9% non-response). A variety of DAA drugs were used, with more than half receiving them in combination with ribavirin (Table 4). Univariable analyses suggest that those who failed to achieve an SVR12 were significantly more likely to be male, older, Black/African/Caribbean/Black British, infected with non-1 genotypes, to have cirrhosis, to have been treated previously, to have HCC, and longer estimated treatment durations but shorter actual treatment durations, and to have alcohol reported as a likely contributing factor, but they did not differ significantly from those achieving SVR12 by country of birth, injecting route of transmission, year of first diagnosis, likely route of transmission, source of referral, post-transplant status, HIV status, renal failure status, or setting of treatment (Tables 5-7). More sophisticated multivariable analyses of these data is outside the scope of this report but will be reported elsewhere.

Table 5. Sociodemographic characteristics of patients in the Hepatitis C patient registry and treatment outcome system who achieved SVR 12 weeks after completion of treatment, compared to those who did not achieve SVR 12.

Variable	Achieved SVR 12 (n= 15,782)	Did not achieve SVR 12 (n= 789)	Significance (P-value)
Sex (% male)	68.7	75.8	P<0.001
Age (Mean ± SD, years)	51.9 ± 11.7	54.9 ± 11.3	P<0.001
Ethnicity (%)			P=0.001
Asian/Asian British	11.7	10.9	
Black/African/Caribbean/Black British	4.7	8	
Mixed/Multiple ethnic groups	1	1.5	
Other	5.2	5.3	
White	77.4	74.3	
Country of birth (%)			NS
UK	67.9	70.8	
Non-UK	32.1	29.2	
Data source: Hepatitis C patient registry and treatment outcome system as at 30 April 2018			

NS: Non-significant

Table 6. HCV infection details for patients in the Hepatitis C patient registry and treatment outcome system who achieved SVR 12 weeks after completion of treatment, compared to those who did not achieve SVR 12.

Variable	Achieved SVR 12 (n= 15,782)	Did not achieve SVR 12 (n= 789)	Significance (P-value)
Genotype (%)			P<0.001
1 unspecified	7.7	6.4	
1a	36	32.8	
1b	13.7	7.3	
2	3.2	5.8	
2 Other	0.4	0.4	
2a	0	0	
3	27	33.1	
3 Other	0.1	0.4	
3a	5.8	6.2	
4	5.3	6.4	
4 Other	0.2	0.1	
4a	0.1	0.1	
5	0.1	0.1	
6	0.2	0.3	
Mixed	0.1	0.4	
Other	0.1	0.1	
Injecting route of transmission (%)			NS
Current/recent PWID (injected in past 3 years)	10.3	8.5	
Past PWID	46.3	48.5	
Never PWID	43.3	43	
Year of first diagnosis (Mean ± SD, years)	2010 ± 6.3	2010 ± 6.5	NS
Likely route of transmission (%)			NS
Mother to child	0.9	0.5	
Non-occupational contact with blood in healthcare setting (e.g. via transfusion, receipt of blood products or use of inadequately sterilised medical equipment)	14.3	14.4	
Occupational exposure	0.8	0.8	
Other	6.4	7.1	
Other Blood exposure e.g. tattoo	5.5	4.1	
PWID (PWID is defined as a person who injects drugs)	64.2	67.4	
Sex between men	5.7	3.3	
Sex Between men and women	2.2	2.4	
Data source: Hepatitis C patient registry and treatment outcome system as at 30 April 2018			

NS: Non-significant

Table 7. Clinical and treatment details for patients in the Hepatitis C patient registry and treatment outcome system who achieved SVR 12 weeks after completion of treatment, compared to those who did not achieve SVR 12.

Variable	Achieved SVR 12 (n= 15,782)	Did not achieve SVR 12 (n= 789)	Significance (P-value)
Disease Stage (%)			P<0.001
No fibrosis	28.2	19.9	
Mild fibrosis (Metavir F1/F2 or equivalent)	24.9	21.8	
Moderate fibrosis (Metavir F3 or equivalent)	10.7	8.7	
Compensated cirrhosis	32.3	40.5	
Compensated cirrhosis with past decompensation	1.2	2.5	
Decompensated cirrhosis	2.7	6.6	
HCC (%)	5.2	9.3	P<0.001
Expected duration of treatment (Mean ± SD, years)	12.2 ± 3.1	12.7 ± 4.3	P<0.001
Alcohol felt to be a contributor to liver disease (%)	13.5	16.9	P<0.01
Source of referral (%)			NS
A&E	0.1	0.4	
Antenatal	0.3	0.1	
Drug services	7.2	6.9	
General medicine/Gastro/ID	30.8	32.8	
GP	46.3	47	
GUM	4.4	3.1	
Other	7.3	7	
Prison/Detention centre	3.2	2.4	
Psychiatry	0.3	0.3	
Post-transplant (%)	2	1.8	NS
HIV positive (%)	8	7.2	NS
Renal failure (eGFR<30 or dialysis; %)	1	0.8	NS
Previous treatment (%)	29	37	P<0.001
Enrolled in HCV Research (%)	10.1	13.6	P<0.01
Actual duration of treatment (Mean ± SD, years)	12.1 ± 3.1	11.3 ± 4.5	P<0.001
Setting of treatment (%)			NS
Community drug service	3.7	2.6	
Other	1.6	1.4	
Prison	2.8	2.5	
Secondary care	91.9	93.5	
Data source: Hepatitis C patient registry and treatment outcome system as at 30 April 2018			

NS: Non-significant

Patients with two treatment episodes in the Register

Whilst the majority of patients had just one treatment episode in the Register, there were 196 people with two treatment episodes recorded. No patients had more than two treatments episodes recorded.

Among the 196 patients with two treatment episodes in the Register, it was possible to determine the outcome of the first treatment in 145 patients (74.0%), 89.7% of whom failed to achieve an SVR at 12 weeks, suggesting that the 10.3% who achieved SVR12 may have subsequently become re-infected. It was possible to determine the outcome of subsequent treatment in 99 of the 196 patients (50.5%), 86.9% of whom achieved SVR at 12 weeks (1.0% breakthrough, 7.1% relapse and 5.1% non-response).

Patients in the Register yet to be treated

As well as recording information on those patients who have undergone treatment, ODNs are encouraged to enter data into the Register on patients known to them but who have not yet been treated with the new DAAs. By the end of April 2018, there were 7,816 patients in this category.

Univariable analyses suggest that patients who were registered but not yet treated, were significantly younger, more likely to be classified as being of White ethnicity and to be UK born (Table 8).

Table 8. Sociodemographic characteristics of patients in the Hepatitis C patient registry and treatment outcome system yet to be treated compared to those with a treatment episode in the Register.

Variable	Not yet treated (n= 7,816)	Treated (n=24,592)	Significance (P-value)
Age (Mean ± SD, years)	46.6 ± 12.2	50.6 ± 11.8	<0.001
Sex (% male)	71.3	70.3	NS
Ethnicity (%)			<0.001
White	83.0	79.1	
Asian/Asian British	8.2	10.6	
Black/African/Caribbean/Black British	3.9	4.6	
Mixed/Multiple Groups	1.0	1.0	
Other	3.9	4.7	
Country of Birth (%)			<0.001
UK	76.5	70.9	
Non-UK	23.5	29.1	
Data source: Hepatitis C patient registry and treatment outcome system as at 30 April 2018			

NS: Non-significant

Patients who were registered but not yet treated had a significantly different genotype distribution, being more likely to be infected with genotype 3 and less likely to be infected with genotype 1, than those with a treatment episode in the Register (Table 9). Univariable analyses suggest that those yet to be treated were also significantly more likely to be current or recent PWID and to have acquired their infections via sex between men (Table 9).

Table 9. Infection details for patients in the Hepatitis C patient registry and treatment outcome system yet to be treated compared to those with a treatment episode in the Register.

Variable	Not yet treated (n= 7,816)	Treated (n=24,592)	Significance (P-value)
Year of first diagnosis (Mean ± SD, years)	2011 ± 8.9	2011± 6.3	NS
HCV Genotype (%)			<0.001
1	49.2	54.3	
2	6.0	4.3	
3	40.1	36.1	
4	4.0	4.8	
5	0.2	0.1	
6	0.2	0.2	
Mixed	0.1	0.1	
Other	0.3	0.1	
Injecting route of transmission (%)			<0.001
Current/recent PWID (injected in past 3 years.)	30.4	16.2	
Past PWID	38.7	46.3	
Never PWID	30.9	37.4	
Likely route of transmission (%)			<0.001
Mother to child	1.0	0.8	
Non-occupational contact with blood in a healthcare setting (e.g. via transfusion, receipt of blood products or use of inadequately sterilised medical equipment)	10.1	12.0	
Occupational exposure	0.4	0.6	
Other blood exposure e.g. tattoo	3.2	5.0	
PWID	68.1	69.7	
Sex between men	13.1	4.5	
Sex between men and women	0.9	2.0	
Other	3.3	5.5	
Data source: Hepatitis C patient registry and treatment outcome system as at 30 April 2018			

NS: Non-significant

Referrals from patients yet to be treated were significantly more likely to come from drug, prison, GUM and GP services rather than from secondary care settings and were far less likely to have undergone any previous treatment for their HCV (Table 10). As might be expected, those yet to be treated were significantly more likely to have mild/moderate liver disease, and less likely to have had a liver transplant, HCC, or renal failure than those with a treatment episode in the Register (Table 10). Those yet to be treated were significantly less likely to be HIV positive or to have alcohol reported as a contributory factor to their liver disease (Table 10).

Table 10. Clinical details for patients in the Hepatitis C patient registry and treatment outcome system yet to be treated compared to those with a treatment episode in the Register.

Variable	Not yet treated (n= 7,816)	Treated (n=24,592)	Significance (P-value)
Source of referral (%)			<0.001
A&E	0.4	0.2	
Antenatal	0.3	0.3	
Drug Services	13.8	10.4	
General Medicine, Infectious Diseases and Gastroenterology	16.4	28.4	
GP	47.2	44.3	
GUM	6.7	4.0	
Prison/Detention	6.9	5.5	
Psychiatry	0.5	0.4	
Other	7.7	6.5	
Previous treatment with interferon/pegylated interferon (+/-ribavirin) (%)	3.4	22	<0.001
Previous treatment with pegylated interferon (+/- ribavirin) and protease inhibitor (%)	0.2	3.5	<0.001
Previous treatment with all oral, interferon-free regimen (%)	0.4	1.4	<0.001
Disease stage (%)			<0.001
No fibrosis	40.8	31.6	
Mild fibrosis (Metavir F1/F2 or equivalent)	30.6	25.9	
Moderate fibrosis (Metavir F3 or equivalent)	12.2	10.4	
Compensated cirrhosis	12.8	28.2	
Compensated cirrhosis with past decompensation	0.7	1.2	
Decompensated cirrhosis	2.8	2.7	
Post-transplant (%)	0.2	1.6	<0.001
Hepatocellular carcinoma (%)	0.6	5.2	<0.001
HIV (%)	2.8	7.2	<0.001
Renal failure (eGFR<30 or dialysis; %)	0.3	1.0	<0.001
Alcohol felt to be a contributor to liver disease (%)	3.9	15.1	<0.001
Data source: Hepatitis C patient registry and treatment outcome system as at 30 April 2018			

Diagnosed patients not in contact with treatment services

In addition to those patients in the Register yet to be treated, it is recognised that there are tens of thousands of people with previously diagnosed HCV infection who are not in contact with treatment services. Many of these people may have been diagnosed when the natural history of HCV-related disease was less certain and/or when treatment options were limited with sub-optimal outcomes. Now that new DAA drugs are available, PHE and NHSE agreed that a priority action was to re-engage HCV-infected people with treatment services. To this end, a national patient re-engagement exercise was launched in September 2018 by PHE and NHS England to help find and treat those people who were diagnosed with hepatitis C in the past and who may not have been treated.

As part of the national hepatitis C patient re-engagement exercise, people diagnosed with HCV in NHS laboratories and reported to PHE, or its predecessor organisations, between 1996 and 2017 with correct and sufficient patient identifiers, were matched by PHE to the NHS Spine patient demographic service (PDS), and to other nationally-held datasets (deaths, transplants, HCV treatment) to generate a list of patients with an HCV diagnosis who are known to be alive, registered with a GP and not known to be on treatment with the new DAAs. Owing to under-reporting, incomplete or incorrect identifiers and therefore failed linkage to other datasets, not all patients who have ever been diagnosed through NHS laboratories will be in the list for ODNs. From over 170,000 laboratory reports received by PHE between 1996 to 2017, following successful matching to PDS and exclusion of those who have died or been treated, 55,329 patient details were shared with their corresponding ODNs (See Appendix 4).

This exercise is supported by The Hepatitis C Trust, the British Viral Hepatitis Group, the British Association for the Study of the Liver, the Royal College of General Practitioners, the BMA General Practitioners Committee, and the British Liver Trust, and treatment uptake will be monitored by recording referrals from this source in the Hepatitis C patient registry and treatment outcome system, and via linkage of patient lists to the registry database.

Conclusions

The creation of the Hepatitis C patient registry and treatment outcome system is a significant milestone in the monitoring of HCV elimination in England, containing more than 32,600 entries for over 32,400 people by the end of April 2018.

Although there was some duplication of information, data completeness exceeded 90% for many key variables, including age, sex, HCV genotype, source of referral, previous treatment, disease stage, as well as expected duration, date and setting of treatment. Where levels of data completeness were sub-optimal (ethnicity 89%, country of birth 71%, injecting route of transmission 61%, and likely route of transmission 54% complete, for example), available data still represent a significant improvement on that previously available in England and it is hoped that the CQUIN incentives put in place by NHS England[10] will support further improvements in data quality, particularly for fields like country of birth, ethnicity, likely route of transmission, year of first HCV diagnosis and postcode .

Amongst those in whom it was possible to establish the outcome of treatment, it was encouraging to see that 95% were achieving an SVR, 12 weeks after completing treatment, with 87% of those having a subsequent course of treatment in the Register achieving SVR by 12 weeks post-treatment following previous treatment failure or re-infection.

Information in the Register has helped us to better understand the socio-demographic, infection and clinical characteristics of people in England who have been diagnosed with chronic HCV infection and have accessed treatment services. These data will be invaluable for targeting allocation of resources for finding and treating patients, improving equity of access to treatment, modelling the future burden of HCV-related disease, and monitoring the progress of elimination, in England.

It is reassuring to see that treatment is already reaching some of the key risk groups, with 11% of those treated being of Asian ethnicity and 29% born outside the UK. Seventy percent of those treated reported injecting drug use as their likely risk for acquiring HCV and 16% of those treated were reported to be either current or recent PWID. While most referrals came from primary care (44%), just 16% came directly from drug services or prisons, which likely represents an improvement on earlier years but needs to be improved further if we are to reach those who are actively transmitting the virus.

Presence or absence variables in the Register suggest that alcohol had contributed to patients' liver disease in at least 15% of those undergoing treatment. It is not possible to fully assess data completeness for those variables that automatically default to 'absent' unless data are entered, since absence of a characteristic cannot be distinguished from

those for whom data were simply missing. For these variables associations are likely to be weakened as there may be some patients with these characteristics in the 'absent' group. Preventing these variables from defaulting to 'absent' would overcome this issue. When modelling the impact of treatment on the future burden of HCV-related disease in England, understanding the disease stage when treated (as well as the risk group) is key.[5] Amongst those with a treatment episode in the Register, disease stage data were available in 96% of cases, and showed that around one third (32%) had cirrhosis prior to treatment Interestingly, 58% had no, or only mild, fibrosis prior to treatment, which suggests that many treatment services have largely completed treating those patients with severe HCV-related disease who are known to them.

Barriers preventing many people with HCV from accessing treatment services are well described,[23],[24] so it is helpful to learn that the vast majority of treatment continues to take place within secondary care, with just 13% of treatments undertaken in drug services, prisons or other outreach settings. As with HCV testing services, it will be important to strive to improve the numbers accessing treatment locally, including within drug services, prisons and via primary care.

When looking at those patients in the Register yet to be treated, univariable analyses suggest that they tended to be significantly younger, of white ethnicity, and UK born, when compared to those who have already accessed treatment. They were also significantly more likely to be current or recent PWID or to have acquired their infections via sex between men. Patients yet to be treated were also significantly more likely to come from drug, prison, GUM and GP services rather than from secondary care settings and were far less likely to have undergone any previous treatment for their HCV. As might be expected, those yet to be treated were significantly more likely to have mild/moderate liver disease, than those with a treatment episode in the Register. Although multivariable analyses are planned to further unpick these data, early findings suggests that PWID and MSM with relatively more recent infection are starting to be identified via local and outreach services. In time it will be possible to tell whether these individuals access treatment and successfully clear their infections.

Data already available in the Register will enable us to better monitor the future burden of HCV-related disease in England. As more data become available, and data completeness improves, our progress eliminating hepatitis C as a major public health threat will be better tracked and interventions more easily identified. Linking these data to other data, like laboratory diagnoses of HCV infection, sentinel surveillance of HCV testing, cancer registry, hospital episode and death data will help inform the cascade of care for people with HCV infection in England.

Appendices

Appendix 1.*WHO GHSS targets[4] for viral hepatitis, relevant to HCV in the UK context, with 2020 targets updated to reflect the draft action plan for the health sector response to viral hepatitis in the WHO European Region.[25]

TARGET AREA	2020 TARGETS[25]	2030 TARGETS[4]
Impact targets		
Incidence: New cases of chronic viral hepatitis C infection	30% reduction	80% reduction
Mortality: Viral hepatitis C deaths	10% reduction	65% reduction
Service coverage targets		
Blood safety:**Proportion of donations screened in a quality-assured manner	100%	100%
Safe injections:*** Percentage of injections administered with safety engineered devices in and out of health facilities	50%	90%
Harm reduction: A comprehensive package of harm reduction services to all PWID[26] including:	At least 200 sterile needles and syringes provided per person who injects drugs per year At least 40% of opioid dependent PWID receive OST 90% of PWID receiving targeted HCV information, education and communication	At least 300 sterile needles and syringes provided per person who injects drugs per year
Proportion of people with chronic HCV diagnosed and aware of their infection	50% [75% of estimated number of patients at late stage of viral hepatitis-related liver disease (cirrhosis or HCC) diagnosed]	90%
Treatment coverage of people diagnosed with chronic HCV who are eligible for treatment	75% (>90% cured) [90% of diagnosed patients with chronic HCV are linked to care and adequately monitored]	80%

* Abstracted from the WHO Global Health Sector Strategy for Viral Hepatitis[4] and modified to reflect the draft action plan for the health sector response to viral hepatitis in the WHO European Region[25]
** In England, 2020 and 2030 targets are already met.[27]
***In England, 2020 and 2030 targets are already met in the health care setting as the UK follows the EU Directive for the prevention of sharps injuries in the health care setting,[28] by using safety engineered devices.

Appendix 2. Variables in the Hepatitis C patient registry and treatment outcome system

Variable	Values	Default
ID	Number	
Provider	Drop down list of providers	
NHS Number	Number	
Local Patient Identifier	Alphanumeric	
Identifier	Number	
Full Name	Text	
First Name	Text	
Last Name	Text	
Date of Birth	Date	
Gender	- Male - Female - Not Specified - Not Completed	
Ethnicity	- White - Asian/Asian British - Black / African / Caribbean / Black British - Mixed/Multiple Ethnic Groups - Other - Not Completed - Unknown	
Postcode	Alphanumeric	
Country of Birth	Drop-down ISO list of countries[29]	
Referral Date	Date	
Year of first HCV diagnosis	Number	
Acoustic Radiation Force Impulse Elastography result	Number	
Created Date	Date	
Created Method	Manual Imported	
Source of Referral	- A&E - Antenatal - Drug Services - General Medicine / Gastro / Id - GP - GUM - Prison / Detention - Psychiatry - Other - Not Completed	
Date of MDT Meeting for current treatment episode	Date	
Treatment ID	Number	
Disease Stage	- No Fibrosis - Mild Fibrosis (Metavir F1 Or F2 Or Equivalent) - Moderate Fibrosis (Metavir F3 Or Equivalent) - Compensated Cirrhosis - Compensated Cirrhosis With Past Decompensation - Decompensated Cirrhosis - Not Completed	
Post Transplantation	True / False	Auto default to False

Variable	Values	Default
HCC	True / False	Auto default to False
Fibroscan result (at point of current treatment decision)	Number	
HCV Genotype	- Genotype 1 (unspecified) - Genotype 1a - Genotype 1b - Genotype 2 - Genotype 2 Other - Genotype 2a - Genotype 3 - Genotype 3 Other - Genotype 3a - Genotype 4 - Genotype 4 Other - Genotype 4a - Genotype 5 - Genotype 6 - Genotype Mixed - Genotype Other - Not Completed	
Interferon/Pegylated Interferon & Ribavirin	True / False	Auto default to False
Pegylated Interferon / Ribavirin+Protease Inhibitor	True / False	Auto default to False
All Oral/ interferon-free	True / False	Auto default to False
HIV	True / False	Auto default to False
Renal Failure (eGFR<30 or dialysis)	True / False	Auto default to False
Alcohol felt to be contributor to liver disease	True / False	Auto default to False
Injecting Route of Transmission	- Current/Recent PWID (Injected In Last 3 Years) - Past PWID - Never PWID - Don't Know - Not Completed	
Likely Route of Transmission	- Mother To Child - Non-Occupational Contact With Blood In Healthcare Setting - Occupational Exposure - Other Blood Exposure E.G. Tattoo - PWID (PWID is Defined as a Person who Injects Drugs) - Sex Between Men - Sex Between Men and Women - Other - Not Completed - Unknown	
In what setting is the current episode of treatment taking place	- Community Drug Service - Prison - Secondary Care - Other - Not Completed	

Variable	Values	Default
Elbasvir/Grazoprevir	True / False	
Sofosbuvir / Velpatasvir	True / False	
Sofosbuvir	True / False	
Ledipasvir	True / False	
Daclastasvir	True / False	
Paritaprevir / Ombitasvir	True / False	
Dasabuvir	True / False	
Ribavirin	True / False	
Pegylated interferon	True / False	
Simeprevir	True / False	
Trial drug (NHS funded)	True / False	
Trial drug (non-NHS funded)	True / False	
Glecaprevir Pibrentasvir (Early Access to Medicines Scheme)	True / False	
Glecaprevir Pibrentasvir (Non-Early Access to Medicines Scheme)	True / False	
Expected Treatment Duration (weeks) agreed at MDT	Number	
Enrolled in HCV Research UK?	True / False	Auto default to False
Treatment start date	Date	
Blue Tech Reference Number (if required)	Number	
Notes	Text	
Outcome	- SVR 12 (Sustained Viral Response - HCV RNA Negative/Cleared The Virus - 12 Weeks After Completion Of Treatment) - Relapse (Achieved Clearance Of Virus During Treatment But Became HCV RNA Positive Again In The Post-Treatment Period) - Breakthrough (Achieved Clearance Of Virus During Treatment But Became HCV RNA Positive Again During Treatment) - Non-Response (Remained HCV RNA Positive And Did Not Clear The Virus At Any Point Throughout The Course Of Treatment Or In The Post-Treatment Period) - Lost To Follow-Up (Did Not Attend 12/24 Week Post-Treatment Follow-Up Appointments) - Died Before Treatment Could Commence - Death (Died After Initiation Of Treatment And Before Testing To Establish 12/24 Week Post-Treatment Outcome) - Other - Not Completed	
Actual Treatment Duration (weeks)	Number	

Appendix 3. Information Governance

PHE is collecting information on patients referred to ODNs to monitor equity and access to hepatitis C treatment, in order to improve prevention, testing and treatment services and monitor progress towards elimination of hepatitis C in England.[4]

Information being collected and shared with PHE are the data entered into the NHS England Hepatitis C patient registry and treatment outcome system. This includes personal identifiers such as name, NHS number, date of birth, demographics (age, sex, ethnicity, country of birth), probable route of infection, year of diagnosis, referral source, disease stage, co-morbidities, treatment history, setting and outcome.

PHE keep personal information on all people diagnosed with hepatitis C (even after death) to help monitor progress of the hepatitis C elimination programme. This personal information is handled confidentially and securely and PHE never publishes any information that could be used to identify anyone with hepatitis C or any other infectious disease.

PHE have a legal right to process confidential patient information for the purposes of the surveillance, prevention and control of communicable diseases and other risks to public health. Specifically, PHE has approval from the Secretary of State for Health under section 60 of the Health & Social Care Act 2001, as re-enacted by section 251 of the NHS Act 2006 and regulation 3 of the Health Service (Control of Patient Information Regulations) 2002. Commonly known as ‘section 251 approval’, this allows PHE to lawfully collect and process confidential and sensitive information without seeking the explicit consent of patients. Section 251 approval is needed by PHE to enable it to collect information on all patients with communicable diseases to ensure that these are rapidly and effectively controlled in order to protect the wider public health.

All the uses of the data collected and processed by PHE under its section 251 approval comply with the requirements of the Data Protection Act. PHE has achieved Level 2 status for the NHS Digital Information Governance Toolkit – the required standard for all health and care organisations processing patient data – and has implemented strong controls to ensure that all its data is collected and processed securely, and that patient confidentiality is protected throughout in accordance with the seven Caldicott principles.

Hepatitis C is also a notifiable organism under the Health Protection (Notification) Regulations 2010. This means that diagnostic laboratories in England have a legal duty to notify PHE of all hepatitis C cases and that this notification should include full patient identifiers. For more information please visit: https://www.gov.uk/guidance/notifiable-diseases-and-causative-organisms-how-to-report#laboratories-report-notifiable-organisms-causative-agents

Appendix 4. Number of patients notified to Operational Delivery Networks as part of the national hepatitis C patient re-engagement exercise to find and treat previously diagnosed patients

Operational Delivery Network	Number of patients*
Barts	1,847
Birmingham	4,862
Bristol and Severn	3,135
Cheshire and Merseyside	2,762
Eastern	3,813
Greater Manchester and Eastern Cheshire	5,429
Humberside and North Yorkshire	1,630
Kent Network via Kings	1,123
Lancashire and South Cumbria	2,604
Leicester	1,050
North Central London	2,724
North East and Cumbria	2,123
Nottingham	2,279
South Thames	3,493
South West Peninsula	1,777
South Yorkshire	2,338
Surrey	1,162
Sussex	1,701
Thames Valley	1,225
Wessex	2,159
West London	2,865
West Yorkshire	3,228
Total	**55,329**

*People diagnosed with HCV in NHS laboratories and reported to PHE, or predecessor organisations, between 1996 and 2017. As laboratory reports contain patient identifiers, where correct and sufficient, PHE matched these patients to the NHS Spine patient demographic service (PDS), and to other nationally-held datasets (deaths, transplants, HCV treatment) to generate a list of patients with an HCV diagnosis who are known to be alive, registered with a GP and not known to be on treatment with the new DAAs. Owing to underreporting, incomplete or incorrect identifiers and therefore failed linkage to other datasets, not all patients who have ever been diagnosed through NHS laboratories will be in the list for ODNs. From over 170,000 laboratory reports received by PHE between 1996 to 2017, following successful matching to PDS and exclusion of those who have died or been treated, 55,329 patient details were shared with their corresponding ODNs.

References

1. World Health Organization. Global Hepatitis report, 2017. Available from: http://www.who.int/hepatitis/publications/global-hepatitis-report2017/en/ [Accessed 09/07/2018].
2. Public Health England. Hepatitis C: Operational Delivery Network (ODN) profile tool. 2018. Available at: https://www.gov.uk/government/publications/hepatitis-c-commissioning-template-for-estimating-disease-prevalence [Accessed 13/11/2018].
3. Public Health England. Hepatitis C in England 2018. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/693917/HCV_in_England_2018.pdf. [Accessed 09/07/2018].
4. World Health Organization. Global health sector strategy on viral hepatitis, 2016-2021. Towards Ending Viral hepatitis. 2016. Available from: http://apps.who.int/iris/bitstream/10665/246177/1/WHO-HIV-2016.06-eng.pdf?ua=1. [Accessed 09/07/2018].
5. Harris RJ, Martin, N. K., Rand E, Mandal S, Mutimer D, Vickerman P, Ramsay ME, et al. New treatments for hepatitis C virus (HCV): scope for preventing liver disease and HCV transmission in England. Journal of Viral Hepatitis. 2016(8):631-43.
6. Martin NK, Vickerman P, Foster GR, Hutchinson SJ, Goldberg DJ, Hickman M. Can antiviral therapy for hepatitis C reduce the prevalence of HCV among injecting drug user populations? A modeling analysis of its prevention utility. Journal of Hepatology. 2011;54(6):1137-44.
7. Martin NK, Vickerman P, Grebely J, Hellard M, Hutchinson SJ, Lima VD, et al. HCV treatment for prevention among people who inject drugs: Modeling treatment scale-up in the age of direct-acting antivirals. Hepatology. 2013;58(5):1598-609.
8. Harris RJ, Thomas B, Griffiths J, Costella A, Chapman R, M R. Increased uptake and new therapies are needed to advert rising hepatitis C- related end stage liver disease in England: modelling the predicated impact of treatment under different scenarios. Journal of Hepatology. 2014;61(3):530-7.
9. Sam Lattimore, Will Ivring, Sarah Collins, Celia Penman, Mary Ramsay and on the behalf of the Collaboration for the Sentinel Surveillance of Blood-Borne Virus Testing. Using Surveillance Data to Determine Treatment Rates and Outcomes for Patients with Chronic Hepatitis C Virus Infection. Hepatology. 2014;59(4):1343-50.
10. NHS England. BI1 Imporving HCV Treatment Pathways through ODNs. 2016. Available from: https://www.england.nhs.uk/wp-content/uploads/2016/11/bi1-improv-hcv-treat-pathways.pdf [Accessed 04/10/2018]
11. National Institute for Health and Clinical Excellence (NICE). Daclatasvir for treating chronic hepatitis C. 2015. Available from: https://www.nice.org.uk/guidance/ta364. [Accessed 09/07/2018]
12. National Institute for Health and Clinical Excellence (NICE). Ledipasvir–sofosbuvir for treating chronic hepatitis C. 2015. Available from: https://www.nice.org.uk/guidance/ta363. [Accessed 09/07/2018]
13. National Institute for Health and Clinical Excellence (NICE). Ombitasvir–paritaprevir–ritonavir with or without dasabuvir for treating chronic hepatitis C. NICE technology appraisal guidance [TA365]. 2015. Available from: https://www.nice.org.uk/guidance/ta365. [Accessed 09/07/2018]
14. National Institute for Health and Clinical Excellence (NICE). Simeprevir in combination with peginterferon alfa and ribavirin for treating genotypes 1 and 4 chronic hepatitis C. NICE technology appraisal guidance TA331. 2015. Available from: http://www.nice.org.uk/guidance/ta331. [Accessed 09/07/2018]

15. National Institute for Health and Clinical Excellence (NICE). Sofosbuvir–velpatasvir for treating chronic hepatitis C. 2017. Available from: https://www.nice.org.uk/guidance/ta430 [Accessed 09/07/2018]
16. National Institute for Health and Clinical Excellence (NICE). Elbasvir–grazoprevir for treating chronic hepatitis C. 2016. Available from: https://www.nice.org.uk/guidance/TA413/chapter/2-The-technology [Accessed 09/07/2018]
17. Innes H, Goldberg D, Dillon J, Hutchinson SJ. Strategies for the treatment of Hepatitis C in an era of Interferon-free therapies: what public health outcomes do we value most? Gut. 2014:1-10.
18. NHS England. Commissioning for Quality and Innovation. 2018 . Available from: https://www.england.nhs.uk/nhs-standard-contract/cquin/ [Accessed 14/09/2018].
19. McLauchlan J, Innes H, Dillon JF, Foster G, Holtham E, McDonald S ea. Cohort Profile: The Hepatitis C Virus (HCV) Research UK Clinical Database and Biobank. 2017. International journal of epidemiology.
20. EASL. European Association for the Study of the Liver. EASL Recommendations on Treatment of Hepatitis C 2018. Available from: https://doi.org/10.1016/j.jhep.2018.03.026 [Accessed 24/09/2018]. Journal of Hepatology. 2018;69(26):461-511.
21. NHS England. Urgent Clinical Commissioning Policy Statement: Retreatment of Chronic Hepatitis C Infection in Adults with Advanced or Decompensated Cirrhosis. 2017. https://www.england.nhs.uk/wp-content/uploads/2017/08/ccp-statement-retreatment-chronic-hepatitis-c-infection.pdf.
22. Public Health England. Hepatitis C in the UK 2018. Available from: https://www.gov.uk/government/publications/hepatitis-c-in-the-uk. Accessed [14/09/2018].
23. World Health Organisation. Barriers and facilitators to hepatitis C treatment for people who inject drugs. A Qualitative Study. Available from: http://www.euro.who.int/en/health-topics/communicable-diseases/hepatitis/publications/2012/barriers-and-facilitators-to-hepatitis-c-treatment-for-people-who-inject-drugs.-a-qualitative-study [Accessed: 20/09/2018] 2012
24. Harris M; Rhodes T. Hepatitis C treatment access and uptake for people who inject drugs: a review mapping the role of social factors. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3686576/. [Accessed: 24/09/2018]. Harm Reduction. 2013;10(7).
25. World Health Organization. Action plan for the health sector response to viral hepatitis in the WHO European Region. 2016. Regional Committee for Europe 66th Session, Copenhagen, Denmark, 12-15 September 2016. Available from: http://www.euro.who.int/en/about-us/governance/regional-committee-for-europe/66th-session/documentation/working-documents/eurrc6610-action-plan-for-the-health-sector-response-to-viral-hepatitis-in-the-who-european-region [Accessed 07/07/2018].
26. World Health Organization. WHO, UNODC, UNAIDS technical guide for countries to set targets for universal access to HIV prevention, treatment and care for injecting drug users – 2012 revision. Available from: http://www.who.int/hiv/pub/idu/targets_universal_access/en/. [Accessed: 09/07/2018]: WHO; 2013.
27. Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee. Guidelines for the Blood Transfusion Services in the UK. Available from: http://www.transfusionguidelines.org/ [Accessed 09/07/2018]
28. European Agency for Safety and Health at Work. Directive 2010/32/EU - prevention from sharp injuries in the hospital and healthcare sector. 2010. Available from: https://osha.europa.eu/en/legislation/directives/council-directive-2010-32-eu-prevention-from-sharp-injuries-in-the-hospital-and-healthcare-sector. [Accessed 09/07/2018]
29. Gov.UK. ISO Country Codes. 2018. Available from: https://www.gov.uk/government/publications/iso-country-codes--2 [Accessed 04/10/2018]