

# Evaluation of a General Practice Based Hepatitis C Virus Screening Intervention

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## Abstract

### Background

In 2003 an estimated 37,500 of Scotland's population was chronically infected with HCV; 44% were undiagnosed former injecting drug users (IDU) - a priority group for antiviral therapy.

### Aim

To evaluate a hepatitis C virus (HCV) screening intervention.

### Design

Outcome measures among two similar General Practice populations in an area of high HCV and drug use prevalence, one of which was exposed to an HCV screening intervention, were compared.

### Methods

Thirty to fifty four year old attendees of the intervention practice were opportunistically offered testing and counselling, where clinically appropriate, (November 2003– April 2004). Outcomes: HCV test uptake, case detection, referral and treatment administration rates.

### Results

Of 584 eligible attendees, 421 (72%) were offered and 117 (28%) accepted testing in the intervention practice; no testing was undertaken in the comparison practice. Prevalences of HCV antibody were 13% (15/117), 75% (3/4) and 91% (10/11) among all tested persons, current IDUs and former IDUs respectively. For 4/15 (27%) evidence of binge drinking following the receipt of their positive result, was available. Of the 11 referred to specialist care because they were HCV RNA positive, nine attended at least one appointment. Two received treatment: one had achieved a sustained viral response as of February 2008.

### Conclusion

While non targeted HCV screening in the general practice

setting can detect infected former IDU, the low diagnostic yield among non IDUs limited the effectiveness of the intervention. A more targeted approach for identifying former IDUs is recommended. Additionally, the low uptake of treatment among chronically infected persons four years after diagnosis demonstrates the difficulties in clinically managing such individuals. Strategies, including support for those with a history of problem alcohol use, to improve treatment uptake are required.

## Introduction

Hepatitis C virus (HCV) infection is one of the most important public health issues of the 21st century. The recent improved efficacy of HCV antiviral therapy, now deemed cost-effective for individuals with mild, as well as those with moderate, disease, has provided the impetus to diagnose and treat people with infection.<sup>1,2,3</sup> Despite this, in 2003, only one-third of the 37,500 persons in Scotland estimated to have chronic HCV infection had been diagnosed.<sup>4</sup> Of the 25,100 undiagnosed individuals, it was estimated that 22,100 had injected drugs and, of these, 16,600 no longer injected.<sup>4</sup> While general practice is the setting where former injectors are most likely to attend (as they often no longer attend drug treatment centres), no UK based studies evaluating the effectiveness of general practice based HCV screening had been undertaken.

In this study we wanted to evaluate an HCV screening intervention designed to increase case detection, referral and management of former IDU with HCV infection in a general practice setting.

## Methods

### Design

The effectiveness of an opportunistic, age criterion based HCV screening intervention was evaluated by comparing HCV test uptake and case yield among attendees of a single general practice offered HCV testing during a six month period (November 2003 - April 2004), with uptake and yield in a similar practice not exposed to the intervention.

## Setting

Two general practices, situated in a single health centre in a socio-economically deprived area of Glasgow with high HCV and IDU prevalence, were selected. The practices' characteristics are shown in Table I.

**Table I: Characteristics of the Intervention and Comparison Practices.**

	Intervention Practice	Comparison Practice
No of doctors (w/e*)	3.75	2
Doctor patient ratio	1:920	1:1311
No of nurses (w/e*)	1.5	1
Size of practice population: All	3450	2622
: Age 30-54 (N)	1165	914
: Males	n (% of N)	n (% of N)
30-39	245 (21)	228 (25)
40-49	280 (24)	210 (23)
50-54	62 (7)	64 (7)
30-54	607 (52)	502 (55)
: Females		
30-39	221 (19)	163 (20)
40-49	238 (23)	174 (19)
50-54	69 (6)	55 (6)
30-54	528 (48)	412 (46)
Proportion of practice populations belonging to the highest deprivation quintile (ie most deprived)	54%	51%
Number of those age 30-54 ever prescribed methadone	97 (8.3)	76 (8.3)
Number of HCV tests undertaken in the six months prior to the intervention	2	1
Number of individuals diagnosed as HCV chronically infected in the six months prior to the intervention	0	0

\*whole time equivalent

## Participants

The 30 to 54 year old age range was identified as the one which potentially would give the highest yield of cases of HCV among former injectors who were at risk of having progressed to moderate hepatitis and, therefore, a priority for antiviral combination therapy. Overall, 1165 persons aged 30-54 years were patients of the intervention practice, and 914 were patients of the comparison practice. The offer was not restricted to those with known risk factors to avoid missing those patients who did not wish to reveal past injecting. Accordingly, all, except previously diagnosed HCV infected individuals attending secondary care services for HCV management, were eligible to be considered for the offer of HCV testing.

## Intervention

Eligible individuals who attended non-urgent appointments with a general practitioner or practice nurse were, where deemed clinically appropriate, offered HCV screening and given an HCV information leaflet. Those accepting the offer could immediately attend, or could return for, an appointment with a study counsellor who was based in the practice. The counsellor undertook full pre test counselling and obtained blood for HCV testing or, where venepuncture proved difficult, oral fluid sampling from consenting individuals. Patients returned to the general practitioner for their results. HCV antibody, HCV RNA positive (or RNA equivocal or not known) individuals were offered referral to a single Hepatology unit for further management.

## HCV tests

Blood or oral fluid samples were sent to the West of Scotland Specialist Virology Centre where HCV antibody (ELISA) testing was performed using the Abbot AxSym version 3.0 ELISA, or, in the case of oral fluid samples, a modified Ortho Diagnostic HCV 3.0 SAVE ELISA (Ortho Diagnostics) using the Orasure Collection Device (Altrix Health Care Cheshire) (sensitivity

92%).<sup>5</sup> Antibody positive blood specimens were then tested by PCR for HCV RNA using the ROCHE Amplicor HCV Monitor test version 2.0 (Roche Diagnostics). In instances where oral fluid tested positive for HCV antibody, a blood test was then required for HCV RNA testing.

## Outcome measures

The outcome measures were rates of HCV test offer and uptake, and HCV diagnosis. For those diagnosed HCV antibody positive, measures included rates of specialist clinic referral uptake, liver biopsy investigation and antiviral therapy administration.

## Data collection

Data on HCV test offer and uptake were sourced from the general practitioners, the study counsellor and the regional HCV testing laboratory. Those consenting to HCV testing provided demographic and HCV risk factor (including IDU status) details through the self completion of a questionnaire. For the intervention practice population, data on "ever methadone" use, a surrogate for ever injecting drug use, were obtained from an electronic record system.

## Statistical analysis

Univariate analysis was conducted using exact logistic regression using LogXact-4 (version 4.1) software, Cytel software Copyright 2000). Multivariate analysis was used to ascertain statistically significant determinants of HCV test uptake and HCV antibody positive diagnosis.

## Results

### Characteristics of Intervention and Comparison General Practices (Table I)

Intervention and comparison practices had similar age and gender distributions, deprivation profiles, proportions of patients with a computer history of ever having been prescribed methadone, and numbers of persons HCV tested and diagnosed during the six months prior to the commencement of the study. The intervention practice had a higher doctor: patient ratio.

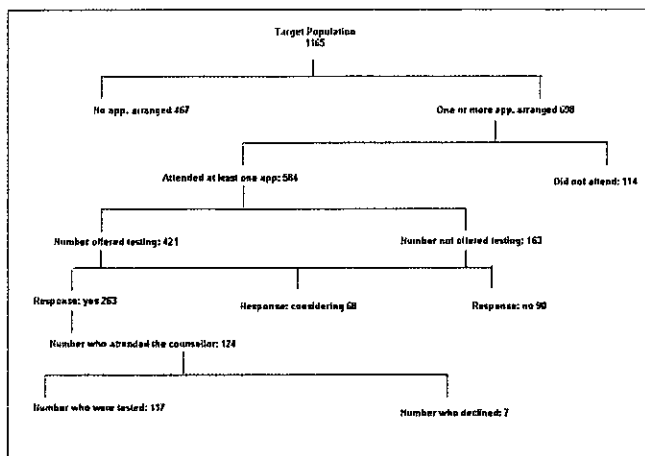
### Uptake of Testing and Case Yield (Figure 1a)

Five hundred and eighty four of the 1165 individuals, belonging to the intervention practice target age range, attended at least one non urgent appointment with a doctor or practice nurse during the study intervention period. Four hundred and twenty one (72%) of these were offered HCV counseling and testing. One hundred and seventeen (27.8%) of those offered were tested; of those an oral fluid was taken from four, all current injectors.

Of the 163 not offered testing by their general practitioner, reasons for the non-offer were available for 118. The main reasons were: forgot to offer (31), patient has mental health problems including problem alcohol use (21), offer inappropriate at the time (16), insufficient time (13), patient known to be HCV infected and in secondary care follow up (10) and patient unstable/intoxicated (9).

No significant gender or age determinants of test uptake were identified on univariate analysis. "Ever methadone" users were slightly, but not significantly, more likely than "never methadone" users to undergo testing following offer (Table II).

Figure 1a: Offer and Uptake of Testing in the Intervention Practice



**HCV Case Yield in the Intervention Practice (Table II)**

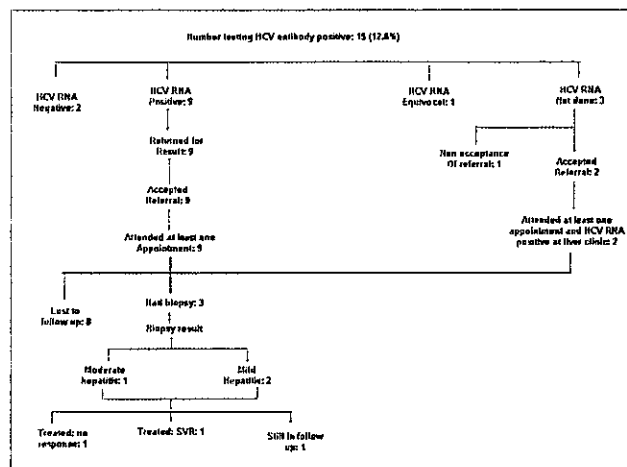
Fifteen out of 117 (12.8%) individuals tested positive for HCV antibody, 14 (93%) of whom had ever injected drugs and 10 of 11 (91%) were former injectors whose previous injection occurred over 12 months prior to testing. The duration of abstinence from injecting among the 11 former injectors ranged from just over one year to 18 years (median seven years).

On univariate analysis, male gender, younger age (30-34) and "ever injecting" were significant determinants of HCV antibody positivity; on multivariate analysis, only "ever injecting" remained, albeit highly, significant [OR:125.36(16.75,4810.79)].

**Uptake of HCV Testing in the Comparison Practice**

During the study intervention period, no individual belonging to

Figure 1b: Referral and Management of PCR Positive Individuals



the target age group was tested for HCV.

**Referral and Management of HCV RNA Positive Individuals (Figure 1b)**

Of the 15 HCV antibody positive persons, three injectors, all current, were diagnosed on the basis of oral fluid, and not blood, testing due to poor venous access. Of the remaining 12, all of whom had blood samples taken, nine were HCV RNA positive. Eleven individuals (nine HCV RNA positive, and two HCV antibody positive (subsequently identified as RNA positive)) accepted the offer of referral to a specialist Hepatology clinic; all attended at least one appointment. As of February 2008, eight of the 11 were lost to follow up, three underwent biopsy, two received antiviral therapy and one achieved a sustained viral response.

Table II: Determinants of HCV Test Uptake and Positivity

Determinants of HCV test uptake						
		Offered	Tested	% tested	OR (Univariate)	
Gender	Male	180	50	28	1.00 ( 0.63, 1.57)	
	Female	241	67	29	1.00 (Baseline)	
Age	30-34	80	18	22	1.00 (Baseline)	
	35-39	105	28	27	1.25( 0.60, 2.64)	
	40-44	103	29	28	1.35 ( 0.65, 2.84)	
	45-49	74	24	32	1.65( 0.76, 3.62)	
	50-54	59	18	31	1.51( 0.71, 3.24)	
Ever prescribed methadone		43	14	33	1.29(0.60,2.64)	
Never prescribed methadone		378	103	27	1.00(Baseline)	
Determinants for HCV positivity						
		Tested	HCV +	% HVC+	OR (Univariate)	OR ( Multivariate)
Gender	Male	50	12	24	6.63 (1.65,38.91)	2.32 (0.03, 176.69)
	Female	67	3	5	1.00 (Baseline)	1.00(Baseline)
Age	30-34	18	5	28	6.25 (1.17,36.14)	1.70(0.071,53.64)
	35-39	28	6	21	4.48 (0.96,23.69)	4.01(0.16,265.26)
	40-44	29	4	14	1.00(Baseline)	1.00 (Baseline)
	45-49	24	0	0		
	50-54	18	0	0		
Never IDU		100	1	1	1.00(Baseline)	1.00 (Baseline)
Current <sup>1</sup> IDU		6	4	67	368.02(39.06,19700.04)	125.36(16.75, 4810.79)
Former <sup>2</sup> IDU		11	10	91		

<sup>1</sup>Defined as injecting within the previous 12 months <sup>2</sup>Defined as no injecting within the previous 12 months

OR - odds ratio

## **Adverse Events Following the Receipt of an HCV Antibody Positive Result**

Of the 15 antibody positive patients, five had adverse reactions within two weeks of receipt of their result. Four binge on alcohol and two misconceived that the result was positive for other blood borne viruses. Two of the five individuals proceeded to comply with secondary care investigation and treatment.

## **Discussion**

### **Summary of the Main Findings**

#### **Uptake of Testing**

The intervention demonstrated that it could effect considerable HCV test uptake; however, uptake was less than anticipated due to a combination of patients not: i) keeping their GP appointments, ii) being offered a test or, iii) accepting testing. Some GPs' reasons for not offering testing, such as insufficient time, are generic to all practice-based screening programmes; nevertheless, their frequent citing of attendees' mental health, including alcohol, problems indicated a perception that HCV test discussion and/or positive diagnosis might be detrimental to the overall wellbeing of certain vulnerable individuals.

#### **Case Yield**

The use of the 30-54 age-related screening criterion led to the identification of several infected individuals who belonged to the target group, namely former injectors who last injected several years before; however, the yield would have risen from 15/117(12.8%) to i) 14/75(18.6%) (at the expense of missing just one case) if eligibility had been restricted to 30-44 years and, ii) 14/17(82.3%) (again at the expense of missing one case) if the offer of testing had been restricted to 30-54 year-old individuals who indicated ever injecting drugs on the questionnaire.

#### **Referral and Management of HCV RNA Positive Individuals**

Altogether, eleven individuals accepted referral for a liver clinic appointment four weeks later and nine attended at least one appointment; however, as of February 2008 only two had received antiviral therapy. Losses to follow up were accrued at most stages of the management process.

#### **Alcohol**

Despite full pre- and post-test counseling, an appreciable minority of those diagnosed HCV antibody positive, binge on alcohol following the receipt of their result. This finding, albeit based on small numbers, demonstrates the potential negative influence of alcohol on the diagnosis, follow-up and treatment of HCV antibody/HCV RNA positive persons. The investigators and their clinical colleagues appreciate, from their own experience, this "alcohol factor" but very few data describing and quantifying the problem have been recorded in the scientific literature. Considering that the role of excessive alcohol consumption in accelerating HCV disease progression is well recognised, it is highly likely that this behaviour is the single most important determinant of health in the HCV infected person.

#### **Strengths of the Study**

This study is the first reported evaluation of a General Practice based HCV screening intervention in the UK. In addition, it is the only General Practice based HCV screening study to

describe patients' adverse reaction to HCV diagnosis and their follow up in secondary care.

#### **Limitations**

The study was undertaken in two small general practices located in a deprived area of Glasgow. The practices were selected on an opportunistic basis: knowing and approaching a general practitioner, known to have a special interest in HCV and drug use, who worked in an area with a high prevalence of these conditions. While the practice's catchment populations are typical of those in Glasgow's areas of deprivation, it is possible that other "less interested" GPs serving similar populations in such areas would have generated different results. Nevertheless, the authors believe that the intervention practices HCV screening experiences are likely to be typical of that of other practices in similar deprived inner city areas.

The use of oral fluid sampling for those with poor venous access led to the identification of HCV antibody positivity among three current IDUs, but the limitation of this approach was demonstrated by them not returning for blood sampling to ascertain past or current infection status through HCV RNA testing; however, two accepted referral to the liver clinic on the basis of their HCV antibody result. The use of near patient testing, currently being evaluated in Scotland, may be advantageous in this respect.

The intervention and comparison practices were similar with regard to key characteristics other than the doctor: patient ratio which was higher in the former. The two practices had near identical, albeit low, numbers of patients tested for HCV during the six months immediately preceding the intervention, suggesting that this factor did not ordinarily lead to increased HCV test uptake. In addition, the lack of any testing of comparison practice patients, belonging to the 30-54 age group, for HCV during the study period, effectively excludes any possibility of "intervention contamination" of the comparison practice.

Any concern that the test was offered more frequently to those individuals whom the clinicians knew to have risk factors for HCV, potentially biasing results, was not borne out; similar proportions of individuals i) with and without a history of ever methadone and, ii) among different age and gender categories were found among those attending, being offered testing and agreeing to testing. It was not possible to ascertain the exact prevalence of ever injecting drug use in the target population as the injecting behaviour of recent initiates to, and occasional exponents of, injecting might not have been recorded in the medical notes or practice computer system.

#### **Comparison with Existing Literature**

The high HCV antibody positive yield, reflecting the catchment area's underlying high HCV prevalence, compares favourably to case yield generated by previous primary care based HCV screening interventions.<sup>6,7,8,9,10</sup>

The few previous general practice-based HCV screening studies did not explore referral and treatment outcomes among persons diagnosed with chronic HCV; nevertheless, the non-attendance of HCV antibody positive patients with a history of ever injecting drug use at referral appointments has been described in audits of HCV management.<sup>11</sup>

## Implications for Future Research and Practice

The findings suggest that a more targeted approach to HCV screening in the primary care setting – one which focuses on "ever injectors" aged over 30 – would generate a high yield of HCV positivity. Targeting individuals likely to have discontinued injecting could be achieved by using age and other information (such as having been administered methadone) indicative of a history of having ever injected. Nevertheless, this study indicates that if optimal diagnosis, referral and treatment outcomes are to be achieved, additional measures need to be introduced. These include better understanding of HCV testing through awareness raising and making available social and psychological support to individuals, particularly those with a history of problem alcohol use, around the time of testing and beyond if they are diagnosed with chronic HCV.

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