International Journal of Drug Policy 72 (2019) 91–98

Contents lists available at ScienceDirect

International Journal of Drug Policy

journal homepage: www.elsevier.com/locate/drugpo

Point-of-care hepatitis C testing from needle and syringe programs: An Australian feasibility study

Bridget Williams[a,*], Jessica Howell[a,b,c,d], Joseph Doyle[a,e], Alexander J. Thompson[c,d], Bridget Draper[a], Chloe Layton[f], Ned Latham[a,i], Frances Bramwell[f], Dean Membrey[f], Maggie Mcpherson[g], Janine Roney[h], Mark Stoové[a], Margaret E. Hellard[a,b,e], Alisa Pedrana[a,b]

[a] Disease Elimination Program, Burnet Institute, Melbourne, Australia
[b] School of Public Health and Preventive Medicine, Monash University, Melbourne, Australia
[c] Department of Gastroenterology, St Vincent's Hospital, Melbourne, Australia
[d] Department of Medicine, University of Melbourne, Melbourne, Australia
[e] Department of Infectious Diseases, The Alfred and Monash University, Melbourne, Australia
[f] Cohealth, General Practice, Melbourne, Australia
[g] North Richmond Community Health, General Practice, Melbourne, Australia
[h] Department of Infectious Diseases, The Alfred, Melbourne, Australia
[i] Department of Infectious Diseases, Monash University, Melbourne, Australia

ARTICLE INFO

Keywords:
Hepatitis C
Point-of-care testing
Harm reduction
Health services accessibility

ABSTRACT

Background: Achieving hepatitis C elimination requires novel approaches to engage people at highest risk of infection into care pathways. Point-of-care-tests may help to overcome some of the barriers preventing people who inject drugs (PWID) accessing testing and progressing to treatment for hepatitis C virus (HCV). We assessed the feasibility and acceptability of HCV point-of-care testing at needle and syringe exchange programs (NSPs) co-located in three community health clinics in Melbourne, Australia.

Methods: NSP clients were offered an oral fluid point-of-care test for HCV antibody by NSP staff. Positive HCV antibody tests were followed by a point-of-care test for HCV RNA alongside standard-of-care laboratory testing for hepatitis C treatment work-up. Participants were offered same-day point-of-care results on site, via phone or text message, or upon return to the service. Participants were scheduled for follow-up review with the study nurse for assessment and linkage to treatment.

Results: A total of 174 participants completed HCV antibody point-of-care test; 150 (86%) had a reactive result. Of these, 140 (93%) underwent a HCV RNA point-of-care test and 76 (54%) tested positive; few participants (5%) waited on site for results delivery, but the majority of RNA positive (63%) attended a follow-up visit for treatment work-up (median time to follow-up visit = 11 days; IQR = 7–20 days). The majority of participants reported a preference for point-of-care tests (66%) and supported NSP staff involvement in testing (90%).

Conclusion: Provision of HCV point-of-care tests, follow-up and linkage to treatment services through NSPs was feasible and acceptable to PWID. Despite few participants waiting to receive same-day results, there was effective linkage to care, suggesting value in further evaluation of this approach.

Introduction

The advent of highly efficacious and well tolerated oral direct acting anti-viral (DAA) therapies that cure hepatitis C virus (HCV) infection within two to three months has revolutionized HCV care and paved the way for elimination (Hellard, Scott, Sacks-Davis, & Pedrana, 2018; Pedrana, Sacks-Davis, Doyle, & Hellard, 2017). Meeting elimination targets set by the World Health Organization requires 90% of the estimated 71 million people living with HCV (Polaris Observatory H. C. V. Collaborators, 2017) to be diagnosed and 80% of those diagnosed to be treated (Taherkhani & Farshadpour, 2017; World Health Organization, 2016, 2017).

While achieving these targets might be considered more feasible in countries that offer unrestricted access to DAA treatments, such as Australia, Portugal, Egypt and Georgia, proactive approaches are still needed to ensure that populations most at risk of HCV infection receive

* Corresponding author at: 85 Commercial Rd, Melbourne, VIC, 3004, Australia.
E-mail address: bridget.williams@burnet.edu.au (B. Williams).

https://doi.org/10.1016/j.drugpo.2019.05.012

diagnostic testing, and are subsequently linked to treatment and cure (Grebely, Dore, Morin, Rockstroh, & Klein, 2017; Pedrana et al., 2017; Scott et al., 2017). In Australia, as in many high-income countries, people who inject drugs account for the majority of the HCV burden and transmission (Alter, 2011; Kirby Institute, 2018). The multi-step process of HCV diagnosis, requiring an initial HCV antibody test, followed by an RNA test, as well as discrimination faced by people who inject drugs in traditional health care settings are major barriers to this group entering and progressing along the cascade of care from initial test to cure (Islam, Topp, Day, Dawson, & Conigrave, 2012, 2013; Jones et al., 2014; Neale, Tompkins, & Sheard, 2008). Utilizing point-of-care diagnostics in non-traditional health care settings may help to overcome this barrier by increasing entry points and avoiding delays in the HCV care cascade (Grebely, Applegate, Cunningham, & Feld, 2017; Morano et al., 2014; Scott et al., 2017). Highly sensitive tests that provide results at the point-of-care are available for both HCV antibodies and RNA (Shivkumar, Peeling, Jafari, Joseph, & Pant Pai, 2012; Khuroo, Khuroo, & Khuroo, 2015; Gupta, Agarwala, Kumar, Maiwall, & Sarin, 2017; McHugh et al., 2017). However, these tests are yet to be approved for diagnostic use in Australia, and are not currently used in HCV testing pathways.

The use of point-of-care tests to detect HCV antibodies has been implemented and tested in a variety of settings (Beckwith et al., 2016; Drobnik et al., 2011; Jewett, Al-Tayyib, Ginnett, & Smith, 2013; Jewett et al., 2012; Smith et al., 2011), however point-of-care testing for detection of HCV RNA, a necessary step for the provision of ongoing care and treatment, is relatively new (Easterbrook & W. H. O. Guidelines Development Group, 2016; Grebely, Lamoury et al., 2017). Research into the impact of HCV point-of-care tests on testing uptake and treatment outcomes is limited (Coats & Dillon, 2015; Jewett et al., 2013; Morano et al., 2014). The Rapid-Eliminate Hepatitis C (Rapid-EC) study aimed to evaluate the acceptability and feasibility of providing HCV point-of-care antibody and RNA testing at needle and syringe programs (NSP) within primary care clinics, to inform strategies to increase the uptake of testing and treatment amongst people who inject drugs.

Methods

Study design

The Rapid-EC study was a pilot single-arm, interventional cohort study evaluating HCV point-of-care testing offered through NSPs to people who inject drugs. It was conducted at three community-based primary care clinics with NSP services in metropolitan Melbourne, Australia. Each site had specialist drug and alcohol services and general practitioners (GPs) able to prescribe DAA treatment for the management of HCV, in line with Australian recommendations (Hepatitis C Virus Infection Consensus Statement Working Group, 2018). The tests used in the study were the OraQuick® HCV Rapid Antibody Test (OraSure Technologies Inc., Bethlehem, PA USA) using oral fluid samples, and the Xpert HCV Viral Load test performed on serum samples using the GeneXpert system (Cepheid, Sunnyvale, CA, USA). Oral fluid samples were preferred over capillary blood samples to reduce the inconvenience of the process to the client. Although the test has greater sensitivity with capillary sampling, the estimated specificity or 99.4% and sensitivity of 95.9% was deemed acceptable for the purposes of this study (Khuroo et al., 2015). The Xpert HCV Viral Load test provides a quantitative assessment of the HCV viral load. However, in this study it was used as a qualitative test only, with HCV RNA detected at any level constituting a positive result. The quantitative results produced by the test were not assessed in this study.

Study staff

The study was implemented by existing NSP staff and clinic nurses, with support from GPs. One of the NSP staff had experience seeing clients individually as a community health worker and the three others NSP staff were primarily responsible for provision of clean injecting equipment and involvement in health promotion campaigns. The nurses had experience working in hepatology and alcohol/other drug sector.

All study staff were trained on the use the point-of-care tests from representatives of Cepheid and Integrated Sciences, the distributor for the OraQuick test in Australia. It also included review of the study protocol, data collection and specimen handling.

Eligibility

All clients aged 18 years or over who attended participating sites during the recruitment period, were able to provide written, informed consent and reported not currently being engaged in care for HCV infection were invited to participate in the study. People currently engaged in HCV care were defined as having received a diagnosis of HCV within the preceding three months, having a planned appointment with a health care practitioner or tests in preparation for HCV treatment, were currently taking treatment, or were within three months of having completed a treatment course. Recruitment occurred from the 29th of June 2017 until the 1st of November 2017, and the initial follow-up period continued at each clinic for two weeks after the date the last participant was recruited. To fit in with availability of staff and clinic rooms, each clinic offered point-of-care testing as part of the study for two days per week.

Recruitment

Posters were displayed in the NSP space to generate awareness of the study. Clients were offered study participation at the NSP desk (point of needles and syringe dispensing) by NSP staff. Staff were instructed to engage clients sequentially in conversations about the study and offer participation. Interested clients were then taken to a private room for consent pre-test counselling and participation.

Sample size

This was a feasibility study; hence a formal sample size was not calculated to make comparison between interventions. The overall aim was to recruit approximately 50 individuals at each site as this would provide enough information to the study team about potential issues with recruitment to inform a future intervention study.

Testing

Clients who consented to participate underwent pre-test counselling for HCV and provided an oral fluid specimen via a mouth swab for the point-of-care HCV antibody test. Participants were offered to self-collect or have assistance from the NSP staff or nurse. Results were determined visually after 20 min and provided to participants on-site. If there was doubt about a test result staff repeated the test. If the result was still uncertain this was documented as indeterminate test result.

Participants with a non-reactive point-of-care antibody test were then offered standard laboratory testing for HCV to confirm the result (as neither of the point-of-care tests used in this study are approved for diagnostic use in Australia) (Hepatitis C Virus Infection Consensus Statement Working Group, 2018). Those with reactive point-of-care antibody tests underwent venipuncture for the serum-based point-of-care RNA test. Venipuncture was performed on-site by the nurse or by self-collection if the participant preferred by self-collection. One blood sample collected in a serum separator tube was centrifuged on site by the nurse or NSP worker using a bench-top centrifuge. Serum was then collected by pipette for testing using a GeneXpert machine at each clinic. Additional blood specimens were collected and sent for standard laboratory based HCV testing and for all tests recommended for DAA

treatment work-up in Australia: full blood count, liver function tests, urea and electrolytes, international normalized ratio, human immunodeficiency virus serology, hepatitis B serology, hepatitis A serology, and hepatitis C viral load and genotype (Hepatitis C Virus Infection Consensus Statement Working Group, 2018).

Receiving results and follow-up

Participants were provided the option of remaining at the clinic for the time taken to reach a result (105 min), or receive the result by text message or telephone call later that day, or the following day if the result was not ready before clinic close, or on return to the clinic either later that day, another day or at follow-up appointment. Text messages used coded language to convey the result to the participant to maintain privacy.

All participants who had blood sent for pathology testing were scheduled for a follow-up visit one to two weeks after their point-of-care tests. At this follow-up visit, participants who were HCV RNA positive were assessed for HCV treatment by the site nurse. Treatment work-up was conducted in line with Australian treatment guidelines (Hepatitis C Virus Infection Consensus Statement Working Group, 2018). Liver fibrosis was first assessed by using the aspartate to platelet ratio index (APRI) and then FibroScan™ assessment if APRI was score ≥ 1.0, as per Australian guidelines (Hepatitis C Virus Infection Consensus Statement Working Group, 2018). Participants were linked to a GP experienced in hepatitis C management within the same service provided there were no indications for specialist management (such as evidence of liver fibrosis, previous HCV treatment, co-infection with HIV or hepatitis B virus, complicated co-morbidities or drug interactions). Where possible, the GP would review the participant directly following the nurse assessment for further counselling and to provide a prescription for treatment. When it was not possible for the GP to review the participant directly after the nurse's assessment, an appointment was organised for the participant to see the GP at a later date.

Data collection and analysis

Whilst awaiting the point-of-care antibody result participants completed a questionnaire that assessed demographic information, risk factors for HCV infection, opinions and attitudes to HCV testing, and experiences of stigma and discrimination within the healthcare setting. Questionnaires were completed on portable electronic devices. Participants had the option of completing the survey independently or to have staff read the questions and record responses. Questionnaires are provided in supplementary information.

At the end of their study participation participants completed a second questionnaire about their experience of point-of-care tests and preferences for testing. Participants were reimbursed AUD 30 for the time taken to participate in the study. This amount was split across two payments –one at the first visit and the other once all components of the study had been completed. Data was collected using REDCap software Version 8.5.11 (Vanderbilt University, Tennessee, USA) and analyzed using Stata version 13 (StataCorp LP, College Station, Texas, USA). Chi-squared tests were used to compare proportions. As this study was not intended to formally compare the intervention across sites, statistical tests for differences reported across sites have not been performed. Ethical approval was granted by the Alfred Health Human Research Ethics Committee (527-16).

Results

Uptake

Due to the busy nature of the services and rapid nature of interactions at the NSP desk, it was not possible to systematically document responses to the offer of study involvement. Limited data collected from 51 individuals offered testing at Clinic 1 (see Supplementary Table 1) suggested that 16% of those offered involvement accepted the offer or had already participated in the study, 25% were interested but preferred to return another day, and 59% declined in involvement. The most common reason cited for declining involvement was being already engaged in HCV care (cited for 70% of those who declined). After several weeks of recruitment clients were approaching staff for participation in the study and rate of recruitment was limited by time taken to implement the testing model. Recruitment ceased due to funding limitations rather than difficulty in recruiting participants.

Participants

A total of 174 participants consented to the study and completed the point-of-care antibody test. The median age of participants was 41 years (interquartile range 35–48 years) the majority (68%) were male, and the vast majority (94%) reported injecting drug use within the preceding six months. Almost all participants (97%) reported ever having a hepatitis C test previously, but only 28% reported this being within the last year. Most reported a previous positive test, either antibody positive only (31%) or RNA positive (44%). Details of participant characteristics are provided in Table 1 and participant flow through the study is shown in Fig. 1.

Point-of-care testing results and initial follow-up

Of the 174 participants who completed the point-of-care antibody test, 150 (86%) had reactive results. Of these, 140 (93%) underwent point-of-care RNA testing and ten were not able to provide a blood sample for testing. Just over half (n = 76, 54%) of the point-of-care RNA tests were positive (see Table 2). Although the study was not intended to evaluate performance of the point-of-care tests, the results were similar to those previously published (see supplementary information for further detail).

Of the 140 participants who underwent point-of-care RNA testing seven (5%) waited to receive their result face-to-face on site, 82 (61%) received their result by phone call or text message, 34 (24%) on return to the clinic (either at their follow-up appointment or opportunistically when returning to use another service at the clinic). Twelve (9%) weren't able to be provided with the result and in five (4%) cases data on mechanism of result delivery were missing Of those who received their result by phone, more preferred a phone call, 55 (66%), than opted for a SMS text message, 28 (34%).The 12 (9%)participants who were not provided with their result could not be contacted and did not return to the clinic (See Table 3). Whilst data on possession of a mobile phone was not collected systematically, notes for 21 (15%) participants who underwent point-of-care RNA testing indicated they did not have a phone on which they could be contacted.

Seventy-six (44%) of participants overall had a positive point-of-care RNA test; 48 (63%) returned for the second study visit for review of all laboratory pathology test results and assessment for treatment. The median time between first visit and second visit was 11 days (interquartile range: 7–20 days). Of the 64 participants who had a negative or invalid point-of-care RNA test, 56 (88%) attended the second study visit to receive their confirmatory testing results (see Table 3). Five participants were documented to have preferred to follow up their results with their usual health care provider directly rather than participate in the second study visit (results were provided to participants' health care providers at participant's request), and two participants could not be followed up due to incarceration.

Participants with unstable accommodation or experiencing homelessness were less likely to attend the follow-up appointment than participants with more stable accommodation (63% compared to 80%, p = 0.033) (See Supplementary Table 2). However, there was no significant difference between follow-up when comparing gender, education, alcohol misuse, whether participants reported receptive needle

Table 1
Participant characteristics.

	Clinic 1 N (%)[a] Total N = 72	Clinic 2 N (%)[a] Total N = 52	Clinic 3 N (%)[a] Total N = 50	Total N (%)[a] Total N = 174
Variable (number of respondents)				
Age (174)				
Median age (IQR)	44 (36 – 50)	44 (38 – 49)	37 (31 – 43)	41 (35 – 48)
Gender (172)				
Male	53 (74)	37 (74)	28 (56)	118 (68)
Female	18 (25)	13 (26)	20 (40)	51 (30)
Other gender	1 (1)	0 (0)	2 (4)	3 (2)
Education (173)				
Above secondary education	15 (21)	14 (27)	7 (14)	36 (21)
Secondary School education	42 (58)	34 (67)	10 (20)	86 (50)
Primary School education or less	15 (21)	3 (6)	33 (66)	51 (29)
Housing (173)				
Owner occupier or renter	37 (52)	26 (51)	21 (42)	84 (49)
Living with family/friends or boarding/guesthouse	11 (15)	12 (24)	10 (20)	33 (19)
Unstable accommodation[b], homeless or other unspecified	24 (33)	13 (25)	19 (38)	56 (32)
Aboriginal and/or Torres Strait Islander (171)				
Yes	8 (11)	10 (20)	15 (31)	33 (19)
No	63 (89)	41 (80)	34 (69)	138 (81)
Alcohol misuse (173)[c]				
Yes	44 (61)	32 (63)	29 (58)	105 (61)
No	28 (39)	19 (37)	21 (42)	68 (39)
Injecting drug use last six months (165)				
Yes	63 (94)	42 (88)	49 (100)	154 (94)
No	4 (6)	6 (12)	0 (0)	10 (6)
Receptive sharing of needle or syringes in last 6 months (173)				
Yes	11 (15)	8 (16)	6 (12)	25 (14)
None reported	61 (85)	43 (84)	44 (88)	148 (86)
Opioid Substitution Therapy (172)				
Current OST	30 (42)	35 (69)	15 (30)	80 (47)
Previous OST	26 (37)	12 (24)	29 (58)	67 (39)
Never on OST	15 (21)	4 (8)	6 (12)	25 (15)
Previous incarceration (171)				
Yes	55 (80)	36 (73)	34 (68)	125 (74)
No	14 (20)	13 (27)	16 (32)	43 (26)
Previous hepatitis C test (173)				
Yes	70 (97)	52 (100)	45 (92)	167 (97)
No	2 (3)	0 (0)	4 (8)	6 (3)
Time since last hepatitis C test (160)				
Last test date within 1 year	21 (30)	20 (43)	3 (7)	44 (28)
Last test date more than 1 year ago	42 (61)	21 (46)	4 (9)	67 (42)
Last test date entered as "unknown"	6 (9)	5 (11)	38 (84)	49 (30)
Last hepatitis C test result (165)				
Ab negative	4 (6)	1 (2)	0 (0)	5 (3)
Ab positive and RNA negative	24 (34)	18 (36)	9 (20)	51 (31)
RNA positive	29 (41)	21 (42)	23 (51)	73 (44)
Don't know/Can't Recall	13 (19)	10 (20)	13 (29)	36 (22)
Previous hepatitis C treatment (172)				
Yes	20 (28)	9 (18)	8 (16)	37 (22)
No	52 (72)	41 (82)	42 (84)	135 (78)

[a] Percentage reported as proportion of respondents to question, rather than proportion of total participants.

[b] Unstable accommodation included accommodation specified as "couch surfing", "squat" or "car".

[c] Alcohol misuse was assessed using the AUDIT-C alcohol screen, with alcohol misuse defined as a score of ≥4 for males, and ≥3 for females.

and syringe sharing or current opioid substitution therapy. A greater proportion of participants who received their positive RNA result prior to the follow-up visit (either waited on site or received the result by phone call or SMS text) returned for follow-up than did others (72% compared to 46%, p = 0.027). However, of the participants with a negative RNA result, the proportions who returned for follow-up did not vary depending on whether they were aware of the result or not (90% compared to 84%, p = 0.392).

Preferences for testing

When asked about their preference for HCV testing, including the possibility of point-of-care RNA testing on capillary blood from finger stick sampling, the majority of participants selected a process with both antibody and RNA point-of-care tests (77/116, 66%) with 13 selecting standard testing (11%). There was a strong preference for same day results (93/117, 75%). There was also widespread support for the involvement of NSP staff (described as 'community workers') in the testing process, with 90% of those who answered this question (104/116) reporting it as very acceptable (see Supplementary Table 3).

Experiences of stigma and discrimination

When asked about experiences of stigma and discrimination in health care services in the preceding 12 months, over half the respondents reported discriminatory treatment due to their injecting drug use at least sometimes (n = 90, 53%), and more than one third reported experiencing this "often" or "always" (n = 69, 41%). Experiences of stigma due to previous incarceration or HCV status were less commonly reported. When asked whether they had experienced poor or different treatment from different types of health care workers, more respondents (34%) reported poor treatment occurring at least sometimes from specialist doctors, than occurring at least sometimes from GPs (31%), nurses (22%) and NSP workers (8%) (see Supplementary Table 4).

Discussion

Our study shows that it is feasible to incorporate community based point-of-care testing into NSPs and have NSP staff conduct testing. The approach was successful at reaching people at high risk of HCV transmission; engaging and retaining them in the initial steps of the cascade of care.

The vast majority (93%) of participants with reactive HCV point-of-care antibody tests went on to have an HCV RNA point-of-care test. This is high compared to recent Australian data, which report that less than 50% of people who are anti−HCV positive have had an HCV RNA test (Iversen et al., 2017; Kirby Institute, 2017, 2018), and data from the United States and Canada, which report less than 30% and 60%, respectively (Janjua et al., 2016; Yehia, Schranz, Umscheid, & Lo Re, 2014). Close to two thirds of participants with a positive RNA point-of-care test returned for assessment for treatment. Whilst data assessing this step in the cascade of care are limited, it has been estimated that 31% of people who inject drugs with active or cured HCV had received a specialist assessment (Iversen et al., 2017). Our study also shows the potential of this model to reach those who remain unengaged in HCV care despite the unrestricted availability of DAA treatment in Australia, with less than a third of the cohort reporting annual testing, which is recommended for individuals at high risk of HCV infection (Hepatitis C Virus Infection Consensus Statement Working Group, 2018). However, it is notable that participants who reported unstable accommodation were significantly less likely to return for follow-up than other participants, highlighting the need to ensure that social and structural determinants of health are not forgotten in the HCV response, and that innovative solutions are sought to bridge gaps in access to care.

The demographic characteristics of our participants are comparable

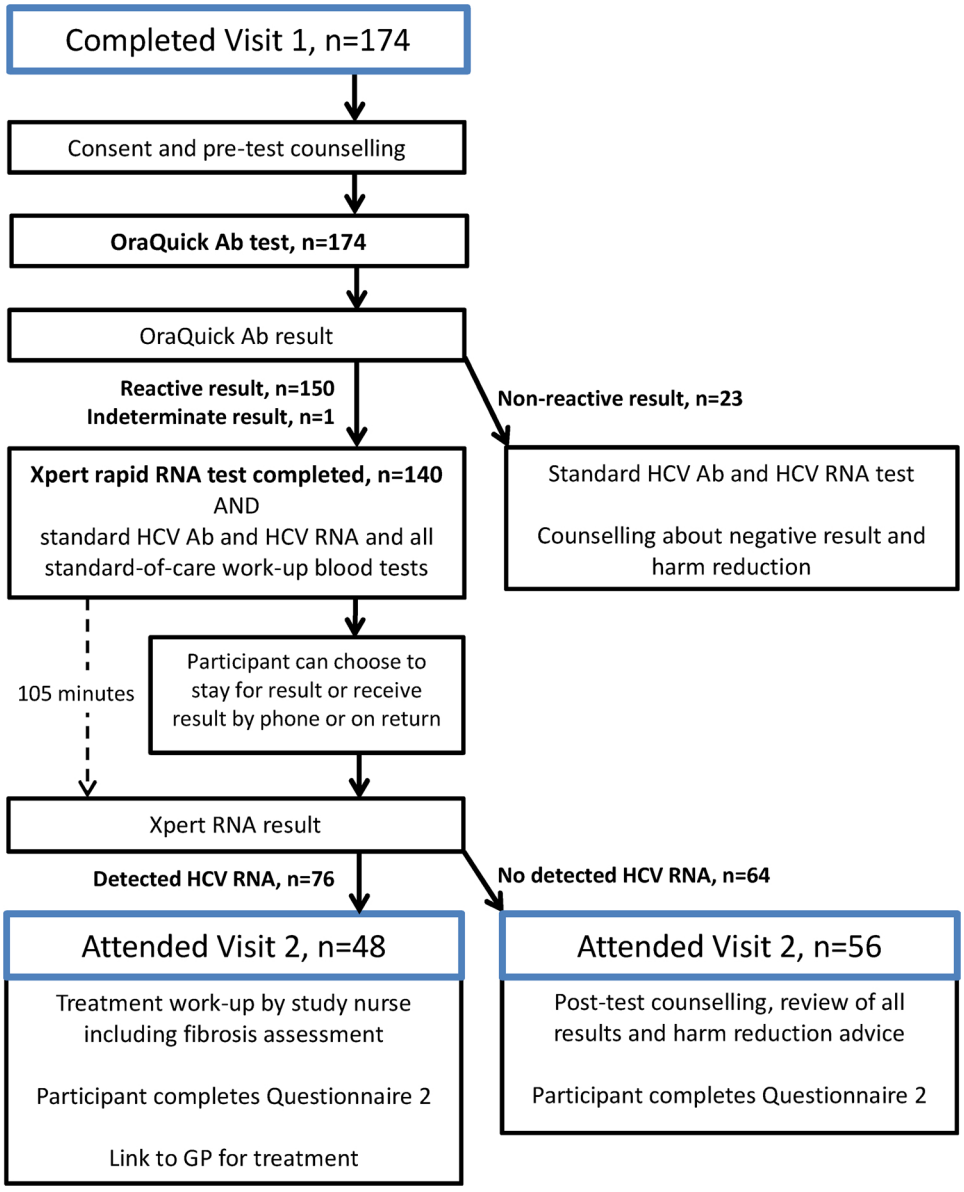

Fig. 1. Study design with participant numbers at each stage of the study.

Table 2
Point-of-care test results.

Results of point of care antibody test				
	Clinic 1 N (%) Total N = 72	Clinic 2 N (%) Total N = 52	Clinic 3 N (%) Total N = 50	Total N (%) Total N = 174
Non-reactive	12 (17)	7 (13)	4 (8)	23 (13)
Reactive	60 (83)	45 (87)	45 (90)	150 (86)
Indeterminate	0 (0)	0 (0)	1 (2)	1 (1)
Results of point-of-care RNA test after reactive point of care antibody test				
	N = 58	N = 38	N = 44	N = 140[a]
RNA Not Detected	31 (54)	14 (37)	17 (39)	62 (44)
RNA Detected	25 (43)	24 (63)	27 (61)	76 (55)
Invalid	2 (3)	0 (0)	0 (0)	2 (1)

[a] 10 participants did not have the point-of-care RNA test performed due to inability to draw blood.

to those in a national survey of people accessing NSPs (Memedovic, Iversen, Geddes, & Maher, 2017); with similar gender distribution (both approximately two thirds male), median age (41 years in our study and 42 years in the 2017 national survey), and proportion who identify as Aboriginal and/or Torres Strait Islander (19% and 18%). Our study population differed from the national survey estimates in reporting a higher lifetime history of HCV testing (97% compared to 81–88%), but lower levels of recent HCV testing in the preceding 12 months (28% compared to 55%). It should be noted that the study design meant it was not possible to collect detailed data on who declined testing.

The high proportion of anti−HCV positivity amongst our participants suggests that antibody testing may be unnecessary in high risk population groups, and that RNA testing could be conducted as the first and only test to diagnose HCV. On the other hand, the prompt results offered by the HCV antibody point-of-care tests may act as an engagement tool to incentivise testing for those who would otherwise not be tested. The 20-minute antibody test incubation period also offers an opportunity to engage clients in a conversation about HCV care and prevention. Given that very few patients waited for their point-of-care RNA test result it may be the case that combining point-of-care

Table 3
Receiving results and initial follow-up after point-of-care RNA test.

	Clinic 1 N (%) N = 58	Clinic 2 N (%) N = 38	Clinic 3 N (%) N = 44	Total N (%) N = 140
Mechanism of receiving results				
Waited on site	1 (2)	2 (5)	4 (9)	7 (5)
Returned to clinic	15 (26)	4 (11)	15 (34)	34 (24)
SMS	11 (19)	15 (39)	2 (5)	28 (20)
Phone call	21 (36)	13 (34)	20 (45)	54 (39)
Unable to contact	8 (14)	4 (11)	0 (0)	12 (9)
Missing or unclear data	2 (3)	0 (0)	3 (7)	5 (3)
Follow up attendance				
Attended follow up within study period	41 (71)	30 (79)	33 (75)	104 (74)
Median time to follow up (IQR)	10 (7 – 14)	7 (7 – 10)	20 (14 – 24)	11 days (7 – 20)
Follow up attendance (if point-of-care RNA positive)	**N = 25 (%)**	**N = 24 (%)**	**N = 27 (%)**	**N = 76 (%)**
Attended follow up within study period	16 (64)	16 (67)	16 (59)	48 (63)
Median time to follow up (IQR)	8 (7 – 13)	7 (7 – 9)	21 (17 – 22)	11 (7 – 17)

antibody testing with standard HCV RNA testing would yield similar results to those in this study. Offering a range of testing pathways may therefore satisfy the diverse needs and preferences of clients.

This study has provided valuable insights into the potential limitations of current point-of-care tests. Whilst we intended to facilitate a single-visit diagnosis, the majority of participants chose not to wait onsite for their HCV RNA result, instead electing to receive their result by phone or on return to the clinic another day. This suggests that, even though 75% of participants reported a preference for same-day results, a wait time of 105 min is too long to facilitate a single-visit diagnosis for most NSP clients. For some participants the requirement for venipuncture was a barrier with 12 (7%) unable to provide a venous blood sample. It is also possible that some clients accessing the NSP declined involvement in the study due to the requirement for venipuncture. This is consistent with existing literature reporting venipuncture as a barrier to HCV care for people who inject drugs (Clements, Grose, & Skirton, 2015; Madden, Hopwood, Neale, & Treloar, 2018). The use of finger stick samples for HCV RNA point-of-care testing has been reported elsewhere and shown to have high levels of accuracy and acceptability and these tests also have a shorter time to result of 60 min (Grebely, Lamoury et al., 2017). The impact of reducing the time to RNA result and the impact of point-of-care tests that can provide diagnosis without venipuncture warrant further investigation. The time required to obtain a diagnosis currently limits testing and treatment from happening in one visit, which may have important implications for treatment uptake (Grebely, Applegate et al., 2017). This idea is supported by the greater proportion of RNA-positive participants who were aware of their result returning for their follow-up visit compared to patients who were unaware, particularly given that phone access can be inconsistent in this population. Interestingly, a greater proportion of RNA-negative participants returned for follow-up than did RNA-positive, and there was no significant difference by awareness of result in this group. Reasons for the proportion of negative participants returning for follow-up are unclear and could include reaching a sample who are particularly concerned about their health, or the reimbursement payments incentivising return for follow-up, or other factors. This highlights the need for further work to formally evaluate the effects of different testing methods.

An important feature of this study was that testing was offered and performed at NSPs by existing NSP site staff. The use of point-of-care tests allowed the entire testing process to happen in a convenient location, designed to be welcoming to people who inject drugs, and be conducted by staff familiar to regular clients of the service, who have experience in harm prevention and the health care needs of people who inject drugs. Given that stigma and discrimination remain barriers to many people who inject drugs accessing HCV care (Jones et al., 2014; Madden et al., 2018), the experiences of discrimination reported by the participants in this study, and the strong support for NSP staff involvement, enabling testing in welcoming environments may be one of the most valuable aspects of HCV point-of-care tests.

Tests that can be performed by staff without extensive clinical training, and provided in a range of settings, including in mobile health care services, may be important for reaching those who experience the most significant barriers to accessing traditional health care services. Point-of-care tests for HIV have helped to improve access to HIV diagnosis, including amongst people who inject drugs (Thornton, Delpech, Kall, & Nardone, 2012). It should be considered how this approach compares with, or could be combined with, other approaches such as peer-led testing and peer navigation (Henderson, Madden, & Kelsall, 2017). Previous research amongst gay and bisexual men showed peer-led point-of-care testing for HIV was highly acceptable and provided valuable opportunities for health education and psychosocial support to high-risk groups (Leitinger et al., 2018). The high prevalence of HCV viraemia amongst our participants supports further exploration of interventions addressing HCV being conducted from NSPs; possibly incorporating peer workers and broader harm reduction activities.

Whilst our study focused on people who inject drugs in a metropolitan Australian setting, this model may also be applicable to reaching people with geographical or cultural barriers to treatment in other settings, particularly in lower-income countries where laboratory capacity may be limited. Point-of-care HCV antibody tests have been implemented in an range of low- and middle-income settings and shown to have high accuracy (Khuroo et al., 2015), and the Xpert HCV viral load test has shown high accuracy in the field in Cambodia (Iwamoto et al., 2019). The model we implemented is similar to that used in a primary health care clinic in Pakistan (Khalid et al., 2018), showing the potential for point-of-care testing to enable HCV treatment in a variety of settings.

Whilst the real-world environment in which our study was conducted was important to the central aim of the study (feasibility of point-of-care testing in NSP services), this contributed to limitations in data. As mentioned, the structure of the services and nature of interactions at NSPs resulted in limited data on testing uptake; as unlike the other data collected for the study, which was collected from consented participants in a private clinic room, the anonymous uptake data was recorded during brief interactions at the point of contact. Furthermore, participants began seeking out study involvement after a few weeks of implementation. This made it difficult to obtain an accurate denominator of health service clients who were offered testing and thereby estimate the overall demand for point-of-care HCV testing amongst all clients of these NSP services and identify factors that contribute to test uptake. Furthermore, the study was only conducted two to three days a week at each service due to the structure of the service, clinic space and

staff capacity. As such our sample may be biased by missing clinic attendees who did not attend on the days the study was offered.

High demand for involvement suggested acceptability of the model, and the majority of participants reported preferences for point-of-care testing and supported NSP staff involvement in testing. However, the survey format used to elicit preferences limited the detail that could be provided by respondents. To better explore nuances of preferences and acceptability, a sub-set of participants participated in interviews, the results of which are reported elsewhere (Latham et al., 2019). Our study did also not assess the costs of the intervention, which would be an important consideration for policy decisions regarding the use of point-of-care tests, in Australia and more broadly. Despite these limitations, the successful implementation of this model and the results suggest that formal evaluation of the impact of point-of-care testing for HCV targeted to people who inject drugs will be useful in guiding policy to reduce the burden of HCV

Conclusion

The Rapid-EC feasibility study demonstrates that providing HCV point-of-care testing through NSP services co-located within community healthcare clinics is feasible and involvement of NSP staff in HCV testing and the use of point-of-care tests are acceptable to people who inject drugs. Whilst many participants did not wait two hours to receive the RNA test result, point-of-care testing was effective at linking people who inject drugs into the HCV care cascade, suggesting that point-of-care tests may offer benefits beyond rapid diagnosis, such as the ability to have testing conducted by a range of people in a range of settings. This study establishes the potential for community-based point-of-care testing for HCV by NSP staff to improve engagement with people who inject drugs.

Funding

This work was supported by The Shepherd Foundation; St Vincent's Hospital Foundation; Gilead Sciences; and Cepheid, who provided in kind support. Funders had no role in the design or evaluation or this research project.

Potential conflicts of interest

The Burnet Institute, MH and JD receive funding support from Gilead Sciences, Abbvie, Merck and BMS for investigator initiated research.

JD or his institution receive consultancy funding from Gilead, Abbvie, and Merck.

AT serves as an advisory board member for Gilead, Abbvie, BMS, Merck, Eisai, Bayer, has served as speaker for Gilead, Merck, BMS, Abbvie, and received research funding from Gilead, Merck, Abbvie.

JH receives research funding from Gilead Sciences.

AP has served as a speaker for Gilead and received research funding from Gilead, MSD and Abbvie.

CRediT authorship contribution statement

Bridget Williams: Data curation, Formal analysis, Methodology, Project administration, Writing - original draft. **Jessica Howell:** Conceptualization, Funding acquisition, Methodology, Project administration, Writing - review & editing. **Joseph Doyle:** Conceptualization, Methodology, Writing - review & editing. **Alexander J. Thompson:** Conceptualization, Funding acquisition, Writing - review & editing. **Bridget Draper:** Data curation, Investigation, Project administration, Writing - review & editing. **Chloe Layton:** Investigation, Project administration. **Ned Latham:** Project administration, Writing - review & editing. **Frances Bramwell:** Investigation, Resources. **Dean Membrey:** Investigation, Resources. **Maggie Mcpherson:** Investigation, Resources. **Janine Roney:** Project administration, Writing - review & editing. **Mark Stoové:** Supervision, Writing - review & editing. **Margaret E. Hellard:** Conceptualization, Funding acquisition, Methodology, Supervision, Writing - review & editing. **Alisa Pedrana:** Conceptualization, Formal analysis, Methodology, Project administration, Supervision, Writing - review & editing.

Acknowledgements

The authors wish to acknowledge the participants of this study and staff at the study sites.

Dr Howell, Dr Pedrana, Dr Doyle, Professor Thompson, Professor Stoove and Professor Hellard all receive Australian National Health and Medical Research Council research grant support. Dr Williams receives funding from the Australian Department of Health via the Specialist Training Program. Dr Howell received funding from Gilead Sciences via the Australia Gilead Research Fellowship (2017). The authors acknowledge the contribution to this work of the Victorian Operational Infrastructure Support Program received by the Burnet Institute.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.drugpo.2019.05.012.

References

Alter, M. J. (2011). HCV routes of transmission: What goes around comes around. *Seminars in Liver Disease, 31*(4), 340–346.

Beckwith, C. G., Kurth, A. E., Bazerman, L. B., Patry, E. J., Cates, A., Tran, L., Noska, A., & Kuo, I. (2016). A pilot study of rapid hepatitis C virus testing in the Rhode island Department of Corrections. *Journal of Public Health (Oxford, England), 38*(1), 130–137.

Clements, A., Grose, J., & Skirton, H. (2015). Experiences of UK patients with hepatitis C virus infection accessing phlebotomy: A qualitative analysis. *Nursing & Health Sciences, 17*(2), 214–222.

Coats, J. T., & Dillon, J. F. (2015). The effect of introducing point-of-care or dried blood spot analysis on the uptake of hepatitis C virus testing in high-risk populations: A systematic review of the literature. *The International Journal of Drug Policy, 26*(11), 1050–1055.

Drobnik, A., Judd, C., Banach, D., Egger, J., Konty, K., & Rude, E. (2011). Public health implications of rapid hepatitis C screening with an oral swab for community-based organizations serving high-risk populations. *American Journal of Public Health, 101*(11), 2151–2155.

Easterbrook, P. J., & W. H. O. Guidelines Development Group (2016). Who to test and how to test for chronic hepatitis C infection - 2016 WHO testing guidance for low- and middle-income countries. *Journal of Hepatology, 65*(1 Suppl), S46–S66.

Grebely, J., Applegate, T. L., Cunningham, P., & Feld, J. J. (2017). Hepatitis C point-of-care diagnostics: In search of a single visit diagnosis. *Expert Review of Molecular Diagnostics, 17*(12), 1109–1115.

Grebely, J., Dore, G. J., Morin, S., Rockstroh, J. K., & Klein, M. B. (2017). Elimination of HCV as a public health concern among people who inject drugs by 2030 - What will it take to get there? *Journal of the International AIDS Society, 20*(1), 22146.

Grebely, J., Lamoury, F. M. J., Hajarizadeh, B., Mowat, Y., Marshall, A. D., Bajis, S., Marks, P., Amin, J., Smith, J., Edwards, M., Gorton, C., Ezard, N., Persing, D., Kleman, M., Cunningham, P., Catlett, B., Dore, G. J., Applegate, T. L., & Live, R. S. G. (2017). Evaluation of the Xpert HCV Viral Load point-of-care assay from venepuncture-collected and finger-stick capillary whole-blood samples: A cohort study. *The Lancet Gastroenterology & Hepatology, 2*(7), 514–520.

Gupta, E., Agarwala, P., Kumar, G., Maiwall, R., & Sarin, S. K. (2017). Point -of -care testing (POCT) in molecular diagnostics: Performance evaluation of GeneXpert HCV RNA test in diagnosing and monitoring of HCV infection. *Journal of Clinical Virology : the Official Publication of the Pan American Society for Clinical Virology, 88*, 46–51.

Hellard, M., Scott, N., Sacks-Davis, R., & Pedrana, A. (2018). Achieving hepatitis C elimination in Europe - to treatment scale-up and beyond. *Journal of Hepatology, 68*(3), 383–385.

Henderson, C., Madden, A., & Kelsall, J. (2017). 'Beyond the willing & the waiting' - the role of peer-based approaches in hepatitis C diagnosis & treatment. *The International Journal of Drug Policy, 50*, 111–115.

Hepatitis C Virus Infection Consensus Statement Working Group (2018). *Australian Recommendations for the Management of hepatitis C virus infection; a consensus statement.* Gastroenterological Society of Australia.

Islam, M. M., Topp, L., Day, C. A., Dawson, A., & Conigrave, K. M. (2012). The accessibility, acceptability, health impact and cost implications of primary healthcare outlets that target injecting drug users: A narrative synthesis of literature. *The International Journal of Drug Policy, 23*(2), 94–102.

Islam, M. M., Topp, L., Iversen, J., Day, C., Conigrave, K. M., & Maher, L. (2013).

Healthcare utilisation and disclosure of injecting drug use among clients of Australia's needle and syringe programs. *Australian and New Zealand Journal of Public Health, 37*(2), 148–154.

Iversen, J., Grebely, J., Catlett, B., Cunningham, P., Dore, G. J., & Maher, L. (2017). Estimating the cascade of hepatitis C testing, care and treatment among people who inject drugs in Australia. *The International Journal of Drug Policy, 47*, 77–85.

Iwamoto, M., Calzia, A., Dublineau, A., Rouet, F., Nouhin, J., Yann, S., Pin, S., Sun, C., Sann, K., Dimanche, C., Lastrucci, C., Coulborn, R. M., Maman, D., Dousset, J. P., & Loarec, A. (2019). Field evaluation of GeneXpert((R)) (Cepheid) HCV performance for RNA quantification in a genotype 1 and 6 predominant patient population in Cambodia. *Journal of Viral Hepatitis, 26*(1), 38–47. https://doi.org/10.1111/jvh.13002.

Janjua, N. Z., Kuo, M., Yu, A., Alvarez, M., Wong, S., Cook, D., Wong, J., Grebely, J., Butt, Z. A., Samji, H., Ramji, A., Tyndall, M., & Krajden, M. (2016). The Population Level Cascade of Care for Hepatitis C in British Columbia, Canada: The BC Hepatitis Testers Cohort (BC-HTC). *EBioMedicine, 12*, 189–195.

Jewett, A., Al-Tayyib, A. A., Ginnett, L., & Smith, B. D. (2013). Successful integration of hepatitis C virus point-of-Care tests into the denver metro health clinic. *AIDS Research and Treatment, 2013*, 528904.

Jewett, A., Smith, B. D., Garfein, R. S., Cuevas-Mota, J., Teshale, E. H., & Weinbaum, C. M. (2012). Field-based performance of three pre-market rapid hepatitis C virus antibody assays in STAHR (Study to Assess Hepatitis C Risk) among young adults who inject drugs in San Diego, CA. *Journal of Clinical Virology : the Official Publication of the Pan American Society for Clinical Virology, 54*(3), 213–217.

Jones, L., Atkinson, A., Bates, G., McCoy, E., Porcellato, L., Beynon, C., McVeigh, J., & Bellis, M. A. (2014). Views and experiences of hepatitis C testing and diagnosis among people who inject drugs: Systematic review of qualitative research. *The International Journal of Drug Policy, 25*(2), 204–211.

Khalid, G. G., Kyaw, K. W. Y., Bousquet, C., Auat, R., Donchuk, D., Trickey, A., Hamid, S., Qureshi, H., Mazzeo, V., Aslam, K., Khowaja, S., & Van den Bergh, R. (2018). From risk to care: The hepatitis C screening and diagnostic cascade in a primary health care clinic in Karachi, Pakistan-a cohort study. *International Health*. https://doi.org/10.1093/inthealth/ihy096.

Khuroo, M. S., Khuroo, N. S., & Khuroo, M. S. (2015). Diagnostic accuracy of point-of-care tests for hepatitis C virus infection: A systematic review and meta-analysis. *PloS One, 10*(3), e0121450.

Kirby Institute (2017). *HIV, viral hepatitis and sexually transmissable infections in Australia: Annual surveillance report 2017*Sydney: Kirby Institute.

Kirby Institute (2018). *HIV, viral hepatitis and sexually transmissible infections in Australia: Annual surveillance report 2018*Sydney: Kirby Institute.

Latham, N. H., Pedrana, A., Doyle, J. S., Howell, J., Williams, B., Higgs, P., Thompson, A., & Hellard, M. E. (2019). Community-based, point-of-care hepatitis C testing: Perspectives and preferences of people who inject drugs. *Journal of Viral Hepatitis*. https://doi.org/10.1111/jvh.13087.

Leitinger, D., Ryan, K. E., Brown, G., Pedrana, A., Wilkinson, A. L., Ryan, C., Hellard, M., & Stoove, M. (2018). Acceptability and HIV Prevention Benefits of a Peer-Based Model of Rapid Point of Care HIV Testing for Australian Gay, Bisexual and Other Men Who Have Sex with Men. *AIDS and Behavior, 22*(1), 178–189.

Madden, A., Hopwood, M., Neale, J., & Treloar, C. (2018). Beyond interferon side effects: What residual barriers exist to DAA hepatitis C treatment for people who inject drugs? *PloS One, 13*(11), e0207226.

McHugh, M. P., Wu, A. H. B., Chevaliez, S., Pawlotsky, J. M., Hallin, M., & Templeton, K. E. (2017). Multicenter evaluation of the cepheid xpert hepatitis C virus viral load assay. *Journal of Clinical Microbiology, 55*(5), 1550–1556.

Memedovic, S., Iversen, J., Geddes, L., & Maher, L. (2017). *Australian needle syringe program survey national data report 2012-2016: Prevalence of HIV, HCV and injecting and sexual behaviour among NSP attendees*Sydney: Kirby Institute.

Morano, J. P., Zelenev, A., Lombard, A., Marcus, R., Gibson, B. A., & Altice, F. L. (2014). Strategies for hepatitis C testing and linkage to care for vulnerable populations: Point-of-care and standard HCV testing in a mobile medical clinic. *Journal of Community Health, 39*(5), 922–934.

Neale, J., Tompkins, C., & Sheard, L. (2008). Barriers to accessing generic health and social care services: A qualitative study of injecting drug users. *Health & Social Care in the Community, 16*(2), 147–154.

Pedrana, A. E., Sacks-Davis, R., Doyle, J. S., & Hellard, M. E. (2017). Pathways to the elimination of hepatitis C: Prioritising access for all. *Expert Review of Clinical Pharmacology, 10*(10), 1023–1026.

Polaris Observatory HCV Collaborators (2017). Global prevalence and genotype distribution of hepatitis C virus infection in 2015: A modelling study. *The Lancet Gastroenterology & Hepatology, 2*(3), 161–176.

Scott, N., Doyle, J. S., Wilson, D. P., Wade, A., Howell, J., Pedrana, A., Thompson, A., & Hellard, M. E. (2017). Reaching hepatitis C virus elimination targets requires health system interventions to enhance the care cascade. *The International Journal of Drug Policy, 47*, 107–116.

Shivkumar, S., Peeling, R., Jafari, Y., Joseph, L., & Pant Pai, N. (2012). Accuracy of rapid and point-of-care screening tests for hepatitis C: A systematic review and meta-analysis. *Annals of Internal Medicine, 157*(8), 558–566.

Smith, B. D., Teshale, E., Jewett, A., Weinbaum, C. M., Neaigus, A., Hagan, H., Jenness, S. M., Melville, S. K., Burt, R., Thiede, H., Al-Tayyib, A., Pannala, P. R., Miles, I. W., Oster, A. M., Smith, A., Finlayson, T., Bowles, K. E., & Dinenno, E. A. (2011). Performance of premarket rapid hepatitis C virus antibody assays in 4 national human immunodeficiency virus behavioral surveillance system sites. *Clinical Infectious Diseases : an Official Publication of the Infectious Diseases Society of America, 53*(8), 780–786.

Taherkhani, R., & Farshadpour, F. (2017). Global elimination of hepatitis C virus infection: Progresses and the remaining challenges. *World Journal of Hepatology, 9*(33), 1239–1252.

Thornton, A. C., Delpech, V., Kall, M. M., & Nardone, A. (2012). HIV testing in community settings in resource-rich countries: A systematic review of the evidence. *HIV Medicine, 13*(7), 416–426. https://doi.org/10.1111/j.1468-1293.2012.00992.x.

World Health Organization (2016). *Global health sector strategy on viral hepatitis 2016-2021*. Geneva: World Health Organization.

World Health Organization (2017). *Global hepatitis report 2017*Geneva: World Health Organization.

Yehia, B. R., Schranz, A. J., Umscheid, C. A., & Lo Re, V., 3rd (2014). The treatment cascade for chronic hepatitis C virus infection in the United States: A systematic review and meta-analysis. *PloS One, 9*(7), e101554.