Hepatitis C prevalence and management among patients receiving opioid substitution treatment in general practice in Ireland

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Abstract:

**Background:** Hepatitis C virus (HCV) infection is a major cause of chronic liver disease and death. Injecting drug use is now the primary route of transmission of HCV in Ireland and globally, with an estimated 80% of new infections occurring among people who inject drugs (PWID). In Ireland and the EU, primary care is a key area to focus efforts to enhance HCV diagnosis and treatment among PWID.

**Objective:** The Heplink study aims to improve HCV care outcomes among opiate substitution therapy (OST) patients in general practice by developing an integrated model of HCV care and evaluating its feasibility, acceptability and likely efficacy.

**Methods:** The integrated model of HCV care comprises outreach of a HCV trained nurse into GP practices, and enhanced access of patients to community-based evaluation of their HCV disease (including a novel approach to diagnosis, i.e. Fibroscan). 14 OST prescribing GP practices were recruited from the professional networks/databases of members of the research consortium. A standardised non-probability sampling framework was used to identify 10 patients from each practice to participate in the study. Patients were eligible if ≥18 years of age, on OST and attend the practice for any reason during the recruitment period. Baseline data on HCV care processes/outcomes were extracted from the clinical records of participating patients.

**Results:** Baseline data was collected from the clinical records of 134 patients. Ninety-six (72%) were male, and the mean age was 43 years (SD=7.6; Range=27-71). One hundred and twenty-four (93%) patients had been tested for anti-HCV antibody in their lifetime. Of those tested, 95 (77%) tested positive. Ninety-seven (72%) patients had received a HIV antibody test in their lifetime. Of those tested, eight (8%) tested HIV positive. Eighty nine (66%) of patients had been tested for HBV in their lifetime, and seven (8%) of those tested were positive. Thirty-three patients (25%) were asked about their alcohol use by their GP in the 12-month period prior to the study, seven (5%) had received a brief intervention, and three (2%) had been referred to a specialist addiction or alcohol treatment service.
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**Conclusions:** With general practice and primary care playing an increased role in HCV care, our findings suggest that the development, evaluation of real world clinical solutions that support patients from diagnosis to completing treatment, are a priority.

**Keywords**

Hepatitis C; primary care; people who inject drugs (PWID), integrated HCV care

**Introduction:**

Hepatitis C Virus (HCV) infection is associated with considerable morbidity and public health burden globally. Worldwide, it is estimated that approximately 115 million people (1.6% of the world’s population) have been infected with HCV, with two-thirds of the infections being active [1]. The number of people infected with HCV infection in the European Union (EU) and European Economic area (EEA) is estimated at 5.6 million [2].

The major burden of HCV infection arises from its progression to chronic infection and associated sequelae [3]. Approximately 74% of acutely infected patients progress to chronic infection [4], with 20% developing cirrhosis within 25 years, and 25% of patients with cirrhosis developing hepatocellular carcinoma and/or decompensated liver disease [5] [6]. In Europe, HCV is now a leading cause of cirrhosis and primary liver cancer [7].

Injecting drug use is now the primary route of transmission of HCV in Ireland and globally, with an estimated 80% of new infections occurring among people who inject drugs (PWID) [8]. Global estimates for the number of anti-HCV positive PWID in 2010 estimate the figure at 10 million [9]. In Ireland, a study of anonymised data from the National Drug Treatment Reporting System (NDTRS) between the years 1991-2014 estimated the total number of injectors up to 2014 as 16,382, with an estimated 56% chronically infected with HCV. After adjusting to account for injectors who had never shared injecting equipment, it was estimated that 12,423 were infected with HCV, with 9,317 chronic infections [10].

HCV infection is mostly asymptomatic in its early stages and rate of progression is slow, with manifest liver disease uncommon within the first 20 years of established infection [11]. As a result, without adequate screening measures, there is a significant potential for an elevated burden of disease among an aging population of former or current PWID. Furthermore, injecting drug use is associated with high levels of problem alcohol use, as well as other factors associated with adverse outcomes [12] [13]. In particular, alcohol use disorders accelerates the progression to fibrosis and associated complications.[14] [15].

In Europe, primary care is increasingly involved in providing continuing care, including opioid substitution treatment (OST), for PWID. The important role of primary care in HCV screening and the provision of complex interventions tailored to the needs of PWID have been highlighted
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[16] [17] [18] [19]. Trials of integrated models of care for HCV treatment (i.e. incorporating treatment for mental health issues and substance abuse) in primary healthcare settings have shown promising results for improving outcomes among PWID [20] [21] [22].

The recent emergence of direct acting antiviral (DAA) treatments has dramatically improved treatment outcomes for people infected with HCV. These treatments have shown a greater than 90% efficacy in achieving sustained virological response (SVR). Utilisation of these new therapeutic agents combined with improved testing, linkage to care, and adherence to treatment, show promise for counteracting the expected rise in future disease burden [23].

Irish and international strategies, plans and guidelines have prioritised the provision of new pharmaceutical regimens for patients with the greatest clinical need initially, seeking to balance the high cost of these drugs at present, with a view to wider implementation of these drug regimens in the future [24, 25]. In addition, HCV screening has been problematic. A cross-sectional survey of patients attending general practice in the Eastern region of Ireland reported HCV testing rates of 34% and a HCV prevalence rate among those tested of 73% [26]. This low rate of screening for HCV in primary care has also been reported in other healthcare systems [27, 28].

In this paper, we aim to describe the current management of HCV among patients on OST attending general practice in Ireland in light of current guidelines aimed at scaling up interventions to reduce chronic HCV infection and associated mortality [29, 30].

**Methods:**

**Study design**

We examined current HCV care practice among patients attending general practice for OST. Data was collected from clinical records as part of a feasibility study of a complex intervention to enhance HCV care. The ‘Heplink’ study is one component of the Hepcare Europe project [31, 32], an EU-supported service innovation project and feasibility study at four European sites (Dublin, London, Seville and Bucharest) to develop, implement and evaluate interventions to enhance identification and treatment of HCV among PWID.

**Setting**

The study sites were 14 OST-prescribing GP practices located in Dublin’s north inner city. In Ireland, currently there are two types of settings in which OST is delivered in the community: specialist addiction clinics and general practice. All patients receiving OST are registered on the Central Treatment List (CTL). ‘Level 1’ GPs are responsible for the treatment of stabilised opiate dependent persons referred from specialist addiction clinics or from ‘Level 2’ GPs. Practice as a ‘Level 1’ GP requires completion of a recognised training programme delivered by the Irish College of General Practitioners (ICGP) and regular educational updates.
The GP is audited by the ICGP / Health Services Executive (HSE) Audit Committee. ‘Level 1’ GPs can treat up to a maximum of 15 patients. A ‘Level 2’ GP has undergone additional training, can initiate OST and prescribe for a greater number of patients (up to a maximum of 35 patients or a maximum of 50 in a partnership with two or more doctors in their own practice [33]). As of 31st August 2016 there were 9,652 patients receiving treatment for opiate use in Ireland (excluding prisons), which included 4,150 patients being treated by 350 GPs in the community [34].

Study population

Fourteen OST-prescribing GP practices in North Dublin were recruited from the professional networks/databases of the research team. Practices were eligible to participate if they were registered to prescribe OST and were located within the Mater Misericordiae University Hospital (MMUH) catchment area. A standardised non-probability sampling framework was used to identify 10 patients from each practice to participate in the study. Based on the recommendations for good practice in feasibility studies [35], and our previous feasibility studies among PWID [36, 37], we estimated that 140 patients (attending 14 general practices) would be adequate to calculate the actual recruitment and retention rates (i.e., feasibility) and provide data on acceptability of study processes and outcome measures, to inform a future definitive intervention trial. Patients were eligible to participate if they were aged at least 18 years, on OST, and attended the practice for any reason during the recruitment period. The researchers instructed participating GPs to recruit consecutively presenting patients who were eligible and interested to participate until they had attained a quota of 10.

GPs provided eligible patients with a verbal explanation of the study and a written information leaflet outlining the study’s purpose, procedures and how the findings would be utilised. Patients who were interested to participate were asked to sign a consent form which was witnessed by the GP or a member of the research team. While the initial approach to participate was from the GP, recruitment was facilitated by a member of the research team being ‘on site’ (where feasible) to support the practice during the recruitment phase and answer any questions potential participants might have. Although practices were instructed to recruit 10 eligible patients, some practices recruited less than 10 as they had a smaller number of OST patients, and some practices recruited more than 10 patients. Ethical approval for the study was received from the MMUH Research Ethics Committee.

Data collection

The clinical records of participating patients were examined by a member of the research team prior to the implementation of the ‘Heplink’ intervention. Baseline data was extracted on: demographic characteristics, care processes / outcomes in relation to HCV and other blood borne viruses (BBV), urinalysis test results, problem alcohol use, chronic illness, and health service
utilisation. Additional data regarding BBV care were extracted from seven of the 14 participating practices (n=60 patients).

**Bloodborne virus care:** Lifetime and past 12-month data on HCV care were extracted from each clinical record, including: HCV antibody testing (yes/no) and status (positive/negative); whether the patient had been referred to a hepatology or infectious diseases specialist (yes/no); had attended a hepatology or infectious diseases specialist (yes/no); been assessed by Fibroscan (yes/no); and initiated HCV treatment (yes/no). Lifetime and past 12-month data in relation to other BBV was also extracted, including: HIV antibody, and Hepatitis B surface antigen (HbsAg) / Hepatitis B core antibody (anti-HBc) testing (yes/no) and status (positive/negative); and whether the patient had received any dose of Hepatitis B (HBV) immunization (yes/no). Additional data on BBV care were extracted on a subset of seven practices (n=60 patients), including: HCV RNA and Antigen (Ag) testing (yes/no) and status (positive/negative); Fibroscan scores (kPa); whether HCV treatment had been completed (yes/no); and whether the patient had received any dose of Hepatitis A (HAV) immunization (yes/no). Lifetime and past 12-month data in relation to these variables was collected.

**Problem drug and alcohol use:** Data extracted from clinical records included results of the last urine drug test, i.e. whether positive/negative for metabolites of non-prescribed drugs of abuse. In addition, clinical records were reviewed to determine whether in the past 12 months GPs had (a) screened/discussed alcohol use (yes/no), (b) conducted a brief intervention (yes/no), and (c) referred the patient to specialised treatment (yes/no).

**Chronic illness and health service utilisation:**
Data was extracted on the presence of chronic illnesses (yes/no), whether the patient had any Emergency Department visits in the past month (yes/no) or GP Out-of-Hours visits in the past month (yes/no).

**Data analysis**
Means, frequencies, and percentages were calculated using Statistical Packages for the Social Sciences (SPSS) version 24.

**Results:**

**Population characteristics**

Fourteen GP practices and 135 patients were recruited to the study. Seven practices were ‘Level 1’ prescribers and seven practices were ‘Level 2’ prescribers. Baseline data was collected from the clinical records of 134 patients. Ninety-six of the 134 patients (72%) were male, and the mean age of the sample was 43 years (SD=7.6; Range=27-71). Fifty six (42%) patients’ most recent urine sample had tested positive for metabolites of non-prescribed drugs of abuse. Forty
four (33%) had at least one chronic illness documented in their clinical record. Three patients (2%) had visited an emergency department in the past month and one patient (1%) had attended a GP OOH service in the past month.

**Screening for bloodborne viruses**

One hundred and twenty-four (93%) patients had been tested for anti-HCV antibody in their lifetime. Of those tested, 95 (77%) tested positive. In the 12-month period before the study, 31 patients (23%) had received an anti-HCV antibody test, with 22 (71%) of those tested testing positive.

Ninety-seven (72%) patients had received a HIV antibody test in their lifetime. Of those tested, eight (8%) tested HIV positive. Twenty-six (19%) patients had been tested for HIV antibody in the previous 12-months, with one (4%) testing positive.

Eighty nine (66%) of patients had been tested for HBV in their lifetime, and seven (8%) of those tested were positive; 30(22%) had been tested in the previous 12-months, one of whom (3%) tested positive.

<table>
<thead>
<tr>
<th>Table 1: Blood-borne virus screening and infection status (n=134)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total (n=134)</strong></td>
</tr>
<tr>
<td>HCV Ab test - lifetime</td>
</tr>
<tr>
<td>HCV Ab positive - lifetime</td>
</tr>
<tr>
<td>HCV Ab test - past year</td>
</tr>
<tr>
<td>HCV Ab positive - past year</td>
</tr>
<tr>
<td>HIV Ab test - lifetime</td>
</tr>
<tr>
<td>HIV Ab positive - lifetime</td>
</tr>
<tr>
<td>HIV Ab test - past year</td>
</tr>
<tr>
<td>HIV Ab positive - past year</td>
</tr>
<tr>
<td>Anti-HBc/HBsAg test - lifetime</td>
</tr>
<tr>
<td>Anti-HBc/HBsAg positive - lifetime</td>
</tr>
<tr>
<td>Anti-HBc/HBsAg test - past year</td>
</tr>
<tr>
<td>Anti-HBc/HBsAg positive - past year</td>
</tr>
</tbody>
</table>

HCV=Hepatitis C Virus; Ab=antibody; Anti-HBc= Hepatitis B core antibody; HBsAg= Hepatitis B surface antigen

**Immunisation against other hepatotrophic viruses**

Fifty-two (39%) patients had received at least one dose of HBV immunisation in their lifetime, and 11 (8%) had received at least one dose in the 12-months prior to the study. Additional data collected from seven practices (n=60 patients) showed evidence that 13 (22%) patients had received at least one dose of HAV immunisation in their lifetime, with one (2%) receiving the vaccine in the past 12-months.
Table 2: Hepatitis A and B immunisation status (n=134)

<table>
<thead>
<tr>
<th>Total (n=134)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any HBV immunisation dose lifetime</td>
<td>52</td>
</tr>
<tr>
<td>Any HBV immunisation dose past year</td>
<td>11</td>
</tr>
<tr>
<td>Any HAV immunisation dose lifetime</td>
<td>13</td>
</tr>
<tr>
<td>Any HAV immunisation dose past year</td>
<td>1</td>
</tr>
</tbody>
</table>

HBV=Hepatitis B Virus; HAV=Hepatitis A Virus

Subsequent care of anti-HCV-antibody-positive patients

Of the 95 patients known to be anti-HCV antibody positive, twelve (13%) patients had undergone a Fibroscan in their lifetime, and five (5%) had undergone a Fibroscan in the previous 12-months. Fibroscan scores were available for nine patients; the mean score was 7.4 kPa (Range:4.5-16.9; SD:3.7).

Fourteen (15%) patients had initiated HCV treatment in their lifetime. Three (3%) had initiated treatment in the past 12-months.

Additional data collected from seven (n=60 patients) of the 14 practices indicates that, among the 47 patients who tested HCV antibody positive in these practices, 27 (57%) had received confirmatory HCV RNA or Ag testing in their lifetime, with 20 (43%) testing positive; six (13%) had received RNA or Ag testing in the previous 12-months, with 4 (9%) testing positive.

Table 3: Management of anti-HCV antibody positive patients (n=95)

<table>
<thead>
<tr>
<th>Total (n=95)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibroscanned - lifetime</td>
<td>12</td>
</tr>
<tr>
<td>Fibroscanned - past year</td>
<td>5</td>
</tr>
<tr>
<td>Initiated HCV treatment - lifetime</td>
<td>14</td>
</tr>
<tr>
<td>Initiated HCV treatment past year</td>
<td>3</td>
</tr>
<tr>
<td>HCV Ag/RNA test - lifetime</td>
<td>27</td>
</tr>
<tr>
<td>HCV Ag/RNA positive - lifetime</td>
<td>20</td>
</tr>
<tr>
<td>HCV Ag/RNA test - past year</td>
<td>6</td>
</tr>
<tr>
<td>HCV Ag/RNA positive - past year</td>
<td>4</td>
</tr>
</tbody>
</table>

ID=Infectious Diseases; HCV=Hepatitis C Virus; Ag=Antigen

Alcohol screening and brief intervention

Thirty-three patients (25%) were asked about their alcohol use by their GP in the 12-month period prior to the study, seven (5%) had received a brief intervention (i.e. a structured discussion around alcohol harms), and three (2%) had been referred to a specialist addiction or alcohol treatment service in the same 12-month period.

Table 4: Screening and Intervention for Problem Alcohol Use in the past year (n=134)
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<table>
<thead>
<tr>
<th></th>
<th>Total (n=134)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol screening past year</td>
<td>33</td>
<td>24.6%</td>
</tr>
<tr>
<td>Alcohol brief intervention past year</td>
<td>7</td>
<td>5.2%</td>
</tr>
<tr>
<td>Referred to specialist addiction or alcohol treatment service past year</td>
<td>3</td>
<td>2.2%</td>
</tr>
</tbody>
</table>

Discussion:

Summary

Our findings suggest that although testing rates for HCV among PWIDs attending GPs for OST have increased since 2003, access to further assessment and antiviral treatment remains a challenge. While 93% of patients had been tested for anti-HCV antibody in their lifetime (of whom 77% tested positive), only 13% had had a Fibroscan and 15% had initiated antiviral therapy.

Comparison with existing literature

93% of patients had been tested for anti-HCV antibody in their lifetime, with 77% testing positive. This shows an increase in the number of patients being tested for anti-HCV antibody compared to data collected in 2003 in a study examining HCV among OST patients in primary care in Ireland (77%) [38] (see Table 5). The percentage of patients testing positive for HCV is higher than previous studies among OST patients in primary care in Ireland [38-40] (see Table 5), and higher than among an at risk cohort from the HepCAT study in primary care in the United States [41]. The percentage of patients testing HCV positive is also considerably higher than available data on prevalence of HCV among injecting drug users in Ireland (41.5%) from the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) [42].

Eight per cent of patients tested positive for HIV and 8% tested positive for HBV (anti-HBc or HBsAg). These rates are lower for HIV, but higher for HBV than data reported by Cullen et al in 2007 (HIV 10%; HBV 4%) [38]. The rates for HIV and HBV are higher than a recent study among OST patients in primary care in Ireland by Klimas et al. (HIV 5.7%; HBV 2.7%) [40] (see Table 5).

<table>
<thead>
<tr>
<th></th>
<th>2017</th>
<th>2013</th>
<th>2003</th>
<th>1999</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>43</td>
<td>40.9</td>
<td>32.2</td>
<td>28</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>96 (72%)</td>
<td>69 (65%)</td>
<td>141 (72%)</td>
<td>409 (72%)</td>
</tr>
<tr>
<td>Tested for anti HCV (lifetime)</td>
<td>124 (93%)</td>
<td>104 (99%)*</td>
<td>151 (77%)</td>
<td>380 (67%)**</td>
</tr>
<tr>
<td>HCV positive</td>
<td>95 (77%)</td>
<td>54 (51%)</td>
<td>104 (69%)</td>
<td>276 (73%)***</td>
</tr>
<tr>
<td>Tested for HIV (lifetime)</td>
<td>97 (72%)</td>
<td>103 (98.2%)*</td>
<td>135 (69%)</td>
<td>326 (57%)</td>
</tr>
<tr>
<td>HIV positive</td>
<td>8 (8%)</td>
<td>6 (5.7%)</td>
<td>14 (10%)</td>
<td>27 (8%)</td>
</tr>
<tr>
<td>Tested for HBV (anti-HBc or HBsAg)</td>
<td>89 (66%)</td>
<td>88 (83.8%)</td>
<td>118 (60%)</td>
<td>316 (55%)</td>
</tr>
<tr>
<td>HBV positive (anti-HBc or HBsAg)</td>
<td>7 (8%)</td>
<td>3 (2.7%)</td>
<td>5 (4%)</td>
<td>43 (14%)</td>
</tr>
</tbody>
</table>

* self-reported data
** 113 of 380 was self-reported data
*** 75 of 276 was self-reported data

Twenty five per cent of patients had been asked about their alcohol use by their GP in the 12-month period prior to the study, 5% had received an alcohol brief intervention and 2% had been referred to a specialist addiction or alcohol treatment service. While these figures show an improvement in screening, brief intervention and referral to treatment for alcohol compared to the baseline data from a recent alcohol intervention study among OST patients in primary care in Ireland [40, 43], nonetheless alcohol screening and brief intervention should be systematically performed among this cohort [44].

**Strengths and limitations**

Limitations of this study include potential bias, and lack of generalizability that may arise from GPs who are more motivated and enthusiastic about the issue under study being over-represented among those recruited. Furthermore, random sampling of patients in the participating practices was not possible as conventional probability sampling methods are often not appropriate for populations of injecting drug users [45]. As a result, a standardized, non-probability sampling framework was used in all participating practices to identify patients on whom data would be collected. In addition, while only data on patients who consented to a researcher having access to their clinical records were collected, consent bias is likely to be minimal, particularly given the high proportion of those asked who provided consent.
Despite these sources of potential bias, the GPs and patients who participated in the study were comparable in their profile to other studies from Ireland [38, 46, 47].

Conclusions

The advent of highly effective DAAs have made eradicating hepatitis C possible, but for this to occur, healthcare systems must address the complex and wide-ranging difficulties associated with effective HCV screening, assessment and treatment in the community. With general practice and primary care playing an increased role in HCV care, our findings suggest that the development, evaluation of real world clinical solutions that support patients from diagnosis to completing treatment, are a priority.

Acknowledgements

We thank the Third Health Programme of the European Union and the Health Service Executive, Ireland for funding this project. We also wish to express our gratitude to the participating general practices that facilitated the research and the patients for consenting for their clinical records to be reviewed for the study.

Authors’ Contributions

RM led the development of the manuscript with other co-authors contributing specific components. WC is principal investigator and conceived the study. RM and WC led preparation of the manuscript with a core group of authors. All authors read and approved the final manuscript.

Conflicts of Interest

The authors report no conflicts of interest

References:


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