

Diagnosis of hepatitis C virus infection in Scotland's injecting drug user population

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SUMMARY

We estimated the extent of undiagnosed hepatitis C virus (HCV) infection in injecting drug users (IDUs) in Scotland. We used record-linkage to determine HCV diagnosis status for 41 062 current/former IDUs attending drug treatment and support services between 1 April 1995 and 31 March 2006; the extent of undiagnosed HCV infection was estimated by comparing the number HCV-diagnosed to the number HCV-infected (estimated from an unlinked anonymous testing survey of 2141 current/former IDUs). In all, 9145 IDUs (22%) were diagnosed HCV antibody-positive since first attendance at drug services (diagnosis rate of 33·6/1000 person-years, 95% CI 32·7–34·4). By 31 March 2006, of the 19 632 current/former IDUs who had attended drug services and were determined to be living with HCV, an estimated 58% (95% CI 45–62) had not been HCV-diagnosed. It is essential that the deployment of resources for identifying at-risk IDUs with a view to offering antiviral therapy is guided by evidence.

Key words: Epidemiology, hepatitis C, injecting drug users (IDUs).

INTRODUCTION

In resource-rich countries, injecting drug use accounts for most hepatitis C virus (HCV) transmission. HCV prevalences exceeding 50% in injecting drug user (IDU) populations, including those in Scotland, are commonplace [1–3]. Although reductions in HCV prevalence have been observed in IDUs in Scotland during the 1990s, the incidence remains high – with

an estimated 1000–2000 new infections per year [4, 5]. In 1999/2000, a national survey of Scotland's current/former IDUs detected an overall HCV prevalence of 44% ($n=2141$), ranging from 23% ($n=40$) in the Forth Valley health board to 62% ($n=611$) in Greater Glasgow [6].

Despite pegylated interferon and ribavirin combination therapy being considered highly cost-effective even for those with mild disease [7, 8] most past and current IDUs in the UK and elsewhere remain untreated [9]. One of the reasons for this is failure to diagnose their HCV infection. A principal aim of Scotland's £43 million Hepatitis C Action Plan,

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launched in May 2008, is to identify as many as possible of the country's estimated 38 000 chronically infected persons, 90% of whom have injected drugs in the past [9].

Understanding the size and characteristics of the HCV-undiagnosed population is crucial if case-finding measures are to be effective. To date, in Scotland, estimates of diagnosed/undiagnosed proportions have depended on (i) analytical studies, where the modelled number of infected persons was compared to the number known to be diagnosed [4, 5], and (ii) surveys of current IDUs, where self-report of HCV status in respondents was compared to their HCV seropositive status [10]. The former approach relies on the accuracy of statistical models to estimate the number of HCV-infected individuals [4], whereas the latter approach is problematic due to the accuracy of self-report data [11, 12].

The existence of extensive country-wide data on the prevalence of HCV in IDUs and two comprehensive national databases – one of IDUs registered as having attended drug treatment and support services, and the other of all laboratory diagnoses of HCV infection made in Scotland – afforded the unique opportunity to determine, through a record-linkage exercise, the extent of undiagnosed HCV infection in IDUs in Scotland, and to ascertain the factors predictive of diagnosis/non-diagnosis. This is the first report of its kind.

METHODS

The design was a retrospective cohort study. Data from three national sources were electronically linked to investigate variables associated with HCV diagnosed status for a large cohort of current/former IDUs.

Study population and data sources

The study population consisted of current or former IDUs in contact with a range of drug treatment and support services, including general practitioners, hospitals, specialist drug clinics, and non-statutory agencies, and reported to the Scottish Drug Misuse Database (SDMD) held by Information Services Division (ISD). These agencies report information on new contacts (defined as either first presentation or repeat presentation if it has been at least 6 months since last attendance) to the SDMD. IDU status was defined according to self-report: if at any attendance

at drug services the client reported having either injected drugs in the past month or having ever injected, they were classified as 'a current/former IDU'. The SDMD contains limited identifying information (forename and surname initials, fourth letter of surname, date of birth, sex, and postcode sector of residence) and data on risk behaviours such as the sharing of injecting equipment. Data for 41 062 IDUs who attended drug services in the period 1 April 1995 to 31 March 2006 were available.

Health Protection Scotland maintains a database of all persons who have been diagnosed HCV positive in Scotland since testing commenced in 1991 [13]; laboratory detection of HCV antibody or a positive PCR test result is a requirement for inclusion. This database contains the following non-named information: surname soundex code, forename initial, date of birth, sex, and the postcode district of residence, as well as data concerning risk activities and the date of the earliest positive specimen. The database contained records for 20 588 persons as of 31 March 2006 [14].

The General Register Office for Scotland (GROS) holds data on all deaths in Scotland. Mortality was not analysed in the current study; however, date of death was required for censoring the follow-up of IDUs in the SDMD.

Unlinked anonymous HCV testing (using residual sera from 2141 current/former IDUs undergoing named anti-HIV testing in 1999/2000; Roy *et al.* [6]) provided estimates of HCV antibody prevalence in IDUs for 11 health boards (i.e. Argyll & Clyde, Ayrshire & Arran, Dumfries & Galloway, Fife, Forth Valley, Grampian, Greater Glasgow, Highland, Lanarkshire, Lothian, Tayside). These health boards are home to 98% of all current IDUs in Scotland [15, 16].

Linkage procedure

Linkage of records between the SDMD, the HCV diagnosis, and the GROS data sources was carried out by ISD using probabilistic record-linkage techniques [17] to match individuals on the SDMD with those on both the HCV diagnosis database and the GROS national death registry. A preliminary step using exact (deterministic) matching identified attendances within the SDMD associated with the same individual. Then, ISD's probabilistic method involved calculating a score for each SDMD attendance record as a potential match to each HCV diagnosis record and each GROS record; an individual on the SDMD

was successfully linked if the score for their top-ranked matching record exceeded a predetermined threshold value. The linked dataset was anonymized before transfer to Health Protection Scotland for analysis. Linkages were approved by the Privacy Advisory Committee, which oversees confidentiality issues involving data held on NHS Scotland patients.

Epidemiological risk factors

Age at first injection was self-reported. However, the values provided were not necessarily consistently reported across attendance episodes; consequently both the earliest reported age first injected and the across-episode mean were derived. The mean age of first injection was used to estimate injection debut and time since onset of injecting. Deprivation quintiles were generated according to the IDU's last known post-code sector of residence using Carstairs social deprivation scores [18] derived from the 2001 census [19].

Health boards were classified into high, mid, and low HCV-prevalence groups according to HCV seroprevalence estimates obtained from unlinked anonymous testing of IDUs in 1999/2000 [6]. These were: high-prevalence (>49%), consisting of Greater Glasgow and Tayside; mid-prevalence (35–49%), consisting of Lothian, Lanarkshire, Ayrshire & Arran, Grampian; and low-prevalence (<35%), consisting of Argyll & Clyde, Dumfries & Galloway, Fife, Forth Valley, Highland.

Outcome measures and statistical analysis

Unadjusted and adjusted odds ratios were computed using logistic regression for the associations between a positive HCV diagnosis and the set of epidemiological variables (above). HCV diagnosis rates subsequent to the estimated injection debut were derived using person-year methods. For each individual, entry to time at risk was delayed until the date of first attendance at drug services, and was defined to end at either the HCV diagnosis date (date of the first positive specimen), death, or the right-censoring date (31 March 2006). Data for individuals whose estimated injecting debut could not be determined ($n=2907$) were excluded, and the remaining data were left-truncated at the date of first attendance at drug services. After excluding a further 2371 IDUs whose HCV diagnosis date preceded date of first attendance, 35 758 records remained for this analysis. Cox proportional-hazards regression analysis was used to estimate the association between time to HCV

diagnosis and the following covariates: sex, deprivation quintile, health board of residence, and period in relation to first attendance recorded on the SDMD. The latter covariate was defined using four categories: 0–60 days, 61–180 days, 181–365 days, and >365 days subsequent to date of first attendance.

To estimate the proportion of diagnosed and undiagnosed HCV infection in IDUs on the SDMD, the numbers of IDUs who had been diagnosed (determined through record-linkage) were compared to the numbers of IDUs estimated to be infected with HCV (determined through HCV seroprevalence estimates from unlinked anonymous testing of IDUs) stratified by health board and age group at 31 March 2006 (<25, ≥25 years). Confidence intervals for the proportion of diagnosed/undiagnosed HCV-infected IDUs were obtained using bootstrapping methods [20]. All statistical analyses were carried out using R version 2.4.0 [21].

RESULTS

Characteristics of the study population

The SDMD contained data for 41 062 IDUs who attended drug services between 1 April 1995 and 31 March 2006. The records for 9145 clients (22% of all IDUs) were linked to the HCV diagnosis database; of these 9145 clients, 81%, 2%, and 17% reported their risk activity leading to infection as IDU, non-IDU and not known, respectively. Five per cent of all IDUs on the SDMD were known to have died as of 31 March 2006 (Table 1). Overall, 21% (8209/39 048) of living IDUs had been diagnosed HCV positive by this date.

The majority of the living IDUs were male (71%), with a mean age at first attendance at drug services (as recorded on the SDMD) of 26.7 years (s.d. = 6.9). The mean injecting debut was 21.8 years (s.d. = 5.5). As of 31 March 2006, longer term injectors (≥10 years since debut) represented 44% (16 076/36 329) of all IDUs for whom the date of first injection could be estimated (Table 2). Almost half of the IDUs (48%) for whom deprivation quintile was available resided in the 20% most deprived localities in Scotland.

Characteristics associated with diagnosed HCV infection

The unadjusted odds ratio (OR) of being HCV-diagnosed increased with age; compared to the

Table 1. Results of record-linkage of the Scottish Drug Misuse Database (ever injected drugs, first attendance between 1 April 1995 and 31 March 2006) to the HCV Diagnosis database and the General Register Office for Scotland deaths registry

	All IDUs		HCV-diagnosed IDUs		% HCV-diagnosed
	<i>n</i>	(%)	<i>n</i>	(%)	
All	41 062	(100)	9145	(100)	22
Dead	2014	(5)	936	(10)	47
Not known to be dead as of 31 March 2006	39 048	(95)	8209	(90)	21

Table 2. Characteristics of all persons in the SDMD who (i) first attended drug services between 1 April 1995 and 31 March 2006, (ii) have ever injected drugs, and (iii) are not known to be dead, and the odds of being diagnosed with HCV by 31 March 2006 associated with these characteristics

Variable	All IDUs		HCV-diagnosed IDUs		Crude odds ratio (95% CI)
	<i>n</i>	(column %)	<i>n</i>	(row %)	
Sex					
Female	11 489	(29.4)	2644	(23.0)	1.0
Male	27 559	(70.6)	5565	(20.2)	0.85 (0.80–0.89)
Age at 31 March 2006					
<20	469	(1.2)	22	(4.7)	0.27 (0.17–0.41)
20–29	14 298	(36.6)	2238	(15.7)	1.0
30–39	18 401	(47.1)	4215	(22.9)	1.60 (1.51–1.69)
40–49	5255	(13.5)	1548	(29.5)	2.25 (2.09–2.42)
≥50	625	(1.6)	186	(29.8)	2.28 (1.91–2.73)
Years since injection debut, relative to 31 March 2006					
<2	1233	(3.4)	40	(3.2)	0.16 (0.20–0.23)
2–3	2996	(8.2)	249	(8.3)	0.43 (0.37–0.49)
4–5	4468	(12.3)	507	(11.3)	0.60 (0.54–0.68)
6–7	5807	(16.0)	1017	(17.5)	1.0
8–9	5749	(15.8)	1272	(22.1)	1.34 (1.22–1.47)
≥10	16 076	(44.3)	4817	(30.0)	2.02 (1.87–2.17)
No information	2719		307	(11.3)	
Deprivation quintile					
1 (least deprived)	1411	(5.8)	353	(25.0)	1.0
2	2128	(8.8)	560	(26.3)	1.07 (0.92–1.25)
3	3705	(15.3)	914	(24.7)	0.98 (0.85–1.13)
4	5427	(22.3)	1540	(28.4)	1.19 (1.04–1.36)
5 (most deprived)	11 616	(47.8)	4563	(39.3)	1.94 (1.71–2.20)
No information	14 761		279	(1.9)	
Health Board of residence					
Greater Glasgow	12 085	(30.9)	3342	(27.7)	1.0
Grampian	5853	(15.0)	1172	(20.0)	0.66 (0.61–0.71)
Lothian	5785	(14.8)	856	(14.8)	0.45 (0.42–0.49)
Tayside	1726	(4.4)	357	(20.7)	0.68 (0.60–0.77)
Other	13 599	(34.8)	2482	(18.3)	0.58 (0.55–0.62)

SDMD, Scottish Drug Misuse Database.

reference age group (20–29 years), IDUs aged 30–39, 40–49 and ≥50 years at the end of follow-up were significantly more likely to be HCV-diagnosed (OR

1.6, 95% CI 1.5–1.7; OR 2.3, 95% CI 2.1–2.4; OR 2.3, 95% CI 1.9–2.7). Compared to the reference group, IDUs aged <20 years were significantly less

likely to be diagnosed (OR 0.3, 95% CI 0.2–0.4). Odds ratios increased with years since injection debut; compared to the reference group (IDUs who started injecting 6–7 years prior to 31 March 2006), the odds of HCV diagnosis for IDUs who injected for the first time <2 years previously were 0.16 (95% CI 0.20–0.23), and the odds of HCV diagnosis for those whose injection debut was ≥ 10 years previously were 2.0 (95% CI 1.9–2.2). Social deprivation was associated with increased odds of HCV diagnosis: IDUs residing in the two most deprived quintiles had significantly elevated odds of being diagnosed compared to the least deprived quintile (OR 1.2, 95% CI 1.0–1.4 and OR 2.0, 95% CI 1.7–2.2, for quintiles 4 and 5, respectively). The odds of diagnosis were significantly lower for males compared to females (OR 0.85, 95% CI 0.8–0.9). The proportion of IDUs diagnosed with HCV infection was highest (28%; 3342/12085) in Greater Glasgow health board, with the odds of diagnosis significantly lower in Lothian, Grampian, Tayside and other health boards compared to Greater Glasgow (ORs of 0.5–0.7).

Table 3 shows the odds of being diagnosed HCV-positive after simultaneously adjusting for sex, age, years since injection debut, and health board of residence. Adjusted odds ratios (aORs) were closely comparable to the crude odds ratios (shown in Table 2) computed for the covariates years since injection debut and health board. The aOR for males (aOR 0.73, 95% CI 0.69–0.77) was smaller compared to the crude OR (OR 0.85, 95% CI 0.80–0.89). The aORs for age were attenuated (<20 years at 31 March 2006: aOR 0.7, 95% CI 0.4–1.1; 30–39 years: aOR 1.1, 95% CI 1.0–1.1; 40–49 years: aOR 1.4, 95% CI 1.2–1.5; ≥ 50 years: aOR 1.3, 95% CI 1.1–1.6). A trend test indicated that the odds of HCV diagnosis significantly increased with time since the onset of injecting ($P < 0.00001$), as expected: the longer the elapsed time the more opportunity for the diagnosis of prevalent HCV infection.

Rate of HCV diagnosis subsequent to first attendance at drug services

Total follow-up time – from date of first attendance at drug services recorded on the SDMD – for analysis of diagnosis rates was 187 250 person-years. Characteristics of the smaller study population used for this analysis, which was restricted to 35 758 IDUs whose first SDMD attendance preceded HCV diagnosis, were comparable to the larger population (Table 2) in

Table 3. *Adjusted odds of being diagnosed with HCV by 31 March 2006 for all persons in the Scottish Drug Misuse Database who (i) first attended drug services between 1 April 1995 and 31 March 2006, (ii) have ever injected drugs, (iii) are not known to be dead, and (iv) reported the age when they first injected (n = 36 329)*

Variable	Adjusted odds ratio for HCV diagnosis (95% CI)	
Sex		
Female	1.0	
Male	0.73	(0.69–0.77)
Age at 31 March 2006		
<20	0.70	(0.45–1.09)
20–29	1.0	
30–39	1.07	(1.01–1.15)
40–49	1.36	(1.25–1.48)
≥ 50	1.36	(1.09–1.61)
Years since injection debut, relative to 31 March 2006		
<2	0.17	(0.12–0.24)
2–3	0.45	(0.39–0.53)
4–5	0.62	(0.55–0.70)
6–7	1.0	
8–9	1.32	(1.20–1.45)
≥ 10	1.85	(1.71–2.01)
Health Board of residence		
Greater Glasgow	1.0	
Grampian	0.77	(0.71–0.83)
Lothian	0.56	(0.52–0.62)
Tayside	0.75	(0.70–0.79)
Other	0.89	(0.78–1.01)

CI, Confidence interval.

terms of sex, deprivation, and health board of residence, but there were fewer IDUs in all but the youngest age groups and in the group whose onset of injecting was ≥ 10 years prior to 31 March 2006, and the proportions diagnosed with HCV in these groups were smaller (30–39 years at 31 March 2006: $n = 2913$, 18.4%; 40–49 years: $n = 899$, 21.4% HCV-diagnosed; ≥ 50 years: $n = 91$, 18.7%; ≥ 10 years since debut: $n = 3522$, 23.4%). The overall diagnosis rate was 33.6 HCV diagnoses per 1000 person-years of follow-up (95% CI 32.7–34.4). Table 4 shows diagnosis rates by the characteristics (a) sex, (b) age group when first injected, (c) deprivation quintile, (d) health board of residence (grouped into high, mid and low HCV-prevalence areas), and (e) period in relation to the first attendance at drug services recorded on the SDMD. Figure 1 displays the cumulative probability of being diagnosed HCV antibody-positive as the joint function of time since injecting debut and characteristics (a)–(d).

Table 4. HCV diagnosis rates of all persons in the Scottish Drug Misuse Database, living and dead, who (i) first attended drug services between 1 April 1995 and 31 March 2006, (ii) have ever injected drugs ($n=35\,758$), and (iii) estimated date of first injection is not missing

Variable	Person-years	<i>n</i>	Rate	95% CI	HR	95% CI
Sex						
Female	51 647	2050	39.7	38.0–41.4	1.0	
Male	135 603	4234	31.2	30.3–32.2	0.80	0.76–0.84
Age when first injected						
<20	81 240	3092	38.1	36.7–39.4	1.27	1.19–1.34
20–24	62 352	1956	31.4	30.0–32.8	1.0	
25–29	29 107	806	27.7	25.8–29.7	0.89	0.82–0.97
≥30	14 550	430	29.6	26.8–32.5	0.97	0.87–1.08
HCV diagnosis date in relation to date of first SDMD attendance						
0–60 days	5043	222	44.0	39.4–50.2	1.37	1.17–1.60
61–120 days	5088	195	38.3	33.1–44.1	1.17	1.00–1.38
121–365 days	20 590	672	32.6	30.2–35.2	1.0	
>365 days	165 529	5195	33.2	32.3–34.1	1.09	1.00–1.19
Deprivation quintile						
1	6824	267	39.1	34.6–44.1	1.0	
2	10 056	417	41.5	37.6–45.7	1.08	0.93–1.26
3	17 379	684	39.4	36.5–42.4	1.05	0.91–1.21
4	24 817	1160	46.7	44.1–49.5	1.22	1.06–1.39
5	56 527	3557	62.9	60.9–65.0	1.40	1.23–1.58
Health Board of residence						
High-prevalence	69 595	2899	41.7	40.2–43.2	1.0	
Mid-prevalence	77 606	2155	27.8	26.6–29.0	0.74	0.69–0.79
Low-prevalence	40 048	1230	30.7	29.0–32.5	0.73	0.69–0.78

n, Number of HCV antibody-positive diagnoses; rate, number of diagnoses per 1000 person-years of follow-up since first SDMD attendance. HR, hazard ratio; CI, confidence interval.

Follow-up was left-truncated at date of first attendance at drug services recorded in the SDMD. Health boards are categorized with respect to HCV seroprevalence, determined from unlinked anonymous HCV prevalence survey data [6]: high-prevalence, seroprevalence ≥50%; mid-prevalence, 35–49%; low-prevalence, <35%.

The rate of HCV diagnosis was highest for IDUs aged <20 years when they first injected (38.1/1000 person-years, 95% CI 36.7–39.4). Considering deprivation quintile, IDUs living within the 20% most deprived localities had the highest overall diagnosis rate (62.9, 95% CI 60.9–65.0). The rate of HCV diagnosis was highest in the 60-day period subsequent to first attendance at drug services recorded on the SDMD (44.0/1000 person-years, 95% CI 39.4–50.2), compared to all periods subsequent to first attendance. Diagnosis rates also varied over the period since injecting debut: 34.0/1000 person-years (95% CI 32.7–35.4), 30.9/1000 (95% CI 29.5–32.3), and 36.0/1000 (95% CI 34.4–37.6), for <5 years, 5–10 years, and ≥10 years following injection debut, respectively.

Results of the multifactorial Cox regression analysis indicated that male sex [hazard ratio (HR) 0.80, 95% CI 0.76–0.84] and residing in a low- or mid-prevalence compared to a high HCV-prevalence

health board area (HR 0.73, 95% CI 0.69–0.78; HR 0.74, 95% CI 0.69–0.79, respectively) were associated with a longer time to HCV diagnosis, and that age <20 years at injection debut compared to 20–24 years (HR 1.27, 95% CI 1.19–1.34) and residing in the two highest deprivation quintiles compare to the lowest quintile (HR 1.22, 95% CI 1.06–1.39; HR 1.40, 95% CI 1.23–1.58, for quintiles 4 and 5, respectively) were associated with a shorter time to HCV diagnosis (Table 4). There was also an increased relative risk of HCV diagnosis in the 60 day period following first attendance at drug services recorded in the SDMD compared to the reference period of 121–365 days (HR 1.37, 95% CI 1.17–1.60).

Extent of undiagnosed HCV infection

Undiagnosed HCV infection (estimated as the proportion of the estimated number of HCV-positive

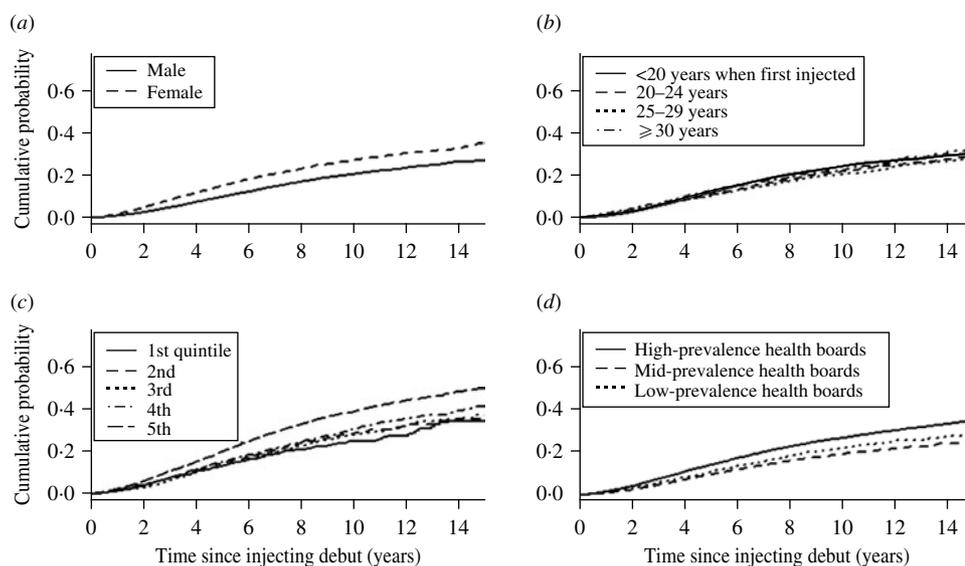


Fig. 1. Cumulative probability of an HCV diagnosis for all IDUs on the Scottish Drug Misuse Database (first attendance between 1 April 1995 and 31 March 2006, ever reported injecting drugs, and injecting debut 1991 or later), as function of (a) sex, (b) age when first injected, (c) Carstairs 2001 deprivation quintile, and (d) health board area (grouped according to 1999/2000 HCV seroprevalence).

IDUs on the SDMD that had not been diagnosed with HCV by 31 March 2006) was largest for the high- and mid-prevalence health board areas: 60% (bootstrapped 95% CI 58–63) and 59% (95% CI 49–62), respectively, of those IDUs estimated to be infected had not been diagnosed, compared to 52% (95% CI 4–60) for the low-prevalence health boards (Table 5). The extent of undiagnosed HCV infection was greater for those IDUs aged ≥ 25 years compared to the < 25 years age group, in the mid- and low-prevalence health board areas. Aggregating over all health boards and age groups, an estimated 58% (95% CI 45–62) of HCV-infected IDUs had not been diagnosed by 31 March 2006.

DISCUSSION

This study has provided important data about the extent of and characteristics associated with HCV diagnosis in IDU attendees recorded on the SDMD in Scotland. Fifty-eight per cent of those IDUs estimated to be infected with HCV had not been diagnosed, and the extent of non-diagnosis was more pronounced in those aged ≥ 25 years, and less pronounced in those health boards with HCV prevalence in IDUs of $< 35\%$, especially in IDUs aged < 25 years.

Diagnosis in IDUs varied according to several key epidemiological variables, but it should be noted that

HCV diagnosis confounds HCV prevalence and HCV test uptake. The prevalence of diagnosed HCV infection was higher for older IDUs, for residents of the Greater Glasgow health board, for those residing in the most deprived localities, and for females. The latter difference is probably due to sex differences in HCV test uptake, as previous studies have found equivalent HCV antibody prevalence for males and females [10, 22]. The adjusted odds of being diagnosed HCV-positive increased with time since injection debut, and was greater for those aged ≥ 30 years.

The overall HCV diagnosis rate – 34/1000 person-years for Scottish IDUs – is an order of magnitude lower than HCV incidence rates predicted by transmission models applied to the Glasgow setting (e.g. 180–300 infections per 1000 injector-years for Glasgow IDUs during 1990–2000 only [4]) and reported for selected IDU populations (119–284/1000 person-years over the period 1993–2002 [6]).

Assuming the national HCV prevalence in all Scottish IDUs (and those IDUs recorded on the SDMD) to be 44%, we estimated that 19 632 of the study population of 39 048 living current/former IDUs were infected with HCV. Given that 8209 have been diagnosed (determined through record-linkage), this suggests that 58% of infected current/former IDUs had not yet been diagnosed by 31 March 2006. This figure is only slightly lower than the two-thirds of all HCV-infected childbearing women (including

Table 5. Estimates of the proportion of all IDUs on the Scottish Drug Misuse Database (SDMD) (who first attended drug services between 1 April 1995 and 31 March 2006 and are not known to be dead as of 31 March 2006; $n=39\,048$) that are undiagnosed with HCV infection, by age at 31 March 2006 and health board area

	< 25 years	≥ 25 years	All
High-prevalence health boards			
% HCV-infected current/former IDUs (est.)	40 % (92/232)	69 % (347/500)	60 % (463/771)
% HCV-diagnosed IDUs in SDMD (linked)	15 % (151/1004)	28 % (3548/12 807)	27 % (3699/13 811)
% undiagnosed with HCV (of IDUs in SDMD estimated to be HCV-infected)	42 % (251/402)	60 % (5289/8837)	60 % (5540/9239)
Mid-prevalence health boards			
% HCV-infected current/former IDUs (est.)	24 % (100/417)	47 % (281/598)	37 % (382/1021)
% HCV-diagnosed IDUs in SDMD (linked)	12 % (299/2555)	19 % (2634/13 850)	18 % (2933/16 405)
% undiagnosed with HCV (of IDUs in SDMD estimated to be HCV-infected)	51 % (314/613)	60 % (4276/6510)	59 % (4190/7123)
Low-prevalence health boards			
% HCV-infected current/former IDUs (est.)	15 % (24/163)	41 % (72/176)	29 % (101/349)
% HCV-diagnosed IDUs in SDMD (linked)	13 % (175/1351)	19 % (1402/7481)	18 % (1577/8832)
% undiagnosed with HCV (of IDUs in SDMD estimated to be HCV-infected)	14 % (28/203)	54 % (1665/3067)	52 % (1693/3270)
All health boards			
% HCV-infected current/former IDUs (est.)	27 % (216/812)	55 % (700/1274)	44 % (946/2141)
% HCV-diagnosed IDUs in SDMD (linked)	13 % (625/4910)	22 % (7584/34 138)	21 % (8209/39 048)
% undiagnosed with HCV (of IDUs in SDMD estimated to be HCV-infected)	49 % (593/1218)	59 % (10 830/18 414)	58 % (11 423/19 632)

The percentage of HCV-infected current/former IDUs was estimated from an unlinked anonymous HCV prevalence survey of current/former IDUs in 1999/2000 [6]. The high-prevalence health board area consists of Greater Glasgow and Tayside (HCV seroprevalence $\geq 50\%$); mid-prevalence health boards include Lothian, Lanarkshire, Ayrshire & Arran, and Grampian (35–49%); the low-prevalence health board area consists of Argyll & Clyde, Dumfries & Galloway, Fife, Forth Valley, and Highland ($<35\%$); excludes Borders, Western Isles, Orkney and Shetland health boards, for which no HCV seroprevalence data were available from the unlinked anonymous HCV prevalence survey [6]. Marginal figures were determined by adjusting for age group and/or health board region.

non-IDUs) estimated to be undiagnosed from a survey undertaken in 2000 [23]. The proportion of undiagnosed IDUs on the SDMD is particularly disappointing, given that these IDUs have been in contact with drug treatment/support services, where referrals for HCV testing can be obtained. The proportion undiagnosed in the total IDU population, including those who have not had contact with drug services ($\sim 10\%$ based on 441 current IDUs recruited from Glasgow street sites during 2004 [24]), would be expected to be higher still.

There are certain limitations with this observational study. Diagnosis rates conflate the prevalence of infection and the uptake of testing. For instance, we found that IDUs residing in the most deprived areas had the highest diagnosis rate, but this almost certainly reflects the highest prevalence of infection (which should lead to increased testing). In order to

attribute clear between-group difference in diagnosis rate to one of these two factors, it is necessary to control for the other, which is not possible without an additional source of information.

Second, the 1.4-fold increased relative risk of HCV diagnosis found for the 60-day period subsequent to first attendance at drug services compared to later periods indicates that IDUs are being referred for HCV testing as a result of this contact. If, due to their contact with drug services, those IDUs recorded on the SDMD are more likely to be tested (and diagnosed) than IDUs not on the SDMD, then we may have overestimated the HCV-diagnosed proportions in the general IDU population. Furthermore, the HCV-diagnosed proportion for recent-onset IDUs may be lower than the proportion estimated in the general IDU population; because a lower proportion of new injectors will have come into contact with

services, this group is likely to be under-represented by the SDMD sample.

Third, an unknown degree of bias will be present due to the limitations of record-linkage with incomplete or missing identifiers, which will influence our estimates of the proportion of IDUs undiagnosed with HCV infection. The deterministic method for identifying unique individuals on the SDMD will result in missed linkages, thus assuming more unique IDUs than in reality. Similarly, unrecovered linkages between the SDMD and the HCV diagnosis database will bias the undiagnosed proportion upwards.

Our comparison of the proportion of IDUs diagnosed with HCV to prevalence relies on seroprevalence estimates from testing carried out in 1999/2000; if prevalence has changed since that time, then we may have under- or over-estimated the extent of undiagnosed infection. However, the prevalence of HCV infection in IDUs in Scotland's four major cities has remained relatively stable since 2000 [25].

In conclusion, the current study has confirmed previous estimates of the relatively low diagnosis of HCV infection in Scotland's IDU population. The key finding concerns the number of positive HCV diagnoses made in members of this at-risk population compared to the numbers estimated to be infected according to seroprevalence studies; the proportion undiagnosed is substantial, even when taking into account variation in prevalence between age groups and across health boards. To bring uptake of HCV testing in line with that reported for countries such as Australia [26] and France [27], improvements are needed in the identification of chronically infected individuals with undiagnosed HCV. This is a major objective of Phase 2 of Scotland's Hepatitis C Action Plan [9], which aims to simplify testing for IDUs by resolving the difficulties in taking a blood sample and delays in result disclosure, through improvements to HCV testing and referral activities, raising awareness campaigns, the evaluation of different approaches to HCV testing/body fluid sampling, and to offering HCV testing and antiviral therapy for HCV carriers.

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DECLARATION OF INTEREST

None.

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