NSW DRIED BLOOD SPOT SELF-SAMPLING HIV AND HEPATITIS C TESTING PILOT PROGRAM

Version 3.8

9 Jan 2024

SYNOPSIS

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Summary

Study title	NSW DRIED BLOOD SPOT SELF-SAMPLING HIV AND HEPATITIS C TESTING PILOT PROGRAM
Protocol version	3.8
Objectives	**Program objective** The primary objective of the program is to reach priority populations who test infrequently for HIV and hepatitis C (HCV). **Evaluation objectives** **Primary objective:** 1. To assess the feasibility of DBS self-sampling HIV and HCV testing (return rate, number of DBS tests done, re-testing rate, mode of distribution of DBS self-sampling kits) **Secondary objectives:** 2. To assess the reach of DBS self-sampling (characteristics of people who use the program – demographics, sexual risk behaviour and past testing history) 3. To evaluate the outcomes of DBS self-sampling HIV testing (HIV positivity, CD4 count at diagnosis, linkage to care) 4. To evaluate the outcomes of DBS self-sampling HCV testing (HCV positivity, linkage to care and treatment initiation) 5. To assess the acceptability of DBS self-sampling testing from the perspective of the participant 6. To assess the performance of the DBS HCV test used for HCV RNA 7. To assess the costs per test and costs per HIV and HCV infection diagnosed
Study design	A pilot implementation research study with two phases: a 'Postal Pathway' (phase 1) and a 'Settings Pathway' (phase 2). Evaluation of the pilot will focus on reach (uptake; demographic, testing and sexual history of target group reached), impact and feasibility (return rate, number of DBS tests done; proportion of individuals who re-test using DBS, mode of distribution of DBS self-sampling kits); outcome (positivity rate, linkage to care following a positive result and treatment initiation); acceptability among a cross-section of DBS kit registrants, assay test performance and costs per test and diagnosis.
Planned sample size	1860
Selection criteria	**Broad inclusion criteria** • Individuals aged 16 years or older who reside in NSW. • Ability to provide independent informed consent to participate in the study, including consent to the provision of a dried blood spot sample for HIV testing, = and willingness to participate in and comply with the pilot program, namely the completion of registration details **Inclusion criteria for DBS self-sampling HIV testing** Individuals who self-select as belonging to one of the following risk groups: • men who have sex with men

	• people who have a transgender history (or their current or previous partners) • People from regions of high HIV prevalence* • People whose current or previous sexual partners are from one of the above groups. ***For the purposes of this study, this is considered to be countries within Africa or Asia, and the following specific countries: Belize, Haiti, Bahamas, Jamaica, Guyana, Barbados, Suriname, Djibouti, Russian Federation, Trinidad and Tobago and Panama.** **Inclusion criteria for DBS self-sampling HCV testing** Individuals who self-select as belonging to one of the following risk groups: • People who identify as Aboriginal or Torres Strait Islander • People who have ever injected drugs • People that are currently or have ever been incarcerated • People who are or have been clients of community corrections services • People who are using or have used drug and alcohol services or mental health services • People who are or have been homeless • People from Africa or the Middle East or regions of high HCV prevalence** **** For the purposes of this study, this is considered to be any country where the participant or their parents were born overseas or a language other than English is spoken in the home.** For settings-based DBS testing (phase 2), settings will be able to provide DBS testing kits to participants who meet the eligibility criteria where they also access a service for which any of the following situations may apply: • Service is unable to collect conventional venepuncture specimens. For example, a remote outreach service, community health setting or online setting • The storage and transport of conventional specimens is problematic • The potential risk of blood contamination prohibits sampling of conventional venepuncture specimens, for example, in outreach settings such as sex on premises venues (SOPV)
Study procedures	Information relating to the pilot and the online registration form will be made available on a dedicated website managed by the DBS Project Coordinator. Self-sampling dried blood spot (DBS) kits will be distributed via two pathways: 1. A 'postal pathway' (phase 1), and; 2. A 'settings pathway' (phase 2). Phase 1 of the pilot will involve individuals self-registering online to receive a DBS kit to a nominated address via post. Registration and kit return, will be the same for both distribution pathways. The NSW State Reference

	Laboratory for HIV, St Vincent's Hospital, Sydney will be the organisation responsible for receiving and testing all DBS samples, and clinical governance, result provision and follow-up will be provided by NSW Sexual Health Infolink (SHIL). Some settings (phase 2 sites) may elect to provide results directly to participants; however SHIL will maintain overarching clinical governance and will monitor follow up. Monitoring and evaluation will be overseen by the NSW Ministry of Health with input from the investigator group.
Statistical considerations	The sample size will focus on the primary objective of the program of reaching high-risk populations who are testing infrequently. Based on behavioural surveys, we assume that 19% of gay men had their last HIV test more than 2 years ago or never, and among CALD populations 40% had never tested. Therefore, to determine if the DBS program is able to reach a 5% or greater proportion of infrequent testers than behavioural surveys, then at least 400 gay and bisexually active men and at least 460 heterosexuals from CALD populations is required for HIV testing. An additional 1000 dual HIV/HCV tests will be performed. In terms of statistical analysis, descriptive analyses (counts and proportions) will be conducted, and relevant outcomes stratified by demographic group, risk behaviour and distribution pathway. Chi-squared tests will be used to assess if there are statistical differences in these outcomes according to these stratifications. Standard deviations will be calculated for means, and interquartile ranges for medians. Also, t-test and Ranksum tests will be used to see differences in means and medians across different participant groups. Sensitivity and specificity will be calculated using standard methods with 95% confidence intervals presented using binomial approximation tests.
Study duration	approx 72 months (until December 2024) unless extended.

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1.BACKGROUND

1.1. DISEASE BACKGROUND

Increasing access to HIV testing is an important tool for reducing onward transmission of HIV as awareness of HIV status may lead to changes in risk behaviour engagement, enable testing of recent partners (contact tracing) and the option of commencing HIV treatment earlier (1,2). The *NSW HIV Strategy 2021-2025* (the Strategy) identifies gay and bisexually active men and people from culturally and linguistically diverse (CALD) backgrounds as two of the priority populations for which initiatives to increase prevention and testing should be targeted. The other priority populations identified in the Strategy are people who inject drugs, Aboriginal people, and people involved in sex work (3).

Gay and bisexually active men are the population group most affected by HIV in Australia and New South Wales, with surveillance data showing about 70% of diagnoses per year are due to male-to-male sexual contact. A further 20% of diagnoses each year are attributed to heterosexual contact, with about half of these diagnoses attributed to people either from high prevalence regions, such as Africa or Asia, or report sexual partners from these countries (4,5).

Surveillance data also show, that among gay and bisexually active men and heterosexuals diagnosed with HIV, nearly a third each year have a CD4 count indicating late diagnosis (defined as a CD4 count at diagnosis of < 350 cells/µL or an AIDS defining illness within 3 months of diagnosis), indicating it is likely that these people have been infected with HIV for about 4-5 years and had not been tested (6). More detailed analysis of NSW surveillance data from 2010-2013 showed the majority of those late diagnosed were in gay and bisexually active men, but late diagnoses were more likely in those aged 50 years or over at diagnosis, speaking a language other than English at home, acquiring HIV overseas, and reporting a history of either heterosexual or injecting drug exposure to HIV (7). Also, an analysis of national data in 2015 showed, specifically among gay and bisexually active men, high rates of late diagnoses in bisexual men, and gay and bisexually active men living in regional/rural locations (8).

Late diagnosis of HIV increases the risk of morbidity and mortality among affected individuals, is associated with increased health care costs and can result in ongoing transmission during the period an individual is unaware of their HIV status (6).

Further, in Australia, in 2013, it was estimated that 14% of people living with HIV (taking into account all exposure groups) were unaware of their positive HIV status. This represents 3,700 of 26,800 people living with HIV nationally and 1,680 of 12,380 in NSW who do not know that they are infected with HIV (5). A recent study in gay men in NSW demonstrated 9% of metropolitan gay men were undiagnosed and half of the men with undiagnosed infection had had a recent HIV test (9), suggesting more frequent or convenient HIV testing is needed. Mathematical models suggest that undiagnosed HIV infections contribute disproportionately to new HIV transmissions in Australia (10) (11).

Clinical guidelines recommend at least annual HIV testing for all sexually active gay and bisexually active men, with 3-6 monthly testing for higher risk men. However, behavioural surveys and clinic data demonstrate that gay men and gay and bisexually active men are not accessing HIV testing at the recommended frequency, about 10% have never been tested, a quarter of non-HIV positive men surveyed have not been tested within the previous 12 months and only a third of high-risk gay and bisexually active men had three or more HIV tests in a year (12). Numerous surveys indicate that

barriers to testing among gay and bisexually active men include psychological factors (not perceiving oneself to be at risk of HIV, fear of a positive result, concerns about stigma and discrimination, concerns about confidentiality, embarrassment about discussing sexuality or risk behaviour with a healthcare provider, fear of blood or needles and anxiety while waiting for a result) (13) and structural barriers (inconvenience of testing, difficulty in finding the time to test, difficulty in getting an appointment with a healthcare provider, not knowing the location of – or not being close to – suitable or acceptable testing services and the need to return to obtain results) (14).

NSW has a large CALD population with almost 27% of the NSW population born overseas and nearly 23% of all residents speaking a language other than English at home, making it one of the most culturally diverse states in Australia (15). However, previous studies have found that – among other high-risk groups – people from CALD backgrounds are more likely to be diagnosed with HIV late in the course of the illness, in addition to experiencing difficulties in accessing health care services and experiencing significant stigma and discrimination which may prevent them from seeking HIV testing or treatment (16).

This evidence suggests there are a large number of missed opportunities to test and diagnose HIV earlier and to link individuals with appropriate care and treatment as soon as possible. Also, current strategies to promote HIV testing in NSW are not reaching groups who are more likely to present late in HIV infection. One method of improving access to testing among populations who do not engage with currently available services for HIV testing, and to increase the frequency of testing among people at risk of HIV infection, is to enable self-sampling of blood specimens in the privacy of an individual's own home. When surveyed, most gay men reported that they would test more frequently if HIV self-tests were available, with the greatest increases in testing expected to be among higher-risk men (17) (18).

Dried blood spot (DBS) is a self-collection method (rather than a self-test) and enables people to collect samples in their own home, post back and receive results without having to attend a health service. Additionally, as a blood sample is collected (rather than oral fluid) acute infections are more likely to be detected and the blood sample enables screening and confirmation to occur using the same sample. DBS testing offers significant advantages when compared to conventional venous blood samples, particularly in relation to logistics such as the transportation of samples to central testing laboratories and in settings where laboratory infrastructure may be limited. DBS offers opportunities for transport because the biological hazards related to liquid samples are mitigated by drying the sample and providing supplementary packaging to contain samples in transit. Appropriately collected and processed samples lend themselves to a postal type distribution network which may improve convenience for participants and increase uptake and frequency of HIV testing.

DBS collection for conventional HIV serological testing has been successfully applied for decades in early infant diagnosis of HIV and in monitoring prevalence of HIV among child-bearing women and injecting drug users (19). There are international quality assurance programs to assess the performance of laboratories conducting testing of DBS samples.

A large scale, public DBS testing program was piloted in the United Kingdom by the Terrence Higgins Trust, Dean Street and Public Health England (PHE) whereby individuals could order self-collection 4th generation DBS HIV test kits online – kits were then posted to the individual's home, a self-collection finger prick specimen was taken and posted back to the reference laboratory for testing with standard HIV serology, and results were relayed to the individual by text message (for negative results) or phone call (for positive results). A strong marketing campaign accompanied the DBS program and led to 17,629 requests for self-sampling kits in the pilot phase between January 2013 and March 2014. The campaign specifically targeted gay and bisexually active men and Black African

heterosexuals, the two groups most affected by HIV in the UK. More than half (59%) of kits were returned to the reference laboratory and 146 HIV diagnoses made, and preliminary data indicated the program was able to reach younger and more rural populations – groups which are less likely to engage with sexual health clinics in the UK (20).

Self-sampling may support increased testing for HIV among high-risk groups who may experience barriers to conventional testing, such as the need to attend a health service to access a test, time taken for test results to be available, difficulties accessing health care providers, stigma and the risk of discrimination. DBS HIV testing may address these barriers through increasing access, supporting autonomy, and providing added confidentiality, privacy and convenience.

People who inject drugs are at greatest risk of hepatitis C infection and are listed as priority populations in the NSW HIV Strategy and the NSW HCV Strategy (21; 22). In Australia, it is estimated that 230,470 people are living with chronic hepatitis C, with approximately 81,900 people from NSW (23). The rate of hepatitis C diagnosis among Aboriginal and Torres Strait Islander people in Australia is almost five times higher than the rate in the non-Indigenous population (23). Aboriginal and Torres Strait Islander people will be eligible for a dual HIV/HCV test within the DBS Project. New direct acting antiviral treatments for HCV are now available on the Pharmaceutical Benefits Scheme and can provide safe and effective treatment for people living with HCV which very high cure rates (24). Appropriate treatment of hepatitis C can prevent the development of the major life-threatening complications of chronic liver disease including cirrhosis and liver cancer (24).

1.2. Rationale for Performing the Study

The purpose of the pilot project is to increase the uptake and frequency of HIV and hepatitis C testing among priority populations in NSW to enable earlier diagnosis of disease and reduce onward transmission.

2. STUDY OBJECTIVES

Primary objective:

1. To assess the feasibility of DBS self-sampling HIV and HCV testing (return rate, number of DBS tests done, re-testing rate, mode of distribution of DBS self-sampling kits)

Secondary objectives:

2. To assess the reach of DBS self-sampling (characteristics of people who use the program – demographics, sexual risk behaviour and past testing history)
3. To evaluate the outcomes of DBS self-sampling HIV testing (HIV positivity, CD4 count at diagnosis, linkage to care and treatment initiation)
4. To evaluate the outcomes of DBS self-sampling HCV testing (HCV positivity, linkage to care)
5. To assess the acceptability of DBS self-sampling HIV/HCV testing from the perspective of the participant
6. To assess the performance of the DBS HCV test used for HCV RNA
7. To assess the costs per test and costs per HIV and HCV infection diagnosed

3. STUDY DESIGN

3.1. DESIGN

Pilot procedures

The design is a prospective pilot implementation study. This protocol refers to both Phase 1 and Phase 2 of the pilot. Phase 1 will involve eligible individuals registering online to receive a DBS kit via post. The point of distribution and return of kits will be the NSW State Reference Laboratory for HIV, St Vincent's Hospital, Sydney.

Phase 2 of the pilot will involve more targeted distribution of kits within particular settings or populations. Site specific ethics applications will be submitted in order for phase 2 to proceed. The NSW State Reference Laboratory for HIV will remain the centralised point of DBS kit distribution and receipt, and participants will still be required to register their details online to activate the kit.

Evaluation

Evaluation of the pilot will focus on feasibility (return rate, number of DBS tests done; proportion of individuals who re-test using DBS, mode of distribution of DBS self-sampling kits); reach (characteristics of people who use the program – demographics, sexual risk behaviour and past testing history), outcomes (HIV and HCV positivity, CD4 count at diagnosis, linkage to care following a positive result); acceptability of the program among DBS kit registrants, assay test performance and cost.

These evaluation indicators will be measured from four data sources (which are detailed further in section 8):

1. Brief online questionnaire at registration
2. Follow-up call (to obtain linkage to care information)
3. Acceptability data collection
4. DBS and conventional laboratory testing results from the laboratory

3.2. NUMBER OF PARTICIPANTS

Phase 1: Based on sample size calculations (section 9), the minimum number of participants required to determine that the program is reaching 10% or more infrequent testers (tested >2 year ago or never) than behavioural surveys is 400 gay and bisexually active men and 460 heterosexual people from CALD populations (860 in total). These individuals may undergo repeat testing and thus the total number of DBS tests, particularly in gay and bisexually active men, may be greater.

Phase 2: To accommodate Phase 2, an additional 1000 testing kits will be included, for a total of 1,860 across all population groups.

3.3. NUMBER OF CENTRES

Phase 1: The pilot will involve centralised distribution of kits from the NSW State Reference Laboratory for HIV, St Vincent's Hospital, Sydney to individuals who register online. NSW Sexual Health Infolink (under the clinical governance of Sydney Sexual Health Centre) will be responsible for ensuring all results are delivered to participants and that participants who receive an HIV and/or HCV detected result are referred to appropriate local services.

Phase 2: Phase 2 will involve more targeted distribution of kits within particular settings defined by a set of principles outlined in the inclusion criteria described below and may include, for example, community outreach services, sex on premises venues, needle syringe program sites, and drug and alcohol services, mental health services, homelessness services, or community corrections that find it difficult to offer conventional laboratory or rapid HIV and/or HCV testing. The NSW Self-Sampling

Dried Blood Spot HIV Testing Pilot Program Steering Committee will provide advice to the Principal Investigators on which sites should be part of Phase 2 of implementation. Services will also have the opportunity to submit an Expression of Interest to the DBS Project Co-ordinator, for inclusion in Phase 2.

Site specific ethics applications will be submitted in order for Phase 2 to proceed at sites wanting to implement DBS testing into the existing service. As in Phase 1, the NSW State Reference Laboratory for HIV will remain the centralised point of DBS kit distribution and receipt, and all participants receiving a kit within specific settings will be required to register their details online to activate the kit.

Selected sites may wish to participate by promoting DBS only. This may include the placement of DBS promotional materials within the site for clients to see. In Phase 2 this may also include the positioning of DBS testing kits for eligible populations to pick-up and take home to register. These sites will not be required to submit a site-specific ethics application but will be considered a distribution point ONLY.

Overall governance for Phase 2 of the pilot will remain with NSW Sexual Health Infolink (SHIL)/Sydney Sexual Health Centre, with local clinical governance provided by the Local Health District within which each particular setting/site is located.

The expected number of sites for Phase 2 is unknown at this stage.

3.4. DURATION

The expected duration of the pilot program will be approximately 72 months from the launch of the website (November 2016) until December 2024 (unless extended).

4. PARTICIPANT SECTION

4.1. INCLUSION CRITERIA

Broad inclusion criteria for both Phase 1 and 2

- Individuals aged 16 years or older who reside in NSW
- Ability to provide independent informed consent to participate in the program, including consent to the provision of a dried blood spot sample for HIV and/or HCV testing, willingness to be contacted after consent to complete follow-up evaluation of their experience using DBS, and willingness to participate in and comply with the pilot program, namely the completion of registration details.

Inclusion criteria for DBS self-sampling HIV testing

Individuals who self-select as belonging to one of the following risk groups:

- men who have sex with men
- people who have a transgender history (or their current or previous partners)
- People from regions of high HIV prevalence*
- People whose current or previous sexual partners are from one of the above groups

***For the purposes of this study, this is considered to be countries within Africa and Asia or the following specific countries: Belize, Haiti, Bahamas, Jamaica, Guyana, Barbados, Suriname, Djibouti, Russian Federation, Trinidad and Tobago and Panama.**

Inclusion criteria for DBS self-sampling HCV testing

Individuals who self-select as belonging to one of the following risk groups:

- People who identify as Aboriginal or Torres Strait Islander;
- People who have ever injected drugs
- People that are currently or have ever been incarcerated
- People who are or have been clients of community corrections services
- People who are using or have used drug and alcohol services or mental health services
- People who are or have been homeless
- People from Africa or the Middle East or regions of high HCV prevalence**

**** For the purposes of this study, this is considered to be any country where the participant or their parents were born overseas or a language other than English is spoken in the home.**

A key modification to protocol version 3.0, approved by the DBS Steering Committee and Principal Investigators, is the HIV and HCV tests will be separated out and offered to individuals based on meeting the eligibility criteria for each test.

For settings-based DBS testing (phase 2), settings will be able to provide DBS testing kits to participants who meet the eligibility criteria where they also access a service for which any of the following situations may apply:

- Service is unable to collect conventional venepuncture specimens. For example, a remote outreach service, community health setting or online setting
- The storage and transport of conventional specimens is problematic
- The potential risk of blood contamination prohibits sampling of conventional venepuncture specimens, for example, in outreach settings such as sex on premises venues (SOPV)

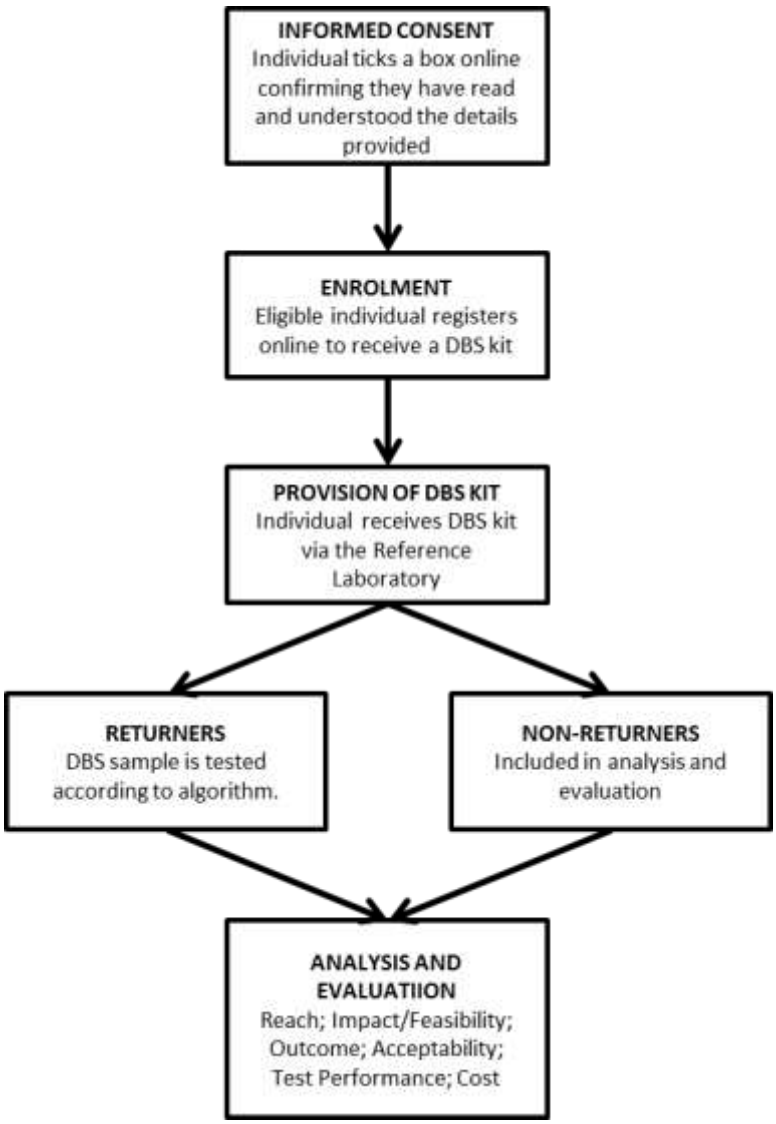
4.2. Exclusion Criteria

- Individuals who do not meet the inclusion criteria outlined above

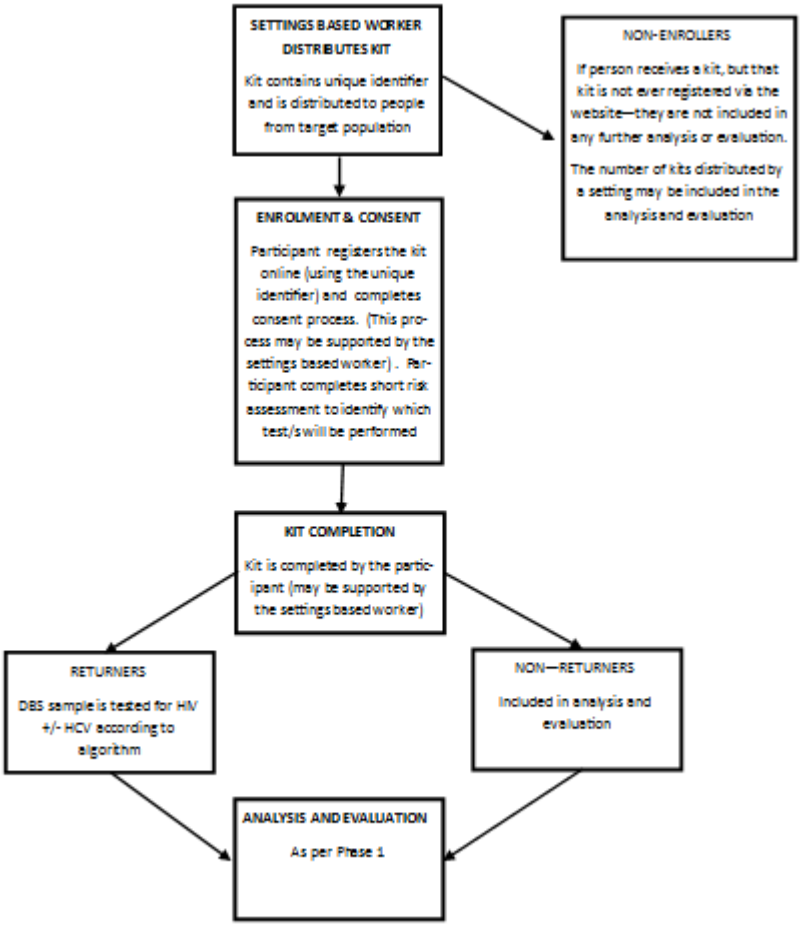
Participants who are excluded will be informed they cannot access HIV and/or HCV testing via the DBS website and will be directed to a local GP or sexual health clinic for testing and sexual health review.

5.STUDY OUTLINE

5.1. STUDY FLOW CHART (PHASE 1)



5.2. STUDY FLOW CHART (PHASE2)



See appendices for more detailed flow diagrams of pilot program procedures.

Timelines/Milestones

The project will commence when all relevant ethical approvals are granted.

MILESTONE	TIMEFRAME
Phase 1 of pilot project 'goes live'	Time zero
Phase 1 of pilot 'open' – Collection of data on individuals who request a DBS kit, those who receive a DBS HIV or HCV test result, and other information e.g. number of visits to website/other social marketing evaluations	Time zero to 72months
Anticipated start of phase 2 – Dependent on site specific ethics approval being granted	Time 6 months to 72 months
Key partners (SHIL and Reference Laboratory) to provide report to NSW Ministry of Health on number of kits distributed, activated, returned and tested, and the positivity rate	Every 3 months from time zero

Analysis of data and completion of report on outcomes of the first 12 months of the DBS pilot	12 months from time zero (allow 3 months to draft evaluation report)
Review of the continuation of the DBS program according to evaluation report	15 months from time zero
Pilot period officially closes	72 months unless extension approved

5.3. GOVERNANCE

Clinical governance

All results will be provided via the Sexual Health Infolink (SHIL), which is under the clinical governance of the Director of Sydney Sexual Health Centre, South-Eastern Sydney Local Health District (SESLHD). The Project Coordinator will be responsible for ensuring pathways for delivery of results are available to participants including referral to appropriate local services.

For phase 1, SHIL will provide results to participants either by text message or email (negative results) or by phone for reactive results. SHIL will contact the patient one week after the delivery of an HIV detected result and after 1 month for a HCV detected result to support a pathway into care and treatment.

During Phase 2, a number of sites may choose to provide results directly to participants. This will be negotiated with each site and will be dependent on there being a clearly defined rationale for the site to provide the results (including adequate clinical skills and knowledge of referral pathways). If this is the case, SHIL will provide results directly to the site and clinical governance will be the responsibility of the site.

Pathology governance

As an accredited pathology provider embedded in SydPath (the Pathology Service of St Vincent's Hospital Sydney), the NSW State Reference Laboratory for HIV will provide pathology governance for the project under the stewardship of the Chief Operating Officer of St Vincent's Centre for Applied Medical Research. Guidance for pathology governance will be provided by five immunopathologists, including two HIV consultant physicians, based at the Reference Laboratory. The laboratory complies with National Pathology Accreditation Standards (NPAAC) and is accredited by the National Association of Testing Authorities, Australia (NATA) for medical testing. St Vincent's Hospital, Sydney will be performing testing of DBS samples within the scope of its accreditation. NSW Health Pathology laboratories also comply with NPAAC standards and are accredited with NATA.

Aboriginal governance

The Aboriginal Health and Medical Research Council Human Research Ethics Committee has provided ethical guidance and approval for Phase 2 of the project.

Governance in correctional settings

The Corrective Services Ethics Committee provides ethical guidance and approval for implementation of the DBS study in correctional settings such as prisons operated by government agencies or private companies or government operated community corrections (probation and parole) services.

Overall governance

A formal agreement has been established by NSW Ministry of Health with the NSW State Reference Laboratory for HIV, St Vincent's Hospital, Sydney Limited and NSW Sexual Health Infolink (SHIL) (which is under the clinical governance of the Director of Sydney Sexual Health Centre as described above) and the Aboriginal Health and Medical Research Council Human Research Ethics Committee to implement the pilot program and deliver a quality assurance and safety package to support the provisions of DBS HIV and hepatitis C testing in NSW.

The NSW Ministry of Health is the lead organisation overseeing implementation, including monitoring and evaluation of the Program.

The NSW State Reference Laboratory for HIV is the organisation responsible for laboratory diagnostic testing of DBS samples, as well as the dispatch, receipt and storage of kits sent back to the laboratory for testing.

The NSW Sexual Health Info Link (SHIL) is the organisation responsible for delivering HIV and HCV test results to clients (or sites where agreed), contact tracing and linking all individuals into follow-up care.

The governance structure of the pilot has been revised to support implementation scale-up across NSW. A single overarching DBS Steering Committee has been established, with membership from partner organisations, Sydney Sexual Health Centre, The Kirby Institute, Sexual Health Infolink, St Vincent's Hospital, Sydney, and the Justice Health and Forensic Mental Health Network and NSW Ministry of Health. Other stakeholders, including selected Local Health District Publicly Funded Sexual Health Service Directors, members of the Aboriginal reference group, the Multicultural HIV and Hepatitis Service (MHAHS) and the AIDS Council of NSW (ACON), will be consulted as required.

A Project Coordinator has been employed to oversee the management of the pilot. The Coordinator is under the clinical governance of Sydney Sexual Health Centre and will be jointly based at SHIL and NSW Ministry of Health within the Blood Borne Virus & Sexually Transmissible Infection Branch of the Centre for Population Health. The project coordinator is responsible for:

- Convening meetings of the Working Group
- Closely liaising with the Steering Group to inform them of the progress of the pilot
- Supporting ethics application submissions and coordinating site-specific assessments
- Liaising with study site staff to organise their participation and kit supply
- Organising development of the website for home testers (https://www.health.nsw.gov.au/dbstest/Pages/order.aspx) This website will also be accessible through www.DBStest.health.nsw.gov.au and the website for site registrations (https://www.health.nsw.gov.au/dbstest/pages/sites.aspx)
- Organising development of the kits and other pilot materials in collaboration with the Steering Group and Working Group
- Managing data collection and organisation in a central and secure database
- Organising staff training on the pilot
- Supporting the communications strategy that will accompany the pilot program. Pilot program promotion and advertising will be in partnership with MHAHS, ASHM (Australasian Society for HIV Medicine), ACON, selected local services and other relevant stakeholders.

5.4. PROMOTION

The DBS HIV and HCV testing program will be promoted through a number of communications and community mobilisation initiatives that are targeted towards priority populations. Traditional media channels, such as community radio and advertising in local community newspapers, will be utilised as well as non-traditional media channels including online and social media/social networking. Promotion of the DBS HIV and HCV testing will be embedded in existing HIV and HCV testing campaigns at the state and local level, and in particular will feature as part of communication and marketing around HIV testing for World AIDS Day and Hepatitis testing week. Direct promotion will also be undertaken with community organisations, Local Health Districts, and other health services (general practices, drug and alcohol services, and emergency departments) as a way to mobilise community and health professionals who work directly with priority populations. Promotional initiatives will be delivered in multiple languages in order to ensure priority CALD communities are engaged.

A formal and detailed communications strategy has been developed following the recruitment of the Project Coordinator, who will develop the strategy under the direction of the DBS Steering Group who will oversee its management and implementation. This strategy incorporates the aims of communications, target audiences, key messages, tools and an implementation plan. Governance of the communications strategy will be through SHIL under the auspices of South Eastern Sydney Local Health District.

The following wording has been specified for use in promotional material:

- Postal HIV and hepatitis C Test
- The Dried Blood Spot (DBS) is a new way to test for HIV and hepatitis C.
- This finger prick test is free, easy and confidential and can be done in the privacy of your own home.
- Order your test kit today!
- Postal hepatitis C Test
- Postal HIV Test
- Free, easy and private
- Everyone who is in prison is eligible for a DBS test
- Complete a self-referral form to see the nurse for testing or more information
- DBS testing is coming to your centre
- Put up your hand to be tested when the DBS test is offered
- Help to register and test is also available

Sites are permitted to develop their own promotional material with any combination of this specific wording ONLY. No commercial logos are permitted to be used with DBS promotional material.

The benefits of participation lie in easier access to HIV and HCV testing for hard to reach populations, and participants access services as they choose in an independent manner.

5.5. RECRUITMENT AND SCREENING

Individuals will not be actively approached for recruitment but will, in Phase 1 of the pilot program, be required to register for DBS HIV or hepatitis C testing and consent to testing and follow-up, Individuals that self-identify as being from the target groups for the DBS pilot program and complete online registration will receive a DBS test kit posted to their nominated address. In Phase 2,

recruitment will be conducted through the agencies providing services to people outlined in the inclusion criteria (including, for example, community outreach services, sex on premises venues, needle and syringe program sites, and drug and alcohol, mental health services, homelessness services, or community corrections that lack the capacity to offer conventional laboratory or rapid HIV testing). These identified services will be selected through a mix of direct contact and an expression of interest process to be disseminated through networks of community organisations and stakeholder groups.

The pilot program will be advertised by the NSW Ministry of Health, Local Health District services, and community representation organisations via community press, social media, online advertisements, banners on websites frequented by priority high-risk populations and through posters and postcards at hospitals, clinics and community sites. A consultation process will be facilitated by the Multicultural HIV and Hepatitis Service, in order to ascertain the optimum mechanisms through which to engage their communities around DBS.

The entire website will be translated into Chinese (Traditional) to extend the reach of the project and increase accessibility by communities speaking Chinese languages.

5.6. Registration

Baseline information for phase 1 participants will be collected via the DBS website (https://www.health.nsw.gov.au/dbstest/Pages/order.aspx) when individuals register to receive or to activate a DBS testing kit. Individuals can also visit via www.DBStest.health.nsw.gov.au and will be redirected to the main website. Baseline information for participants being assisted to register with a registered site will be collected via a separate DBS website (https://www.health.nsw.gov.au/dbstest/pages/sites.aspx). This baseline information will include demographic and contact details (including full name, date of birth, telephone number and address), preferred method of results provision (mobile/telephone, SMS or email), Aboriginality, country of birth, and injecting drug use history. Identifiable information (name, date of birth, telephone number and address) only be shared between health service providers for the purpose of clinical care. Only de-identified information will be used in reporting or publication.

Website text incorporating standard data collection at online registration, attached to this submission.

5.7. Online and Verbal Informed Consent Process

Once eligibility to the study has been ascertained and before the registration of details, participants will be asked to provide their independent informed consent for participation in the study. The text in this online consent form is based on standard National Health and Medical Research consent form templates for non-interventional studies. The information is provided in a language that is easily understood to enable people to make an independent informed decision about DBS sampling and HIV/HCV testing. The website contains information about the DBS test, eligibility, testing process and results, privacy, withdrawing from the study and has links for more information. A participant information sheet (PIS) is also made available for download. A Participant Information and Consent Form (PICF) will also be made available to the client. The website and PIS also describe the limitations of the test including the window period and the need for repeat testing if there has been a recent risk event or illness. Finally, participants will be able to select the DBS tests for which they are eligible.

The process of online consent is considered necessary for this study due to the volume of participants to be recruited in the program, plus the nature of the pilot program (in which home-

based participants/postal pathway do not have face-to-face interaction with research or clinic staff) prevents a paper-based approach from being effective and practicable. The benefit of an adapted online consent form also provides increased accessibility particularly for participants who opt for DBS HIV/HCV testing due to the added privacy and confidentiality it affords. The online consent form will require people to confirm their ability to provide independent informed consent to participate in the program and their understanding of the program aims, processes and possible risks. As with standard consent procedures, participants will still have the opportunity to clarify any questions they have with research staff (by telephone or email) and they will be able to keep an electronic or printable copy of their consent form.

For the settings pathway (registered sites), verbal consent is introduced to expedite the testing process. In this setting, participant registration and testing will be assisted by a staff member or trained assistant who will explain the study, its processes, risks, results, referral pathways and other necessary information. The staff member or trained assistant will provide their signature that verbal consent was received.

During Phase 2, some sites may have difficulty with internet access, such as those accessing participants in remote NSW. In this instance, paper-based records for registration and acknowledgement of verbal consent will be provided.

The minimum information that will be provided before the client consents (or not) to receiving a DBS HIV/HCV kit is:

- A description of DBS for HIV and HCV testing
- The eligibility criteria for DBS testing
- A description of how the sample should be taken and how the laboratory test is conducted
- Requirement to complete data collection activities (such as questionnaires)
- A description of privacy and confidentiality related to testing and results
- Information about test accuracy, including the window period, false negative results, false positive results and the need to confirm reactive results
- Information about provision and interpretation of results
- The potential implications of not being tested
- Ability to withdraw consent for follow-up at any time without prejudice

These Participant Information Sheets will also be offered in Chinese (Traditional). Translation into these priority languages will be finalised as soon as possible after the pilot commences. Other translated material will also be available on the DBS website.

Consent to participate in the follow-up evaluation processes will be requested at the time of registration as per procedures used in a range of other previous studies. Follow-up information will be collected via a variety of methods, for example a cross-sectional survey of participants or semi-structured interviews and will include questions about acceptability of self-sampling, testing preferences and confidence regarding the performance of self-sampled DBS HIV or HCV test.

A formal evaluation of the pilot is planned. Further detail regarding the follow-up of participants will be provided to relevant Human Research Ethics Committees as an additional amendment as soon as possible. Follow-up of participants will not commence until formal ethics approval has been granted for this process. Participants who wish to withdraw their consent for the study, will be directed to the online “consent withdrawal” form. However, withdrawal of consent will also be accepted by

phone, SMS or email. In this event, as much information as to the circumstances for withdrawal of consent, will be documented.

5.8. Enrolment Procedure

Individuals will be enrolled into the pilot program once they have confirmed they meet the inclusion criteria for the pilot and have completed the informed consent process on the website or verbally consented when being assisted to test at a registered site. If the individual is completing the DBS test unassisted, they will be assigned a DBS Study program validation number via SMS or email to confirm their contact details, and this will be documented in the individual's DBS study program record and on all program documents. If the individual is completing the DBS test with assistance from a trained worker, clinician or peer worker, a validation code is not required. Instead, the trained worker will enter the DBS kit code and their own contact details for third point of validation.

5.9. DBS Testing Kit Distribution Process

All kits will be coded with a unique identifier and stored at the NSW State Reference Laboratory for HIV. A register of kit distribution will be kept by the Project Coordinator in order to assess uptake by distribution method and to track kits from point of distribution to point of return to the Reference Laboratory for testing and outcome of results. All kits will need to be activated by participants or assisting trained workers on the dedicated DBS website, using the allocated validation code for participants registering independently of a site, or using the DBS kit code where a trained worker is assisting the participant.

In the event of a participant attempting to register on the website a second time, while their initial testing kit remains outstanding; SHIL will delete the second registration and make contact with the participant using their preferred method of contact, to advise that the initial validation code remains valid.

The DBS HIV testing kits will be distributed via the following mechanisms:

(i) **Postal pathway** (commencing in Phase 1): Individuals self-identify as being eligible for the DBS study program and complete online registration and validation code to receive a DBS testing kit posted to a nominated address, self-sample a DBS specimen and post the used kit back to the central laboratory for testing.

(ii) **Settings pathway** (commencing in Phase 2): Individuals directly receive DBS HIV/HCV testing kits in selected settings. Unassisted individuals receiving kits via this pathway will be required to enter the DBS website to activate the kit and receive a validation code. Depending on the setting, individuals may be supported by staff to complete online or paper-based registration and self-sampling at the point of distribution or will need to take the kit to a preferred location to complete registration and self-sampling. If the individual is completing the DBS test with assistance from a trained worker, clinician or peer worker, a validation code is not required. Instead, the trained worker will enter the DBS kit code and their own contact details for third point of validation. Inclusion criteria for eligible settings are outlined in the appropriate section above.

Information provided on the registration website will include information on referral to local services for testing and treatment for HIV, HCV and other sexually transmitted infections, reputable Australian sources of further information including community support groups, and safe sex and safe injecting messages.

See Appendix A for the testing kit distribution flowchart.

DBS HIV/HCV testing kits

The collection kit will include:

- instructions on how to collect a DBS testing sample,
- two alcohol swabs,
- a cotton fibre blood collection blotting test card (or Guthrie card),
- a desiccant sachet (to ensure the sample is dried),
- two single-use retractable lancets for collecting the finger prick blood sample,
- two cotton wool balls,
- two band aids,
- a plastic zip locked bag, and
- a reply-paid envelope for posting back the specimen.

The collection kit will be in a plain envelope so the contents of the package cannot be identified, and privacy is maintained.

5.10. Participant Specimen Collection Process

Upon receipt of the DBS HIV/HCV testing kit, the participant will be required to enter the validation code that they received via SMS or email when they registered on the website on the space allocated on the test card included in the kit. If the individual is completing the DBS test with assistance from a trained worker, clinician or peer worker, a validation code is not required. Instead, the trained worker will enter the DBS kit code and their own contact details for third point of validation. Those using paper-based forms will note the unique identifier issued to each kit will enter this on their paper forms. This will ensure that the bio-specimens received are from the person who registered online. The validation code will then be verified at the laboratory to ensure there is a match with the patient information recorded online.

The participant will collect their own blood specimen according to the instructions included with the DBS HIV/HCV testing kit. The kit packaging is designed to be discreet and practical. The instructions contain advice and diagrams to guide the participant through the sample collection process step by step.

During Phase 2, some participants may be assisted by health care workers or peers to complete the specimen collection process. Training will be provided to staff and peers at the phase 2 sites, to ensure that they comply with infection control procedures.

5.11. Venepuncture substudy

At selected clinics, participants will be asked to provide a paired sample of blood (5ml) collected via venepuncture by a healthcare professional. This will be optional for participants. Up to 1300 participants will be enrolled in the venepuncture sub study. Participants can take part in the DBS HIV and HCV study without providing this sample. The primary objective of this sub-study is to compare the analytical performance of DBS as a sample type for the diagnosis of hepatitis C (antibody and RNA) to standard of care (venous-collected samples). All samples will be tested at NSW Health Pathology laboratories. Results delivery will be as per standard of care by NSW Health Pathology to the service ordering the tests. Participants will not receive HCV treatment as part of this study. Participants that are RNA positive will be linked to standard of care to assess for HCV treatment eligibility. Reactive DBS hepatitis C results will not need a confirmatory test as the sample will be paired to a venous sample tested as per standard of care. See Appendix D.

5.12. Laboratory Testing Procedures

Once the package is received at the NSW State Reference Laboratory for HIV, the sample will be processed then tested. HIV testing will use one of the Abbott Alinity i automated anaylser, HIV antigen/antibody combo assay. HCV testing will use the Hologic Panther, Aptima HCV Quant Dx assay which is an in vitro nucleic acid amplification test (NAAT) performed on automated platforms.

All DBS samples received by the laboratory will be tested according to a specific algorithm described below and in Appendix B (see Appendix B for the testing flowchart).

The HIV 4th generation EIA has a sensitivity of >99%, a specificity of >99% and window period of 15-21 days (26). Samples found reactive by EIA will have a Western Blot test conducted consistent with routine practices. Trial data suggests the Aptima HCV NAAT has a specificity of 98.6%, and is highly sensitive (27).

All commercially available laboratory tests for HIV are not intended for use with DBS samples. HIV testing is highly regulated in Australia by the TGA and application of in-vitro diagnostic devices with alternate sample types not supported by the manufacturer involves using the product 'off-label' under the Therapeutic Goods Administration's Clinical Trial Notification (CTN) Scheme.

Testing will be done frequently to ensure a fast turn-around time for receipt of results. The NSW State Reference Laboratory for HIV has successfully participated in an established external quality assurance scheme (EQAS) for HIV testing in Dried Blood Spot samples coordinated by the US Centers for Disease Control (CDC) for more than 20 years. It is anticipated that DBS samples received by the testing laboratory will be tested and results made available within one week. This would include confirmation of HIV reactive samples by HIV Western blot. The advantage of testing of samples in a reference laboratory allows for a variety of supplemental tests to be applied in the confirmation of true test positivity. This testing may also include TGA approved nucleic acid tests for HIV for which manufacturers have made claims to support the use of DBS sample types.

DBS sample collection for HIV and HCV as an alternative to conventional venepuncture has been used for 28 years in the Needle Syringe Program surveillance system among people who inject drugs throughout Australia and has been used successfully in a growing program of early infant HIV diagnostic testing targeting resource limited and remote settings (28). Laboratory testing strategies have been successfully developed and applied for detection of HIV antigens and antibodies plus hepatitis C RNA in DBS samples. In the context of early infant diagnosis, the detection of nucleic acid (HIV pro-viral DNA) indicates HIV infection of the infant, however the detection of HIV antibodies may be due to the presence of maternal HIV antibodies in the infant sample (28,29).

5.13. Result Provision

All results will be provided via the Sexual Health Infolink (SHIL), which has an established service for providing results of HIV and sexually transmissible infections to individuals and linking the person to local care. The *Sexual Health Infolink Operations Manual 2023*outlines the responsibilities of SHIL in providing test results (29). The provision of results for the DBS study will be integrated with current operating procedures at SHIL.

Negative results will be sent to the participants via text message or email by SHIL using the following standard script: "Hi, your DBS test result is negative (ok). Stay Safe and Test often. Call (02) 9382 7681 for more info" and "Hi, Your test result is negative (ok). Test often. Call 1800 451 624 (open weekdays 9am to 5:30pm) for more information. Regards, (Nurse) NSW Sexual Health Infolink" If a

participant calls SHIL back, the DBS Results Management Business Rule outlines how SHIL staff are to proceed.

With respect to participants who return a negative result and do not have contact details (due to lack of access to a working phone, email address or stable home address) the following process will apply: sites delivering negative results will make a record of the result in the patient file and ensure mechanisms are in place to alert staff should the individual subsequently return to the service so that the result can be given.

Participants who return an invalid test result will be sent a text message or email using the following script: "Hi, please call (02) 9382 7681 for your DBS test results (weekdays, 9-5). (Nurse).

Participants who return a test result detecting HIV or HCV will be sent a text message or email using the following script: "Hi, Please call me on (02) 9382 7681 (open weekdays 9am to 5.00pm) for your DBS test results. Regards, (Nurse) Clinical Nurse – NSW Sexual Health Infolink.

A trained clinical nurse specialist from SHIL will speak to participants about having a confirmatory venous HIV or Hepatitis C test done and will provide advice about where participants can go for testing, such as local public sexual health clinics, GPs, or relevant clinicians in the HIV Support Program run by the Ministry of Health where appropriate. Where SHIL is delivering results on behalf of a registered site, nurses will ask the client for permission to provide this result to the associated site for assistance in engaging the client in confirmatory testing, treatment and ongoing care. Procedures for referral and booking of participants for follow-up care are outlined in the DBS Results Management Business Rule. As part of this pilot, SHIL will routinely follow-up all participants (or the relevant site) with a detectable HIV result one week after notification to ensure they have attended testing, been linked to care and offer further referrals if required.

All participants who return a detectable HIV result will be actively contacted on 5 attempts, as per recommended guidelines in the DBS results management Business Rule. If contact remains unsuccessful, the Project Coordinator and clinical governance lead at Sydney Sexual Health Centre will be alerted for follow-up.

During Phase 2, a setting/site may request to provide results directly to participants. In this situation, SHIL will provide results to a clinician at the site. The site will then provide the results to the participants. In the case of a suspected new positive HIV result, SHIL will follow up with the site to ensure that results have been provided and linkage to care has been supported. Information on participants' treatment initiation will be collected from sites via a standardised case report form. For new HIV cases, sites will confirmatory follow up venous test results (HIV), CD4 results (HIV) and information on linkage to care and treatment initiation to SHIL or the DBS Study Coordinator, and SHIL will ensure all confirmatory results are forwarded to the NSW State Reference Laboratory for HIV (St Vincent's Hospital Sydney). A specific consent process has been developed for participants to consent to site delivery of results. (Approved in amendment 6 application).

See Appendix C for the test results flowchart.

5.14. Study Procedure Risks

DBS self-sampling for HIV and HCV testing should be used in circumstances where it can be demonstrated that the benefits to be gained from their use outweigh any potential risks.

Minimum performance requirements for point of care testing (PoCT) for HIV have been published by the Therapeutic Goods Administration and have been endorsed by NSW Ministry of Health (31), and

similar requirements for self-testing are relevant to DBS self-sampling for HIV testing, including the need for:

- Individuals to be given appropriate information, clear instructions in their preferred language on how to perform the test and support regarding the potential disadvantages of HIV and/or HCV self-sampling for testing in comparison to a laboratory test. In particular, individuals need a full understanding of test accuracy, including the window period and the need for re-testing.
- Appropriate support for individuals who have undergone or are about to undergo self-collection for a HIV or HCV test, including online and telephone services. Referral details for existing support services, such as "healthdirect" (which provides 24 hour access), should be provided with the device, and DBS testing kits should have clear instructions for use.
- Providing reliable, accurate and accessible information on DBS self-sampling for HIV and HCV testing with the device to ensure users understand the purpose and limitations of the screening devices, as well as promoting locally available support services such as appropriate health information phone lines and websites to enable linkage to care and support services. This will include providing information in multiple languages and pictorial instructions.
- Informing users with negative test results and recent/on-going risk of the necessity to re-test frequently.
- Systems in place to support users who receive an HIV or HCV detected test result.

The standard testing algorithm for this study outlines this process (see Appendix B).

NSW Health notes that there is no evidence from other jurisdictions where home-based or self-sampling testing is approved that use of self-sampling devices will reduce a person's access to professional health care.

Other specific risks relating to the pilot program are as follows:

(i) Incorrect or mislabelled dried blood spot specimens

As a way of ensuring the veracity of the sample sent to the laboratory, the participant will receive a validation code when registering for the study online. The validation code will be cross-checked prior to testing of the DBS sample and again before test results are released to the participant. If participants have lost their validation code they may also call the Sexual Health Infolink on 1800 451 624 to retrieve this upon correct identification. If the individual is completing the DBS test with assistance from a trained worker, clinician or peer worker, a validation code is not required. Instead, the trained worker will enter the DBS kit code and their own contact details for third point of validation.

(ii) Inaccurate results dependent on the window period and sensitivity and specificity of the test

The patient information sheet (attachment 1) and information provided on the DBS website will provide appropriate information required for informed consent. This will include how the test performs in comparison to conventional laboratory HIV or HCV testing, the limitations of the test including the window period, and the need for repeat testing if there has been a recent risk event or illness. Results of DBS samples found to be reactive will not be provided to the participant until a validated confirmatory test such as Western Blot has been conducted. Information will be provided on the registration website directing individuals to seek clinical review for Post-Exposure Prophylaxis (PEP) if they think they have had an exposure to HIV within the previous 72 hours.

(iii) Bleeding, discomfort and bruising can occur from a finger prick test.

(iv) Participants may experience stress and anxiety while waiting for their DBS HIV or HCV test result

(v) Participants may feel embarrassed answering some of the questions in the client survey regarding sexual behaviour. However, this has been minimised by using an online format, enabling people to provide the information in the comfort of their own home or other private location

(vi) Participants may experience stress and anxiety and adverse personal relationship effects as a consequence of testing positive for HIV or HCV

(vii) Sample may be from someone other than named participant

Risks (iv), (v), (vi) and (vii) could occur during routine clinical practice in sexual health and general practice clinics and are not unique to this study. Participants may withdraw from the study without penalty or any adverse effect. If participants are distressed, they will be able to contact SHIL to speak to a trained registered nurse who will be able to provide referral for support if required. This will be made clear to participants on the DBS website and during the online registration process. Participants who return a detected HIV or HCV result will receive intensive support and follow-up, as is standard clinical practice.

6. SAFETY

6.1. ADVERSE EVENT REPORTING

Any adverse events in this study related to the use of dried blood spot specimens with the 4th generation EIA test will be recorded by the NSW State Reference Laboratory for HIV and the Project Coordinator at SHIL, and de-identified data on the event will be reported to the ethics review committee responsible for the pilot program overall. De-identified data relating to adverse events will also be reported by the Reference Laboratory and Project Coordinator to the principal investigators for discussion and review by the DBS pilot steering and working group at group regular meetings during the pilot period.

The psychological and physical wellbeing of pilot participants will be prioritised during the management of any adverse event. Complaints regarding the pilot will be managed by the Project Coordinator and de-identified data on the complaint will be reported to the principal investigators and ethics committee. Participants will be provided with the contact details of the Project Coordinator should they wish to make their complaint. The process of handling complaints will be conducted in accordance with Chapter 5.6 of the *National Statement on Ethical Conduct in Human Research, 2007* (31).

7. EVALUATION OUTCOMES AND DEFINITIONS

The key study outcomes and their definitions are listed below

1. **Return rate:** proportion of DBS samples which were returned for testing. This will also be disaggregated by target population.
2. **HIV test positivity rate:** The numerator for calculating HIV positivity is the number of laboratory confirmed HIV positive individuals with Western Blot testing. The denominator is the number of individual 4^{thd} generation EIA tests performed during the pilot period.
3. **HCV test positivity rate:** The numerator for calculating HCV positivity is the number of laboratory confirmed HCV positive individuals with RNA testing on the Hologic Panther analyser. The denominator is the number of individual HCV RNA tests performed during the pilot period.
4. **Proportion of participants who are infrequent testers:** The proportion of DBS participants who reported at the first registration they had never tested for HIV before or had tested over 2 years

ago. This outcome measure will also be disaggregated by target population and test combination (HIV only compared to HIV/HCV dual testing).

5. **Linkage to care rate:** proportion of DBS participants who return an HIV detected test result and are reviewed by a referral clinician within 2 weeks of diagnosis. Linkage to care will be verified by the registered nurse making the follow-up call to newly diagnosed participants one week after notification of results, and information will be self-reported by the participant. Linkage to care will be reported separately for participants who receive a reactive HIV result, and those who receive a reactive HCV RNA test result.
6. **Mean CD4 count at diagnosis:** calculated in laboratory confirmed HIV positive individuals using flow cytometry
7. **Re-testing rate:** Proportion of DBS participants who had two or more DBS tests in the study period
8. **Acceptability of DBS test process:** Proportion of DBS participants who reported they found the DBS testing processed acceptable or highly acceptable
9. **Cost per DBS test** conducted: the costs to the health system of each DBS test done
10. **Cost per HIV infection diagnosed** by DBS test: the costs to the health system of each positive DBS test
11. **Cost per HCV infection diagnosed** by DBS test: the costs to the health system of each positive DBS test

8.EVALUATION DATA SOURCES AND PROCEDURES

a. Brief online questionnaire at registration

All participants will complete an online survey at registration. The survey will cover socio-demographics and injecting drug use history.

b. Follow up call at 7 days

SHIL will follow up with phase 1 people who receive an HIV or HCV detected test result one week after receiving their results via a telephone call, as part of the standard of care that would include provision of assistance, support and linkage to care services for newly diagnosed people. Sites managing their own results will be responsible for ensuring people are linked to follow up care and treatment as necessary. SHIL will follow up people with detected results in the case that sites have elected for SHIL to manage results. ”

c. Follow-up evaluation processes

Consent to participate in the follow-up evaluation processes will be requested at the time of registration as per procedures used in a range of other previous studies. Follow-up information will be collected via a variety of methods, for example a cross-sectional survey of participants or semi-structured interviews and will include questions about acceptability of self-sampling, testing preferences and confidence regarding the performance of self-sampled DBS HIV or HIV/HCV test. Follow-up of both registrants who have sent a DBS kit for testing and those who do not complete DBS testing will occur to better understand the factors influencing completion of DBS testing by individuals who register for the service. A formal evaluation of the pilot is planned from December 2022. Further detail regarding the follow-up of participants will be provided to relevant Human Research Ethics Committees as an additional amendment as soon as possible. Follow-up of participants will not commence until formal ethics approval has been granted for this process.

d. Cost

The evaluation objective assessing cost (costs per test and costs per HIV or HCV infection diagnosed) relates to all costs relating to staffing, delivery DBS HIV testing kits, laboratory testing and result

communication and follow-up. The cost of staff wages will be estimated using data from the participating centres. Data on the cost of the DBS kit and laboratory testing will be sourced from the NSW State Reference Laboratory for HIV, St Vincent's Hospital, Sydney and includes the DBS collection kit, postage, labour, reagents, consumables and specimen storage. A cost pathway will be developed, outlining all steps involved and costs collated in an Excel spreadsheet.

9. SAMPLE SIZE

The sample size will focus on the primary objective of the program of reaching priority populations who are testing infrequently. Based on behavioural surveys, we assume that 19% of gay men had their last HIV test >2 years ago or never (34) and among CALD populations, 40% had never tested (16). Therefore to determine if the DBS pilot study is able to reach a 5% or greater proportion of infrequent testers than behavioural surveys, then at least 400 gay and bisexually active men and at least 460 heterosexuals from CALD populations is required.

An additional 1000 dual HIV/HCV tests will be available in Phase 2.

10. STATISTICAL ANALYSIS*

Descriptive analyses (counts and proportions) will be conducted and relevant outcomes stratified by demographic group, risk behaviour and distribution pathway. Chi-squared tests will be used to assess if there are statistical differences in these outcomes according to these stratifications.

Standard deviations will be calculated for means, and interquartile ranges for medians. Also t-test and Ranksum tests will be used to see differences in means and medians across different participant groups.

Sensitivity and specificity will be calculated using standard methods with 95% confidence intervals presented using binomial approximation tests.

11. CONFIDENTIALITY AND STORAGE AND ARCHIVING OF STUDY DOCUMENTS*

All of the clinical data required for the DBS pilot study will be routinely recorded in secure patient management systems used by South East Sydney Local Health District (SESLHD), which provides clinical governance to SHIL. All clinic staff members within the health services participating in this pilot are bound by the terms of the following NSW Health Policy Directives which relate to confidentiality within this working environment: *Code of Conduct*; *Notifiable Disease Data Security and Confidentiality*; and *HIV Confidentiality: A Guide to Legal Requirements*.

A central database containing de-identified study data will be established and managed by the Project Coordinator at NSW Sexual Health Infolink/NSW Ministry of Health and the NSW State Reference Laboratory for HIV, where the research staff will collate the de-identified study data. Only the Principal Investigators, Project Coordinator or other staff nominated by the Principal Investigators will have access to this password-protected central study database. De-identified study data will be stored for 15 years after completion of the study and publication, with the intention of data being made available for potential related research projects (if feasible) during this time period. At the end of the 15 year period, electronic data will be erased and hard data will be shredded.

Identifiable patient data will be held on the password-protected local health network at SESLHD and will be accessible only by SHIL Registered Nurses and the Project Coordinator for patient care purposes. Patient medical records will be stored for a minimum of 7 years before they can be securely destroyed. Medical information on any patient returning a detectable HIV or HCV result may be kept indefinitely.

Privacy and confidentiality is mandatory at SHIL when disclosing results and other personal health information. Data presented in reports and publications will be published in aggregate form and in a manner that does not identify individuals.

12. REPORTING AND PUBLICATION

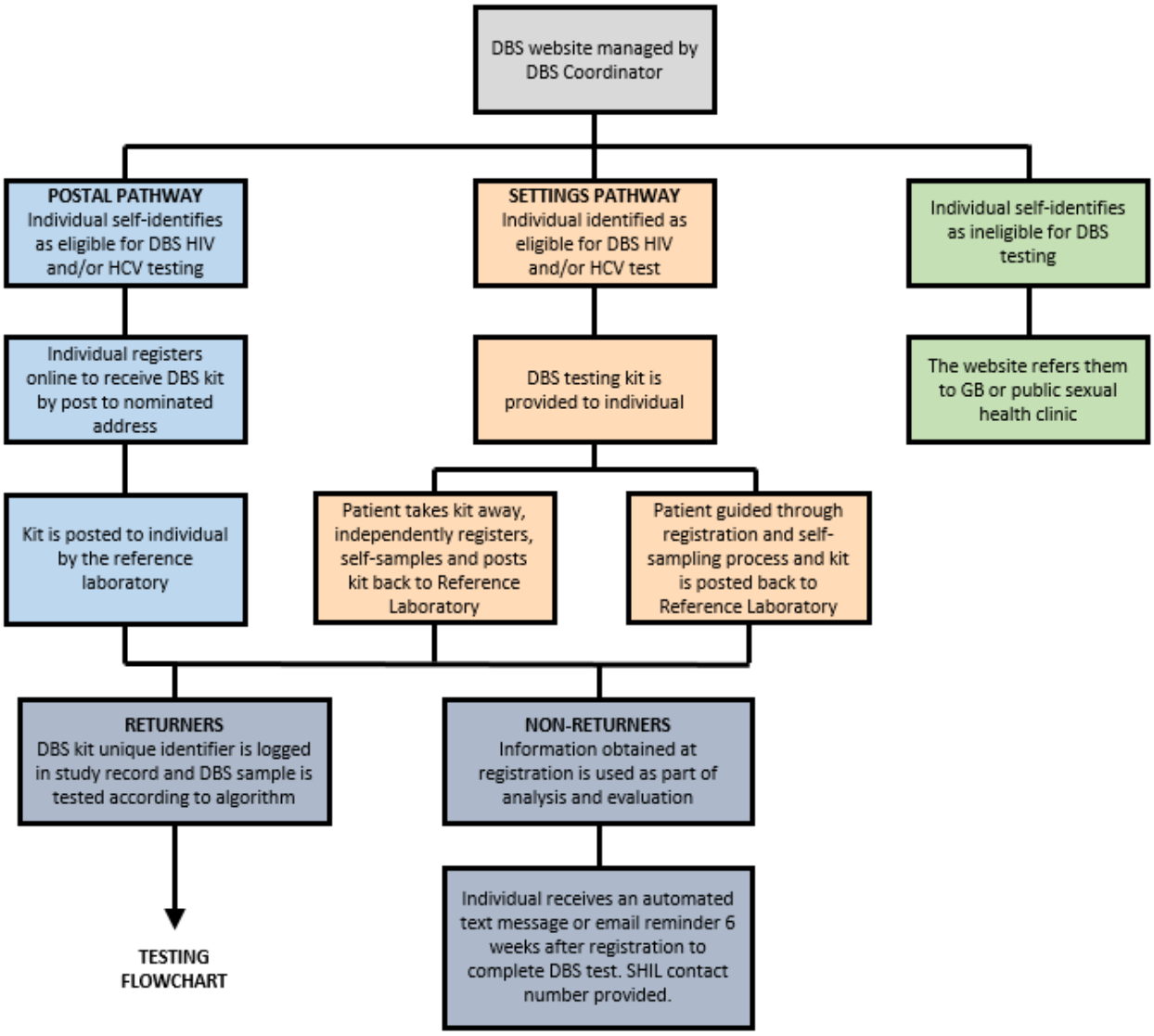
The NSW State Reference Laboratory for HIV and SHIL will be required to provide monthly reports on the number of kits distributed, activated, returned and tested; and on the positivity rate of samples by distribution pathway to the BBV & STI Unit, NSW Ministry of Health and to the Steering Committee. Final evaluation of the Program will commence in the final quarter of the last 12 month period (month 45 onwards).

The results of this study will be presented in a report for use by NSW Ministry of Health, NSW Sexual Health Infolink, Sydney Sexual Health Centre, St Vincent's Hospital Sydney, the Kirby Institute for Infection and Immunity in Society (UNSW Australia), the Centre for Social Research in Health (UNSW Australia), Local Health Districts involved in the pilot, and other peak organisations.

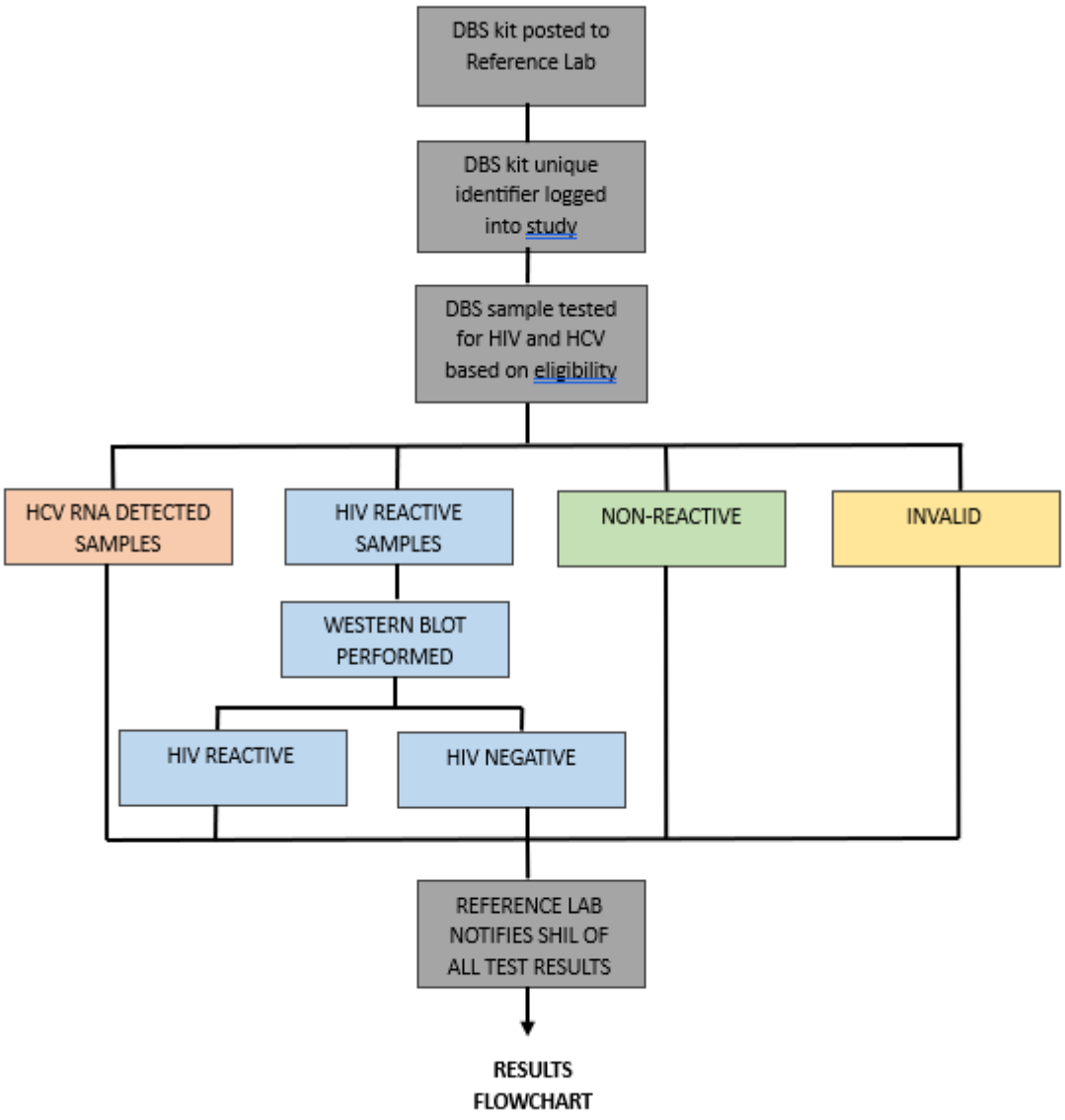
Analysis of data will be the responsibility of the BBV & STI Unit at the NSW Ministry of Health. All reports and papers written in relation to this pilot program will be overseen by the BBV & STI Unit in the Centre for Population Health at the Ministry with input provided by other members of the Steering Committee. Any information published or circulated to key stakeholders will be presented in aggregated form and in such a way that individuals cannot be identified. Any publication of results from this project will be approved by a person at the level of Deputy Secretary within NSW Ministry of Health; in practice, this role generally falls to the Chief Health Officer.

13. APPENDICES

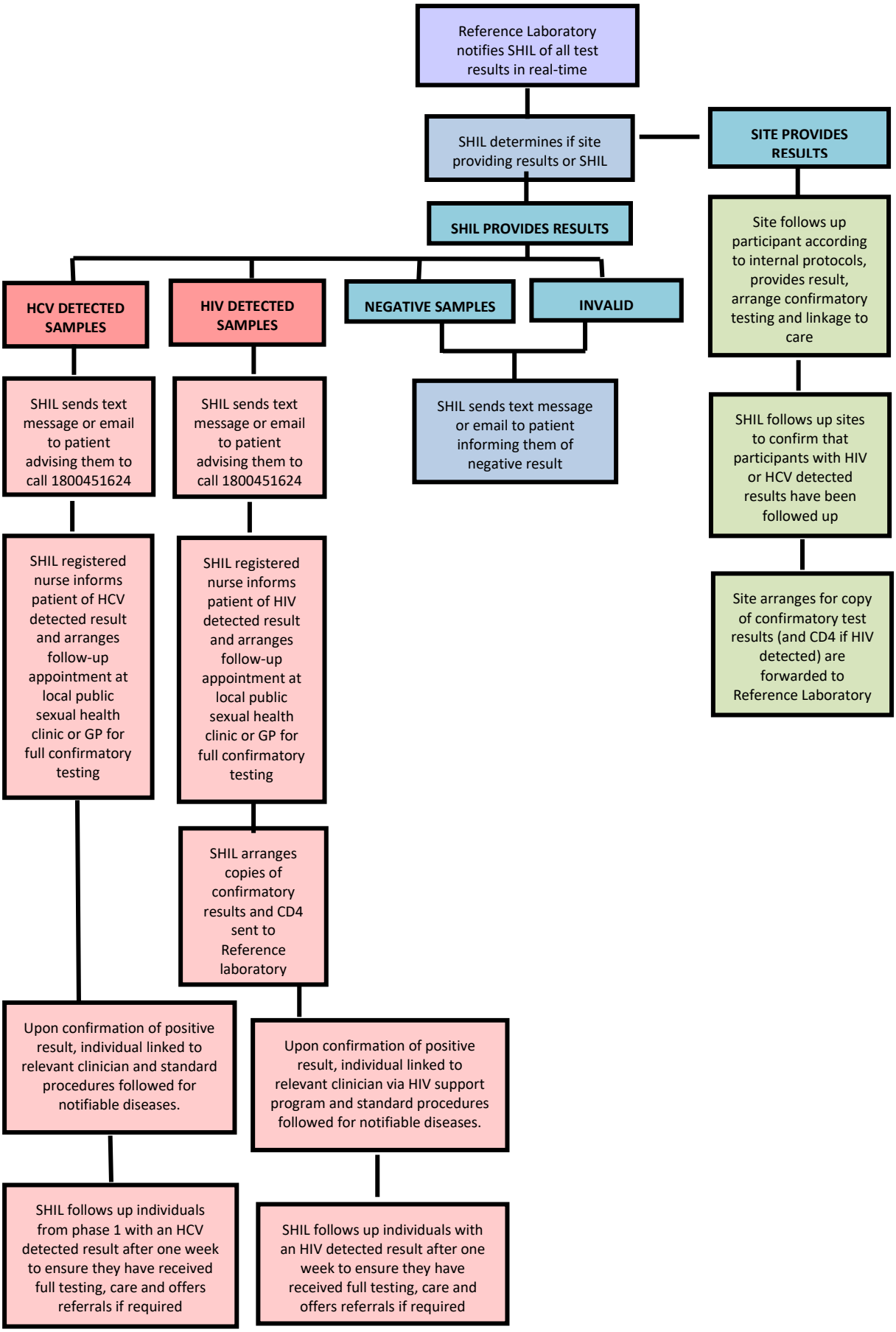
APPENDIX A: DISTRIBUTION FLOWCHART



APPENDIX B: TESTING FLOWCHART MAIN STUDY



APPENDIX C: RESULTS FLOWCHART MAIN STUDY



Appendix D: Substudy

Title	Validation of dried blood spot sampling for the detection of HCV RNA: A sub-study of the NSW Dried Blood Spot Self-Sampling HIV and Hepatitis C Testing Pilot Program.
Background and Rationale	Declines in annual HCV RNA testing and treatment is threatening Australia's ability to meet the HCV Targets outlined in the Fifth National Hepatitis C Strategy and the NSW Health Hepatitis C Strategy (2022-2025). 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 [1]. Stigma and discrimination associated with HCV and how it was acquired can be a barrier to testing and treatment initiation [2]. Dried Blood Spot (DBS) as an alternative sampling and testing option has been shown to increase testing and linkage to care [3,4]. It is valuable in settings where venepuncture is not available, when venous access is poor or where other barriers to accessing services may be present. Samples are produced from finger-stick collection of capillary whole-blood (50-100 μl) onto specialised filter paper. Once dried, samples have good stability, are easy to store and do not require cold chain transport [5,6,7]. Collection of DBS samples does not require a trained clinician and can be performed by a lay person with minimal training [5]. Literature on HCV DBS testing has shown an overall sensitivity of > 97% and specificity >99% for diagnostic accuracy of HCV RNA [8,9,10] and sensitivity of >96% and specificity of >99% for HCV antibody [9,11]. There are currently no hepatitis C serological or molecular laboratory assays available within Australia that include DBS as a registered sample type and approved by the Therapeutic Goods Administration (TGA). Therefore, the NSW DBS Pilot was implemented as a research study under the TGA Clinical Trial Notification (CTN) Scheme. The DBS sample type requires validation against paired venous sample in a National Association of Testing Authorities (NATA) Australia accredited laboratory, to provide the scientific evidence required by the TGA for approval of this device in routine clinical settings. This validation study aims to compare the use of capillary whole blood dried blood spots obtained via fingerstick, against the use of conventional venous plasma for HCV RNA and antibody testing. If deemed an acceptable alternative method of sample collection, it is likely to increase compliance with testing and reduce the need for repeat blood

	collection in patients who are unable to provide a venous-collected specimen, such as those with a history of drug-use and children, as well as provide access to testing to those living in remote/isolated areas where access to laboratory facilities is limited.
Study objectives	This primary objective of this sub-study is to compare the analytical performance of DBS as a sample type for the diagnosis of hepatitis C (antibody and RNA) to standard of care (venous-collected samples).
Study design	Participants will be recruited from sites participating in the HIV and HCV Dried Blood Spot Testing Pilot with a focus on sites with high testing volumes. Clinic staff will identify participants and offer participation in the sub-study. After providing consent, participants complete a capillary blood finger-stick DBS sample and a venous blood sample. The paired identically labelled samples will be sent to the Serology & Virology Division, NSW Health Pathology, Randwick (SAViD NSWHP) for testing. Results delivery will be as per standard of care by NSW Health Pathology to the service ordering the tests. Participants will not receive HCV treatment as part of this study. Participants that are RNA positive will be linked to standard of care to assess for HCV treatment eligibility.
Inclusion criteria for participants	**Inclusion criteria** Participants are eligible for inclusion if the following criteria are met: a. Provide informed consent. b. ≥ 18 years of age. c. Have a risk factor for the acquisition of HCV infection (such as current or past injecting drug use, previous incarceration) OR:

	d. Are attending a service 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). **Exclusion criteria** Is unable or unwilling to provide informed consent or abide by the requirements of the study.
Study procedures	**Enrolment visit and sample collection** Trained healthcare providers will engage with people at risk of HCV infection to determine eligibility for participation in the study. Participants fulfilling the inclusion criteria will be asked to provide consent. Following informed consent, the patients will undergo collection of paired venous blood via venepuncture and capillary blood via finger-stick for dried blood spot samples. Whatman 903© Cards (Merck, Germany) with five circles will be used to collect the capillary blood via finger-stick. The five circles will need to be fully filled with blood, with the paper saturated and covering the same surface when viewed at the back of the card. A minimum of 4 fully filled circles will be accepted. Following air drying overnight, the card will be placed in a paper envelope, followed by a zip lock plastic specimen bag containing a desiccant sachet, and transported at room temperature to the nearest NSW Health Pathology service as per standard practice. A dedicated request form for HCV serology and RNA on the paired venous and DBS samples will accompany the specimens. **Testing** *RNA Testing:* One dried blood spot from the paper cards will be processed and tested in parallel with matched venous blood plasma for the presence of HCV RNA using the Cobas© HCV 6800/8800 assay, following the manufacturer's instructions. Invalid results will be addressed by re-testing. *Antibody Testing:* One dried blood spot from the paper card will be processed and tested in parallel with matched venous blood plasma for the presence of anti-HCV using the Alinity i Anti-HCV assay, as per manufacturer's instructions. Reactive plasma samples will be centrifuged at 10,000 g for 10 min and retested in duplicate. Remaining samples will be stored for the duration of the study period and may be used for quality improvement testing on other more advanced HCV antibody or RNA assays should they become available.

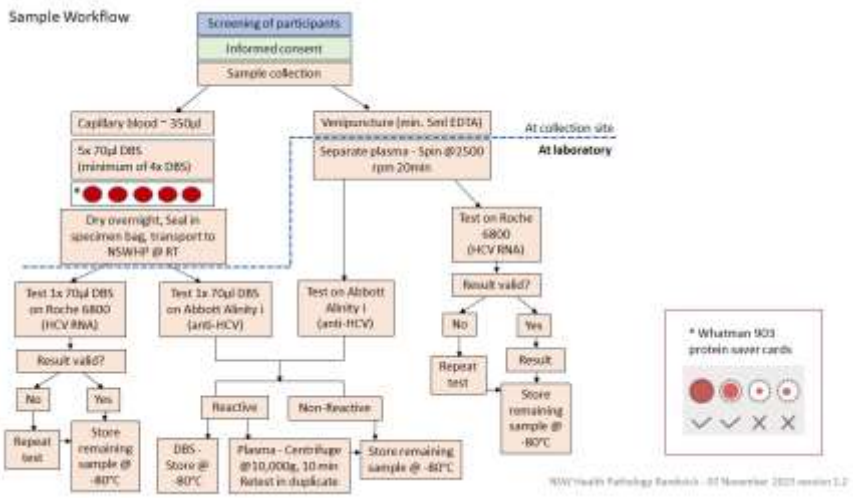


Figure 1: Outline of the workflow for HCV RNA and antibody testing on dried blood spots from finger-stick and venous plasma collected via conventional venepuncture. Processes above the blue dotted line will be performed at the collection sites and those below the line at the laboratory.

Study population

Participants will be recruited from sites participating in the *NSW HIV and HCV Dried Blood Spot Testing Pilot.*

Study Analysis

A comparison of the results obtained from testing of conventional venous plasma and capillary DBS will be performed and the following will be determined:

- Sensitivity
- Specificity
- Negative and positive predictive values
- reproducibility (intra- and inter- assay)
- Additional analytical performance analyses for HCV RNA will include: limit of detection, stability, and analytical specificity (interfering substances and cross-reactivity with other microorganisms)

The validation data will be submitted to the TGA for assessment.

This validation study is based on a sample size of 1300 patients referred for HCV testing, with an anticipated HCV RNA prevalence rate of 8% however, prevalence may be higher in some areas such as prisons or Drug and Alcohol settings.

Total sample size	Number of evaluable HCV RNA detectable specimens	Number of evaluable HCV RNA undetectable specimens	Sensitivity	Lower bound 95% CI	Upper bound 95% CI
1000	87	913	97.5%	91.3%	99.7%
1100	88	1012	97.7%	92.0%	99.7%
1200	96	1104	97.9%	92.7%	99.8%
1300	104	1196	98.1%	93.2%	99.8%

	• Assuming 99% specificity for all comparisons • The calculations were performed using the diagnostic test evaluation calculator MedCalc (https://www.medcalc.org/calc/diagnostic_test.php)
Dissemination	Findings from this sub-study may be submitted to peer-reviewed journal(s). Study findings will be presented at international and domestic conferences and seminars, when applicable. This information will be outlined in the Participant Information Sheet and Consent Form.
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