Prevalence of diagnosed HIV infection among persons with hepatitis C infection: England, 2008-2014

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Abstract

Objective: In persons with hepatitis C (HCV), HIV co-infection leads to faster progression to advanced liver disease. We estimate diagnosed HIV prevalence among people with evidence of current HCV infection (PCR+), and examine predictors of co-infection.

Methods: Adults (≥15yrs) with a current HCV infection reported to the PHE sentinel surveillance of blood borne viruses were linked to the PHE national HIV database using a deterministic methodology. Descriptive and multivariate analyses were conducted.

Results: Between 2008 and 2014, 5.0% (999/20,088) of adults with a current HCV infection were diagnosed with HIV co-infection. The majority acquired HIV through sex between men (441, 64.9%), followed by injecting drug use (153, 22.5%) and heterosexual contact (84, 12.4%). 65.5% of persons co-infected had been diagnosed with HIV >6 months before their HCV diagnosis, 41.4% of whom had a negative anti-HCV test between their HIV and HCV diagnosis.

In a multivariable model among persons with current HCV, a HIV diagnosis was more likely among men (aOR: 3.29, 95% CI 2.60-4.16) and person of black ethnicity (aOR: 3.19; 95% CI 1.36-7.46), and less likely among older adults (aOR: 0.85 per 10-year increase, 95% CI 0.79-0.92) and persons of Asian ethnicity (aOR: 0.59, 95% CI 0.41-0.86).

Conclusion: Our results indicate that the majority of diagnosed HIV and current HCV co-infection are among men who have sex with men. Safer sex campaigns should include awareness of transmission of HCV among MSM living with HIV.

Introduction

In the United Kingdom (UK), an estimated 214,000 persons are chronically infected with hepatitis C (HCV) and 101,200 are living with HIV (1,2). Within the UK, the highest prevalence of HCV is reported among persons who inject drugs (PWIDs), whilst the highest prevalence rates of HIV are among men who have sex with men (MSM) and persons of black African ethnicity (2).

Although HCV remains more prevalent in PWIDs when compared to other groups at risk of HCV, in recent years there has been an increase in the number of MSM being diagnosed with HCV across Europe and the United States, particularly those HIV positive. HCV transmission has been linked to recreational drug use and high-risk sexual behaviours (3–5). Co-infection with HCV and HIV leads to faster progression to advanced liver disease (6,7), and there is conflicting evidence as to whether co-infection worsens HIV-associated outcomes, such as AIDs-defining events and HIV-associated mortality (8–11).

The prevalence of HCV antibodies (anti-HCV), a marker of ever being infected, in HIV positive MSM in England was noted to be 4.1% in 2002-2003 and 7.1% in 2008-2009 (12,13). Furthermore, the UK Collaborative HIV Cohort (UK CHIC) study estimated HCV prevalence for HIV positive persons in 2011 at 10.0% overall, corresponding to an estimated 10,000 people, and 9.9% in HIV positive MSM, compared to 83.3% in HIV positive PWIDs (14). However, these estimates, along with those from other studies (8,15,16), have used HIV as the base population and there has been less focus on HIV prevalence among persons HCV positive in the UK. Dougan et al. found 0.8% of persons

79 with HCV were diagnosed with HIV when they matched laboratory confirmed HCV cases
80 between 1996 and 2003 to the national HIV database, although the authors
81 acknowledged it was likely an underestimate given the majority of reported cases from
82 genitourinary medicine (GUM) clinics were missing personal identifiers (12), and Barclay
83 et al. (17) found that 6.5% of patients being treated for HCV between 2012 and 2014
84 were co-infected with HIV. Using a large sentinel surveillance database linked to the
85 national HIV database, we estimate HIV co-infection among persons with evidence of
86 current HCV infection, and examine risk factors associated with diagnosed co-infection.

Methods

HCV data

The Sentinel Surveillance of Blood Borne Virus Testing (SSBBV), held at Public Health England (PHE), collects information on hepatitis A-E, HIV and HTLV tests, regardless of result, from 23 participating sentinel laboratories in England. It is estimated to cover 40% of HCV and HIV testing in England. Alongside the test result, SSBBV collects information on demographics and the service requesting the test. The methods have previously been described but, in brief, data from participating laboratory information systems in England were extracted and records of individuals were deduplicated and linked to all other test results using a combination of soundex (phonetic algorithm for indexing names), date of birth, National Health Service (NHS) number and hospital number. Demographic and testing data on all anti-HCV, combined antibody/antigen and PCR testing between January 2008 and December 2014 were extracted from SSBBV. Tests were excluded if they were quality control samples, tests to confirm a previous diagnosis, from persons participating in a study and/or from persons less than 15 years of age when first tested.

All persons with a HCV antibody or combined antibody/antigen test within the period were included in the study, and an overall 'anti-HCV result' was assigned based on the combination of HCV tests and results recorded for each testing episode. A person's first positive anti-HCV test (indicative of ever being infected with HCV), requester service and first subsequent HCV PCR test (to confirm current infection) were identified.

HIV data

Two PHE data sources were used to identify HIV positive persons: SSBBV and the HIV and AIDS Reporting System (HARS), which collects information on persons diagnosed with HIV and any subsequent access to care at an NHS HIV service in England. From SSBBV, all positive HIV antibody tests were extracted and a person's first positive test date was identified. The HARS datasets was linked to SSBBV using deterministic (where identifiers have to match exactly), and probabilistic (which scores matches using weighted probabilities) methodology. Identifiers used for linkage included hospital number, GUM number, soundex, first name initial, date of birth, sex and region of test. Of persons identified as HIV positive, 60.6% were identified from HARS only, 34.3% from SSBBV and HARS and 5.1% in SSBBV only. Following data linkage, the earliest date of HIV presentation between the two data sources was established and appended to the HCV testing records. Route of HIV transmission was only available for persons identified as HIV positive from the HARS database, as route of HIV transmission is not recorded in SSBBV.

Definitions

Persons who tested positive for anti-HCV were regarded to have ever been infected with HCV, and persons who tested HCV PCR positive (i.e. were viraemic) were regarded to have a current HCV infection.

To ensure concurrent co-infection, as around 25% will spontaneously clear their HCV infection (the majority in the first 6 months) and persons may have been treated for their HCV(18), persons were defined as co-infected at the time of HCV diagnosis if there was evidence of a HIV diagnosis at any time prior to their anti-HCV test, or they were newly

diagnosed with HIV in the six months following their anti-HCV test, and they were subsequently identified as HCV PCR positive.

Statistical Analysis

Statistical analysis was carried out in STATA SE (version 13) with Chi-squared and Fishers Exact tests being used to compare categorical variables and Wilcoxon rank-sum tests to compare continuous variables. Predictors of diagnosed co-infection in persons with a current HCV infection were examined using a multivariate logistic regression, which included sex, age at date of anti-HCV test (continuous), ethnicity (including where not reported, as the majority of people testing in sexual health services do not have an ethnicity reported), year of positive anti-HCV test and speciality requesting their anti-HCV test (excluding HIV specialist services). All proportions reported in the text exclude unknowns.

Results

Between 2008 and 2014, 1,368,424 persons aged 15 years and over were tested for anti-HCV in the SSBBV network, of whom 2.6% (35,682) were positive, indicative of a person ever having been HCV infected (current or past infection) (table 1 and figure 1). Overall, 4.4% (1,560/35,682) of persons who had ever been infected with HCV had also been diagnosed with HIV. Of persons ever HCV infected and diagnosed with HIV, most were male (84.3%), of white ethnicity (66.9%) and tested for HCV in a sexual health service (67.1%). A higher prevalence of HIV infection was found in men than women (5.6% vs 2.0%; p<0.001). Persons of black ethnicity had a higher prevalence and persons of Asian ethnicity had a lower prevalence of HIV infection, when compared to persons of white ethnicity (9.6% vs 4.5%; p<0.001and 1.9 vs 4.5%; p<0.001 respectively).

HCV-HIV co-infection

A PCR test was conducted on 80.5% (28,708) of persons who were anti-HCV positive, with current HCV infection identified in 70.0% (20,088). Among those with a current HCV infection, 5.0% (999) had been diagnosed with HIV at any time prior to or in the 6 months following their anti-HCV test (co-infected). Persons co-infected were mostly male (87.8%), of white ethnicity (70.6%), tested for HCV at a sexual health service (67.3%) and slightly younger at HCV diagnosis (median: 38 vs 40 years; p<0.001) than those with current HCV infection only.

The highest prevalence of co-infection was among men (6.3%) and persons aged between 30 and 54 years (5.3%). Prevalence of co-infection was lower in persons of Asian ethnicity when compared to persons of white ethnicity (2.1 vs 5.1%; p<0.001). Prevalence varied

by speciality, with the highest prevalence of co-infection among persons found infected with HCV at a sexual health service (31.9%), followed by persons tested at speciality liver services (6.8%) and at emergency departments (5.6%).

Route of HIV transmission was available for 80.7% (796) of co-infected persons, with the most frequent route of transmission for HIV being sex between men (520, 65.3%), followed by injecting drug use (175, 22.0%) and heterosexual contact (97, 12.2%). Of those where route of transmission was reported as sex between men, 3.1% (16) were also reported to have injected drugs. A higher proportion of co-infected women acquired HIV through injecting drug use than men (44.3% vs 18.9%; $p<0.001$). Regardless of probable route of HIV infection, the majority of persons had their first positive HCV test in a sexual health service.

Of those co-infected, 65.5% were diagnosed with HIV more than 6 months before their HCV diagnosis, 18.2% were diagnosed with HIV in the 6 months before their HCV diagnosis, and 11.5% were diagnosed with HCV and HIV on the same day (figure 1). 4.8% were diagnosed with HIV in the 6 months after their HCV diagnosis. 66.8% and 57.8% of co-infected males and females respectively had their HIV infection diagnosed more than 6 months before their HCV infection.

Of persons with a HIV diagnosis more than 6 months before their positive anti-HCV test, 41.4% (271/654) had a negative anti-HCV test between their HIV and HCV diagnosis between 2008 and 2014. Where route of infection was reported (88.2%), 95.8% (n=229) acquired their HIV following sex between men.

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187 *Factors associated with diagnosed co-infection*

188 In a multivariable model, persons with a current HCV infection were more likely to be
189 diagnosed as co-infected if they were male (adjusted odds ratio (aOR): 3.29, 95%
190 Confidence Interval (CI) 2.60-4.16) or of black ethnicity (aOR: 3.19, 95% CI 1.36-7.46);
191 diagnosed co-infection was less likely among older adults (aOR: 0.85 per 10-year age
192 increment, 95% CI 0.79-0.92) and among persons of Asian ethnicity (aOR: 0.59, 95% CI
193 0.41-0.86)(table 2).

194 Compared to persons tested for HCV in general practice, those tested in sexual health
195 services (aOR: 143.50, 95% CI 104.98-196.14), specialist liver services (aOR: 7.79, 95% CI
196 5.40-11.24), emergency departments (aOR: 6.03, 95% CI 3.44-10.56) and other secondary
197 care services (aOR: 3.71, 95% CI 2.72-5.06) were more likely to be diagnosed as being co-
198 infected.

199 *Testing HIV positive more than 6 months after HCV test*

200 Among persons not defined as co-infected at the time of HCV diagnosis, 0.19%
201 (37/19,089) of persons with a current HCV infection were diagnosed with HIV more than
202 6 months after their HCV diagnosis, 75.7% (28) of whom were male. Unlike when HIV was
203 diagnosed prior to or at the time of HCV, most persons (where reported; 54.1%, n=20)
204 diagnosed with HIV more than 6 months after their HCV diagnosis reported injecting drug
205 use as their route of HIV transmission (50.0%, n=10), followed by sex between men
206 (35.0%, n=7), of which 2.7% (1) also indicated drug use, and heterosexual contact (15.0%,
207 n=3).

Discussion

Between 2008 and 2014, one in twenty (5%) persons with a current HCV infection were diagnosed with HIV either prior to or in the six months after HCV diagnosis. Overall men and persons of black ethnicity were significantly more likely to be diagnosed as co-infected. Most persons meeting our criteria for diagnosed co-infection had been diagnosed with HIV more than 6 months before their HCV diagnosis; a large proportion of these had also previously tested negative for anti-HCV between 2008 and 2014, suggesting that persons with HIV continue to engage in behaviour after their diagnosis that puts them at increased risk of HCV.

We found that all persons tested for HCV within SSBBV, regardless of result, had a higher prevalence of diagnosed HIV than the national average (2.4% vs 0.2%); diagnosed prevalence was also higher than that among PWID (0.9%), the main group affected by HCV (2,19). Previous estimates of HIV infection amongst persons ever HCV infected, through linking laboratory confirmed HCV cases (anti-HCV positive) between 1996 and 2003 to national HIV databases, were significantly lower than our results (0.8% compared to 4.4%) (12), but our prevalence of diagnosed co-infection among persons currently HCV infected was similar to that found by Barclay et al. (5.0% vs 6.5%) (17). The difference with Dougan et al. is likely to be due to improved availability of identifiers for matching the two datasets, particularly for those attending sexual health services.

Whilst injecting drug use is the predominant risk factor within the UK for HCV (around 90% of cases are acquired through this route (20)), among those co-infected only a quarter of cases acquired their HIV through injecting drug use. In comparison, a higher

proportion (78%) acquired their HIV infection through sexual transmission, of which 84% was sex between men. In co-infected women a higher proportion reported injecting drug use (44%), although women constituted only around 10% of the co-infected population.

When using the setting of the test as an indicator of likely risk, persons were over 140 times more likely to be diagnosed as co-infected with HIV when testing for HCV in sexual health services. Whilst PWID do frequent sexual health clinics, such services are more likely to be frequented by persons participating in high-risk sexual behaviours (15). Furthermore, HIV prevalence is known to be low in PWID who access drug services, following the implementation of harm reduction strategies, and such services would also routinely undertake BBV testing in people who report injecting drug use. Using the probable route of infection as recorded through HIV surveillance, 65% of those co-infected reported their risk to be sex between men. Research into HCV infections in HIV positive MSM have also found relatively low rates of injecting drug use (10-40% of persons co-infected) and reported associations with sexual behaviours, such as condomless anal sex, fisting, high rates of partner change and sex under the influence of recreational drugs, also known as 'chemsex' (sex under the influence of psychoactive substances), and concomitant sexually transmitted infections, but not typically "conventional" injecting drug use (3,15,21). Testing guidelines are also likely to drive testing within sexual health services, as they recommend regular HCV testing for MSM who are HIV positive or who disclose recreational drug use or 'chemsex' during their consultation (22). However, in those attending sexual health clinics, injecting drug use may be underreported as the most likely route of transmission due to not being considered socially acceptable.

Two-thirds of persons diagnosed as co-infected were diagnosed with HIV more than 6 months before their HCV diagnosis, a significant proportion of whom had previously tested HCV negative, confirming the results of previous studies that identify continued behaviours following a HIV diagnosis that put individuals at increased risk of sexually transmitted infections, including HCV (15,23). While some HIV positive MSM modify their risk behaviour (serosorting or only having condomless anal sex with other HIV positive MSM) in an attempt to prevent onwards transmission (24), tackling the risk of HCV and other sexually transmitted infections remains a challenge for HIV and sexual health services.

Our findings support the British HIV Association guidelines, which indicate that persons with HIV should be tested regularly for HCV, with the majority of persons in our study diagnosed with HCV a number of months after their HIV diagnosis. However, it is also important, that a HIV test is considered following an HCV diagnosis as, although only a small proportion were diagnosed with HIV post HCV. Despite an HIV test following an HCV diagnoses being recommended by British HIV Association HIV testing guidelines, only 45% of persons with a positive HCV antibody test within SSBBV who were not already diagnosed with HIV received an HIV test in the six months following their HCV test (21). As co-infected persons have faster liver disease progression it is important that persons are tested for other blood borne viruses once diagnosed with either HCV or HIV (6,7), and that they continue to be offered tests when reporting behaviours that put them at increased risk of co-infection.

Important limitations to this study include that tests within sexual health services have limited patient identifiers and so true matches may have been missed when linking the

datasets. Secondly, we are only able to report on persons diagnosed with HCV and HIV, we do not know how they would differ from the co-infection rate in persons undiagnosed, which will be influenced by the proportion of undiagnosed HIV and HCV infection in different sub-populations. As heterosexuals have higher rates of undiagnosed HIV in England, (2) this is most likely to be an issue among people who acquire HIV through heterosexual sex than among MSM. In addition there are no guidelines for HCV testing other than in individuals who report injecting drug use or are HIV positive, and populations not covered by these guidelines may be under-represented in our HCV testing database. Thirdly, as SSBBV is a sentinel system it will not include earlier HCV tests that occurred outside of our centres. This could result in persons who had previously tested positive outside of SSBBV, who were then tested within SSBBV, having a later HCV diagnosis date assigned to them. SSBBV coverage by Local Authority ranges from 0%-100%, with higher coverage in urban areas, but on average it is estimated to cover 40% of HCV testing in England. Additionally, we were not able to determine how many people who were not diagnosed with HIV had been tested for the infection elsewhere. This would have helped to better understand the potential impact of undiagnosed HIV infection on co-infection prevalence.

We found rates of diagnosed HIV infection in persons with a current HCV infection to be higher than those found in PWID and that most HIV infections were among MSM, indicating that diagnosed co-infection is mainly associated with high risk sexual behaviour, rather than injecting drug use, the dominant risk factor for those HCV mono-infected. As an HIV diagnosis preceded a HCV infection in the majority of those co-infected (many of whom will be engaged in care, receiving HIV treatment and have

299 previously tested HCV negative), more needs to be done to increase awareness of HCV
300 risk, the need for regular testing and encourage safer sex, as well as understand the
301 contribution of ‘chemsex’ to HCV and HIV risk.

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Table 1: Characteristics of persons diagnosed with HIV[1] among persons tested for anti-HCV between 2008 and 2014 in sentinel laboratories in England.

	All anti-HCV tested	Ever HCV infected			Current HCV infection		
Demographic variable	n	n	HIV+ (n)[1]	HIV+ (%)[1]	n	HIV+ (n)[1]	HIV+ (%)[1]
	1,368,424	35,682	1,560	4.4	20,088	999	5.0
Sex							
Male	719,273	23,494	1,315	5.6	13,985	877	6.3
Female	628,839	11,537	231	2.0	5,771	116	2.0
Unknown	20,314	651	14	2.2	332	6	1.8
Age at anti-HCV test							
15-29 years	405,570	6,177	241	3.9	3,298	162	4.9
30-39 years	359,016	11,441	585	5.1	6,542	388	5.9
40-54 years	313,666	13,197	633	4.8	7,672	396	5.2
55+ years	283,507	4,627	98	2.1	2,513	53	2.1
Unknown	6,665	240	3	1.3	63	0	0.0
Ethnicity							
White	834,180	23,185	1,044	4.5	13,811	705	5.1
Asian	155,713	3,564	69	1.9	2,112	45	2.1
Black	26,103	271	26	9.6	127	8	6.3
Other	36,593	569	31	5.4	288	21	7.3
Unknown	315,835	8,093	390	4.8	3,750	220	5.9
Year positive HCV test							
2008	156,110	5,534	300	5.4	3,041	197	6.5
2009	169,716	5,248	238	4.5	2,934	146	5.0
2010	167,806	4,990	207	4.1	2,782	134	4.8
2011	173,022	5,019	179	3.6	2,904	110	3.8
2012	195,174	4,989	208	4.2	2,930	133	4.5
2013	234,434	4,926	219	4.4	2,824	145	5.1
2014	272,162	4,976	210	4.2	2,673	134	5.0
Service requesting HCV test							
General Practice	376,038	10,553	100	0.9	6,407	57	0.9
Specialist drug service	28,997	5,642	31	0.5	3,572	24	0.7
Sexual health services	253,016	4,555	1046	23.0	2,105	672	31.9
Prison services	28,149	3,570	25	0.7	1,995	15	0.8
Emergency departments	16,897	562	23	4.1	304	17	5.6
Other Primary Care	95,205	355	1	0.3	119	-	0.0
Specialist liver service	48,013	1,443	94	6.5	955	65	6.8
Specialist renal service	52,292	439	8	1.8	182	4	2.2
Other Secondary Care	468,764	8,507	231	2.7	4,428	144	3.3
Unknown	1,051	56	1	1.8	21	1	4.8

[1] Persons diagnosed with HIV at any time before their anti-HCV test or in the six months following their HCV diagnosis.

Table 2: Factors associated with a HIV diagnosis among persons with current HCV infection in England, 2008-2014

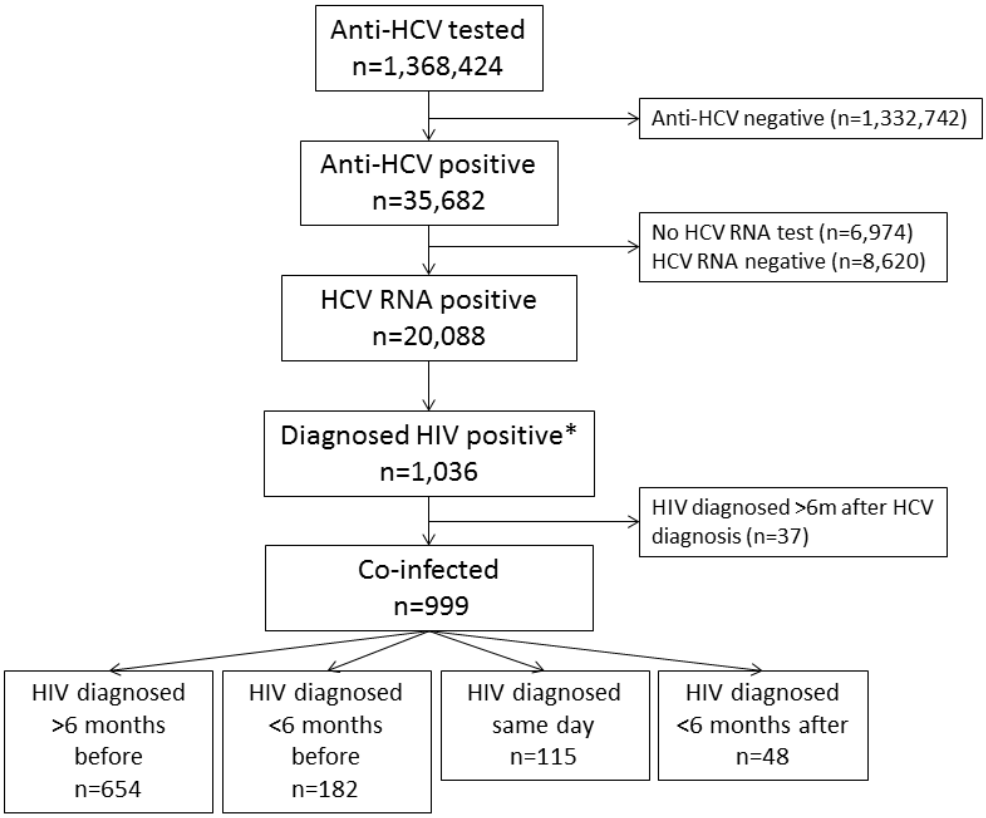
		Current HCV infection[1]	Co-infected[1]	Adjusted[2]		
				OR	95% CI	p-value
Sex						
	Female	5,737	98	1		<0.001
	Male	13,875	796	3.29	2.60-4.16	
Age						
	per 10 year increase			0.85	0.79-0.92	<0.001
Ethnicity						
	White	13,620	629	1		
	Asian	2,061	38	0.59	0.41-0.86	<0.001
	Black	121	8	3.19	1.36-7.46	
	Other	279	16	1.42	0.77-2.64	
	Not reported	3,531	203	0.11	0.09-0.14	
Year of positive HCV test						
	2008	2,976	180	1		
	2009	2,870	135	0.81	0.61-1.06	
	2010	2,717	128	1.04	0.79-1.38	0.15
	2011	2,848	99	0.84	0.62-1.12	
	2012	2,850	117	0.76	0.58-1.01	
	2013	2,753	126	1.00	0.76-1.33	
	2014	2,598	109	0.78	0.58-1.04	
Requester Type						
	General Practice	6,333	57	1		
	Specialist drug service	3,484	23	0.67	0.41-1.09	
	Sexual health services[3]	1,921	571	143.50	104.98-196.14	
	Prison services	1,944	14	0.93	0.52-1.69	<0.001
	Emergency departments	302	17	6.03	3.44-10.56	
	Other Primary Care	115	0	-	-	
	Specialist liver service	949	64	7.79	5.40-11.24	
	Specialist renal service	181	4	2.68	0.96-7.53	
	Other Secondary Care	4,383	144	3.71	2.72-5.06	

[1] includes only persons with complete data on all variables (excluding ethnicity) included in the model

[2] adjusted for all other variables

[3] excluded persons tested positive in specialist HIV services

Figure 1: Flow diagram of HIV diagnoses relative to HCV diagnoses in persons co-infected (n=999) between 2008 and 2014.



* Includes people diagnosed with HIV >6 months after HCV diagnosis, who are not included in our co-infected definition