INTEGRATING HIV AND HCV TESTING

NASTAD

APHL ASSOCIATION OF PUBLIC HEALTH LABORATORIES

OVERVIEW

Increasingly health departments (HDs) are seeking new strategies to improve the productivity and yield of HIV testing and linkage programs, expand availability of and access to testing for hepatitis C virus (HCV), and to optimize public health resources. In the context of the ongoing opioid epidemic and in serving high-risk communities including people who inject drugs (PWID) and gay, bisexual, and other men who have sex with men (MSM), the ability to detect both HIV and HCV is imperative for successful prevention and linkage to treatment efforts. Integration of HIV and HCV testing services, at multiple levels, can help HDs achieve these aims. This toolkit will provide HDs with current information regarding HIV and HCV testing technologies, describe factors HDs should consider in determining when integration of testing is beneficial, and discuss how various testing technologies and strategies for using these technologies can facilitate integration. This toolkit focuses on integration of HIV and HCV testing services, but some of the strategies discussed and tools provided have relevance for integration of testing for sexually transmitted diseases (STDs). When appropriate, integration of hepatitis B and STD testing is addressed. HDs may wish to refer to CDC's Planning and Implementing HIV Testing and Linkage Programs in Non-Clinical Settings: A Guide for Program Managers for detailed discussion and tools to support program implementation. While the Guide was developed to support implementation of HIV testing in non-clinical settings, it provides information, tools, and tips which are applicable to HCV testing, and is also relevant for clinical settings.

INTRODUCTION TO HIV TEST TECHNOLOGIES

Diagnosis of HIV infection requires conducting a series of tests, or testing algorithm, beginning with a series of antibody (Ab) and/or antigen (Ag) tests, and potentially requires a nucleic acid test (NAT) that detects HIV RNA. Older antibody tests, such as the Western blot, detect only Immunoglobulin G (IgG) antibodies, which appear later in the course of HIV infection. IgG antibody tests have the longest window periods at approximately 5 weeks. More recent antibody tests detect both IgG and Immunoglobulin M (IgM) antibodies, which appear earlier in infection than IgG antibodies. These tests have a window period of approximately 3 weeks. The newest and most sensitive tests for HIV detect both HIV antigen and HIV antibodies (Ag/Ab tests). The window period of Ag/Ab tests is approximately 2.5 weeks. Nucleic acid tests which may be required for supplemental testing to confirm HIV infection directly detect HIV. The median window period for HIV NATs is under 2 weeks. The laboratory markers of HIV are presented below in Figure 1. The window periods for specific HIV tests, relative to laboratory markers of infection, are presented in Appendix A.

FIGURE 1: LABORATORY MARKERS OF HIV INFECTION

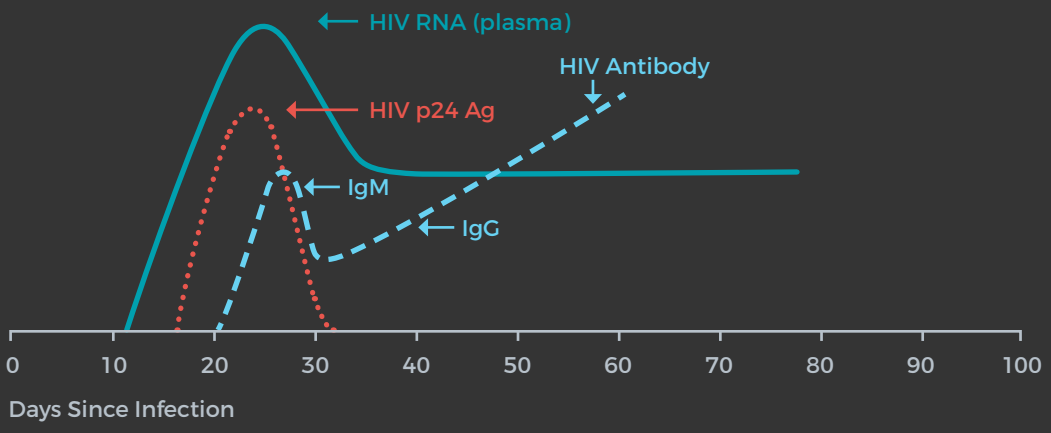


Figure adapted from Delaney et al., CID 2017:64 and provided by M. Owen, NCHHSTP, CDC.

Oral Fluid Testing: Oral fluid HIV tests are less sensitive during early infection than laboratory-based screening tests designed for use with serum and plasma and have a longer window period than any blood-based laboratory or rapid tests. Among HIV tests approved for use with oral fluid, the sensitivity and specificity of these tests is lower when used with oral fluid as compared to blood specimens.

[1]*Approximate window periods, based on the most current evidence (for plasma), are summarized in Table 1 and additional details are presented in Appendix A.*

SENSITIVITY refers to a **test's ability to identify an individual with infection as positive**. A highly sensitive test identifies most individuals with the infection (true positive), but may also identify individuals as positive that do not have the infection (false positive).

SPECIFICITY refers to a **test's ability to identify an individual who does not have an infection as negative**. A highly specific test will not detect infection for individuals who are not infected (true negative), but may also fail to identify infection in individuals that actually have infection (false negative).

Testing algorithms take advantage of the trade-offs between sensitivity and specificity. The screening test should be highly sensitive to minimize the chance that individuals with the infection are missed. All positive tests should be confirmed with a different highly specific test to ensure that the individual truly has the infection.

HD testing and linkage programs use rapid tests at point of care, and there are several rapid HIV tests from different manufacturers available. Most rapid HIV tests currently used by HDs are IgG antibody tests, while some rapid HIV tests detect both IgG and IgM antibodies. Detailed information is available from the CDC. Rapid HIV tests that are IgG sensitive have a window period of approximately 5 weeks, while those that are IgG/IgM sensitive have a window period of approximately 3 weeks. Many rapid tests detect, but do not distinguish between HIV-1 and HIV-2. There are two FDA-approved rapid tests that may be used with either blood or oral fluid specimens. There is one rapid HIV test suitable for use at point of care which detects both HIV antigen and antibodies (Appendix A).

The approximate window periods for HIV tests performed on plasma are summarized in Table 1, below.

HIV TESTS:
MEDIAN WINDOW PERIOD IN DAYS BASED ON PLASMA

	Laboratory-Based Tests	POC Rapid Tests
Ag/Ab	17.8	19.2
IgM/IgG	23.1	29.3
IgG	30.6	31.1

As HIV testing continues to evolve, newly developed tests will focus on further decreasing the window period and expanding the options for testing at point of care. There are several tests, including NATs suitable for use at point of care that are under investigation by multiple diagnostic manufacturers. ■

INTRODUCTION TO HCV TEST TECHNOLOGIES

Diagnosis of HCV requires an antibody test to be performed, and if positive, followed by a NAT that detects HCV RNA. The window period for HCV antibody tests has improved over the decades with newer assays. The currently available serologic assays have a window period of approximately 8-11 weeks. HCV RNA can be detected approximately 2–3 weeks after infection. The laboratory markers of HCV infection are presented in Figures 2, below.

FIGURE 2: LABORATORY MARKERS OF HCV INFECTION

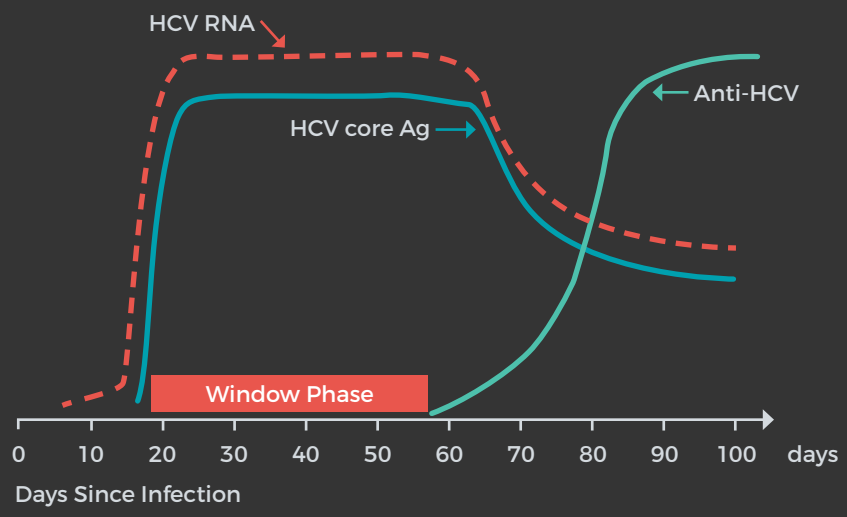


Figure provided by S. Kamili, DVH, CDC.

Some HCV NAT tests are FDA-approved for both diagnosis (i.e. qualitative result) and viral load (i.e. quantitative result). HCV antibody and NAT tests conducted in laboratories must be performed with serum or plasma specimens. There are no laboratory-based HCV tests for use with oral fluid. There is only one FDA-approved rapid HCV antibody test. This test can be performed on either fingerstick or venous whole blood. The performance of this test (i.e. sensitivity and specificity) is similar to laboratory-based HCV antibody tests for all specimen types.

Development of new tests for diagnosis of HCV is focused on detecting current infection. While not yet available in the United States, an assay that can detect core antigen, an early marker of infection, is commercially available in other countries.

NASTAD and APHL's 2017 webinar, *Advances in HIV and HCV Testing*, addressed current and near future testing technologies and strategies and can be an additional resource. A recording from the webinar and slides are available for download. ■

TESTING STRATEGIES FOR HIV AND HCV

HD testing and linkage programs can use two basic testing strategies: (1) laboratory-based (sometimes referred to as "conventional" testing); and (2) point-of-care rapid testing. Integration of HIV and HCV testing may be achieved through either strategy.

Laboratory Testing: Laboratory testing involves obtaining a specimen from a patient and sending it to a laboratory for processing.

Most laboratories use several different tests in a sequence (i.e. an algorithm) to diagnose HIV or HCV infection. If the first test result is positive, one or more subsequent tests may be conducted to confirm the result. If testing is performed "in house," such as within the same clinic or hospital, results may be available within several hours. If testing is performed elsewhere, such as in a public health or commercial laboratory, test results may be available within several days. Some laboratories do not perform all the supplemental testing needed to confirm diagnosis and may send specimens to other laboratories (i.e. reference laboratories) for supplemental testing or request that the provider submit a second specimen to a reference laboratory. Laboratory-based testing can detect infection earlier than rapid testing due to the shorter window periods for laboratory tests (Appendix A). If testing is performed by multiple laboratories because a specimen is referred or a second sample is required, the gains in earlier detection may be lost due to longer turnaround times.

It is important to understand where each step of testing is performed and which tests are conducted in order to identify additional testing that may be required (e.g. to confirm infection), correctly interpret results, and to report accurately identified cases to public health surveillance. Additionally, every laboratory operates slightly differently so it is important to learn how and when specimens are transferred between laboratories, how frequently tests are performed (e.g. if tests are batched), and mechanisms by which results will be reported to the testing provider, patient, and the health department (e.g. electronically, by fax).

The CDC published recommendations for Laboratory Testing for the Diagnosis of HIV Infection. The CDC recommends a testing algorithm which begins with an HIV antigen/antibody (Ag/Ab) test. A negative result indicates no HIV antibodies or antigen have been detected. Persons with a negative screening test could still have an acute infection and NAT testing may be considered for persons at high risk or with recent exposures. A positive result on the first test is followed by a second antibody test that allows differentiation of HIV-1 from HIV-2 infection. A negative or indeterminate result on the second test is followed by a NAT. Because this algorithm begins with an Ag/Ab combination test, it enables identification of HIV infection within two to three weeks of infection. Use of the NAT in this algorithm enables identification of acute HIV infection. Most public health laboratories currently use the CDC-recommended algorithm. Additional information about HIV testing practices in public health laboratories is available from APHL.

The CDC published Testing for HCV Infection: An Update of Guidance for Clinicians and Laboratorians which recommends that testing for HCV infection begin with an HCV antibody test. A positive result indicates either current HCV infection, resolved HCV infection, or a false positive result. A positive antibody result is followed by a NAT. If NAT testing detects HCV RNA, this indicates current infection. The completion of the diagnostic testing algorithm enables providers to distinguish between current infection and past infection, and provides the impetus to link a patient to care. A negative result indicates no HCV antibodies were detected. The diagnostic algorithm for HCV does not identify acute infection, and an HCV NAT may be considered for individuals with HCV antibody negative results but with recent exposure. Most public health laboratories perform HCV antibody testing. Additional information about HCV testing practices in public health laboratories is available from APHL.

In addition to laboratory-based testing for HIV and HCV, most diagnostic tests for sexually transmitted infections are also performed in the laboratory. Some, like syphilis, also employ a multi-step algorithm for diagnosis. Testing for other infections such as chlamydia and gonorrhea may be accomplished with a single NAT.

Point-of-Care Rapid Testing: There are a number of rapid HIV tests and one rapid HCV test that may be used outside of a laboratory setting, at point of care. Many of these tests have been categorized as waived tests under the Clinical Laboratory Improvement Amendments (CLIA) (also see Appendix C). Point-of-care rapid testing is just that: tests conducted where the client receives services and which typically make results available on the same day/visit. Positive test results are typically considered preliminary and usually require supplemental testing to confirm a diagnosis of HIV or HCV. A provider who performs a rapid test may provide supplemental testing through one of three ways: (1) use of a second rapid test (by a different manufacturer) at the point of care (available for HIV only); (2) by taking a blood specimen and sending it to a laboratory; or (3) by referral to another provider who can conduct supplemental testing, perhaps along with other tests needed for evaluation for treatment. If supplemental testing is conducted in a laboratory, final results are typically available within several days.

As described previously, most rapid tests detect HIV or HCV antibodies only and have median window periods of 3-5 weeks for HIV (plasma) and up to 8-11 weeks for HCV in blood samples. For oral fluid testing refer to the section above (also refer to Appendix A). In general, antibody tests that use blood from a vein can detect HIV sooner after infection than tests performed on blood from a fingerstick or oral fluid. Many HIV rapid tests used at point of care detect but do not distinguish between HIV-1 and HIV-2. There is currently only one HIV rapid test, suitable for use at point-of-care, which detects HIV antibodies and antigen. This test allows the user to determine whether HIV antibody and/or antigen are present. The CDC has published an information sheet on the use of this test in the laboratory algorithm.

In addition, there is one FDA-approved rapid syphilis test that is suitable for use at point of care, but may not be ideal in populations with a high likelihood of prior infection. Syphilis diagnosis also uses a multi-step algorithm so a positive rapid test must be confirmed with laboratory testing. ■

USING TESTING STRATEGIES FOR INTEGRATION

Laboratory testing has the advantage of facilitating integration of HIV and HCV testing and related services, as well as STD and viral hepatitis services (e.g. such as vaccination for hepatitis B), by enabling screening for multiple infections using a single specimen and/or simplified reporting. Laboratories frequently employ automated platforms for testing which can improve testing efficiency and may be used to test for multiple pathogens. In some laboratories, a single specimen can be tested for HIV, HCV, and other pathogens using the same automated platform. In other laboratories, multiple specimens may be required to test for multiple pathogens, but results for a patient may all be delivered to the testing and linkage provider on a single report, thereby facilitating linkage to care, and improving the quality of care that a patient receives. Commonly used HIV and HCV automated platforms for which there are tests for multiple pathogens are presented in Appendix B.

Integration of screening for multiple pathogens can also be achieved in a point-of-care setting, however multiple tests and samples would be required and a positive result on any of the tests may require follow-up testing performed in a laboratory. This strategy does not, however, preclude immediate linkage to medical care for further evaluation and treatment. Tests suitable for use at point of care are presented in Appendix C.

The ability to test for multiple pathogens is an important consideration for populations or communities where co-morbidity is a concern, such as gay men/MSM, for whom co-morbidity of HIV and syphilis is a concern, or HIV and HCV co-infection among people who use injection drugs. Health department HIV and HCV programs should discuss with stakeholders the potential benefits, drawbacks, and feasibility of various testing strategies to find an optimal approach for testing for relevant infections (and co-infections), thereby facilitating appropriate treatment. Stakeholders may include local testing and linkage providers, STD programs, HIV programs, viral hepatitis programs, public health and other laboratories, health department surveillance programs, and importantly, representatives from affected communities.

A comparison of testing strategies is presented in Table 2, below:

TABLE 2

COMPARISON OF TESTING STRATEGIES

Comparison Categories	Laboratory-Based Testing (using CDC-recommended serum/plasma algorithms)		Point-of-Care Rapid Testing (using CLIA-waived tests)	
	HIV	HCV	HIV	HCV
Approximate window period	2-3 weeks	8–11 weeks	3-5 weeks (blood specimens)[2]	8–11 weeks
Able to detect acute infection	✓ Yes	Yes, when interpreted in conjunction with clinical information such as symptoms	✗ No	Yes, when interpreted in conjunction with clinical information such as symptoms
Able to distinguish between HIV-1 and HIV-2	✓ Yes	Not applicable	✗ No	Not applicable
Final results	All tests in algorithm may be performed on one specimen		Negative results from single test/specimen; Positive results require supplemental testing with second specimen	
Testing for multiple infections	✓ Yes, multiple tests may be performed on single specimen		✗ No, separate specimens needed for other tests	
Timeframe for delivering results	Several hours to several days to final result, depending on setting and work flow		Negative results delivered same visit/day. For positive results, several hours to several days to final results depending on setting and requirements for supplemental testing	
FDA-approved specimen types	Serum or plasma[1]		Whole blood, serum, or oral mucosal transudate (HIV only)	
Specimen collection and processing	Specimen collection via venipuncture. Specimen requires centrifuging and possibly temperature controlled shipping		Specimen collection varies by test and can include venipuncture, finger stick, or oral fluid	
Quality assurance and monitoring	QA is managed by the laboratory performing the testing. Requires limited quality assurance by testing and linkage providers		Requires more extensive quality assurance by testing and linkage providers (e.g. temperature and lot control, staff proficiency testing, storage space)	

[1]Some laboratories may have validated additional specimen types for testing such as dried blood spots (DBS) or oral fluid but the assays are not FDA-approved for these types of samples. [2] Studies are being done to verify the window period for tests that use whole blood and oral fluid specimen types. Existing data for oral fluid tests used outside the US or for the at-home oral fluid HIV tests suggest that antibody cannot be reliably be detected for up to or 3 months. Another study found that point-of-care oral fluid testing detects fewer infections than other methods and is best reserved for circumstances precluding fingerstick or venipuncture. Refer to the Oral Fluid section above for additional information.

SELECTING A TESTING STRATEGY

There are many factors for HDs to consider when selecting an overall testing strategy. Health departments should use a testing strategy which ensures accurate and timely results. Optimally, HDs should use tests and testing strategies which can identify HIV or HCV as early in the course of infection as possible and facilitate linkage to and engagement in medical care to treat infection. It is important to note, however, that a single testing strategy may not be appropriate in every situation, setting, or for every population. There may also be situations where integration of HIV and HCV testing serves the needs of the population and the HD, and there may be other situations where integration does not.

In making decisions about testing strategies, HDs should consider population-, client-, and program-level factors. The factors are summarized in Table 3, below:

TABLE 3

FACTORS TO CONSIDER IN SELECTING A TESTING STRATEGY

Population-Level Factors

- HIV and HCV Prevalence
- HIV and HCV Incidence
- HIV-2 prevalence
- Co-morbidity of HIV and HCV, and/or with other conditions such as STDs and hepatitis B virus (HBV)

Client-Level Factors

- Likelihood of acute HIV infection (e.g. symptomatic, recent exposure)
- Likelihood of current HCV infection (i.e. recent or unresolved infection)
- Likelihood that clients will return for 2nd visit to receive final result or supplemental testing and linkage to care
- Understanding of the accuracy of testing strategy, specific tests
- Acceptability of the testing strategy (e.g. specimen type, length of time for result delivery, method of result delivery)
- Appropriateness and relevance to client needs and priorities (e.g. co-morbidity with STDs or HCV, utilization of HIV PrEP, pregnancy status, previously diagnosed HIV infection)
- Cost to client for testing and treatment, including insurance coverage, as applicable
- Readiness to engage in treatment
- Access to treatment (e.g. availability of treating providers, insurance coverage restrictions)

Program-Level Factors

- Staff capabilities to conduct testing
- Staff perceptions and attitudes about tests and testing strategy
- Feasibility of introducing strategy into existing workflow or setting
- Laboratory capacity to implement required tests, including CDC-recommended testing algorithms
- Delivery of related prevention and treatment services (e.g. HIV PrEP, syringe access services, substance use disorder prevention and treatment, STD treatment)

Health departments may decide to support different testing strategies for different clients, settings (e.g. clinics or community-based organizations), or populations, or they may decide to support just one strategy across all testing programs.

For example, a HD may elect to use rapid testing in conjunction with outreach testing activities and laboratory-based testing for testing performed in fixed-site testing programs. Alternatively, a HD may decide to provide laboratory-based testing for priority populations such as gay men/MSM in order to maximize accuracy of test results for those seeking HIV PrEP, or to individuals with history of injection drug use to efficiently identify HIV and HCV co-infection.

Here are two examples which consider selecting testing strategies based on the population, client, and programmatic factors described in Table 2.

EXAMPLE 1:

The Health Network operates a syringe services program (SSP) in conjunction with other HIV prevention programming. The SSP has provided HIV rapid testing for several years. The SSP plans to expand their services to include HCV testing and linkage services. During the last quarterly meeting with the health department and other regional service providers, the Health Network learned of a 12% increase in the number of individuals diagnosed with both HIV and HCV infection statewide compared with the prior year. The Health Network also learned about several very recent cases of acute HIV infection in their service area among people who use injection drugs. Based on the new information and health department encouragement to integrate HIV and HCV testing, the Health Network re-examined their plan. While the Health Network had planned to implement HCV testing using rapid HCV test kits, based on the new co-infection rates and the recent incidence of acute HIV infections, a laboratory-based strategy for co-testing for HIV and HCV would be a better option for most SSP clients. The public health laboratory has the capacity to perform testing for both infections and the health department will provide training for Health Network staff on phlebotomy and specimen submission.

EXAMPLE 2:

The health department funds a network of 10 community-based organizations (CBOs) and 5 community health centers (CHCs) to provide HIV testing and linkage services to gay men/MSM. Recently services were expanded to include HIV pre-exposure prophylaxis (PrEP). A subset of the network providers serves other populations, including people who use injection drugs. Historically, the CBOs have provided rapid HIV testing, while the CHCs conducted a mix of rapid testing at point of care and laboratory-based testing. The health department requires laboratory-based testing for PrEP initiation due to the fact that the population has a high risk of sexually transmitted infections coupled with the possibility of acute HIV infection. In conjunction with PrEP implementation, all CHCs shift to laboratory-based testing for HIV to meet health department requirements and they also add co-testing for syphilis, gonorrhea, and chlamydia. With training and assistance from collaborating CHCs, several of the CBOs are able to offer laboratory-based testing to support PrEP initiation as well. CBOs that are not able to develop the capacity to offer laboratory-based testing refer patients to collaborating CHCs. These CBOs continue to offer point-of-care rapid HIV testing for clients who are not seeking PrEP. Among the subset of CBOs which also provide services to persons who use injection drugs, they also begin to offer rapid HCV testing. Clients with positive HIV or HCV rapid tests are linked to a collaborating CHC for supplemental testing and treatment.

How to Decide? Health departments should develop plans for implementation through collaborative consultation with their HIV and HCV programs, and their public health laboratory (PHL). All decisions to change testing strategies at the laboratory or within the HD HIV or HCV program(s) have the potential to impact the other. Therefore, the HIV and HCV programs and PHL should discuss current and future testing capacity, priorities, and plans, as well as, the impact any potential changes will have on the laboratory and/or the HD.

HIV and HCV surveillance programs, testing providers, clinical laboratories, as well as members of target populations are also relevant stakeholders. In planning for integration of testing services, it is essential that health departments consider surveillance, program, and other sources of data to identify gaps and opportunities in services. HDs also need to consider the technical capacity of laboratory partners, the experience and expertise of program managers, and staff providing testing services, as well as the communities served by HD testing and linkage programs. Drawing on the expertise and experience of a diverse range of stakeholders will ensure that HDs consider perspectives necessary to make well-informed decisions regarding which tests and testing strategies to use, in which settings, and with which populations.

Table 4, below, presents various factors that health departments should consider in selecting a testing strategy to support integration of testing services.

TABLE 4

EXAMINING IMPLEMENTATION FACTORS TO SUPPORT INTEGRATION OF TESTING SERVICES

Population-Level Factors	Considerations
• HIV and HCV prevalence • HIV and HCV incidence	• Use epidemiologic data to characterize incidence and prevalence of HIV, HCV, and as relevant, STDs, and HBV. Segment the analysis by geographic area, testing provider or venue, and population.
• HIV-2 prevalence	• Compare epidemiologic data with other data regarding current levels of testing and prevalence; e.g. program service data or medical claims data to identify gaps and opportunities for improvement or redirection.
• Co-morbidity of HIV and HCV, and/or with other conditions such as STDs and HBV	• Reviewing multiple sources of data can help a HD "match" strategies and populations, geographic areas, and venues to determine which strategies are appropriate, and whether a single or multiple testing strategies are appropriate.

Client-Level Factors	Considerations
• Likelihood of acute HIV infection and/or recent HCV infection	• Train testing staff to employ a brief set of screening questions to identify patients who have symptoms suggestive of acute infection or behaviors suggestive of possible recent exposure who may benefit from testing best suited to identify those infections, and provision of HIV PrEP or PEP, if appropriate. • Implement a protocol to facilitate immediate linkage to medical care for patients with symptoms or risk suggestive of acute HIV infection.
• Likelihood that clients will return for 2nd visit to receive final result or supplemental testing	• Make test results available to clients via telephone or electronically, if permitted under regulation or law. Implement strategies to remind clients to return for results (e.g. text message reminders). • Develop simple messages that testing staff can use with clients to help them understand the need for supplemental testing and for returning for test results. This will be particularly important if a mix of point-of-care rapid and conventional tests are used to accomplish integration of testing services. • Implement protocols to facilitate immediate linkage to clinical providers for testing, and if appropriate, medical evaluation and treatment including: (1) clients tested with negative rapid test results, but with recent exposure or symptoms; (2) clients with positive rapid test results; and (3) clients with symptoms suggestive of acute HIV infection.
• Understanding the accuracy of testing strategy and specific tests employed	• Train testing program staff to use simple messages regarding the accuracy of tests, and the approximate window period of tests to optimize client understanding of test limitations. This will be important for clients who may express a preference for point-of-care rapid testing but who would benefit from laboratory-based testing using the CDC-recommended algorithm, as well as, immediate linkage to medical care. Such clients include those who have symptoms or risk suggestive of acute HIV or recent HCV infection, including those who have a negative rapid HIV test result. This is also important for clients who may have recent possible HIV exposure and for whom re-testing may be appropriate.

Client-Level Factors	Considerations
• Acceptability of the various features of the testing strategy (e.g. which infections are being tested for, specimen type(s) and methods for obtaining specimens, length of time for result delivery)	• During program planning, assess target population awareness and understanding of various tests and testing strategies, and priorities for testing (e.g. a target population may be more interested in testing for one infection, but may be at risk for several). This will help to identify the best testing strategy and also suggest messages for clients that will increase their understanding and acceptance of the tests and testing strategies used by the program. Consider conducting interviews or focus groups with representatives of the target population(s) to explore different testing strategies. This will help to understand which factors are likely to be a barrier or facilitator to using particular testing strategies. • Train testing staff to employ simple messages regarding the strengths of the tests and testing strategy, and to provide clear and succinct information to the client regarding when they can expect to learn their test results, and how they can expect to receive them. Results associated with testing for multiple infections may not be complete or available at the same time, and clients should be aware of this so that they can have realistic expectations of when they will receive final results.
• Appropriateness and relevance to client needs and priorities (e.g. co-morbidity with STDs, HCV, utilization of HIV PrEP, pregnancy status, previously diagnosed HIV infection)	• Testing strategies should optimally enable screening for relevant (to the client) co-infections, thereby facilitating treatment for these infections, regardless of HIV status. Some clients may be more interested in, or concerned with HCV infection than with HIV (or STDs), for example. Staff may require training to help them assess and communicate to clients risk for and relevance of tests for multiple infections. Testing staff should employ simple messages to help clients understand the value of being tested for multiple infections.
• Cost to client for testing and treatment	• Provide training and tools to help testing staff assess the extent to which the actual or perceived costs associated with testing and treatment of HIV, HCV, or any other infection for which the client may be tested are a concern for the client. Identify opportunities for reduced or no cost (to the client) testing and treatment services. • Train staff to clearly and simply communicate to clients whether there will be a cost to them for testing services, how much the cost will be, and payment options, including situations where health insurance will be billed. There may be different costs associated with testing for multiple infections, depending on the specific test used, the infections tested for, and testing history (e.g. the frequency and intervals of prior tests for an infection).

Client-Level Factors	Considerations
	• As part of program planning, assess availability of treatment, health insurance coverage for treatment, and resources which can assist clients with engagement in treatment. Access to, and availability of treatment, as well as, insurance coverage for treatment may vary by infection. It may be helpful to prepare a summary of coverage of testing and treatment services for common health insurance plans that can be used as a reference by program staff. This may be particularly relevant for HCV treatment, where coverage of treatment is often more complicated than for HIV (or STDs). The Health Law & Policy Clinic of the Center for Health Law and Policy Innovation publishes reports on qualified health plan coverage of HIV and HCV treatment for a number of states, and these reports may be a resource for health departments.
• Readiness to engage and access to treatment	• Some clients may be more or less interested in, or concerned with treatment for one infection versus another. Testing staff should employ simple messages and techniques such as motivational interviewing to help clients accept treatment as relevant, and to understand its availability, means to access treatment, and the value of treatment.

Program-Level Factors	Considerations
• Staff capabilities to conduct testing	• During program planning, consider the knowledge, skills, and attitudes that program and laboratory staff will need to perform testing and/or sample collection using the selected strategy. Provide appropriate training and/or cross-training on requirements associated with different tests and testing strategies, and the processes associated with the testing strategy employed (e.g. turnaround time associated with each test performed). For example, staff collecting samples may need to acquire an additional volume of sample to enable testing for both HIV and HCV; samples may need to be packaged and sent to different laboratories; or, if rapid tests are used, tests for different infections or from different manufacturers have different requirements to conduct each test.
• Staff perceptions and attitudes about tests and testing strategy	• Staff should receive information and training that will help them to understand the different infections which are being tested for, test performance, and the factors that impact performance (e.g. type of test, specimen type). Staff should also receive information and education about the benefits associated with the selected testing strategy.

Program-Level Factors	Considerations
• Feasibility of introducing strategy into existing workflow or setting	• Conduct a work flow analysis to determine where in an existing workflow the various components (e.g. specimen acquisition, specimen preparation) of testing can feasibly be introduced. If different strategies are to be used to test for different infections, or for patients with different circumstances, this should be addressed in planning workflow (e.g. rapid testing for HIV and conventional testing for HCV and syphilis; rapid HIV and HCV testing, except when acute HIV infection is a consideration).
• Laboratory capacity to implement the required tests, including CDC-recommended testing algorithms	• Determine the tests and testing algorithms being used by the laboratory where testing will be performed in order to determine what changes in laboratory capacity (e.g. tests conducted, platforms used) or workflows will be required in order to accomplish integration of testing services. The PHL (if it is not the laboratory that will perform testing) may be able to provide training and technical assistance to enhance laboratory capacity, implement new algorithms and work flows, or adopt CDC recommended laboratory-based testing algorithms.
• Delivery of related prevention and treatment services (e.g. HIV PrEP, syringe access services, substance use disorder prevention and treatment)	• Assess related prevention and treatment services which will be offered in conjunction with, or available to recipients of testing services to ensure that the selected testing strategy appropriately supports and facilitates those services. For example, delivery of PrEP engagement or navigation services may be best served by laboratory-based strategies which can identify acute HIV infection, and simultaneously screen for HCV and STDs, including hepatitis B. Similarly, if prevention and support services target individuals who inject drugs, the selected testing strategy should support screening for both HIV and HCV.

Here are two examples which illustrate how a health department considers the factors described in Table 3 in making decisions about testing strategies.

EXAMPLE 1:

There has been a 5% increase in new HIV cases reported to the health department in each of the past three years among people with a history of injection drug use. Screening for hepatitis C, using rapid tests, is offered through several outreach programs supported by the health department. Approximately 30% of those tested are HCV antibody positive, only 10% of whom go on to get RNA testing. In light of these data, the health department wants to expand both HIV and HCV testing for people who use injection drugs (PWID), and to ensure that they are linked to medical treatment. The health department HIV and HCV prevention programs, in collaboration with their public health laboratory, develop a plan wherein fixed site community-based HIV testing and linkage programs serving PWID will expand services and will test all PWID seeking testing services for both HIV and HCV. All testing will be performed by the public health laboratory, including reflex testing to confirm HIV and HCV antibody reactive results. Agency staff will receive training in phlebotomy and the public health laboratory will provide technical assistance to develop specimen preparation and handling protocols. The health department HIV and HCV prevention programs will collaborate to develop training to support integrated testing services, including development of sample "scripts" that test counselors can use to explain the benefit of co-testing and availability of treatment. Health department HIV partner services staff will also receive training to improve their skills to provide risk reduction relevant to HCV and injection risk, and to increase their knowledge of HCV prevention and treatment resources.

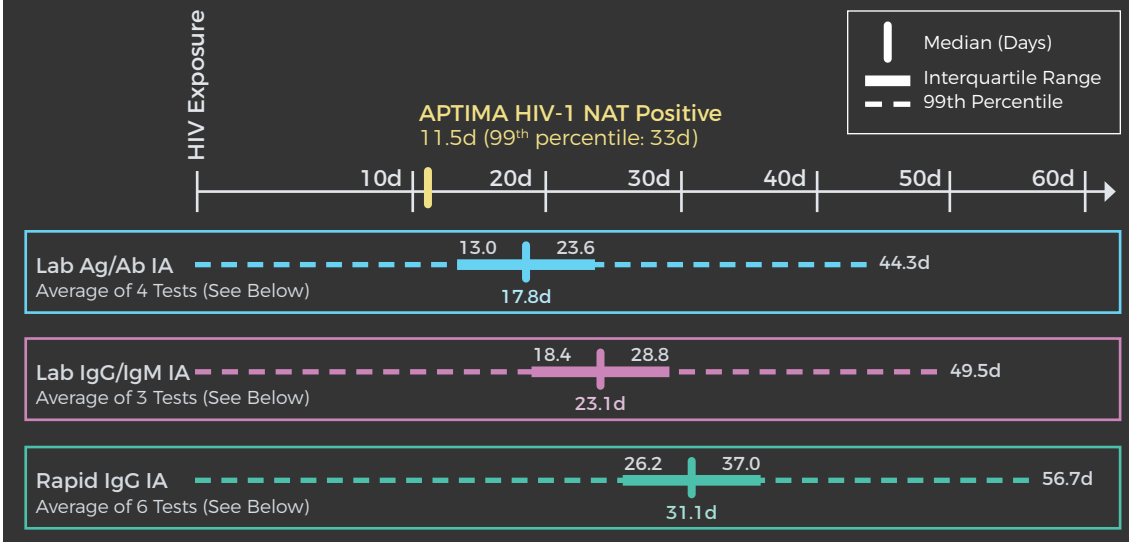
EXAMPLE 2:

The health department HIV prevention program funds a network of community-based organizations (CBOs) and community health centers (CHCs) to provide HIV testing and linkage services to men who have sex with men (MSM), including HIV pre-exposure prophylaxis (PrEP). A subset of the network providers serves other populations, including people who use injection drugs. Historically, the CBOs have provided rapid HIV testing, while the CHCs conducted a mix of rapid testing at point of care and laboratory-based testing. With the implementation of PrEP, given that this is a population with a high risk of sexually transmitted infections, coupled with the possibility of acute HIV infection, the health department decides to require laboratory-based testing for PrEP initiation. The health department also prioritizes expansion of HCV testing targeted to PWID. Therefore, all CHCs supported by the health department will be required to shift to laboratory-based testing for HIV and also add co-testing for syphilis and HCV. With technical assistance and training from the health department, several CBOs are able to initiate phlebotomy and offer testing for both HIV and HCV. CBOs send samples to the public health laboratory, which conducts screening for both HIV and HCV. Through a contract with a clinical laboratory, the public health laboratory refers samples requiring HIV and HCV NAT. CHCs submit specimens to the public health laboratory for clients who are not patients of the CHC, or who have no insurance. CBOs which lack capacity to implement phlebotomy are provided training by the health department to screen for referral to a collaborating CHC clients who may have acute HIV infection or who are recommended PrEP. The public health laboratory provides training and proficiency testing to these CBOs to enable them to implement point-of-care rapid HCV testing, and to continue to provide rapid HIV testing. The health department HIV and HCV prevention programs collaborate to develop training to support integration of HCV testing into services, including skills-development to identify injection-related risk, explanation of the benefit of testing for HIV, HCV, and syphilis, as well as treatment options.

Resources to support integration of testing services remain a challenge. Health departments should leverage multiple sources of funding to support integration. State and federal funding streams for HIV, viral hepatitis, STDs, and substance use prevention and treatment services, have more or less flexibility regarding integration of testing services, including allowable expenditures for co-testing or testing for multiple infections. To the greatest extent possible, HDs should optimize resources made available through 3rd party reimbursement of testing services. Many PHLs currently have the capacity to bill Medicaid and other insurers for testing services performed by the PHL, but may not be utilizing that capacity to bill for HIV, HCV, or related infections. NASTAD's Billing Coding Guide for HIV Prevention includes information and examples of billing for HIV, HCV, and STD testing services. ■

APPENDIX A

ESTIMATED WINDOW PERIODS FOR TESTS USING PLASMA SPECIMENS*



HIV TESTS	Median (IQR) (days)	99th Percentile (days)
Laboratory Ag/Ab Immunoassays (IA)		
ARCHITECT HIV Ag/Ab Combo	17.9 (13.6, 23.1)	41.6
BioPlex 2200 HIV Ag-Ab	17.4 (12.8, 23.2)	43.1
GS Combo Ag/Ab EIA	17.4 (11.4, 24.6)	50.5
Siemens Combo HIV Ag-Ab	18.4 (14.1, 23.6)	42
Rapid Ag/Ab Immunoassay (IA) [Not included in Figure]		
Determine HIV-1/2 Ag/Ab Combo	19.2 (14.8, 24.6)	43.1
Laboratory IgM/IgG Immunoassay (IA)		
ADVIA HIV 1/O/2 Enhanced	21.5 (16.1, 28.0)	53.5
GS HIV-1/HIV-2 PLUS O EIA	24.7 (20.4, 30.0)	48.4
VITROS Anti-HIV-1 + 2 Assay	23.1 (19.0, 28.3)	46.6
Rapid IgG/IgM-sensitive Immunoassay (IA) [Not included in Figure]		
INSTI HIV-1/HIV-2 Antibody Test	26.1 (21.9, 31.2)	49.8
Uni-Gold Recombigen HIV	32.5 (26.5, 39.4)	64.9
Rapid IgG Immunoassay (IA)		
Clearview COMPLETE HIV-1/2	31.7 (26.9, 37.5)	56.7
Clearview HIV 1/2 STAT-PAK	31.3 (26.1, 37.4)	56.7
DPP HIV-1/2	30.3 (25.6, 36.0)	55
Multispot HIV-1/HIV-2 Rapid Test[b]	27.9 (23.5, 33.1)	51.3
Oraquick ADVANCE Rapid HIV-1/2 Antibody Assay	35.3 (29.2, 42.4)	64.6
Reveal G2 Rapid HIV-1 Antibody Test	30.3 (25.9, 35.8)	55.8

Abbreviations: (Ab) antibody, (Ag) antigen, (EIA) enzyme immunoassay.

Estimated median, interquartile range (IQR), i.e. the 25th and 75th percentiles, and 99th percentiles of the window period distribution, the duration of time between HIV exposure and immunoassay reactivity, in days. Percentiles are means of respective percentiles from four computational methods. Window period estimates were sums of 10,000 simulated days ITRI, using parameters from the observed data (testing of plasma specimens), and 10,000 simulated eclipse period days as graphed in Figure 1 of the manuscript.

*Adapted from Delaney et al., CID 2017:64. Estimates based on simulations and parameters from observed data with plasma specimens.

APPENDIX B

FDA-APPROVED HIV, HBV, HCV, AND STD DIAGNOSTIC OR MONITORING TESTS BY MANUFACTURER AND PLATFORM

SEROLOGIC ASSAYS

Manufacturer	Platform	HIV	HAV	HBV	HCV	Chlamydia, Gonorrhea, Syphilis
Abbott	Architect	HIV Ag/Ab Combo	Anit-HAV IgG, Anti-HAV IgM	Anti-HBs, HBsAg Qual, HBsAg Qual Conf., Anti-Hbc, Anti-HBc IgM,	Anti-HCV	Syphilis TP
Bio-Rad	EVOLIS	HIV Combo Ag/Ab EIA, HIV-1/HIV-2 Plus O EIA	MONOLISA Anti-HAV EIA, MONOLISA Anti-HAV IgM EIA	MONOLISA Anti-HBs EIA, MONOLISA Anti-HBc, GS HBsAG EIA 3.0, GS HBsAG Confirmation 3.0		Syphilis IgG
	BioPlex 2200	HIV Ag-Ab				Syphilis Total & RPR assay
	Manual	HIV Combo Ag/Ab EIA, HIV-1/HIV-2 Plus O EIA, Geenius HIV-1/2 Supplemental Assay	MONOLISA Anti-HAV EIA, MONOLISA Anti-HAV IgM EIA	MONOLISA Anti-HBs EIA, MONOLISA Anti-HBc, GS HBsAG EIA 3.0, GS HBsAG Confirmation 3.0		
Ortho-Clinical Diagnostics	VITROS Eci/ EciQ	Anti-HIV1+2	Anti-HAV IgM, Anti-HAV Total	Anti-HBc, Anti-HBC IgM, Anti-HBe, Anti-HBs, HBeAg, HBsAg	Anti-HCV	
	VITROS 3600	Anti-HIV1+2, VITROS HIV Combo	Anti-HAV IgM, Anti-HAV Total	Aniti-HBc, Anti-HBC IgM, Anti-HBs, HBsAg	Anti-HCV	
	VITROS 5600		Anti-HAV IgM, Anti-HAV Total	Anti-HBc, Anti-HBC IgM, Anti-HBs, HBsAg	Anti-HCV	
Roche	Cobas e 411		Elecsys Anti-HAV IgM, Anti-HAV Total	Elecsys Anti-HBc Total, Anti-HBc IgM, HBsAg, HBsAg Confirmatory, Anti-HBs	Elecsys Anti-HCV II	Elecsys Syphilis (Treponemal)
	Cobas e 601		Elecsys Anti-HAV IgM, Anti-HAV Total	Elecsys Anti-HBc Total, Anti-HBc IgM, HBsAg, HBsAg Confirmatory, Anti-HBs	Elecsys Anti-HCV II	Elecsys Syphilis (Treponemal)
	Cobas e 602	Elecsys HIV Combi PT	Elecsys Anti-HAV IgM, Anti-HAV Total	Elecsys Anti-HBc Total, Anti-HBc IgM, HBsAg, HBsAg Confirmatory, Anti-HBs, HBeAg	Elecsys Anti-HCV II	Elecsys Syphilis (Treponemal)
Siemens	ADVIA Centaur XPT	HIV Ag/ AB Combo, EHIV 1/O/2 Enhanced		Anti-HBs2, HBc IgM, HBc Total,	HCV	Syphilis (Treponemal)
	ADVIA Centaur XP/ CP	HIV Ag/ AB Combo, EHIV 1/O/2 Enhanced		Anti-HBs2, HBc IgM, HBc Total, HBsAg, HBs Ag Confirm.	HCV	Syphilis (Treponemal)
	IMMULITE 2000/Xpi			Anti-HBs, Anti-HBs Quant., Anti-HBc IgM, Anti-HBc Total, HBsAg, HBsAg Confirm.		Syphilis Screen (Treponemal)

APPENDIX B

FDA-APPROVED HIV, HBV, HCV, AND STD DIAGNOSTIC OR MONITORING TESTS BY MANUFACTURER AND PLATFORM

MOLECULAR ASSAYS

Manufacturer	Platform	HIV	HAV	HBV	HCV	STD
Abbott	m20000	RealTime HIV-1 (Viral Load)		RealTime HBV (Viral Load)	RealTime HCV (Viral Load), RealTime HCV Genotype II	RealTime CT/NG
Roche	cobas 6800/8800	cobas HIV-1 (Viral Load)		cobas HBV (Viral-Load)	cobas HCV (Dual-Claim)	
	cobas 4800				COBAS AmpliPrep/ COBAS Taqman HCV Test, v2.0 (Dual Claim)	cobas 4800 CT/NG
	cobas AmpliPrep	COBAS AmpliPrep/ COBAS Taqman HIV-1 Test, v2.0 (Viral Load)		COBAS AmpliPrep/ COBAS Taqman HBV Test, v2.0 (Viral Load)		
	Manual			COBAS Taqman HBV Test (Viral Load)	COBAS Taqman HCV Test (Viral Load)	
Hologic	Panther	Aptima HIV-1 Quant (Viral Load)		Aptima HBV Quant (Viral Load)	Aptima HCV Quant Dx (Dual-Claim)	APTIMA Combo2 for CT/NG, APTIMA CT, APTIMA GC, APTIMA TV
	Tigris					APTIMA Combo2 for CT/NG, APTIMA TV
	Manual	Aptima HIV-1 RNA Qual (Diagnosis)			Aptima HCV RNA Qual (Diagnosis)	
Siemens	VERSANT				VERSANT HCV Genotype 2.0 (LiPa)	

APPENDIX C

FDA-APPROVED RAPID TESTS FOR HIV, HCV, AND SYPHILIS

	Manufacturer	Pathogen	Assay Name	Sample Type	Time to Result	Detects
CLIA-WAIVED	Alere	HIV	Determine HIV-1/2 Ag/Ab Combo	Fingerstick whole blood	20 min	HIV-1 and HIV-2 antibodies, HIV-1 antigen
	bioLytical Laboratories	HIV	INSTI HIV-1/HIV-2 Antibody test	Fingerstick whole blood	<2 min	HIV-1 and HIV-2 antibodies
	Chem-Bio	HIV	DPP HIV-1/2	Fingerstick wholeblood, venous whole blood, oral fluid swab	10-40 min, specimen type dependent	HIV-1 and HIV-2 antibodies
			HIV 1/2 STAT-PAK	Fingerstick whole blood, venous whole blood	15 min	HIV-1 and HIV-2 antibodies
			SURE CHECK HIV 1/2 Assay	Fingerstick whole blood, venous whole blood	15 min	HIV-1 and HIV-2 antibodies
	OraSure	HIV	OraQuick ADVANCE Rapid HIV-1/2 Antibody Test	Fingerstick whole blood, venous whole blood, oral fluid swab	20 min	HIV-1 and HIV-2 antibodies
		HCV	OraQuick HCV Rapid Antibody Test	Fingerstick whole blood, venous whole blood	20 min	HCV Antibodies
	Trinity BioTech	HIV	Uni-Gold Recombigen HIV-1/2	Fingerstick whole blood, venous whole blood	10 min	HIV-1 and HIV-2 antibodies
		Syphilis	Syphilis HealthCheck	Fingerstick whole blood, venous whole blood	10 min	Trepnonemal Antibodies
HOME USE	OraSure	HIV	OraQuick In-Home HIV Test	Oral fluid swab	20 min	HIV-1 and HIV-2 antibodies
MODERATELY COMPLEX	Alere	HIV	Determine HIV-1/2 Ag/Ab Combo	Serum, plasma, whole blood	20 min	HIV-1 and HIV-2 antibodies, HIV-1 antigen
	bioLytical Laboratories	HIV	INSTI HIV-1/HIV-2 Antibody test	Plasma, whole blood	<2 min	HIV-1 and HIV-2 antibodies
	Chem-Bio	HIV	DPP HIV-1/2	Serum, plasma, whole blood, and oral fluid swab	10-40 min, specimen type dependent	HIV-1 and HIV-2 antibodies
			HIV 1/2 STAT-PAK	Serum, plasma, whole blood	15 min	HIV-1 and HIV-2 antibodies
			SURE CHECK HIV 1/2 Assay	Serum, plasma, whole blood	15 min	HIV-1 and HIV-2 antibodies
	MedMira	HIV	Reveal G3 Rapid HIV-1 Antibody Test	Serum, plasma, whole blood	<2 min	HIV-1 antibodies
	OraSure	HIV	OraQuick ADVANCE Rapid HIV-1/2 Antibody Test	Plasma, whole blood, oral fluid swab	20 min	HIV-1 and HIV-2 antibodies
	Trinity BioTech	HIV	Uni-Gold Recombigen HIV-1/2	Serum, plasma, whole blood	10 min	HIV-1 antibodies
		Syphilis	Syphilis HealthCheck	Serum, plasma, whole blood	10 min	Trepnonemal Antibodies