Increasing uptake of hepatitis C virus infection case-finding, testing, and treatment in primary care:

evaluation of the HepCATT (Hepatitis C Assessment Through to Treatment) trial

INTRODUCTION
Hepatitis C (HCV) is a bloodborne virus. Acute infection is usually asymptomatic, with symptoms not appearing until after several years of chronic infection, when the liver may be severely damaged, leading to patients presenting late with cirrhosis and liver disease. In the UK, injecting drug use is the main route of HCV transmission; other routes include unscreened blood transfusion, unsafe health care, exposure to blood-contaminated needles, for example, by tattooing, and sexual practices that lead to exposure to blood. Research from 2019 suggests that up to 43% of future hepatitis C infections could be prevented if transmission among people who inject drugs was reduced. Treatment of chronic HCV infection results in sustained viral clearance in a high percentage (>95%) of treated patients. An estimated 143 000 people in the UK have chronic HCV infection; however, HCV has been described as a silent epidemic, with <50% of those infected aware of their HCV status and with many more not receiving treatment, who are therefore at increased risk of morbidity, mortality, and onward transmission. HCV screening interventions have been effective in increasing case finding in target populations, for example, in migrants and attenders at drug treatment centres, however, those not in contact with specialist services are not systematically being assessed. The crucial role of primary care in stemming the HCV epidemic and preventing HCV-related illness has been highlighted, although many primary care patients at risk of HCV infection have not been tested. The World Health Organization (WHO) has called for an increase in HCV diagnosis, setting a target of 90% of infected people in Europe knowing their status by 2030. To increase diagnosis and treatment, the National Institute for Health and Care Excellence (NICE) recommends implementing cost-effective interventions to increase case finding in primary care; however, robust evidence is lacking, and case finding and treatment rates in many sites are low.

The Hepatitis C Assessment Through to Treatment (HepCATT) trial was conducted to assess whether a complex intervention...
in primary care could increase the identification and treatment of HCV-infected patients compared with usual care. The HepCATT intervention, following NICE recommendations, consisted of training practice staff about HCV; providing patients with information about HCV; and use of an electronic patient record algorithm to identify patients with HCV infection risk factors or patients who had been previously diagnosed and not referred for treatment. During the trial, 2071 (16%) of patients identified in the intervention practices and 1163 (10%) in the control practices were tested for HCV, giving an overall intervention effect as an adjusted risk ratio of 1.59 (95% CI = 1.21 to 2.08, \( P < 0.001 \)). Intervention practices had a greater yield of positive antibody tests compared with control practices (6.2% versus 4.2%; rate ratio 1.42; 95% CI = 0.95 to 2.13), and the intervention was demonstrated to be highly cost-effective for the NHS. Recommendations have been made by the trial team to implement the HepCATT intervention across the UK.

How this fits in
Although the Royal College of General Practitioners and the National Institute for Health and Care Excellence provide guidance for GPs on testing for hepatitis C, research suggests that the current practice of case-finding, testing, and treatment is not effective. This study examined the implementation of the HepCATT (Hepatitis C Assessment Through to Treatment) trial complex intervention, which consists of training practice staff, providing patient HCV posters and leaflets; and using an electronic patient record algorithm for proactive case-finding of patients with HCV infection risk factors or patients diagnosed >1 year previously with no evidence of referral for treatment. The intervention was found to be feasible and acceptable to staff, and could be effective in supporting primary care to follow hepatitis C infection testing and treatment guidelines.

METHOD
Study design
The HepCATT trial was a pragmatic two-armed practice-level cluster randomised controlled trial in 45 primary care practices (22 intervention and 23 control) in the southwest of England. Practices were randomised to either control (usual care) or intervention. The intervention comprised:

- online HCV educational resources (Royal College of General Practitioners e-learning module — Hepatitis C: Enhancing Prevention, Testing and Care) and 1-hour face-to-face staff training on the epidemiology, diagnosis, management of HCV infection, and trial processes;
- patient posters and leaflets explaining HCV risk factors and treatment options in practice waiting rooms; and
- Audit+ software [Informatica Systems Ltd] integrated into practice electronic patient record systems and used to identify patients with risk factors for HCV infection or patients who had been diagnosed >1 year previously without a referral for treatment.

Patients identified by the audit tool were invited by letter/email (and followed up by telephone, email, or text) for an HCV test, and automatically flagged by the software by creating on-screen pop-ups to encourage opportunistic testing if the patient attended a consultation.

Semi-structured interviews were conducted with staff in intervention practices involved in implementing the intervention to investigate their views and experiences of the intervention; the acceptability and feasibility of the intervention; the impact on working practice; and attitudes to future implementation.

Sampling and recruitment
Purposive sampling was used to capture maximum variation in views and experiences, and to reflect a range of practices [in relation to size and location based on socioeconomic deprivation], and staff [in relation to professional roles]. The socioeconomic status of practice populations was estimated using the Index of Multiple Deprivation decile. Staff from all 22 intervention practices were invited to participate in an interview after delivering the intervention for ≥1 month via email or telephone. Sample size was informed by the concept of “information power”, with analysis and sampling conducted in parallel and continuous assessment of the suitability of the information within the sample with regard to study objectives.

Data collection
Telephone interviews were conducted by an experienced social science researcher.
Audio-recorded verbal consent was gained before the interviews, which lasted between 12 and 47 minutes, with an average time of 25 minutes. A flexible topic guide was used to assist questioning but allow participants to introduce new issues (Box 1).

Data analysis
Interviews were audio-recorded, transcribed, anonymised, imported to NVivo (version 10), and thematically analysed. Transcripts were coded inductively to establish an initial analysis framework and three researchers coded a subset of two transcripts; discrepancies were discussed to ensure a coding consensus and maximise rigour. The four normalisation process theory constructs were used to further develop themes across the dataset. Normalisation process theory proposes that implementation of interventions is dependent on staff fulfilling four criteria (Box 2).

RESULTS
Fourteen healthcare professionals (HCPs) (seven GPs, three nurses, and four practice staff) were interviewed from across 12 practices — five in areas of high deprivation (Table 1). Findings are presented for each of the normalisation process theory constructs, illustrated with anonymised verbatim quotes.

1. Coherence (sense making)
All HCPs described their practice of HCV testing before HepCATT as opportunistic and sporadic, testing patients with a history of drug dependency, abnormal liver function, and/or other infections such as HIV or hepatitis B. Only two HCPs described other HCV infection risk factors, such as blood transfusions given abroad, a family member with HCV, or high-risk sexual activity:

‘If somebody came, you know, and we found they had HIV, we definitely tested. Um, I think if they had a hepatitis B they were tested as well but I don’t think it was routinely picked up on for anybody else.’ (Site 17, Nurse)

Participants understood the relevance of the intervention and valued its perceived impact. Initial engagement was led by an interest in finding out whether there were patients with HCV infection risk factors at their practice who had not yet been previously identified:

‘I was interested to see whether we would have anybody, because my first thoughts were “oh, we will be fine because you know[doctor] does it and the drugs workers do it all” … I thought “oh, maybe we have missed people but we will wait and see”.’ (Site 6, GP)

‘I think it would be a sensible thing to do because I think that if we can diagnose

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Box 1. Interview discussion topic guide

- Existing HCV identification practice before HepCATT intervention
- Acceptability of the intervention
  - Experiences of using the software
  - Views on opportunistic prompts
- Feasibility of the intervention
  - Appropriateness of patients identified
  - Difficulties experienced with offering the test
  - Support needs
- Approaching patients for testing opportunistically
  - Patient information support needs
  - Perceived patient views about being approached for testing
- Future implementation of the intervention in primary care
  - Improvements to intervention
  - Potential barriers
  - Recommendations for roll-out of the intervention

HCV = hepatitis C virus. HepCATT = Hepatitis C Assessment Through to Treatment

Box 2. Normalisation process theory criteria

1. Coherence: sense making — understanding and opinion of the intervention purpose
2. Cognitive participation: buy-in — engagement with the intervention
3. Collective action: the work of putting the intervention into operation
4. Reflexive monitoring: appraisal of the intervention

| Practices | Deprivation decile | Patient population |
|-----------|-------------------|-------------------|
|           | High (n=9000) | Low (n=>13 000) | 9000-13 000 | >13 000 |
| GPs       | 7 2 5 4 1 2 |
| Nurses    | 3 0 3 0 2 1 |
| Practice managers | 1 1 0 0 | 0 0 |
| Information technology/ administrators | 3 2 1 1 2 0 |
| Total     | 14 5 9 5 6 3 |

*Index of Multiple Deprivation.*

(Index 10, GP)
people with hepatitis C earlier than potentially we can reduce their risk of becoming cirrhotic. [Site 9, GP]

2. Cognitive participation (buy-in)
Participants valued the training for enhancing HCV awareness and increasing knowledge, particularly in practices with lower levels of patients with existing HCV. Even those with previous experience of HCV believed the training had expanded their knowledge of risk factors for HCV infection and who to target for testing:

‘Hepatitis C was something I was aware of anyway, perhaps more so than other GPs because of my work as a drugs lead … certainly that was always a population that I’m aware that we should be screening … but I think that the way HepCATT worked was potentially broadening out that … it was a broader remit to think of hepatitis C.’ [Site 11, GP]

‘I don’t think it was on people’s radar particularly because there’s so many other things going on … the doctors all said “you know, we hadn’t even thought about that”’. [Site 18, Nurse]

The training itself acted as a prompt for opportunistic testing:

‘I think having the discussion at the beginning of the trial to raise awareness and remind people about the risk factors of hepatitis C probably led to some people offering the test perhaps where they wouldn’t have done.’ [Site 11, GP]

3. Collective action (putting HepCATT into operation)
Audit tool. Some practices encountered ‘a few teething problems’ [Site 11, GP] with setting up the audit tool, compatibility issues, and not always having the necessary time and resources; however, with support from the trial team and the software company, difficulties were resolved, and practices went on to use the audit tool without issue:

‘It took a bit of getting used to but I felt like we had support to find our way around it … you had to take the time just to focus on it and get used to it, but it worked fine when you were familiar with it … that [support from trial team] helped a lot.’ [Site 2, Administrator]

Participants saw the benefits of identifying patients using the audit tool and most liked that it was ‘straightforward’ to use and helpful in ‘identifying the right people’. [Site 2, Administrator]

‘I think it’s fairly robust at identifying the patient that is at risk.’ [Site 9, GP]

Screening lists of patients with HCV infection risk factors produced by the audit tool were perceived to be mostly appropriate. Although the algorithm automatically excluded certain patients (such as those on opioid patches for pain relief or who were terminally ill), issues arose in some practices with inconsistencies in medical record coding leading to inappropriate patients being identified. This was particularly pertinent to how drug users were categorised. This meant that, for some, the benefits of using the Audit+ software were offset by additional resource and time needed to screen lists. To reduce GP workload, in some practices administrators or nurses reviewed patient lists before GP screening:

‘I think the only problem was about the codes that we’d used … we had one partner in particular who tended to code this little lady who couldn’t get off her sleeping tablets as drug dependent and that was a problem for us, because that’s flagged up unnecessary ones.’ [Site 5, GP]

‘She [administrator] would pull off the lists and have a quick scan … highlight the ones she thinks aren’t right … then I look through it … so 10 sets of notes … I would pull the notes up, quickly have a look to see if there is anything that I mean is palliative care, they have just had a consultation that hasn’t been coded.’ [Site 6, GP]

HCV testing via invite letters. Some participants were initially concerned about the resources needed to implement the intervention. Resource concerns were threefold: first, to manage the mail-out to identified patients; second, to deal with patient queries; and, third, to conduct the HCV tests. To address this, practices sent letters out in batches:

‘We haven’t sent out the whole lot, we would only do like 20 at a time, so we didn’t want 20 people to ring up saying they wanted a test, that would have had a big impact on the practice, but it didn’t turn out to be the case.’ [Site 6, GP]

Participants also worried about disappointing patients by not being able to schedule a test promptly. They believed this
would result in patients not trying to book a test at a later date. Therefore, one practice appointed a dedicated nurse to liaise with patients and conduct tests:

“We don’t want them [patients] to be disappointed, because if they ring up and we say “oh, that’s in a month’s time” … they won’t be interested.” [Site 6, GP]

A few practices commented that engaging patients with a history of injecting drug use was challenging because they often did not respond to HCV testing invite letters and the practice had to ‘chase up the patients’ [Site 18, Nurse]; however, most HCPs described that patients were happy to be approached and they did not receive any negative feedback:

“We haven’t had any negative erm comments from patients saying “Why have I been picked?” or anything like that … if the doctors have identified more risk for the letter, then obviously, I go through it with them and explain why their name has come up. And they’re very understanding of why their name has been picked up.” [Site 13, Nurse]

A few HCPs described being cautious about approaching patients for testing with risk factors other than injecting drug use, such as organ transplants or past blood transfusions, because they did not want to scare them, but the intervention allowed for testing options to be discussed:

“But it [intervention] kind of opened up the conversation with them … we had to be very careful, we didn’t want to scare patients and the ones that probably fell into that ball park were the ones who’d had transfusions or some sort of procedure where they might be at risk but a long time ago. That was a little bit difficult, but once we had explained it to them, why it was a problem and why it might be a risk and they kind of were happy to then go ahead.” [Site 5, GP]

Only one practice described a negative response from a small number of HIV-positive patients, because they felt they were being stigmatised and they were already screened regularly for HCV at the local hospital:

“Some of our HIV patients, I mean two or three, were a little bit upset and also you know when I went into their records, they’re all seen regularly at hospital and they do have regular Hep C tests there.” [Site 11, Administrator]

**Opportunistic HCV testing via ‘pop-up’ computer screen alerts.** Because of the busy nature of primary care, the computer screen alerts or pop-ups to opportunistically identify patients with HCV risk factors during routine consultations were commonly not welcomed or used by GPs. Patients often presented with complex needs and immediate clinical problems were prioritised over discussing HCV risk and testing given the limited consultation time. Participants also spoke of pop-up fatigue, of having too many screen pop-ups when dealing with a patient and therefore the impact of the alerts becoming diluted. Using the screen pop-ups was also made more challenging by the requirement for GPs to log in to the Audit+ software to activate them, which they often forgot or opted not to do:

“Just remembering to switch it on in the morning was probably the biggest issue … but then I suspect that probably GPs because of the number of pop-ups it fired at you would have ignored it or try to switch it off at some point.” [Site 11, GP]

“We recognised that people were just a bit swamped and couldn’t factor that into their 10-minute appointment.” [Site 5, GP]

Although GPs did not welcome the screen pop-ups, some nurses thought they could be useful to keep HCV testing on people’s ‘radar’:

“I’m always very happy with the opportunistic testing because if I’ve got a pop-up box it’s fantastic. I will see it and speak to the patients about it.” [Site 18, Nurse]

### 4. Reflexive monitoring (appraisal of HepCATT intervention)

When appraising the intervention and making recommendations for future implementation, participants suggested streamlining information technology systems. Integrating the algorithm and screen pop-up systems within existing electronic patient record systems (for example, EMIS) would remove the need for HCPs to additionally log in to the Audit+ software:

“Trying to make that alert part of EMIS might be better, because having a separate bit of software … it did rely on each doctor logging in every morning and so perhaps...”
having a prompt in EMIS might be more reliable … as we tend to use prompts in
EMIS more.’ (Site 10, GP)

The record search algorithm was based
on a large number of Read codes and
risk factors were not weighted. A few
participants suggested refining the search
algorithm so it could be tailored by the
practice to focus on more high-risk patients
and reduce the number of inappropriate
patients identified. This would in turn reduce
practice staff workload in screening lists of
patients identified and sending invites, and
would allow realistic financial planning:

‘Being a bit more focused on the patients
who are more at risk … it felt like it was
literally picking everyone up who might have
the minutest risk of hepatitis … and it didn’t
always feel appropriate … maybe it felt like
the search could be narrowed down a bit
than perhaps using a too broad a remit.’ (Site 11,
GP)

‘We send out a lot of letters for a minimal
response … when there’s more acute
patients that could be identified … whether
that’s something in the audit or the coding
… that identifies the high-risk rather than
medium-risk patients.’ (Site 13, Nurse)

Some participants suggested changing
the wording of the HCV testing invite letter
to alleviate staff concerns regarding sending
the letters to certain patient groups:

‘If you have, you know, something like
“please don’t be offended but we are just
sending letters out to anybody who’s had a
Hep C blood test in the last 20–25 years” …
we did have to be sort of careful if somebody
might have had one for fertility blood test
and they maybe now had a new partner,
you know, whether picked up that letter
it’s, you know, they might be thinking “oh,
you know, why have you got this?”.’ (Site 11,
Administrator)

Implementing HepCATT in more practices
could be enabled by increasing activities
to raise patient and HCP awareness and
acceptance of HCV and testing. A public
health campaign and ongoing clinician
training were suggested:

‘My awareness will gradually fade.’ (Site 14,
GP)

‘I think it’s the patients accepting it … but
then that’s education of the public isn’t it?
Everybody knows if you have bleeding down
below, you have to go and see your doctor, if
you cough up blood, go and see your doctor
as there has been big public campaigns …
but as far as I’m aware, I haven’t seen them
[hepatitis C campaigns].’ (Site 6, GP)

Some participants suggested additional
resources would be required for practices
to implement the intervention:

‘If you’re asking more practices to do more
work then practices need to be funded to do
more work, you can’t just expect surgeries
to take on more work. You get people
phoning and speaking to the receptionist
about the letter they received, you get
people making appointments, you have the
cost of the blood test … they might need an
appointment to discuss the results.’ (Site 8,
GP)

DISCUSSION

Summary

The HepCATT intervention was valued
by primary care staff for enhancing
systematic identification of patients with
HCV infection with the potential to benefit
from treatment, compared with previous
opportunistic and sporadic HCV testing.
HepCATT training enhanced awareness
of HCV and improved knowledge of HCV
infection risk factors. Although there were
initial teething problems with setting up
the audit tool in some practices, most
staff found it straightforward and helpful,
and valued having a comprehensive list
of patients to target for testing. Extra
resources were required to screen lists and
to conduct tests, and practices often drew
on the expertise of nurses to reduce GP
workload. Fees for running the algorithm
and contingency staff management to
conduct tests should be considered in
wider implementation of the intervention.
Staff valued the opportunity to discuss HCV
testing with patients, especially those who
may not have been previously aware of HCV
risk; however, practices need to be cautious
not to additionally stigmatise patients with
conditions such as HIV, particularly those
who may receive regular screening for HCV
in secondary care. Although the algorithm
excluded patients who had been tested
for HCV within the previous 12 months, it
relied on patient record data. Therefore,
if a patient had recently received an HCV
test in secondary care, test results may not
have been apparent on patient records at
the time of the record search. As with any
algorithm-based intervention, the quality
and completeness of medical records are
critical for its effectiveness.
Funding
The trial (ISRCTN161788850) was funded by the National Institute for Health Research (NIHR) Health Policy Research Programme (Evaluation of interventions designed to increase diagnosis and treatment of patients with hepatitis C virus infection in primary care and drug treatment settings, 015/0309). This study was designed and delivered in collaboration with the Bristol Randomised Trials Collaboration, a UK Clinical Research Collaboration Registered Clinical Trials Unit (CTU), which, as part of the Bristol Trials Centre, is in receipt of NIHR CTU support funding. Support was given by NIHR Health Protection Research Unit (HPRU) in Evaluation of Interventions and NIHR HPRU Blood Borne & Sexually Transmitted Infections, NIHR programme Grant EPIToPe, and NIHR Applied Research Collaboration West, NIHR School for Primary Care Research, and Centre for the Development and Evaluation of Complex Interventions for Public Health Improvement. The views expressed in this article are those of the authors and not necessarily those of the NHS, NIHR, or the Department of Health and Social Care.

Ethical approval
NHS ethics approval was received from the National Research Ethics Service (ref: 15/SW/0094).

Provenance
Freely submitted; externally peer reviewed.

Competing interests
The authors have declared no competing interests.

Acknowledgements
The authors would like to thank the general practices and patients that participated in the trial, Informatica Systems Ltd, and the NIHR Clinical Research Network West of England, which assisted with identifying and accessing GP practices to participate in the trial. The Hepatitis C Trust provided expertise and support on hepatitis C virus prevention, and essential health education materials.

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When considering further use of the intervention, participants suggested refining the search algorithm to weight risk factors to reduce the number of inappropriate patients identified. Participants also recommended fully integrating information technology systems, especially computer screen pop-up software with electronic patient record systems. Views on the value of screen pop-up prompts were mixed, with some GPs highlighting ‘pop-up fatigue’, while some nurses valued reminders to consider HCV testing. Pop-up alerts have been found to be beneficial in influencing clinicians’ behaviour; however, the danger of electronic patient record-based alerts overload, producing ‘pop-up fatigue’, is a common phenomenon.

Future implementation of HepCATT should ensure that on-screen pop-ups are tailored to ensure a balance between adequate alerting and burden.

Strengths and limitations
Participants were recruited using a diverse sample of practices, GPs, practice nurses, and information technology and/or administration staff to ensure that all aspects of the intervention were captured, including software installation and use, case finding, patient consultation, and testing. Analysis demonstrated a high degree of similarity between views and experiences, suggesting acceptability across practices serving different communities. The use of normalisation process theory to inform analysis allowed for examination of issues with both the intervention design and its implementation. A study limitation is that no interviews were conducted with patients, which should be taken into consideration when interpreting the results. Although HCPs did discuss how the intervention was received by patients, which provided some insight into patients’ views, there were no problems raised by HCPs except for a few patients living with HIV. These patients, because of delays with previous HCV test results from secondary care, should have been excluded from screening lists.

Comparison with existing literature
HepCATT trial findings demonstrated an effective and cost-effective intervention. Although the effect size was modest, the intervention is very low cost to implement. Previous research has suggested that a high proportion of patients at risk of HCV are not being tested in primary care as a result of clinicians not remembering to test patients with risk factors, and not being able to quickly and reliably determine HCV risk and status from EMIS coding. The current study demonstrates that HepCATT can overcome these issues, with staff valuing the intervention as a straightforward means of identifying at-risk patients and providing an opportunity to discuss HCV testing. As HCV infection is usually asymptomatic, staff welcomed the HepCATT intervention proactive case finding based on HCV risk factors. The HepCATT intervention aligns with the ‘new service model for the 21st century’ aspiration of the NHS Long Term Plan to be more proactive in providing services to enable individuals ‘to take more control of how they manage their physical and mental wellbeing’. As other HCV primary care interventions have found, the current study indicated resource concerns for proactive case finding and increasing HCV testing; however, the findings demonstrate that nurses might be considered to alleviate increased GP workload. Previous research has also identified nursing support as a critical facilitator to increasing primary care HCV testing and as effective in supporting adherence to HCV testing and treatment guidelines.

Implications for practice
With adequate resources and technology, primary care can play an important role in identifying patients with HCV infection who have the potential to benefit from treatment. While there needs to be a multipronged approach to increase HCV testing in a range of settings, including prisons and drug treatment centres, the cost-effective HepCATT intervention provides primary care with a range of tools to improve the identification and care of patients with HCV infection, and prevent HCV-related illness. This could help the UK to reach the WHO target of 90% of infected people knowing their status by 2030 and help to stem the HCV epidemic, reducing the risk of morbidity, mortality, and onward transmission.
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