Identifying former injecting drug users infected with hepatitis C: an evaluation of a general practice-based case-finding intervention

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ABSTRACT

Background In Scotland, a general practice-based case-finding initiative, to diagnose and refer hepatitis C virus (HCV) chronically infected former injecting drug users (IDUs), was evaluated.

Methods Testing was offered in eight Glasgow general practices in areas of high deprivation and high HCV and IDU prevalence to attendees aged 30–54 years with a history of IDU. Test uptake and diagnosis rates were compared with those in eight demographically similar control practices.

Results Of 422 eligible intervention practice attendees, 218 (52%) were offered an HCV test and, of these, 121 (56%) accepted. Poor venous access in 13 individuals prevented testing. Of 105 tested, 70% (74/105) were antibody positive of which 58% (43/74) were RNA positive by PCR. Of 43 chronically infected individuals identified in intervention practices, 22 (51%) had attended specialist care within 30 months of the study, while 9 (21%) had defaulted. In control practices, 8 (22%) of 36 individuals tested were antibody positive. Test uptake and case yield were approximately 3 and 10 times higher in intervention compared with control practices, respectively.

Conclusions Targeted case-finding in primary care demonstrated higher test uptake and diagnosis rates; however, to optimize diagnosis and referral of chronically infected individuals, alternative means of testing (e.g. dried blood spots) and retention in specialist care (e.g. outreach services) must be explored.

Keywords epidemiology, primary care, screening

Introduction

The hepatitis C virus (HCV) presents a major public health challenge with an estimated 170 million people infected worldwide.1 Of 38 000 people living in Scotland estimated to be chronically infected with HCV and at risk of cirrhosis and liver failure/cancer,2 <40% had been diagnosed, 20% had ever been in specialist care and only 5% had received antiviral therapy by the end of 2006.2 By comparison, in 2005/2006, 46% of injecting drug users (IDUs) who
underwent HCV testing in England were unaware of their infection.3

Improvements in the efficacy of combination antiviral therapy in clearing the virus,4–6 thus averting the risk of severe liver disease, mean that case finding and assessment for treatment are more important than ever, particularly as the treatment of mild, moderate and severe hepatitis with pegylated interferon and ribavirin in patients aged over 18 is considered clinically and cost-effective.7,8

In the UK, HCV is principally transmitted through injecting equipment sharing among IDUs; it is estimated that 90% of the 23 300 individuals living in Scotland with undiagnosed chronic HCV have been infected this way, and of these, 16 300 no longer inject.2 Approximately 40% of these former IDUs reside in the Greater Glasgow and Clyde (GGC) NHS Board area, particularly in areas of high socioeconomic deprivation.9 Accordingly, there is a need to intensify case-finding initiatives among this group to reduce their risk of developing advanced liver disease and to encourage other risk factor modification (e.g. alcohol consumption).

The first UK-based HCV screening intervention, undertaken in Glasgow in 2004, among general practice attendees aged 30–54 years, aimed to identify ‘older’ HCV-infected individuals in line with the recommendations of the Royal College of Physicians of Edinburgh Consensus Statement on HCV who were considered a priority for screening given their higher risk of progressing to severe liver disease.10 The study demonstrated that it could effect considerable test uptake; however, the yield of infected individuals would have risen from 13% (15/117) to 82% (14/17) if the offer of testing had been restricted to individuals who disclosed ever injecting drugs.11

Published cost-effectiveness studies have since suggested that (i) targeted case finding in general practice among 30–54 year olds with a history of IDU is more cost-effective than opportunistic testing of all those aged 30–54 years12 and (ii) case finding among IDUs in general practice is more cost-effective than in prisons, GUM clinics or drug/alcohol services, particularly among older individuals who have ceased injecting.13 Based on these findings, we aimed to evaluate the effectiveness and acceptability of a targeted screening intervention in general practices in Glasgow in terms of detecting, referring and, where appropriate, treating chronically infected former IDUs.

**Methods**

**Study design**

The effectiveness of a targeted screening intervention to identify HCV-infected former IDUs was evaluated through comparison of test uptake and case yield between patients attending eight general practices exposed to the intervention and those attending an equivalent number of demographically comparable control practices. The intervention ran for a maximum of 6 months in each practice during February–October 2007.

**Setting**

**Intervention practices**

To generate a high HCV positivity yield, 29 of a total of 274 practices in NHS GGC were targeted; these 29 practices were selected as they resided in areas of high socioeconomic deprivation, and high HCV and IDU prevalence (determined through three sources: Carstairs Deprivation Index,14,15 Scotland’s HCV diagnoses database16 and the Scottish Prescribers’ Association methadone database (details available from authors). The 29 practices were contacted via letter and invited to participate. Ten (34%) practices agreed; however, two later had to withdraw due to time constraints and limited availability of surgeries for blood testing. No differences in profile were apparent between participating and non-participating practices.

**Control practices**

Eight demographically comparable control practices in NHS GGC were identified and were matched for patient age and gender distribution to the eight intervention practices. Control practices were not aware of their involvement. Neither control nor intervention practices were randomized to the intervention.

**Participants**

Intervention practices’ clinical administration systems, all of which employed the General Practice Administration System for Scotland (GPASS), were interrogated using a search protocol designed to identify registered patients who (i) were aged 30–54 years and (ii) had indicators of past IDU (i.e. had ceased injecting at least 6 months prior to the intervention) (see Appendix I). On review of the search results, any identified individuals considered by general practitioners (GPs) to be unsuitable for testing (i.e. those failing to meet the inclusion criteria referred to in (i) and (ii) above, or individuals with a psychiatric condition for whom HCV testing would be inappropriate) were excluded. All remaining individuals who attended the practice for a non-urgent consultation during the intervention period were eligible to participate; this included individuals who had been
previously diagnosed and who had been referred to, but had defaulted from, specialist care.

**Intervention**

Eligible persons were informed of the intervention, provided with information leaflets, and offered testing by their GP/practice nurse. Individuals accepting the test provided signed consent and completed a short questionnaire, informed by a previously validated data collection tool. As per routine practice, a pre-test discussion was provided by the GP/practice nurse. Participants returned to the practice to receive their results as part of a post-test discussion with their GP. Training (either an on-site half-day seminar or detailed pre- and post-test discussion documentation) was offered to practices; one requested a seminar and the remaining seven received documentation. Chronically HCV-infected individuals were offered referral for specialist evaluation and treatment, where appropriate (i.e. no contraindications to antiviral therapy). To encourage practice participation and reduce the clinical burden, practices were each asked to offer testing to 20 patients over the intervention period, receiving £100 remuneration for each test offer.

**HCV blood tests**

All venous blood samples were sent to the West of Scotland Specialist Virology Centre (WoSSVC) for antibody testing using an enzyme linked immunosorbent assay (ELISA). The sensitivity and specificity of the third generation ELISA test was 97 and 100%, respectively [Abbott AxSYM antibody to HCV (v02)]. Antibody positive samples were subjected to RNA testing by the polymerase chain reaction (PCR); an ‘in-house’ real-time RT-PCR assay was used which had a lower detection level of 50 IU/ml.

**Data collection**

Data on test offer, acceptance and result among intervention practice patients, and the referral of infected individuals for specialist evaluation, were recorded by GPs/practice nurses. Participants provided demographic and risk factor information via a self-report questionnaire. Test results from intervention and control practices were sourced from the WoSSVC laboratory database. In addition, specialist clinical staff recorded numbers (i) referred, (ii) attended and (iii) treated.

Following the intervention period, practices reverted to their chosen testing procedure and no further data on test uptake were collected.

**Face-to-face interviews**

To determine the acceptability of the intervention, all practice staff and participants were invited to take part in face-to-face semi-structured interviews, informed by previously validated tools. These were conducted in a private room with consenting participants and staff at each intervention practice.

**Statistical analysis**

Data were analysed using SPSS Version 14.0. Multivariable logistic regression analysis was undertaken to ascertain the significant determinants of (i) test uptake among those offered, and (ii) HCV positivity among those tested. Qualitative interview data were anonymized and subjected to content analysis.

**Results**

**Characteristics of intervention and control practices**

Intervention and control practice populations totalled 35,449 and 37,724, respectively; 62 and 60% of the respective intervention and control practice populations resided in the 15% most deprived datazone areas. Of intervention and control practice populations, 37 and 38% were aged 30–54 years, respectively (Table 1).

**Test uptake and case yield in intervention practice**

Of 13,037 individuals aged 30–54 years registered at intervention practices, 838 (6.4%) were identified via the search protocol as having indicators of past IDU, and 485 (3.7% of the practice population aged 30–54 years) formed the target population following the review by GPs (Tables 1 and 2, Fig. 1). Over the 6-month intervention period, 422 (87%, range 67–97% across practices) of the 485 eligible individuals attended one of the practices for a non-urgent consultation. Of 422 individuals attending, 218 (52%, range 5–88%) were offered testing, although asked to offer an HCV test to 20 individuals, test offer by practice varied during the intervention period (1–56 patients). Of 218 offered testing, 121 (56%, range 35–100%) accepted. The four most commonly reported reasons for test refusal, as reported by potential participants at the time of consultation, were (i) never having injected drugs (by 15, 15% of those who refused testing), (ii) poor venous access (by 13), (iii) already attending an HCV specialist (by 12) and (iv) having previously received an HCV-positive diagnosis (by 13) as verified by the GP. Females were significantly more likely than males...
to accept a test [adjusted OR: 2.33 (95% CI: 1.26–4.28), P = 0.01], while individuals aged 40–54 years were significantly less likely than those aged 30–39 years to accept testing [adjusted OR: 0.53 (95% CI: 0.28–0.99) P = 0.05].

Of 121 individuals who accepted testing, 105 (87%) were tested, 13 (11%) experienced venepuncture failure due to poor venous access and three (2%) failed to return for testing. Of 105 participants tested, 74 (70%) were found to be antibody positive, of which 58% (43/74) were PCR positive (i.e. chronically infected). Approximately a quarter (21/74) of those found to be antibody positive had already been diagnosed HCV positive prior to the intervention. No significant differences were found in antibody positivity by gender and age category among those tested.

No adverse events following receipt of an antibody positive result were reported by staff or participants; however, staff in one practice noted heightened anxiety among participants at the prospect of testing.

### Comparison with test uptake and case yield in control practices

During the intervention period, 36 individuals (0.25% of the practice population) aged 30–54 years were tested across eight control practices (range one to seven tests per practice). Eight (22%) of the 36 individuals tested were antibody positive, of whom 5 were PCR positive. Test uptake and case yield among those aged 30–54 years in the intervention practices were approximately 3 and 10 times higher, respectively, than in control practices (Table 3).

### Referral and management of HCV PCR-positive individuals in intervention practices

By May 2010 (2.5 years after completion of the intervention), 31 participants from intervention practices had been referred to HCV specialist centres: 26 were PCR positive (61% of the 43 PCR-positive cases identified within intervention practices), two were antibody positive/PCR negative, one was antibody positive (with no PCR test data) and two had been referred for testing due to venepuncture failure. Of 31 individuals referred for specialist assessment, 7 (23%) had attended one appointment, 15 (48%) had attended two or more, while 9 (29%) had failed to attend. Of the 15 individuals who had attended two or more appointments, 2 had been treated and had achieved a sustained virological response, 1 had received treatment unsuccessfully, 1 was on therapy, 3 were awaiting treatment, 1 had declined, 3 had been assessed but not offered treatment due to contraindications and no information was available for the remaining four. No referral or treatment data were available for HCV-positive individuals from control practices.

### Acceptability of intervention from patient perspective

Sixty-one participants consented to be interviewed (50% of those accepting testing). Of this self-selected sample, 23 (38%) interviews were conducted: involving 13 (57%) females; 8 (35%), 13 (57%) and 2 aged 30–34, 35–39 and 40–44 years, respectively, and all were receiving methadone.

### Table 1 Demographic characteristics of the intervention and control practice populations

<table>
<thead>
<tr>
<th></th>
<th>All intervention practices, n (% of n)</th>
<th>All control practices, n (% of n)</th>
</tr>
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<tbody>
<tr>
<td>(a) All ages</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Practice population (n)</td>
<td>35 449 (100)</td>
<td>37 724 (100)</td>
</tr>
<tr>
<td>Proportion of practice population living in datazones defined as the 15% most deprived</td>
<td>21 872 (62)</td>
<td>22 725 (60)</td>
</tr>
<tr>
<td>Proportion of practice population in receipt of methadone prescription as on 18 May 2006a</td>
<td>487 (1.4)</td>
<td>509 (1.3)</td>
</tr>
<tr>
<td>(b) Aged 30–54 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Practice population (n)</td>
<td>13 037 (100)</td>
<td>14 189 (100)</td>
</tr>
<tr>
<td>Males</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30–34</td>
<td>1319 (10)</td>
<td>1357 (10)</td>
</tr>
<tr>
<td>35–39</td>
<td>1508 (12)</td>
<td>1640 (11)</td>
</tr>
<tr>
<td>40–44</td>
<td>1493 (11)</td>
<td>1653 (12)</td>
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<tr>
<td>45–49</td>
<td>1334 (10)</td>
<td>1462 (10)</td>
</tr>
<tr>
<td>50–54</td>
<td>1041 (8)</td>
<td>1158 (8)</td>
</tr>
<tr>
<td>Total</td>
<td>6695 (51)</td>
<td>7270 (51)</td>
</tr>
<tr>
<td>Females</td>
<td></td>
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</tr>
<tr>
<td>30–34</td>
<td>1146 (9)</td>
<td>1328 (10)</td>
</tr>
<tr>
<td>35–39</td>
<td>1410 (11)</td>
<td>1458 (10)</td>
</tr>
<tr>
<td>40–44</td>
<td>1453 (11)</td>
<td>1565 (11)</td>
</tr>
<tr>
<td>45–49</td>
<td>1292 (10)</td>
<td>1439 (10)</td>
</tr>
<tr>
<td>50–54</td>
<td>1041 (8)</td>
<td>1129 (8)</td>
</tr>
<tr>
<td>Total</td>
<td>6342 (49)</td>
<td>6919 (49)</td>
</tr>
<tr>
<td>With history of IDUb</td>
<td>485 (4)</td>
<td>not known</td>
</tr>
<tr>
<td>Patients tested for HCV during intervention period</td>
<td>105 (0.8)</td>
<td>36 (0.3)</td>
</tr>
<tr>
<td>Patients tested HCV antibody positive during intervention period</td>
<td>74</td>
<td>8</td>
</tr>
<tr>
<td>Patients tested HCV PCR positive during intervention period</td>
<td>43</td>
<td>5</td>
</tr>
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*Identified through search of Scottish Prescribers’ Association methadone database.

*Identified through search protocol and following review by GP.
Of the 23 interviewees, 15 (65%) were HCV antibody positive and, of these, 13 were PCR positive.

When asked to consider the acceptability of the intervention, all interviewees responded positively, several stating that they were ‘fine about it’, others reporting ‘it’s better to know’ or ‘I wasn’t surprised to be asked’. None of the 23 interviewees was offended by such an offer.

**Acceptability of intervention from practice staff perspective**

Following the intervention, interviews were conducted with practice staff (six GPs, two practice managers and one nurse). Staff in six practices viewed the intervention as an opportunity to facilitate identification, and subsequent referral, of HCV-infected individuals; prior to the intervention, competing priorities had hindered testing. In the remaining two practices, pre-intervention efforts had been made to ascertain the HCV status of (i) new patients with appropriate risk factors or (ii) patients initiating methadone maintenance treatment; however, practice staff felt the intervention could aid the detection of other HCV-infected individuals not previously tested, and facilitate the re-referral process for those who had previously tested positive, but who had not engaged with specialist care.

As a group, practice staff made repeated reference to the difficulties of accessing former IDUs. Although many within this group attend their GP regularly to receive methadone, and can be approached for testing, others have ceased injecting and rarely consult their GP. Further barriers to testing/referral included: (i) current clinical administration system limitations, (ii) the myriad health and social problems facing many former IDUs, rendering opportunistic HCV testing inappropriate for many and time consuming for others and (iii) poor venous access experienced by many.
Offer and uptake of HCV testing in the intervention practices. *These figures should be considered in the context of the fact that each intervention practice was asked to offer an HCV test to 20 individuals over the 6-month intervention period.

Table 3 HCV test uptake and result among control and intervention practices

<table>
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<th>Population</th>
<th>Control practices</th>
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<tr>
<td></td>
<td>Total</td>
</tr>
<tr>
<td>Practice population size (all ages)</td>
<td>37 724</td>
</tr>
<tr>
<td>Practice population (aged 30–54 years), n (% of n)</td>
<td>14 189 (100)</td>
</tr>
<tr>
<td>HCV test undertaken, N1 (% of n)</td>
<td>36 (0.3)</td>
</tr>
<tr>
<td>HCV antibody positive, N2 (% of N1)</td>
<td>8 (22)</td>
</tr>
<tr>
<td>HCV PCR positive, N3 (% of N1)</td>
<td>5 (14)</td>
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</tbody>
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<table>
<thead>
<tr>
<th>Population</th>
<th>Intervention practices</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
</tr>
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</tr>
<tr>
<td>Practice population (aged 30–54 years), n (% of n)</td>
<td>13 037 (100)</td>
</tr>
<tr>
<td>HCV test undertaken, N1 (% of n)</td>
<td>105 (48)</td>
</tr>
<tr>
<td>HCV antibody positive, N2 (% of N1)</td>
<td>73 (70)</td>
</tr>
<tr>
<td>HCV PCR positive, N3 (% of N1)</td>
<td>43 (41)</td>
</tr>
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</table>
Discussion

Main findings of this study

The effectiveness of this targeted approach to identify HCV-infected former IDUs was demonstrated by the significantly higher rates of test uptake and case yield in the intervention, compared with control, practices. Moreover, these outcomes will likely be conservative given that each practice was asked to offer testing to 20 individuals during the intervention period. The high antibody positive yield (70%) among intervention practices compares favourably to that generated by previous primary care-based screening interventions; however, the low treatment uptake rate demands attention.11,25–30 This study, therefore, indicates that if optimal diagnosis, referral and treatment outcomes are to be achieved, additional measures need to be introduced. These include alternative means of testing (e.g. dried blood spot testing, the sensitivity of which has been established31 and which has the potential to increase test uptake by improving opportunities for testing32) and of retaining individuals in specialist care (e.g. outreach services and primary care-based treatment delivery33).

What is already known on this topic

To date, published general practice-based HCV screening studies have predominantly been undertaken in France; these have adopted various universal and targeted approaches to identify and test patients, and all have relied on GPs’ willingness to participate.25–29 Elsewhere, in Ireland for example, Cullen et al.30,34 have made considerable efforts to highlight the role of GPs in stemming the HCV epidemic. In the UK, the authors of the only previous HCV screening intervention recommended that a targeted approach in the primary care setting would generate a high yield of HCV positivity,11 an approach in line with previous modelling studies.35

What this study adds

While the potential benefits of HCV screening initiatives are clear, these study findings will help to inform their future development. Analysis indicated that women and those aged 30–39 years were significantly more likely to accept testing than men and those aged 40–49 years, respectively. Although infected individuals aged 30–39 years, identified via this route, are less likely to have advanced to serious liver disease given their younger age, treatment of individuals diagnosed with mild, moderate or severe hepatitis is considered to be cost-effective and is recommended.7 Given the reduced odds of men and older patients agreeing to testing, alternative methods of accessing these groups to improve case detection are needed.

While acknowledging the increased case detection associated with the intervention, its implementation has highlighted several barriers to testing within general practice and subsequent referral to specialist care; it is imperative that these are considered in future interventions. As highlighted by several practices, the process of offering testing and obtaining a blood sample was more time consuming than first anticipated with multiple appointments required in many cases. In light of the extreme demands on GPs’ time, alternative methods of testing (e.g. oral fluid or dried blood spot testing) need to be explored. Further work relating to the cost-effectiveness of this intervention is also required.

Although no adverse reactions to positive results were reported, it was noted that opportunistic screening can lead to anxiety among some individuals. This underlines the need for additional counselling support to facilitate testing and referral of chronically infected individuals. The failure rate to attend specialist appointments (21% of participants failing to attend an initial appointment) likewise highlights the need for such support.

These findings confirm the important role of general practices in the testing, diagnosis and referral process, as highlighted in the Scottish Government’s Action Plan (Phase II).2 The major Government investment (totalling £43 million over 3 years) associated with the Plan will enable NHS boards and other stakeholders to deliver high-level actions, including the development and implementation of innovative approaches (such as the targeted approach evaluated here), to improve HCV testing and referral activities by GPs and other community setting practitioners. Greater attention also needs to be paid to the treatment of chronically infected current IDUs, given recent modelling work illustrating that this could reduce the prevalence of infection in this population.36

Limitations of this study

As this study focused on practices located in areas of high deprivation, and high HCV and IDU prevalence, of which only 29 were identified, and relied upon their willingness to participate (34% agreed), randomization of practices to intervention and control groups was not feasible. Selection bias and the reduced generalizability of any results associated with this non-randomized study design must be given due consideration. Nevertheless, promising results indicate that a randomized controlled trial, considering all practices and taking into account HCV prevalence variation, is warranted.
Given the resource implications of the intervention for GPs/practice nurses, the majority of practices declined to be involved despite financial incentives. Furthermore, although a sufficient sample size was achieved, test uptake ranged considerably between intervention practices despite reimbursement for test offers. Nevertheless, resource issues may need to be reconsidered to ensure GPs devote sufficient time to HCV testing, diagnosis and referral; for example, inclusion of HCV testing as part of the UK GP Quality and Outcomes Framework, for which payments are made against evidence-based indicators for particular health conditions (e.g. diabetes and cardiovascular disease), warrants consideration.

The current complexity of general practice administration systems makes the identification of former IDUs extremely difficult, particularly given the inconsistency of HCV test result, HCV status and IDU coding. The reliability of the intervention search protocol could, thus, be improved through development of the Read coding system employed by general practices.

While efforts were made to ensure the comparability of key characteristics of intervention and control practices, thus highlighting any differences in HCV test uptake, a lack of control practice referral and treatment data limits the interpretability of this aspect of the study. From the poor attendance of intervention practice participants at specialist care appointments, however, it is clear that improvements are needed across the general practice setting to retain patients in the patient care pathway.

Acknowledgements

The authors gratefully acknowledge the assistance of Paul Turner, Ian Mackie, Alasdair Buchanan and members of the NHS Greater Glasgow & Clyde Primary Care GP IT Mentoring Team which was integral to the development of the search protocol. The support of June McGill in the recruitment of practices, the contribution of Brownlee Centre staff (Sandy McLeod, Maxine Burke, Laura Mathers and Dr Roger Wong), Dr Rosalind Adam and staff at C-level (Claire Morris and Moira Washington) to the development of pre- and post-test discussion training materials and the assistance of Toni Williams in data extraction, are gratefully acknowledged. Sincere thanks are extended to the staff of the eight participating practices (Dr Cherry & Partners, Springburn Health Centre, Dr Clegg, Clydebank Health Centre, Dr Cole & Partners, Easterhouse Health Centre, Dr Connell & Partners, Balmore Surgery, Dr Jaberoo & Partners, Clydebank Health Centre, Dr Mackenzie, Lighthburn Medical Centre, Dr Muir, Woodside Health Centre, Dr Robertson & Partner, Pennan Practice), the West of Scotland Specialist Virology Centre and the participating HCV specialist centres (Brownlee Centre and Gastroenterology Unit, Gartnavel General Hospital and the Gastroenterology Department, Glasgow Royal Infirmary) for their commitment and support which have been crucial to the testing, diagnosis and assessment of patients. The involvement and encouragement of Steering Group members in the design and implementation of the intervention are gratefully acknowledged. This work was submitted by the principal author in partial fulfilment of the degree of Master of Public Health at the University of Glasgow; Dr Elisabeth Fenwick’s guidance is greatly appreciated.

Funding

This work was financially supported by the Scottish Government, the Schering-Plough Corporation and the Greater Glasgow and Clyde Development Directorate.

References


**Appendix I**

**Search protocol**

The clinical administration systems within the eight general practices were interrogated using a search protocol designed to identify registered patients who (i) were aged 30–54 years and (ii) had indicators of past IDU (i.e. had ceased injecting at least 6 months prior to the intervention).

All practices employed the GPASS to hold patients’ clinical records.

A search protocol was developed and piloted in collaboration with representatives of GPASS, the Glasgow Local Medical GP Sub-Committee and the GP Information Technology Mentoring Team for NHS Greater Glasgow and Clyde Primary Care Division. Search terms included (i) age parameters of 30–54 years, (ii) Read code information indicative of IDU, opiate type dependency and/or previous HCV testing and (iii) prescription details for methadone or another substitute drug (e.g. buprenorphine and naltrexone).
Identified individuals considered by GPs to be unsuitable for HCV testing (i.e. those who failed to meet the inclusion criteria or individuals with a psychiatric condition for whom HCV testing would be inappropriate) were excluded. All remaining individuals who attended the practice for a non-urgent consultation during the intervention period were eligible to participate in the intervention.