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Establishing the cascade of care for hepatitis C in England–benchmarking to monitor impact of direct acting antivirals.

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Running head:

Cascade of care for hepatitis C in England

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Abstract

Little is known about engagement and retention in care of people diagnosed with chronic hepatitis C (HCV) in England. Establishing a cascade of care informs targeted interventions for improving case-finding, referral, treatment uptake and retention in care. Using data from the Sentinel Surveillance of Blood Borne Virus testing (SSBBV) between 2005-2014 we investigate the continuum of care of those tested for HCV in England.

Persons ≥1 years old, with an anti-HCV test and subsequent RNA tests between 2005-2014 reported to SSBBV were collated. We describe the cascade of care, as the patient pathway from a diagnostic test, referral into care, treatment, and patient outcomes.

Between 2005-2014, 2,390,507 samples were tested for anti-HCV, corresponding to 1,766,515 persons. 53,038 persons (35,190 men and 17,165 women) anti-HCV positive were newly reported to SSBBV. An RNA test, was conducted on 77.0% persons anti-HCV positive, 72.3% of whom were viraemic (RNA positive) during this time period, 21.4% had evidence of treatment, and 3130 49.5% had evidence of a sustained virological response (SVR). In multivariable models confirmation of viraemia by RNA test varied by age and region/test setting; evidence of treatment varied by age, year of test and region/test setting; and SVR varied by age, year of test and region/setting of test. In conclusion,

Our findings provide HCV cascade of care estimates prior to the introduction of direct acting antivirals. These findings provide important baseline cascade estimates to benchmark progress towards elimination of HCV as a major public health threat.

Key words:
Barriers, Cascade, DAA HCV, SVR, Treatment

Introduction

An estimated 160,000 persons (0.4% of the population) in England are infected with hepatitis C virus (HCV) (1), a leading cause of liver disease worldwide. Over 85% of those diagnosed with HCV in England acquired their infection through injecting drug use (2). Both the incidence and prevalence of HCV infection, as well as associated morbidity and mortality are influenced by changes in treatment innovations, healthcare policy and delivery of services, socio-demographic factors and risk behaviours. Historically, the diagnosis, referral, treatment, and care of persons infected with HCV has been challenging due to the difficulty of health worker and patient engagement, with HCV disproportionately affecting persons from socially excluded groups [people who inject drugs (PWID), prison inmates, migrants] who generally have poorer health care access and outcomes (3).

The previous standard of care, involving complex, poorly tolerated and long periods of treatment with ribavirin and pegylated interferon, provided a challenge to optimal treatment initiation and retention in care. Improvements to care and health outcomes are, however, expected through the introduction of the new direct acting antiviral (DAA) treatments, which are more efficacious, of shorter treatment duration and have a better side effect profile than the previous treatment options. The timely use of the DAAs is

expected to lead to individual health benefits and to a reduction in the pool of infectious people, who are the source of onward transmission. Several modelling studies have shown that increased HCV treatment among PWID will reduce prevalence and onward transmission (4-8), especially when combined with opioid substitution therapy and high coverage of needle and syringe programmes (7). Modelling predicts that rapid scale up of HCV treatment in those with moderate to severe liver disease will curtail morbidity and mortality from end stage liver disease (9, 10), but to make a substantial impact on transmission, treatment of mild disease is also required (11). In the era of the new DAAs it is important, therefore, to have a baseline measure of the previous standard of care against which to assess the impact of treatment strategies with DAAs, and highlight where gaps in the patient pathway persist.

In England little is known about engagement and retention in care, with modelling of pharmacy dispensing data for ribavirin and pegylated interferon between 2006 and 2011 suggesting that only 3% of chronically infected persons were on treatment (10, 12). A study in Nottingham identified that less than half of diagnosed persons between 2001 and 2002 were referred to care, with only 10% of patients being treated (13). A repeat pathway audit following improvements, by the same group, for patients diagnosed between 2010 and 2011 showed an improvement in the referral rate to 80%, with 37% of patients receiving treatment (14). However, this local audit is likely to represent the best-case scenario of the cascade of care for patients, the pathway from a person's diagnostic test, to care, treatment, and outcome, having been undertaken in an area with well-established clinical pathways and networks; it may therefore not be representative of the national picture.

Establishing a nationally representative cascade of care for HCV infected patients is critical for identifying where and which groups drop out of the care pathway to inform targeted interventions to improve case-finding, referral, treatment uptake and retention in care. In the absence of large and costly patient registries and cohorts, Sentinel Surveillance of Blood-Borne Virus (SSBBV) testing can be used to indirectly estimate the proportion of individuals in each step of the care pathway.

Using data collected by the SSBBV between 2005 and 2014, we investigated the care and management of those tested for HCV in England. In this paper, we describe differences in testing, confirmation of current infection, treatment initiation, and treatment outcome by patient demographic characteristics, year of testing, geographical region of testing and setting or specialty of diagnosis.

Methods

SSBBV is a unique surveillance system that captures all blood-borne virus tests regardless of the result for tests conducted at any one of 23 sentinel laboratories across England. Participating laboratories are estimated to cover approximately 65% of the English population for primary and reference HCV testing and are broadly representative of most laboratories providing HCV testing. Data collection methods for SSBBV have been described previously (15). In summary, demographic and testing data for all individuals tested for hepatitis C-specific antibody (anti-HCV), indicative of current or past infection ("ever infected") and HCV-RNA (indicative of viraemia, i.e. current infection) are extracted from participating laboratory information systems. Individuals were de-duplicated, and test

results for each individual were linked over time using a combination of soundex code (a coding based on the person's surname), first initial, date of birth and NHS number.

Results from all persons ≥1 year old, with an anti-HCV test between 2005 and 2014 were collated with subsequent HCV-RNA tests where available. Persons aged <1 year were excluded due to the possibility of false-positive results from maternal antibodies, as were persons testing in renal services and all reference laboratories as these tests are unlikely to reflect normal testing practises. Persons with an RNA test prior to the first reported anti-HCV result within SSBBV testing were also excluded as this was assumed to be evidence of previous HCV diagnosis outside of the SSBBV laboratory network.

We describe the cascade of care as the patient pathway from the first anti-HCV test, referral into care, treatment, and patient outcomes. All persons had at least one year of follow-up following an initial anti-HCV test. The cascade of care was described for persons diagnosed anti-HCV positive by sex, age, source of anti-HCV test, and region of anti-HCV test.

The following patient pathway was described: the number of persons tested for anti-HCV, and the number anti-HCV positive; for the anti-HCV positive patients, the number for whom an RNA test was conducted. The setting of a person's anti-HCV test was grouped into one of 10 clinical specialities based on the requesting department reported by the laboratory: general practitioner, community drug services, sexual health services (including HIV medicine), prisons, occupational health, antenatal and maternity services, accident and emergency department, liver specific services, general medicine, and other. General practice, emergency departments, community drug services, and prisons were categorised as primary care specialties; the rest, as secondary care.

Treatment Algorithm

Evidence of treatment was derived using an algorithm where four or more sequential HCV-RNA test results within a 390 day period of an initial positive RNA result was considered suggestive of monitoring during treatment with the standard of care (ribavirin and pegylated interferon based regimens) (15). Persons with a final negative HCV-RNA test result within the 390-day period were considered to have responded to therapy, and to have achieved a sustained virological response (SVR) (16). The algorithm was validated using a clinical cohort database in Nottingham, the algorithm results were found to have high sensitivity, specificity, PPV, NVP and inter-rater agreement.

Treatment uptake was estimated for all persons with a positive HCV-RNA regardless of when the test was conducted following a positive anti-HCV result. Among those for whom there was evidence of treatment initiation, the proportion with SVR was estimated.

Statistical Analysis

The cascade of care among those newly testing positive for anti-HCV was examined using descriptive analysis. Proportions were compared using the X^2 test. Three multivariable models identified factors associated with having an RNA test following a positive anti-HCV test result, initiating treatment following a positive RNA result, and achieving SVR following treatment initiation, adjusting for year of diagnosis, age, sex, region and setting of diagnosis. An interaction between region and speciality of test was found to be significant ($p<0.001$) for both variables, and thus we re-categorised these two variables to create a new variable (London Primary Care, London Secondary Care, Outside London Primary Care, and Outside London Secondary Care). Statistical analyses were performed using STATA version 10 (Stata Corp., College Station, TX, USA).

The research presented as part of the present study was undertaken within the National Institute for Health Research Health Protection Research Unit (NIHR HPRU) in Blood Borne and Sexually Transmitted Infections at University College London.

Results

Of the 2,390,507 samples, corresponding to 1,766,515 persons, tested for anti-HCV between 2005 and 2014, 118,308 tests (5.0%), and 70,674 persons (4.0%) were found to be anti-HCV positive. London had the highest number of persons presenting for a HCV test (538,253), and by service type general practice had the highest number of persons tested (468,481). In contrast, the highest proportion of positive tests was in the North West (5.9%, 19260/325,697), and among persons attending drug services (26.9%, 10,328/38,431), followed by prisons (17.4%, 6284/36,087).

Among patients with a positive anti-HCV result (70,674), 66,716 had their first anti-HCV positive result between 2005 and 2014; 13,678 of these patients were excluded from further analysis as there was an RNA test reported to SSBBV prior to the first anti-HCV result. Table 1 shows the characteristics of those tested and the remaining 53,038 persons (35,190 men and 17,165 women) newly anti-HCV positive within SSBBV. The median age at anti-HCV diagnosis was 39 years (interquartile range [IQR]: 31-47), with males representing 67.2% of new anti-HCV positive persons, and 54.3% of persons were diagnosed anti-HCV positive in primary care settings. By source of referral, 28.2% were tested in general practice, 14.8% within community drug services, 13.0% in sexual health clinics including HIV services, 12.1% in general medical departments, 10.8% in other services, 9.7% in prisons,

5.4% in liver specific services, 3.5% through antenatal and maternity services, 1.5% in emergency departments, and 0.93% through occupational health.

An RNA test, to determine whether a person had a current HCV infection, was conducted on 40,856 (77.0%) anti-HCV positive patients; of these, 29,557 (72.3%) were HCV RNA positive; 6326 (21.4%) of those known HCV RNA positive patients had evidence of treatment, of whom 3130 (49.5%) were estimated to have achieved an SVR. Overall, of all 53,038 newly anti-HCV positive persons, 6326 (11.9%) had evidence of treatment, and 3130 (5.9%) had evidence of a SVR. Figure 1 shows a simulated cascade of care for all persons chronically infected within England using these distributions.

Among persons with an RNA test (40,856), for 26,537 (65%), the test was performed within seven days of the anti-HCV result (which indicates "reflex testing" of the original anti-HCV positive serum sample). A previous negative anti-HCV result was available for 3354 (6.3%) of anti-HCV positive persons, with the highest proportions of persons with a previous negative test among persons diagnosed in sexual health services (9.8%; 673/6889) or antenatal and maternity services (7.1%; 132/1854).

Table 2a-c show unadjusted and adjusted associations between setting of test and demographic factors and whether an RNA test was conducted (2a), evidence of HCV treatment (2b), and evidence of SVR (2c).

In adjusted models region and setting of anti-HCV test remained associated with an RNA test following an anti-HCV positive result. Compared to persons testing in primary care settings in London, persons testing in secondary care settings in London were more likely to have had a subsequent RNA test [Odds Ratio (OR): 1.11 (95% confidence interval: 1.02-1.20)], persons testing in primary care settings outside London were also more likely

[OR=1.21 (1.13-1.30)] whereas persons testing in secondary care services outside London were less likely to have had an RNA test [OR=0.75 (0.70-0.80)]. Furthermore, an RNA test was more likely for among those testing between 2008 and 2010 [OR=1.18 (1.11-1.24)] and between 2011 and 2014 [OR=1.12 (1.07-1.18)] when compared to 2005 and 2007. Finally, persons aged 50 years and over were less likely to have an RNA test [OR=0.92 (0.87-0.98)] compared with persons aged 30-39 years.

In a multivariable model investigating predictors for treatment, region and setting of anti-HCV test remained an independent predictor for evidence of treatment. Compared to persons testing in primary care settings in London, persons testing in secondary care settings in London and secondary care settings outside London were more likely to have evidence of treatment [OR=1.15 (1.03-1.29) and OR=1.14 (1.03-1.26), respectively]. Furthermore, evidence of treatment was more likely between 2008 and 2010 [OR=1.19 (1.11-1.28)], and less likely between 2011 and 2014 [OR=o.76 (0.71-0.82)] when compared to years between 2005 and 2007 (table 1b) and more likely for all age groups when compared with persons aged 30-39 years [<15 years OR=2.73 (1.74-4.28) 15-29 years OR=1.11 (1.02-1.21), 40-49 years OR=1.38 (1.28-1.48), and ≥50 years OR=1.45 (1.34-1.57)].

Finally, in a multivariable model investigating evidence of SVR among persons treated, region and setting of anti-HCV test remained an independent predictor for evidence of SVR. Compared to persons testing in primary care settings in London, persons were more likely to have evidence of SVR outside of London regardless of setting [Outside London Primary Care OR=1.58 (1.34-1.87), and Outside London Secondary Care OR=1.50 (1.26-1.79)], and less likely in London secondary care [OR=0.74 (0.60-0.91)]. Evidence of SVR was less likely for persons aged 50 years and over when compared to those 30-39 years [OR= 0.76 (0.66-0.88)]

and more likely among persons diagnosed between 2008 and 2010 and between 2011 and 2014 when compared to those diagnosed between 2005 and 2007 [OR=1.13 (1.00-1.27)] and OR=2.05 (1.80-2.33), respectively], (table 2c).

Discussion

Our analysis demonstrates that in the pre-DAA era, confirmation of a current HCV infection occurred in 77% of persons positive for anti-HCV, with a low uptake of treatment of 11.9%, and attainment of SVR 5.9% overall. If restricting the cascade to those who were RNA positive following an anti-HCV positive result, around a fifth had evidence of treatment and half of those were estimated to have been cured.

Confirmation of current infection (viraemia) following a positive anti-HCV result is a critical first step in the cascade that triggers referral for and consideration of treatment. Among our population 65% of patients had had a test where the timing of the RNA test suggested that the same sample as for anti-HCV testing was used. Alternative pathways result in the antibody and RNA tests being conducted on separate samples requiring patients to re-attend for a blood test, increasing the likelihood of loss to follow up. To counter this, NICE recommend that RNA testing be conducted on the same sample, referred to as "reflex testing" (17); this approach has been shown to reduce referral and testing costs, with a faster treatment initiation following a reflex test (18).

Progression through the cascade varied considerably by patient demographics, setting, geography and year of diagnosis. Our data indicate that the distribution of positive anti-HCV results is consistent with populations disproportionately affected by HCV, with a higher proportion of men and those testing at community drug clinics and within prisons positive

for HCV. However, although positivity rates for anti-HCV and RNA were highest in those testing in community drug services and prisons, treatment coverage was the lowest at 6.6% and 5.9% respectively, compared with general practice where 17.7% of those with a positive RNA result being on treatment. Similarly, attainment of SVR was highest in general practice and secondary care services and lowest among persons initially presenting in drug services and prisons. These findings are likely a function of transient and mobile populations, access to care pathways, referral practice, local policy and/or clinician dependent offer of HCV therapy as well as uptake and compliance in the patient population. These disparities are similar to those observed in a two year retrospective cohort in Nottingham, where treatment initiation was highest in those diagnosed through general practice (43%), followed by secondary care (39%), drug services (32%), and then prisons (26%) (14). These cascade data reinforce well-articulated recommendations that community-based and patient-focused treatment delivery, including in prisons and drug services, are needed to reduce disengagement particularly among socially excluded groups (19, 20).

Our findings provide baseline cascade of care estimates as new regimens based on DAAs are being introduced into England. The low overall treatment rate of 11.9% is consistent with those published for the USA, Canada, and Australia, with these published rates ranging from 1.1%-25.6% (21-27). Those studies identified a number of factors associated with treatment initiation, with older age (21-23), current drug and alcohol use (21, 23, 26), and comorbidities (21, 23, 26) being associated with a reduced likelihood of treatment. In addition, patients reported deferring treatment until the availability of better therapies, because of treatment related perceptions, ability to comply, and concerns with side effects (24, 28).

In our data, the lower rates of treatment in recent years compared to 2007-2011 could reflect this deferral of treatment (whether clinician or patient driven) in anticipation of introduction of the DAA in 2014 /2015. The association between age and treatment uptake with under 15 and over 50 year olds having higher treatment coverage also likely reflect clinical prioritisation of the young to prevent liver chronic liver disease, and of older persons to curtail progression of liver disease. Conversely higher levels of attaining SVR in patients diagnosed in 2011-2014 may reflect more effective drug combinations and compassionate use of DAA (through the NHSE expanded access programme) in patient groups with decompensated cirrhosis /per-transplantation, while lower SVR attainment in older persons is expected as older age is associated with advanced disease stage and other co-morbidities which lower success of treatment.

There were also wide variations in the different components of the cascade between geographic regions. For example, RNA testing following a positive HCV result ranged from 69 to 80%; treatment initiation following a positive RNA test ranged from 7-20%; and SVR rates ranged from 2-13%. Although the reasons for these differences are multifactorial and likely reflect current and historical differences in the affected population structure, case mix, clinical networks, patient pathways and commissioning, and so are not necessarily directly comparable or simple to disentangle, regions should be aware of these disparities so they can reflect on where improvements could be made in their own models and adopt good practice from elsewhere.

The recent national roll out of DAAs through the NHS, which are injection-free, easier to tolerate, and of shorter treatment duration is likely to transform the treatment landscape and increase treatment uptake and completion among those chronically infected with HCV

– thus potentially narrowing a gap in the cascade. However, inequalities in access to and outcome of treatment among socially excluded groups who have high rates of infection such as prisoners and PWID, as highlighted in this study, may persist and even widen with new DAAs if prevention and treatment services are not commissioned or delivered following an equitable approach. Future analysis of SSBBV data will enable persistent gaps to be identified and acted upon in the era of DAAs.

Our study is limited by the fact that initial and follow-up testing for HCV may have occurred outside the 23 sentinel surveillance laboratories if patients moved location, thereby resulting in an under-estimate of upstream (e.g. where initial anti-HCV test was not found) and downstream activities (e.g. RNA testing for monitoring treatment not found) within the cascade. Additionally, data on dried blood spot (DBS) testing which is being increasingly used in prison and community drug services, is most frequently tested in commercial laboratories and not captured by SSBBV, preventing follow up of individuals tested by DBS which is necessary for cascade of care estimations.

This study provides important cascade estimates to benchmark progress towards elimination of HCV as a major public health threat, providing a baseline cascade of care for the pre-DAA period. These data will enable persistent barriers to be identified, as well as inequities in performance across geographical regions. The cascade of care contributes to the evaluation of clinical and public health HCV control strategies, which may inform the allocation of resource for health service planning. Furthermore, understanding and addressing patient and structural factors that influence engagement in the patient care pathway will impact the overall goal to reduce HCV transmission and HCV-associated cirrhosis, cancer and death. Collective and concerted efforts are needed to improve the

cascade of care for HCV within England, and to realise the population benefits from prevention and treatment interventions.

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Author Contributions

RS undertook the analysis and had access to the complete dataset; SM, SL, MR, and SI came up with the initial concept. All authors provided critical input to the manuscript and approved all revisions.

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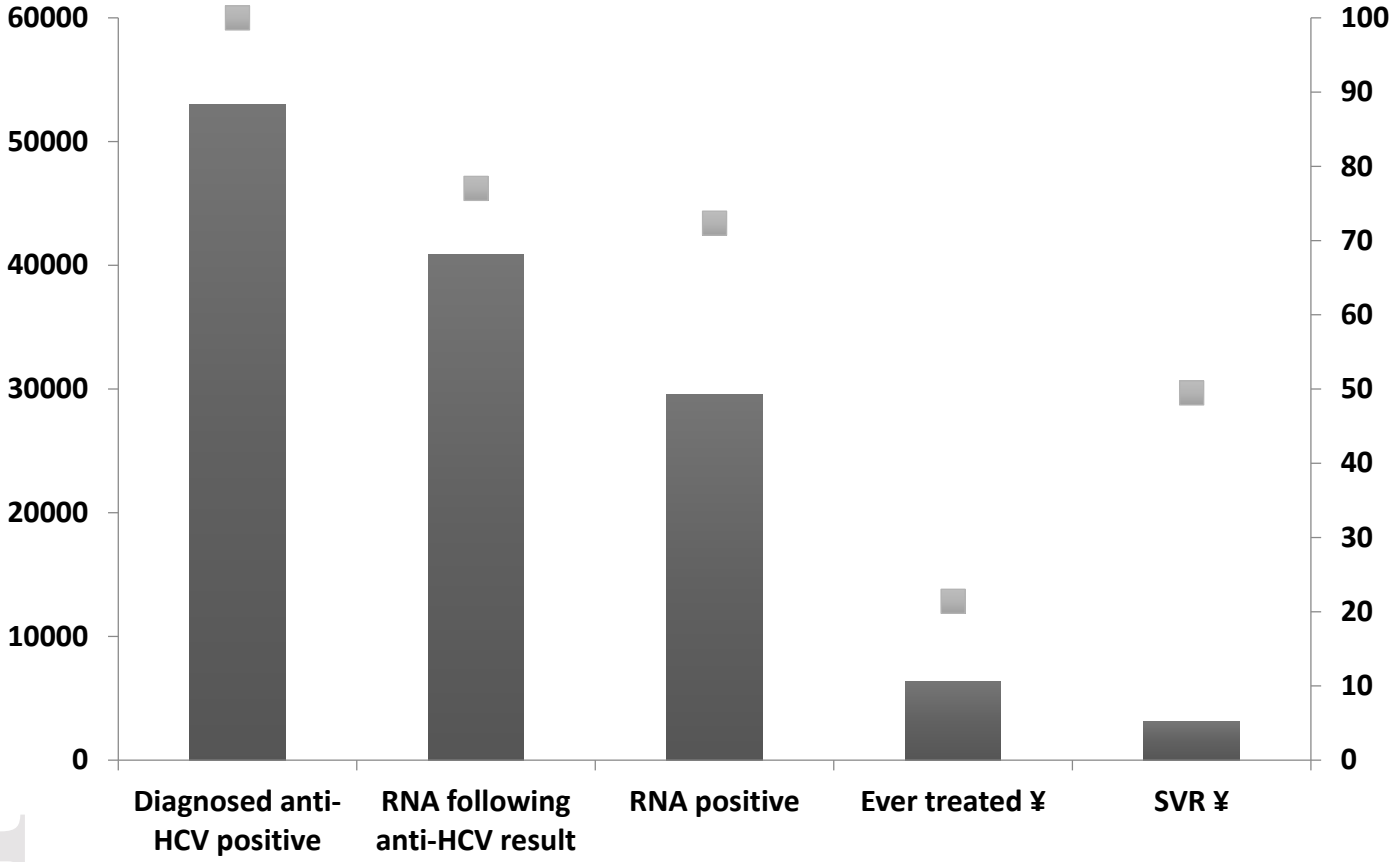
Table 1: Distribution of persons through the care cascade following a positive anti-HCV result, reported to sentinel surveillance 2005-2014.

	Anti-HCV tested	Anti-HCV Positive *		Had an RNA test		Ever RNA positive		Evidence of treatment		Evidence of SVR	
	n	n	%	n	%	n	%	n	%	n	%
Total	1,766,515	53038	3.0	40856	77.0	29557	55.7	6326	11.9	3130	5.9
Sex											
Male	926,534	35,190	3.8	27,313	75.8	20,701	58.8	4,479	12.7	2,180	6.2
Female	807,015	17,165	2.1	13,156	65.2	8,580	50.0	1,842	10.7	947	5.5
Not Reported	32,966	683	2.1	387	71.3	276	40.4	5	0.7	3	0.4
Age Group											
<15	26,802	189	0.7	130	65.4	85	45.0	32	16.9	18	9.5
15-29	517,654	9,891	1.9	7,593	69.7	5,294	53.5	1,061	10.7	561	5.7
30-39	463,382	17,428	3.8	13,565	72.7	9,863	56.6	1,813	10.4	909	5.2
40-49	300,534	14,583	4.9	11,398	72.7	8,284	56.8	1,961	13.4	981	6.7
≥50	472,811	10,583	2.2	8,032	73.9	5,935	56.1	1,458	13.8	661	6.2
Not Reported	9161	364	4.0	138	69.6	96	26.4	1	0.3		0.0
Source of referral											

Emergency Department	21,871	799	3.7	604	73.7	445	55.7	63	7.9	23	2.9
Drug Services	38,431	7,833	20.4	6,378	78.1	4,984	63.6	516	6.6	273	3.5
General Practice	468,481	14,931	3.2	12,100	74.4	8,998	60.3	2,643	17.7	1,400	9.4
Sexual Health (including HIV)	335,436	6,889	2.1	4,974	63.7	3,166	46.0	489	7.1	149	2.2
Occupational Health	132,703	494	0.4	358	39.4	141	28.5	23	4.7	9	1.8
Prison	36,087	5,152	14.3	3,868	71.8	2,776	53.9	306	5.9	128	2.5
Liver Services	71,182	2,846	4.0	2,486	76.5	1,902	66.8	545	19.1	294	10.3
Maternity/Antenatal Care	177,201	1,854	1.0	1,303	59.6	777	41.9	205	11.1	119	6.4
General Hospital	203,523	6,396	3.1	4,295	72.4	3,111	48.6	718	11.2	310	4.8
Other	280,042	5,698	2.0	4,387	72.5	3,179	55.8	814	14.3	423	7.4
Not reported	1558	146	9.4	103	75.7	78	53.4	4	2.7	2	1.4
Region											
East Midlands	142,098	3,118	2.2	2,573	75.6	1,946	62.4	470	15.1	279	8.9
East of England	78,083	1,842	2.4	1,111	75.9	843	45.8	232	12.6	164	8.9
London	538,253	13,173	2.4	10,312	68.6	7,078	53.7	1,542	11.7	595	4.5
North East	110,293	2,817	2.6	2,204	80.3	1,770	62.8	453	16.1	123	4.4
North West	325,697	14,192	4.4	10,243	71.3	7,301	51.4	1,306	9.2	784	5.5
South Central	42,867	993	2.3	743	75.2	559	56.3	66	6.6	49	4.9
South East Coast	142,190	3,814	2.7	2,925	71.6	2,095	54.9	259	6.8	173	4.5
South West	130,979	5,323	4.1	4,831	70.4	3,400	63.9	716	13.5	120	2.3
West Midlands	73,219	2,022	2.8	1,247	76.1	949	46.9	147	7.3	75	3.7
Yorkshire and the Humber	182,798	5,744	3.1	4,667	77.5	3,616	63.0	1,135	19.8	768	13.4
Not Reported	38										
Year of anti-HCV test											
2005	104,618	4,930	4.7	3,566	75.9	2,705	54.9	542	11.0	255	5.2
2006	111,710	5,565	5.0	4,190	72.9	3,055	54.9	648	11.6	271	4.9
2007	129,383	5,590	4.3	4,273	71.1	3,039	54.4	755	13.5	320	5.7
2008	160,030	5,807	3.6	4,452	69.9	3,113	53.6	800	13.8	337	5.8
2009	174,503	5,572	3.2	4,417	69.2	3,058	54.9	803	14.4	318	5.7
2010	171,689	5,155	3.0	4,078	70.1	2,859	55.5	690	13.4	384	7.4
2011	178,437	5,177	2.9	4,181	71.8	3,004	58.0	667	12.9	391	7.6
2012	201,962	5,101	2.5	3,923	74.5	2,921	57.3	545	10.7	326	6.4
2013	241,903	4,988	2.1	3,899	74.2	2,893	58.0	501	10.0	311	6.2
2014	292,280	5,153	1.8	3,877	75.1	2,910	56.5	375	7.3	217	4.2

* 3958 persons were excluded as their first anti-HCV positive result known to SSBBV was prior to 2005, and 13,678 persons were excluded as there was an RNA test reported to SSBBV prior to the first anti-HCV result.

Figure 1: The cascade of care for persons with chronic HCV in England in the era of ribavirin and pegylated interferon treatment (Bars), and the proportion of persons who move to the next stage of the care pathway (squares), using the sentinel surveillance of blood borne virus testing database, 2005-2014.



¥ Derived using an algorithm where four or more sequential RNA test results within a 390 day period of an initial positive RNA result was considered to be monitoring during treatment with the standard of care in the study period which included ribavirin and pegylated interferon.

Table 2: Results from logistic regression analysis to identify factors associated with a. having an RNA test following a positive anti-HCV result, b. evidence of treatment among persons with a current infection (RNA positive), and c. evidence of achieving an SVR, reported to sentinel surveillance 2005-2014.

a.

	Unadjusted		Adjusted	
	OR	**95% CI**	**OR**	**95% CI**
Year of anti-HCV test				
2005 - 2007	1		1	
2008 - 2010	1.21	1.44-1.27	1.18	1.11-1.24
2011 - 2014	1.18	1.12-1.24	1.12	1.07-1.18
Age Group				
<15	0.66	0.48-0.92	0.74	0.54-1.03
15-29	0.96	0.90-1.02	0.97	0.91-1.03
30-39	1		1	
40-49	1.02	0.97-1.08	1.03	0.97-1.08
≥50	0.89	0.84-0.94	0.92	0.87-0.98
Sex				
Male	1		1	
Female	0.94	0.90-0.98	0.96	0.92-1.00
Region / Source of Referral				
London Primary Care	1		1	
London Secondary Care	1.12	1.03-1.21	1.11	1.02-1.20
Outside London Primary Care	1.22	1.40-1.31	1.21	1.13-1.30
Outside London Secondary Care	0.74	0.69-0.79	0.75	0.70-0.80

b.

	Univariate		Multivariate	
	OR	**95% CI**	**OR**	**95% CI**
Year of anti-HCV test				
2005 - 2007	1		1	
2008 - 2010	1.21	0.13-1.29	1.19	1.11-1.28
2011 - 2014	0.77	0.72-0.83	0.76	0.71-0.82
Age Group				
<15	2.74	1.76-4.28	2.73	1.74-4.28
15-29	1.11	1.02-1.21	1.11	1.02-1.21
30-39	1		1	
40-49	1.37	1.28-1.48	1.38	1.28-1.48
≥50	1.43	1.33-1.55	1.45	1.34-1.57
Sex				
Male	1		1	
Female	0.99	0.93-1.05	0.99	0.93-1.05
Region / Source of Referral				
London Primary Care	1		1	
London Secondary Care	1.17	1.04-1.31	1.15	1.03-1.29
Outside London Primary Care	1.01	0.92-1.11	1.07	0.97-1.17
Outside London Secondary Care	1.14	1.03-1.26	1.14	1.03-1.26

c.

	Univariate		Multivariate	
	OR	**95% CI**	**OR**	**95% CI**
Year of anti-HCV test				
2005 - 2007	1		1	
2008 - 2010	1.08	0.96-1.22	1.13	1.00-1.27
2011 - 2014	1.92	1.70-2.18	2.05	1.80-2.33
Age Group				
<15	1.28	0.63-2.59	1.21	0.60-2.53
15-29	1.12	0.96-1.30	1.09	0.92-1.25
30-39	1		1	
40-49	1.00	0.88-1.14	0.99	0.87-1.13
≥50	0.83	0.72-0.95	0.75	0.66-0.88
Sex				
Male	1		1	
Female	1.12	1.00-1.25	1.09	0.97-1.22
Region / Source of Referral				
London Primary Care	1		1	
London Secondary Care	0.75	0.61-0.93	0.74	0.60-0.91
Outside London Primary Care	1.60	1.36-1.90	1.58	1.34-1.87
Outside London Secondary Care	1.44	1.21-1.72	1.94	1.26-1.97