The National Australian HCV Point-of-Care Testing Program: An observational cohort study to evaluate the use of finger-stick point-of-care hepatitis C testing to enhance diagnosis and treatment of HCV infection – HCV antibody testing minimal dataset

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Protocol Synopsis

Title	**The National Australian HCV Point-of-Care Testing Program: An observational cohort study to evaluate the use of finger-stick point-of-care HCV testing to enhance diagnosis and treatment of HCV infection – HCV antibody testing minimal dataset**
Protocol registration no.	NCT05713136
Background and rationale	The advent of simple direct-acting antiviral hepatitis C (HCV) therapies with cure rates >95% is one of the greatest medical advances in decades, having led to a reversal in liver-related mortality. In Australia, treatment uptake has declined between 2016 (32,000 treated) and 2019/20 (2019: 11,500; 2020: 8,500).[1] Progress towards HCV elimination has been impeded by COVID-19, affecting the delivery of national and state-based HCV strategies. Improving HCV treatment uptake to reduce disease burden is a key aim of global, national and state-based HCV strategies.[2-4] Scale-up of HCV testing and treatment will be required to achieve elimination by 2030. Increasing HCV testing is hampered by diagnostic pathways requiring multiple visits and loss to follow-up, amplified in key populations, such as people who inject drugs. In Australia, 81% of people have had HCV antibody testing (indicates exposure), but only 47% have been HCV RNA tested (indicates active infection and the need for HCV treatment).[5] Mathematical modelling suggests that HCV RNA testing needs to increase by at least 50% annually to achieve elimination in Australia by 2030.[6] The approval of the Xpert® HCV Viral Load Fingerstick test for detection of active HCV infection in one hour at the point-of-care by the Therapeutic Goods Administration is a 'game-changer'. This HCV point-of-care test enables diagnosis and treatment in a single-visit, increases testing acceptability, and reduces loss to follow-up, addressing the drop-off in the HCV care cascade. The Kirby Institute is an international leader in research evaluating the Xpert HCV assay *(Grebely Lancet Gastro Hep 2017)*, having built a large network of Xpert platforms for HCV testing in needle and syringe programs, prisons, drug treatment clinics, tertiary hospitals,

	and Aboriginal Community Controlled Health Service. In Kirby-led research, point-of-care HCV testing interventions in needle and syringe programs and prisons have resulted in high HCV treatment uptake (70-90%). The Kirby Institute and Flinders University will establish the Australian National HCV Point-of-care Testing Program for the scale-up of point-of-care HCV RNA testing in services with high prevalence of HCV infection, including community health centres, drug treatment clinics, needle and syringe programs, and prisons. This program will include the development of standard operating procedures, logistics/deployment, initial set-up, an operator training program, and quality assurance and competency assessment program. In settings with lower HCV antibody prevalence, immediate point-of-care HCV RNA testing may not be cost-effective ($60/test), and a screening strategy using a point-of-care HCV antibody test (approximately $10/test) followed by a HCV RNA test in people who are HCV antibody positive may be more cost-effective and time efficient. However, although there are HCV antibody tests available for use in Australia, there are none currently approved by the Therapeutics Goods Administration. It is critical to evaluate the cost and time effectiveness of different testing strategies to optimise testing and government funding and to inform clinical utility. Understanding and addressing implementation challenges is critical to rapidly translate HCV point-of-care testing into practice and policy. This protocol describes an observational cohort study that will be established to evaluate initial point-of-care antibody testing before reflex HCV RNA testing. There are currently no TGA approved HCV antibody tests, so testing can only be evaluated within a research study with appropriate informed consent. An evaluation of the HCV treatment uptake following scale-up of point-of-care HCV antibody testing followed by HCV RNA testing is therefore needed.
Study objectives	**Primary Objective** To evaluate the proportion of HCV infected (HCV RNA quantifiable) participants who initiate HCV treatment at 12 weeks following HCV RNA testing.

	Secondary Objectives 1. To evaluate the proportion of people who accept point-of-care testing among those offered testing. 2. To evaluate the prevalence of current HCV infection (HCV RNA quantifiable) among people tested. 3. To evaluate the HCV antibody prevalence among people tested. 4. To evaluate the time to treatment uptake among people receiving point-of-care HCV antibody testing with reflex HCV RNA testing in those who are HCV antibody detectable who received HCV treatment; 5. To evaluate the proportion of HCV RNA positive participants who initiate HCV treatment at 12 months (52 weeks) following HCV RNA testing. 6. To evaluate the proportion of participants who complete HCV direct-acting antiviral (DAA) treatment following point-of-care HCV antibody testing with reflex HCV RNA testing in those who are HCV antibody detectable who received HCV treatment; 7. To evaluate the proportion of participants who achieve an SVR (defined as HCV RNA below the lower limit of quantitation at post treatment week 12) following point-of-care HCV antibody testing with reflex HCV RNA testing in those who are HCV antibody detectable who received HCV treatment. 8. To evaluate the proportion of participants who are HCV RNA negative at 12 months (52 weeks) following HCV RNA testing. 9. To evaluate the cost-effectiveness of this testing strategy.
Participant population	Participants will be included from settings that provide services to people with a risk factor for the acquisition of HCV infection, including drug treatment clinics, needle and syringe programs, prisons, mobile outreach services, community health services, mental health services, homelessness services, and other appropriate settings nationally. It is anticipated that approximately 100,000 participants will be screened for HCV infection using point-of-care HCV testing. ***Inclusion criteria***

	Participants are eligible for inclusion if the following criteria are met: a. Provide informed consent b. ≥ 18 years of age. ***Exclusion criteria*** a. Is unable or unwilling to provide informed consent
Study design	This is an observational cohort study. Participants will attend a single visit where they will provide informed consent and receive point-of-care HCV testing. All other study procedures will comprise data collection only.
Treatment of participants	No treatment will be prescribed as a part of this study. Participants who are HCV RNA detectable will be linked to standard of care for any other clinical assessments and treatment initiation.
Study procedures	All participants receiving HCV testing at sites participating in this study, and who meet the study criteria will be identified and offered participation in the study. Participants will undergo verbal or written informed consent followed by HCV point-of-care testing. As this is an observational cohort study, further study procedures will comprise data collection only. For participants who have previously been told they have HCV infection, or for people who have previously received HCV treatment, testing will be performed using point-of-care HCV RNA testing via Xpert HCV Viral Load Fingerstick assay using the GeneXpert machine (results in one hour). For all other participants who have not previously been told they have HCV infection nor have previously received HCV treatment, testing will be performed using point-of-care HCV antibody testing. If the result is HCV antibody positive, individuals will undergo reflex HCV RNA testing. Participants will not receive treatment as a part of this study. Participants who are HCV RNA positive will be linked to standard of care for any other clinical assessments and treatment initiation.

Statistics	**Primary outcome** The proportion of HCV RNA detectable participants who initiate HCV treatment within 12 weeks of HCV RNA testing. **Sample size** Overall, 100,000 point-of-care HCV tests will be performed in different settings as part of the Australian National HCV Point-of-care Testing Program. It is estimated that the HCV prevalence will be 10% (n=10,000 people who are HCV RNA detectable) and the treatment uptake following testing will be 65% (n=6,500). Under these assumptions, the 95% confidence intervals around the estimate for HCV treatment uptake will be 64.1%-65.9% and for HCV RNA prevalence will be 9.8 %-10.2%. For analyses evaluating factors associated with HCV treatment uptake, we will have 90% power to detect an odds ratio of 1.15 or greater (alpha=0.05) for a variable that is 50% prevalent (i.e. recent injecting drug use). Analysis will follow the STROBE guidelines for observational studies. The analysis of the primary outcome will occur when all patients have completed 12 weeks of follow-up (from enrolment) or have been permanently lost to follow-up. Participant flow will be summarised, showing the numbers of participants included.

1. Background and rationale

In Australia, hepatitis C virus (HCV)-related morbidity and mortality have doubled in the past decade, with health care costs of $220 million per annum.[1] In 2019, 128,000 Australians were living with HCV infection.[2] The majority of new (90%) and existing (80%) cases of HCV infection in Australia occur among people who inject drugs (PWID).[1,2]

The advent of simple direct-acting antiviral (DAA) HCV therapies with cure rates >95% is one of the greatest medical advances in decades, having led to a reversal in liver-related mortality.[11] In Australia, treatment uptake has declined between 2016 (32,000 treated) and 2019/20 (2019: 11,500; 2020: 8,500).[1] Progress towards HCV elimination has been impeded by COVID-19, affecting the delivery of national and state-based HCV strategies. Improving HCV treatment uptake to reduce disease burden is a key aim of global, national and state-based HCV strategies.[2-4]

Globally, HCV testing and diagnosis remains low.[4] Testing pathways involve an HCV antibody test to confirm exposure and an HCV RNA test to detect active infection. This two-step pathway requires up to 5 visits to practitioners and off-site phlebotomists, leading to a drop-off in the diagnosis of active infection.[2] In Australia, 81% of people have had HCV antibody testing (indicates exposure), but only 47% have been HCV RNA tested (indicates active infection and the need for HCV treatment).[5] Mathematical modelling suggests that HCV RNA testing needs to increase by at least 50% annually to achieve elimination in Australia by 2030.[6]

Point-of-care HCV testing increases linkage to care.[7] Our group led the first evaluation of a point-of-care HCV RNA assay[8,9], the Xpert HCV Viral Load Fingerstick point-of-care test, enabling same-day diagnosis of active infection in one hour (sensitivity and specificity, 100%) at the point-of-care, enabling diagnosis and treatment in a single visit, improving treatment uptake.[9] This research facilitated the recent approval of the assay by the Therapeutics Good Administration (TGA), providing an unprecedented opportunity to scale-up HCV testing and treatment. Scale-up of HCV testing will be most impactful in settings with high HCV prevalence (e.g. those providing care for people who inject drugs), including prisons, drug treatment clinics, and needle and syringe programs. Point-of-care HCV RNA testing can also be combined with outreach models and mobile clinics to provide access to testing and treatment to those who may not have been tested or treated to date. The next step is to translate this novel discovery into routine clinical practice to scale-up testing and treatment to facilitate HCV elimination.

The Kirby Institute is an international leader in research evaluating the Xpert HCV assay, having built a large network of Xpert platforms for HCV testing in needle and syringe programs, prisons, drug treatment clinics, tertiary hospitals, and Aboriginal Community Controlled Health Services. In Kirby-led research, point-of-care HCV testing interventions in needle and syringe programs and prisons have resulted in high HCV treatment uptake (75-90%). The Kirby Institute and Flinders

University also have a strong track record of implementing point-of-care testing for STIs and COVID-19, providing an ideal foundation to scale-up point-of-care HCV testing in Australia.

The Kirby Institute and Flinders University will establish the Australian National HCV Point-of-care Testing Program for the scale-up of point-of-care HCV testing in services caring for people with risk factors for the acquisition of HCV infection (e.g. drug treatment clinics, needle and syringe programs, prisons, mobile outreach services, community health services, mental health services, and homelessness services).

In settings with lower HCV antibody prevalence, immediate point-of-care HCV RNA testing may not be cost-effective ($60/test), and a screening strategy using a point-of-care HCV antibody test (approximately $10/test) followed by a HCV RNA test in people who are HCV antibody positive may be more acceptable to clients and service providers given a quicker turnaround time for an HCV antibody detectable result. However, although there are HCV antibody tests available for use in Australia, there are none currently approved by the Therapeutics Goods Administration. Therefore, testing can only be evaluated within a research study with appropriate informed consent. It is critical to evaluate the cost and time effectiveness of different testing strategies to optimise testing and government funding and to inform clinical utility.

This protocol describes an observational cohort study that will be established to evaluate HCV treatment uptake following scale-up of point-of-care HCV antibody testing followed by HCV RNA testing. This information will provide critical information on the effectiveness of this testing strategy to enhance HCV treatment.

2. Hypotheses

Primary Hypothesis

An intervention integrating HCV RNA testing (predominantly through point-of-care testing) will lead to a high uptake of HCV treatment (>65%) among people at increased risk for HCV infection.

3. Study objectives

Primary Objective

To evaluate the proportion of HCV infected (HCV RNA quantifiable) participants who initiate HCV treatment at 12 weeks following HCV RNA testing.

Secondary Objectives

1. To evaluate the proportion of people who accept point-of-care testing among those offered testing.
2. To evaluate the prevalence of current HCV infection (HCV RNA quantifiable) among people tested.

3. To evaluate the HCV antibody prevalence among people tested.
4. To evaluate the time to treatment uptake among people receiving point-of-care HCV antibody testing with reflex HCV RNA testing in those who are HCV antibody detectable who received HCV treatment;
5. To evaluate the proportion of HCV RNA positive participants who initiate HCV treatment at 12 months (52 weeks) following HCV RNA testing.
6. To evaluate the proportion of participants who complete HCV direct-acting antiviral (DAA) treatment following point-of-care HCV antibody testing with reflex HCV RNA testing in those who are HCV antibody detectable who received HCV treatment;
7. To evaluate the proportion of participants who achieve an SVR (defined as HCV RNA below the lower limit of quantitation at post treatment week 12) following point-of-care HCV antibody testing with reflex HCV RNA testing in those who are HCV antibody detectable who received HCV treatment.
8. To evaluate the proportion of participants who are HCV RNA negative at 12 months (52 weeks) following HCV RNA testing.
9. To evaluate the cost-effectiveness of this testing strategy.

4. Participant population

Participants will be included from settings that provide services to people with a risk factor for the acquisition of HCV infection, including drug treatment clinics, needle and syringe programs, prisons, mobile outreach services, community health services, mental health services, homelessness services, and other appropriate settings nationally. It is anticipated approximately 100,000 participants will be screened for HCV infection using point-of-care HCV testing.

Inclusion criteria

Participants are eligible for inclusion if the following criteria are met:

a. Provide informed consent
b. ≥ 18 years of age.

Exclusion criteria

b. Is unable or unwilling to provide informed consent

5. Study design

This is an observational cohort study. Participants will attend a single visit where they will provide informed consent and receive point-of-care HCV testing. All other study procedures will comprise data collection only.

Participants will be offered treatment as standard of care. Participants who are HCV RNA detectable will also be linked to standard of care for any other clinical assessments and treatment

initiation, and local health staff may provide counselling and medical advice for these tests, and link participants with support services available in their state or territory.
Participants who return to the same site at a later date and require further HCV testing (as standard practice or due to a risk factor) can do so through the study without having to consent and enrol again. There is no time restrictions for when participants can receive another test, this is dependent on the individual case.

6. Treatment of participants

No treatment will be prescribed as a part of this study.

7. Study procedures

7.1 Visits and Procedures

All participants receiving HCV testing at the participating sites will be identified. Site staff will discuss the research study will participants, and written or verbal consent will be obtained. If written consent, the participant will date and sign the participant information sheet and consent form together with the data and signature of the person conducting the consent discussion. If verbal consent is utilised the person conducting the consent will sign the verbal consent form to confirm that the study has been explained to the participant and consent has been given. A copy of the signed participant information and consent form will then be offered to the participant. Participants will then undergo HCV point-of-care testing. Further study procedures will comprise data collection at Week 12 and Week 52 only.

For participants who have previously been told they have HCV infection, or for people who have previously received HCV treatment, testing will be performed using point-of-care HCV RNA testing via Xpert HCV Viral Load Fingerstick assay using the GeneXpert machine (results in one hour). For all other participants who have not previously been told they have HCV infection nor have previously received HCV treatment, testing will be performed using point-of-care HCV antibody testing (results within 20 minutes). If the result is HCV antibody positive, individuals will undergo reflex HCV RNA testing. Where possible, the HCV RNA test will be performed via Xpert HCV Viral Load Fingerstick assay using the GeneXpert machine. If not available, HCV RNA testing will be performed via other standard of care methods.

If the HCV antibody test result is negative, but site staff suspect a recent infection and deem an HCV RNA test clinically relevant, they may proceed with conducting the HCV RNA test.

The following participant information will be collected as part of this study, from the participating sites existing medical records available at the site, by site staff:

- Name code
- Aboriginal and Torres Strait Islander status
- Gender

- Age
- Medical Record Number (optional)
- HCV testing and status
- Post code (optional)
- Previous HCV status and treatment (optional)
- Known history of injecting drug use (optional)
- Collection of other potential risk factors (optional)
- Currently receiving opioid agonist therapy (optional)

Additional data collection for HCV RNA positive patients only (if available):

- HIV testing and status
- HBV testing and status
- HCV treatment regimen prescribed
- HCV prescription date
- HCV treatment proposed duration
- HCV treatment start and end date
- Treatment completion (including reasons for not completing treatment)
- Treatment outcome (including reasons for not responding to treatment)

Additionally, a record of the overall number of patients who declined a point-of-care HCV test will be obtained from sites that record this data.

Assessment / Procedure	**HCV Testing**	**Data Review* (Week 12)**	**Data Review* (Week 52)**
Provide informed consent	X		
Basic demographics	X		
Finger-stick point-of-care HCV testing	X		
Treatment uptake		X	X
Treatment outcome		X	X
HCV RNA status			X
HIV/HBV testing and status			X

*Data review of medical records for patients who are HCV RNA detectable only

7.2 Study case report forms (CRFs)

Electronic case report forms will be completed for each participant to capture study specific information. Data will be collected through electronic case report forms designed for this study and through secure IT/connectivity solutions designed for the transmission of testing results.

7.3 Process evaluation

Process outcomes will be tracked via our central point-of-care test database that captures deidentified individual patient and quality management electronic test results from the GeneXpert platform (includes valid/invalid results). Using connectivity software, data are captured in real-time, cleaned and analysed to generate process outcomes, displayed on our internal dashboard, and available for real-time reporting. We will evaluate the proportion of tests with an invalid/error/no result (usually <5% but an important indicator of problems with point-of-care testing procedures and prompt review of training). We record the numbers of staff trained (initial and refresher courses), and frequency/outcomes of quality assurance/competency testing.

8. Statistics

8.1 Primary outcome

The proportion of HCV RNA detectable participants who initiate HCV treatment within 12 weeks of HCV RNA testing.

8.2 Sample size

Overall, 100,000 point-of-care HCV tests will be performed in different settings as part of the National Australian HCV Point-of-care Testing Program. It is estimated that the HCV prevalence will be 10% (n=10,000 people who are HCV RNA detectable) and the treatment uptake following testing will be 65% (n=6,500). Under these assumptions, the 95% confidence intervals around the estimate for HCV treatment uptake will be 64.1%-65.9% and for HCV RNA prevalence will be 9.8%-10.2%. For analyses evaluating factors associated with HCV treatment uptake, we will have 90% power to detect an odds ratio of 1.15 or greater (alpha=0.05) for a variable that is 50% prevalent (i.e. recent injecting drug use).

Analysis will follow the STROBE guidelines for observational studies. The analysis of the primary outcome will occur when all patients have completed 12 weeks of follow-up (from enrolment) or have been permanently lost to follow-up. Participant flow will be summarised, showing the numbers of participants included. The primary endpoint will be the proportion of participants who initiate HCV treatment within 12 weeks of HCV RNA testing. The secondary endpoints will be:

- Proportion of people who accept point-of-care testing among those offered testing.
- Proportion of people who are HCV RNA detectable among people tested.
- Time to HCV treatment uptake following finger-stick point-of-care HCV antibody testing with reflex HCV RNA testing among people who receive treatment.

- Proportion of HCV RNA detectable participants who initiate HCV DAA treatment at 12 months (52 weeks) following enrolment.
- Proportion of participants who complete HCV direct-acting antiviral (DAA) treatment.
- Proportion of participants who achieve an SVR (defined as HCV RNA below the lower limit of quantitation at post treatment week 12).
- To evaluate the proportion of HCV RNA detectable participants who are HCV RNA negative at 12 months (52 weeks) following finger-stick point-of-care HCV antibody testing with reflex HCV RNA testing.
- Cost-effectiveness of different testing strategies.

Participant characteristics at baseline will be summarised. Factors hypothesised to be associated with treatment initiation within 12 weeks of testing will be determined *a priori* and will include age, gender, Aboriginal and Torres Strait Islander status, and geography. Logistic regression will be used to assess factors associated with treatment initiation. Secondary analyses will be performed on these outcomes with stratified analyses performed where possible.

A detailed statistical analysis plan will be developed towards completion of the study, and prior to analyses being performed.

9. Data collection, source documents and record retention

The Principal Investigator and the institution where the study will be conducted will permit study-related monitoring, audits and ethics committee review providing direct access to source documents. Flinders University, NSW Pathology (NSW study sites) and Cepheid may also request to conduct an audit or inspection at sites. Prior to this they would seek permission from the site to access study related records physically at site.

Data will be collected on study specific electronic or paper copy case record forms. The Principal Investigator is responsible for ensuring the data collected are complete, accurate and recorded in a timely manner.

Data will be collected in a de-identified format and submitted to the Kirby. All data will be stored in the secure study database, RedCap, and will be kept on a secure password protected server hosted by UNSW Sydney, until its destruction. Only approved site staff and study staff, will have access to this data. Site staff will be responsible for collecting and entering the data for their site, and will only have access to the study data collected at their own site.

De-identified data collected from this research project may be used in future research projects following separate review and approval from a Human Research Ethics Committee (HREC).

The informed consent forms will be stored at site level according to the site's local process, and in accordance with ICH-GCP guidelines. Archiving and subsequent secure destruction of the informed consent forms and other study specific documents at site level are the responsibility of the Principal Investigator. When the period for archiving has elapsed, sites will be notified by the Sponsor, UNSW Sydney, to securely destroy the documents in accordance with ICH-GCP guidelines.

10.1 Submission of data

Electronic CRFs: Following each participant HCV test or medical record review, the designated site staff will complete the visit specific CRF. Once all required information is received the CRF shall be considered complete. Project Team staff will then monitor the data for completeness and accuracy. Any CRF discrepancies, either manual or automatic, will be addressed with the site staff for clarification.

The site Principal Investigator is responsible for ensuring the completion of accurate source documentation to support data collected on case report forms.

It is not acceptable for the CRF to be the only record of study participation and progress must also be recorded in each participant's medical record. This is to ensure that anyone accessing the medical record has adequate knowledge that the participant is a clinical trial participant.

Any document that acts as a source document (the point of the initial recording of a piece of data) should have evidence of who the person recording or reviewing the data is. Persons completing the source documents must be listed as a site staff member.

The sponsor's monitor might visit sites to conduct monitoring. Flinders and/or Cepheid may also visit the sites to access study related documents.

The Principal Investigator is responsible for retaining all essential documents listed in ICH Good Clinical Practice guidelines. These must be organised in a comprehensive filing system that is accessible to study monitors and other relevant personnel.

10.2 Archiving

The Principal Investigator is responsible for ensuring all study documents are retained for a minimum of 7 years or as per local site guidelines, whichever is longer, following completion and publication of the study.

11. Ethics committee/regulatory approval

The sponsor is responsible for ensuring regulatory approval for the study is obtained where required.

The site Principal Investigator is responsible for obtaining IRB/EC approval for the protocol in compliance with local regulatory requirements prior to entering any participant into the study. The approval letter/document must clearly identify the protocol and all documents approved by the IRB/IEC including version number & date of the protocol. A copy of the approval document must be sent to the study sponsor.

The site Principal Investigator must also obtain approval for any amendments to the protocol. The Principal Investigator must comply with all IRB/IEC reporting requirements for all adverse events, annual updates and end of study reports and must agree to abide by any IRB/IEC conditions of approval.

The site Principal Investigator (or designee) is responsible for ensuring freely-given consent is obtained from each potential participant prior to the conduct of any protocol-specific procedures. The Principal Investigator may delegate the task of obtaining consent to appropriately qualified Sub-investigator(s).

Consent for this study will occur either via hardcopy or verbal consent, depending on the site/participant preference. If hardcopy, the participant will date and sign the participant information and consent form together with the date and signature of the person conducting the consent discussion. If verbal consent is utilised the person conducting the consent will sign the verbal consent form to confirm that the study has been explained to the participant and consent has been given.

For hardcopy consent, if the participant is illiterate, an impartial witness should be present during the entire consent discussion. Once the discussion is complete, the participant must sign and date the informed consent form, if capable. The impartial witness must also sign and date the consent form along with the person who conducted the consent discussion.

A copy of the participant information and consent form will be offered to the participant, either hardcopy or electronic copy (via email or SMS) to keep. The participant must be informed in a timely manner of any new information that becomes available during the course of the study that may affect their willingness to continue study participation.

This study shall be conducted in accordance with the ethical principles laid out in the Declaration of Helsinki (most current issued version) and the National Statement on Ethical Conduct in Research Involving Humans (most current issued version).

12. Confidentiality of data

By signing the Clinical Trial Agreement, the site Principal Investigator affirms to the sponsor that information provided to them by the sponsor will be maintained in confidence and divulged only as necessary to the ethics committee and institution employees directly involved in the study. Both ethics committee members and employees must also understand the confidentiality requirements for any information divulged to them. The data generated by this study will be considered confidential, except where it is included in a publication as agreed in the publication policy of this protocol.

All patient data will be stored in a de-identified form and individuals will only be identified by a study number and age. Data will be stored in a secure location for a minimum of 7 years, or as per local site guidelines, whichever is longer.

Data confidentiality will be maintained at all times and no documents containing the participating institution's name or other identifying information will be made publicly available.

13. Governance

The study is sponsored by UNSW and coordinated through the Kirby Institute. It is funded by the Commonwealth Government, the National Health and Medical Research Council, and NSW Health. The Kirby Institute has established governance and implementation structures which use resources efficiently to deliver program objectives on schedule.

14. Quality Control (QC) and Quality Assurance (QA)

The sponsor agrees to be responsible for implementing and maintaining quality control and quality assurance systems with written standard operating procedures to ensure the study is conducted and data are generated, documented and reported in compliance with the protocol, Good Clinical Practice standards and all applicable local laws and regulations relating to the conduct of a clinical trial.

15. Publication Policy

The results of this study may be published and presented at scientific meetings. Publication of data derived from this protocol will be governed by the Project Team. All published data will be non-identifiable group data.

17. List of References

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8. Grebely J, Lamoury FMJ, Hajarizadeh B, et al. Evaluation of the Xpert HCV Viral Load point-of-care assay from venepuncture-collected and finger-stick capillary whole-blood samples: a cohort study. Lancet Gastroenterol Hepatol 2017; 2(7): 514-20.
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18. Abbreviations List

CRF	Case Report Form
DAA	Direct Acting Antiviral
HCV	Hepatitis C Virus
IRB	Institutional Review Board (Human Research Ethics Committee)
PWID	People Who Inject Drugs
POCT	Point of Care Testing
RNA	Ribonucleic Acid

19. Appendices

19.1 The perspectives of key stakeholders in the prison setting in integrating and scaling up point-of-care testing for hepatitis C infection in prisons: a qualitative study

Title	**The perspectives of key stakeholders in the prison setting in integrating and scaling up point-of-care testing for hepatitis C infection in prisons: a qualitative study**
Background and Rationale	The National Hepatitis C Point-of-Care Testing Program has been operational since 2022, providing same day hepatitis C testing and treatment in a variety of settings, including prisons. Previous research has identified the reduced clinical pathway timeline (Sheehan et al., 2023) and patient perceptions of acceptability of hepatitis C point-of-care testing in the prison setting (Lafferty et al., 2022). However, a key gap in the literature is the perceptions of key stakeholders (operational, managerial, and policymakers) in integrating hepatitis C point-of-care testing into the prison environment, and informing national scale up. Through qualitative interviews with people in prison (including people who accept and decline offers of hepatitis C point-of-care testing), frontline workers (officers and healthcare workers), prison and prison health management (governors, managers of security, and nurse unit managers), and prison / prison health policymakers, this study will seek to address this knowledge gap.
Proposed Project Plan	Investigators from the Centre for Social Research in Health (CSRH) and the Kirby Institute, UNSW Sydney will lead, develop, and implement a qualitative sub-study investigating implementation and scale up of point-of-care HCV testing in the prison setting. Only researchers from CSRH and Kirby Institute will be involved in data collection and access to raw data.
Study Aims	1) To understand motivations and barriers of people who are incarcerated for accepting/declining point-of-care HCV testing during regular/routine testing models and high intensity testing campaigns 2) To investigate whether point-of-care HCV testing as currently implemented is acceptable to prison personnel (officers, healthcare workers, and prison administrators) and to identify areas for improvement. 3) To investigate high level policy considerations that support or inhibit point-of-care HCV testing
Study Design	Semi-structured, in-depth qualitative interviews (approx. n=101) with people who are incarcerated accepting (n=10) and declining (n=10)

	point-of-care HCV testing (including during regular/routine testing models and within high intensity testing campaigns); people involved directly and peripherally in point-of-care HCV testing in prison (prison healthcare workers, n=20; and correctional officers, n=20) and people influencing the governance and policy of prisons and prison health (prison administrators [governors, managers of security, and nurse unit managers], n=21, and policymakers, n=20)
Study Population	There are five distinct participant groups for this study: Group 1: People who are incarcerated Group 2: Correctional officers Group 3: Prison healthcare workers Group 4: Prison administrators (e.g., governors, managers of security, nurse unit managers) Group 5: Prison policymakers (including prison and prison health)
Inclusion Criteria for Participants	All participants will: - provide verbal informed consent; - be incarcerated (Group 1), or work in prisons (Groups 2-4), or have policy oversight of prison/s (Group 5), where the National HCV Point-of-Care Testing Program is operational; - and sufficient proficiency in English
Study Procedures	This social science sub-study will investigate the barriers and enablers to point-of-care HCV testing in the prison setting. Potential participants will be recruited via key contacts within prisons through the broad network of the National HCV Point-of-Care Testing Program. People who are incarcerated (Group 1), correctional officers (Group 2), prison healthcare workers (Group 3), and prison administrators (governors, managers of security, and nurse unit managers) (Group 4) participants will be recruited from prisons across Australia where the National HCV Point-of-Care Testing Program is currently operational. Policymaker participants (Group 5) will be selected based on their policy influence on prisons and/or prison health within states and territories. Selection of prison sites will include those who have and/or are currently conducted/ing point-of-care testing for hepatitis C infection. Research team members will attend prisons operating hepatitis C point-of-care regular/routine testing models and those implementing high intensity testing campaigns to conduct on-site interviews with people who are incarcerated (Group 1), correctional officers (Group 2), prison healthcare workers (Group 3), and prison administrators

	(governors, managers of security, and nurse unit managers) (Group 4). In these instances, potential participants will first be approached by a project coordinator who will introduce the qualitative study to potential participants; following verbal preliminary agreement to participate, the project coordinator will introduce the potential participant to the interviewer. Interviews will be conducted in a private space within the prison / health clinic. *Recruitment of people who are incarcerated:* Healthcare workers who implement point-of-care testing will be verbally introduce the study to people undergoing and declining point-of-care testing. The inmate identification number and first two initials of first and surname of those who provide preliminary verbal consent will be provided to the project coordinator. This information will then be shared with the interviewer prior to a site visit – or tele-meeting (e.g., Teams within health clinic) – to conduct interviews. During point-of-care testing, healthcare workers conducting point-of-care testing and research team members will verbally introduce the study to people undergoing and declining point-of-care testing. Those who provide preliminary verbal consent will be introduced to the interviewer. The interviewer will then review the Participant Information Statement and Consent Form before obtaining informed consent. *Recruitment of correctional officers and prison healthcare workers:* A project coordinator within the National HCV Point-of-Care Testing Program will contact (via email) the governors and nurse unit managers at each of the selected prisons to notify of the qualitative sub-study, and their support sought for personnel participation within their respective prisons. A list of potential correctional officers and prison healthcare workers will be sought along with permission/support for a healthcare worker trained in point-of-care testing to directly approach prison personnel (correctional officers, healthcare workers) for study participation. Potential personnel participants who provide preliminary verbal consent to participate will be contacted by a member of the research team to schedule an interview. The Participant Information Statement and Consent Form for correctional officers and prison healthcare workers will be attached to the preliminary email.

	For on-site recruitment of prison personnel (prison officers and healthcare workers), members of the research team will directly approach correctional officers and healthcare workers engaged with / supporting high intensity testing campaigns and introduce the study. Personnel who provide preliminary verbal consent will be introduced to the interviewer. The interviewer will then review the Participant Information Statement and Consent Form before obtaining informed consent. *Recruitment of prison administrators:* A project coordinator within the National HCV Point-of-Care Testing Program will contact Group 3 potential participants (prison governors, managers of security, and nurse unit managers) via email inviting them to participate in an interview. The Participant Information Statement and Consent Form will be attached to the preliminary invitation email. *Recruitment of policymakers:* The Principal Investigator of the National HCV Point-of-Care Testing Program will approach potential policymaker participants via email, informing them of this qualitative sub-study and seeking preliminary interest to participate. The Participant Information Statement and Consent Form will be attached to the preliminary invitation email. The research team will be notified of any potential participants who have provided preliminary consent to participate in an interview. The interviewer will directly contact the potential participant via email to re-confirm preliminary interest and setup a time for the interview convenient to the participant. Interviews may also be conducted via telephone or a virtual platform, such as Teams or Zoom, with the preferred platform selected by the participant. Prior to commencing any interview, the Participant Information Statement and Consent Form will be verbally reviewed with the participant; informed verbal consent will be obtained on a separate audio recording. All interviews will be audio recorded. The interview guide for people who are incarcerated seeks to understand patient motivators for accepting / declining point-of-care

	HCV testing during point-of-care testing and identify patient-perceived barriers to point-of-care HCV testing. The interview guides for prison personnel and policymaker participant groups seek to identify the barriers and enablers to implementation of HCV point-of-care testing within the prison setting, including perceptions of the role of point-of-care testing within prison, implementation/integration of routine point-of-care testing compared with high intensity testing campaigns using point-of-care testing, and health intervention prioritisation and decision making. For Group 1, if allowed and according to corrective services policy and procedure, participants will receive remuneration paid into their prison account for their time (only applicable in states that approve this process).
Data Access and Storage	Only the research team will have access to the data. Data will be stored for a minimum of seven years, all data will be destroyed in a confidential manner. Audio recordings will be saved to a secure UNSW OneDrive folder. Only Kirby and CSRH team members will have access to this folder, along with a professional transcriber who has signed a confidentiality agreement. The transcriber will access audio recordings, then upload transcripts to this folder. Kirby and CSRH personnel will proof and de-identify transcripts; following this step, audio recordings will be permanently deleted.
Study analysis and Dissemination	De-identified data (transcripts) will be thematically analysed. Study findings will be presented at scientific forums including national and international conferences, and published in peer-reviewed journals. Findings will also be made available via other dissemination strategies, such as newsletters and staff meetings.
References	Lafferty, L., Cochrane, A., Sheehan, Y., Treloar, C., Grebely, J., & Lloyd, A. R. (2022). “That was quick, simple, and easy”: Patient perceptions of acceptability of point-of-care hepatitis C RNA testing at a reception prison. *International journal of drug policy, 99*, 103456. doi:https://doi.org/10.1016/j.drugpo.2021.103456 Sheehan, Y., Cunningham, E. B., Cochrane, A., Byrne, M., Brown, T., McGrath, C., . . . Grebely, J. (2023). A 'one-stop-shop' point-of-care hepatitis C RNA testing intervention to enhance

	treatment uptake in a reception prison: the PIVOT study. *Journal of Hepatology*. doi:10.1016/j.jhep.2023.04.019

19.2 Implementation Process Mapping of Hepatitis C Point-of-Care Testing

Title	Implementation Process Mapping of Hepatitis C Point-of-Care Testing
Background and Rationale	Developing new complex pathways of care requires an understanding of the underlying processes, variation in approaches, and influences on implementation. Process mapping is commonly used to map clinical pathways with stakeholder consultation and can be a useful implementation planning tool to map clinical or patient behaviours that could be targeted for change, or to co-design interventions to optimise practice.[1-3]
Study Objectives	Our study objectives are to: a) map existing processes for the current HCV diagnostic pathway (HCV antibody test for exposure, HCV RNA for active infection, and one or more assessments to commence treatment) and patient journeys/experiences through the health system. b) map processes for the proposed HCV diagnostic pathway (i.e. point-of-care testing and treatment) and anticipated patient journeys.
Study Aims	Through this implementation qualitative sub-study, we aim to: 1. Gain a clearer understanding of current hepatitis C point-of-care testing procedures and workflow. 2. Develop setting specific implementation process maps that identify commonalities and variation in hepatitis C point-of-care testing practices. 3. Identify implementation barriers and enablers to hepatitis c point-of-care testing.
Study design	Re-coding of qualitative interviews described in sub-study 19.1 to implementation science frameworks such as the Consolidated Framework for Implementation Research[5] (CFIR). Follow up qualitative interviews and focus groups may be conducted to clarify anything that is unable to be re-coded and confirm the

	barriers/enablers identified, as well as process maps generated, from the original interviews. Follow up interviews and focus groups would only take place with people who work in prisons (Groups 2-4 from sub-study 19.1). After re-coding the information gathered, the research team will design an implementation platform to optimise Point-of-Care Testing for Hepatitis C Infection in prisons. We will engage stakeholders through follow up email contact and/or interviews and focus groups (based on the preference/availability of participants) to consider the proposed new model of care, barriers and facilitators to its implementation and identify potential implementation strategies, to provide structured opportunities to co-refine and further develop implementation strategies.
Inclusion Criteria for Participants	Participants will be recruited for qualitative interviews as described in sub-study 19.1.
Study Procedures	Point-of-Care testing providers will participate in qualitative interviews described in sub-study 19.1. These interviews will then be re-coded to CFIR 2.0[5] through deductive qualitative analysis techniques to a) map existing processes for the current HCV diagnostic pathway (HCV antibody test for exposure, HCV RNA for active infection, and one or more assessments to commence treatment) and patient journeys/experiences through the health system. During the same re-coding exercise we will b) map processes for the proposed HCV diagnostic pathway (i.e. point-of-care testing and treatment) and anticipated patient journeys. If there is information that needs to be clarified with a participant in group 2-4, sub-study 19.1, a follow-up interview and/or focus group may be conducted by the research team (phone/videoconferencing/in-person) and will be audio-recorded and transcribed. Transcripts will be coded using a mixed inductive/deductive qualitative analysis approach. Content analysis will identify steps in existing care pathways and inform the development of visual, software-generated process maps (Microsoft PowerPoint). To identify barriers and enablers to the implementation of point-of-care testing structured according to the key steps in the care pathway, data will be coded to implementation science frameworks (CFIR 2.0[5]). Re-coding of qualitative interviews will be used to: map audit data to existing

	processes; use maps to understand changes needed to support the new approach; prospectively map audit data through the trials to determine where the gaps are in a 'live' fashion; use data to measure change in processes/quality/fidelity to the new approach over time; use interview data for barrier/facilitator analysis to inform the design of targeted implementation strategies. Triangulating the information gathered from objectives a-b, the research team will design an implementation platform to optimise Point-of-Care Testing for Hepatitis C Infection in prisons. Using 'implementation mapping' methodology, and informed by the combined use of implementation frameworks, the platform and resources will be designed to overcome identified barriers and maximise existing facilitators for optimising evidence-based intervention implementation. The implementation platform will be presented back to key stakeholders, providing structured opportunities to co-refine and further develop implementation strategies. The research team will synthesise information gathered to present the platform, and an accompanying logic model (to demonstrate mechanisms of action for Point-of-Care Testing for Hepatitis C Infection in prisons implementation strategies), for optimal iterative improvements to implementation.
Study Population	Our study population are key prison workers (clinical, allied health, corrections or administrative) stakeholders across the approved sites (including prison settings) that have been interviewed as part of sub-study 19.1 and are involved with the delivery of point-of-care testing for hepatitis C.
Study analysis	**Process maps:** Process maps will be developed through a content analysis of the qualitative interviews from sub-study 19.1. An individual process map will be developed for each point-of-care testing service model. **Qualitative analysis:** During qualitative data collection for process map development, we will simultaneously ask about any experienced barriers or facilitators with the current process for hepatitis C point-of-care testing. Additional barriers and facilitators will be coded to the CFIR 2.0[5] through deductive qualitative analysis techniques.

Dissemination	The findings from this study will inform the development of a peer-reviewed manuscript.
References	1. Elwyn G, Kreuwel I, Durand MA, et al. How to develop web-based decision support interventions for patients: a process map. Patient education and counseling 2011; 82(2): 260-5. 2. Kononowech J, Landis-Lewis Z, Carpenter J, et al. Visual process maps to support implementation efforts: a case example. Implementation Science Communications 2020; 1(1): 105. 3. Morrow A, Hogden E, Kang Y-J, et al. Comparing theory and non-theory based implementation approaches to improving referral practices in cancer genetics: a cluster randomised trial protocol. Trials 2019; 20(1): 1-12. 4. Damschroder, L.J., Reardon, C.M., Widerquist, M.A.O. et al. The updated Consolidated Framework for Implementation Research based on user feedback. Implementation Sci 17, 75 (2022). https://doi.org/10.1186/s13012-022-01245-0