

## GUIDANCE DOCUMENT FOR THE IMPLEMENTATION OF HIV SCREENING SERVICES FOR PRIVATE GP CLINICS IN SINGAPORE

Dr Tan Kok Kuan, Dr Matthew Tan, Dr Sophia Archuleta, Dr Wong Chen Seong, Prof Roy Chan, Dr Martin Chio, Dr Choy Chiaw Yee

### ABSTRACT

**This document is intended for private practice general practitioners (GP) and family physicians in Singapore who wish to initiate or expand on HIV testing services in their clinics. It provides a consolidated source of pertinent information and complements current national guidelines on HIV testing. The objective of this document is to increase HIV testing among patients, identify patients with unrecognized HIV infection and link them to care and reduce the risk of infection to patients who are currently uninfected with HIV but continue to be at risk.**

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### INTRODUCTION

Human Immunodeficiency Virus (HIV) remains a major global public health threat. In Singapore, 9,129 Singapore residents have been infected with HIV as of end-2021, of whom 2,255 had passed away. Sexual transmission remains the most common mode of transmission, accounting for more than 95 percent of all HIV-infected cases. Sixty-two percent of patients had late-stage HIV infection at diagnosis.<sup>1</sup>

Accurately diagnosing a patient's HIV status remains the most important pillar in strategies to prevent HIV transmission.<sup>2</sup> Persons diagnosed with HIV can be linked to life-sustaining anti-retroviral therapy that also reduces their likelihood of transmitting HIV to others. When a HIV-positive person's viral load is undetectable, the HIV is non-

transmittable (U=U).<sup>3</sup> Persons who are not infected with HIV but are at risk can leverage on a variety of behavioural and biochemical tools such as HIV Pre-Exposure Prophylaxis (PrEP) and Post-Exposure Prophylaxis (PEP) to remain uninfected. Partner notification can lead to early diagnosis and abort the infection chain.

Current anti-retroviral therapy (ART) for HIV is highly effective in preventing morbidity and helping people living with HIV (PLHIV) attain normal or near-normal life expectancy.<sup>4</sup> Availability of fixed dose combination medicines has significantly reduced the patient's pill burden. Conversely, failure to diagnose and treat HIV can result in acquired immune deficiency syndrome (AIDS) and onward transmission of HIV to others.

Only an estimated 82 percent of PLHIV in Singapore are aware of their status. This falls short of the Joint United Nations Programme on HIV and AIDS' (UNAIDS) 90-90-90 targets.<sup>5,19</sup> HIV testing is routinely offered to all inpatients in public hospitals, all antenatal mothers, and to all males enlisted for National Service.<sup>6,7</sup> Action for AIDS runs an Anonymous HIV testing centre and Mobile HIV Testing Service. There are also nine private GP clinics designated as Anonymous HIV Testing sites.

Private GP practices are usually based within residential communities and are more accessible than the Accident & Emergency department or the Specialist Outpatient clinics. GPs are hence uniquely positioned to offer HIV testing as well as provide prevention counselling and encourage HIV testing in the general population and especially high-risk groups.

This article aims to provide GPs and family physicians with knowledge and information required to initiate and conduct HIV screening in their practices.

### METHODS

Relevant publications used in this paper were searched for via PubMed. In determining if they were suitable references, the following search criterion was used: English publications in peer reviewed journals between 2000 to 2021. Local Singaporean guidelines were obtained from Singapore Government websites.

### BASIC BIOLOGY OF HIV AND RECOGNISING ACUTE HIV INFECTION

HIV is a single-stranded RNA Lentivirus in the Retrovirus Family that infects humans. It has an outer envelope that surrounds two copies of single-stranded RNA as well as several viral proteins. Upon infection, the envelope 120 Glycoprotein attaches to CD4 receptors expressed on the surface of lymphocytes. Attachment is followed by fusion

DR TAN KOK KUAN  
Director, Dr Tan Medical Centre

DR MATTHEW TAN  
Physician, Dr Tan Medical Centre

DR SOPHIA ARCHULETA  
Director, National HIV Programme

DR WONG CHEN SEONG  
Deputy Director, National HIV Programme

PROF ROY CHAN  
Senior Consultant, National Skin Centre

DR MARTIN CHIO  
Senior Consultant, National Skin Centre

DR CHOY CHIAW YEE  
Consultant, National Centre for Infectious Diseases

of the virus membrane with the cell membrane. The RNA is converted to DNA via the action of reverse-transcriptase enzymes. The viral DNA migrates to the cell nucleus and integrates as proviral DNA into the host cell DNA.

The HIV virus then uses the intracellular machinery of the host cell to replicate HIV RNA and synthesise HIV proteins. New HIV RNA and HIV proteins move to the cell membrane and assemble as an immature HIV virus. New HIV viruses bud off from the cell membrane. Proteases within the virus cleave the long HIV protein chains, turning the virus into its mature and infectious form.

If left untreated, HIV infection results in a gradual decline in CD4 cell count, eventually progressing to AIDS, which is characterised by the development of opportunistic infections or specific malignancies. This occurs at a median of 10 years after initial infection with HIV.<sup>8</sup>

Acute HIV infection may present with a constellation of nonspecific symptoms. In 10 to 60 percent of cases, early HIV infection may be asymptomatic.<sup>9</sup>

In patients who do develop symptoms, the usual time from HIV exposure to the development of symptoms is 2-4 weeks and are often described as a mononucleosis-like syndrome.<sup>10</sup> The severity and duration of symptoms vary widely from patient to patient, but these are often self-resolving. In Singapore, the most common symptoms of acute HIV infection are fever, rash, and diarrhoea, which occur in more than 50 percent of patients.<sup>9,11</sup> Symptoms of acute HIV infection can mimic that of dengue. Seroprevalence of HIV infection among patients with dengue-like illness was reported at 2.1 percent. Providers are advised to consider HIV testing in patients who present with dengue-like illness but test negative for dengue.<sup>12</sup>

## TYPES OF HIV TESTS

HIV testing options in Singapore include lab-based tests and Point-of-Care (POC) tests.

Lab-based tests require a venipuncture blood draw and may take up to a week to return a result. They are more sensitive and specific compared to POC tests and have a shorter window period.<sup>13</sup> A positive lab-based screening HIV test automatically triggers a confirmatory test using the same blood sample. POC tests are performed on saliva, finger-stick whole blood, or blood from a venipuncture that was already drawn for other routine blood tests. They provide patients and providers with immediate results. However, they are less sensitive and have a longer window period compared to lab-based tests.

HIV POC test kits are a Class D Medical Device, the control of which falls under the purview of the Health Science Authority (HSA) and is regulated under the Health Products Act, Health Products (Medical Devices) Regulations 2010.

HSA maintains a directory of approved medical devices. Information on the status of device registration can be found

on the Singapore Medical Device Register, available online at: <https://www.hsa.gov.sg/e-services/infosearch>. Each product has its unique performance characteristics, storage conditions, materials, procedures, and interpretations. The details can be found in the product insert that accompanies the test kits.

Reactive, inconclusive, or erroneous results on the POC tests must be followed up by a venous blood sample sent to a diagnostic clinical laboratory for confirmatory testing. Lab-based and POC HIV tests are further subdivided into different generations.<sup>14</sup>

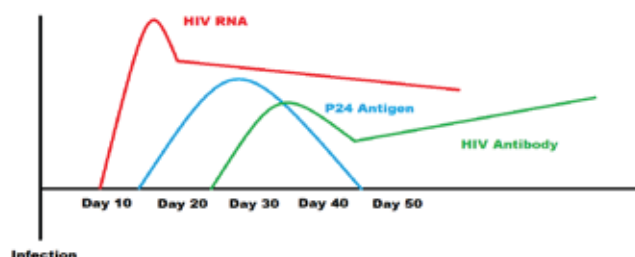
1 <sup>st</sup> Generation	This test uses antigens from a lysate of HIV viruses grown in cell culture and detects anti-HIV-1 and anti-HIV-2 IgG antibodies. It employs labelled antihuman IgG for detection of IgG antibodies. The HIV-1 Western Blot assay uses 1 <sup>st</sup> Generation testing principles.
2 <sup>nd</sup> Generation	This test uses synthetic peptides or recombinant HIV protein antigens and detects anti-HIV-1 and anti-HIV-2 IgG antibodies. It employs labelled antihuman IgG or Protein A for detection of IgG antibodies. It improves on both the sensitivity and specificity from 1 <sup>st</sup> Generation tests.
3 <sup>rd</sup> Generation	This test uses synthetic peptides or recombinant HIV protein antigens bound to HIV antibodies in an antigen sandwich format. This allows it to detect anti-HIV-1 and anti-HIV-2 IgG and IgM antibodies. The ability to detect IgM antibodies increases sensitivity during early seroconversion. It improves on the window period from 2 <sup>nd</sup> Generation tests.
4 <sup>th</sup> Generation	This test combines the detection of p24 antigen with 3 <sup>rd</sup> Generation HIV tests. Inclusion of p24 antigen capture allows detection of HIV-1 before seroconversion. This assay improves on the window period from 3 <sup>rd</sup> Generation tests.

## HIV TESTING WINDOW PERIOD

The HIV testing window period is defined as the period of time from exposure to HIV infection to when the body produces sufficient HIV antibodies to be detected by standard HIV tests. The window period varies between tests and is determined by the marker that is targeted by the particular assay as well as the lower detection limit of the test. There is also a variability in the time needed for

markers of infection to rise to detectable levels in different individuals. The window period is therefore a distribution of time rather than a fixed duration of time that is identical to every patient (refer to **Figure 1**).

**Figure 1. After a HIV infection, the body responds by undergoing a series of serologic events and produce virus, antigens, and antibodies in an expected manner.**



Immediately after infection, there is a period of time where it is not possible to detect any markers of infection. This is known as the “Eclipse Period” and lasts for about 10 days.<sup>15,16</sup>

Approximately 10 days after infection, HIV-1 RNA becomes detectable by Nucleic Acid Amplification Tests in plasma. Levels peak between 20 to 30 days.<sup>17</sup>

Next, HIV-1 p24 antigen is expressed and can be detected by 4<sup>th</sup> generation immunoassays within 4-10 days after the initial detection of HIV-1 RNA. Levels continue to rise until day 25 to 30, at which point antibodies are able to complex with circulating p24. By day 50, p24 is often cleared from the bloodstream entirely.

Next, IgM antibodies are expressed, which can be detected by 3<sup>rd</sup> and 4<sup>th</sup> generation immunoassays 3-5 days after p24 antigen is first detectable, approximately 10 to 13 days after the appearance of viral RNA, i.e., 20-23 days from infection.

Finally, IgG antibodies are expressed beginning day 30 to 35 from infection and persist throughout the course of HIV infection.

In rare cases, antibodies may not be detectable for a number of months.<sup>16</sup>

Taking into account all antibody-based tests including rapid HIV tests, and applying statistical confidence limits (99 percent) to the average time that standard HIV screening tests become detectable to declare a person is uninfected, a clinician can say with confidence that a person with a negative HIV antibody test has not acquired HIV infection after 12 weeks, provided there has not been any further exposure.<sup>8</sup>

Laboratory testing using antigen/antibody tests detects HIV infection earlier than other available tests that detect only antibodies. If a person gets a negative laboratory-based antigen/antibody test on blood plasma less than 45 days after a possible HIV exposure, follow-up testing can be done 45 days after the possible HIV exposure.<sup>18</sup> For all other tests,

HIV tests should be repeated at least 90 days after high-risk exposure.<sup>13</sup>

POC tests have an undefined window period. When using POC tests, after a negative test in the window period, a patient should be retested 90 days or more after a HIV exposure.<sup>8,13</sup> A patient who is concerned about waiting this long can be offered a lab-based 4<sup>th</sup> Generation test 45 days after exposure.

## SETTING UP AND CONDUCTING A HIV TESTING SERVICE

Any private GP clinic with a Ministry of Health Clinic License is allowed to conduct HIV testing.

A doctor registered and licensed with the Singapore Medical Council can conduct HIV testing. There are no additional licenses or mandatory training or certification required. This applies to both engaging the services of a commercial clinical laboratory for lab-based HIV testing as well as HSA-approved POC tests.

There is no need to obtain a signed written consent from the patient for HIV testing in Singapore. A HIV test may be obtained if medically indicated or as part of the overall medical management of the patient.<sup>19</sup>

The Infectious Diseases Act requires that the identifiable information of any persons diagnosed with HIV be provided to MOH. These are reported by laboratories upon confirmation through confirmatory HIV testing (e.g., western blot or antibody differentiation immunoassay) or detectable quantity from virologic tests (e.g., nucleic acid, viral culture, or p24 antigen test including neutralisation assay).<sup>20</sup>

The confidentiality of a patient’s HIV status is protected by the Infectious Diseases Act Section 25 “Protection of identity of person with HIV infection or other sexually transmitted diseases”; however, potential limitations apply.<sup>21</sup>

### Limitations to confidentiality:

- Providers should encourage patients to disclose their HIV status to their spouse, current, and previous sex partners. These partners should also be encouraged to test for HIV. Providers may offer to assist patients to notify their partners without disclosing the patient’s identity.<sup>21</sup>
- Providers should inform persons who receive a new diagnosis of HIV infection that they will be contacted by health ministry staff for an index interview to discuss notification of their partners and collect epidemiological information for statistical purposes and for education outreach programmes.<sup>22</sup>
- Patients should also be informed that they are required to inform potential sexual partners on the risk of contracting HIV and the partner must accept the risk voluntarily prior to engaging in any sexual activity.<sup>23</sup>

Doctors and staff aware of a patient's HIV status are not permitted to disclose any information that may identify the patient except:

- With the consent of the patient
- When providing notification as required by the Infectious Diseases Act
- When it is necessary as part of a criminal investigation
- When ordered to do so by a court
- To any medical practitioner or health staff who is treating the patient
- To the victim of a sexual assault by the patient
- To the next-of-kin of the patient upon the patient's death

HIV testing should be offered at least once to all patients above the age of 21. HIV testing should be offered to<sup>19</sup>:

- Patients who are diagnosed with Tuberculosis
- Patients diagnosed with a Sexually Transmitted Infection including viral hepatitis.
- The presence of any symptom or diagnosis that could be indicative of HIV infection
- Pregnant women at the first antenatal visit

Repeat HIV testing (at least annually) should be offered to:

- Sexual partners of HIV-infected persons with a viral load that is above the limit of detection
- As part of routine monitoring for individuals on PEP or PrEP
- Persons who exchange sex for drugs or money and their sex partners
- Persons with a history of injection drug use or who engage in sexual activities under the influence of alcohol or other drugs, and their partners
- Persons with multiple sexual partners

Other reasons for HIV testing include:

- Contact tracing
- A specific request for HIV testing (voluntary screening)

To confirm the results of a HIV self-test or HIV test performed outside of Singapore

## Pre-Test Counselling

Pre-test counselling is essential prior to routine HIV testing except for individuals who test regularly where excessive pre-test counselling may unintentionally deter testing.<sup>19</sup> The content and duration of pre-test counselling should be tailored to individual patient needs. Ideally counselling is done in a private space and appropriate language used to ensure patients fully understand the reason and need for HIV testing.

Topics to be covered during pre-test counselling include the following:

- Reason for testing and risk assessment (refer to **Table 1**)
- Timing of risk and option for HIV PEP\*

- Need to test for other Sexually Transmitted Infections (STIs) and bloodborne infections
- History of previous HIV testing
- Confidentiality and privacy issues around testing, including potential limits to confidentiality in the event of a positive result
- Implication of positive results including availability of treatment and linkage to care
- Implications of a negative result including explanation of the window period
- Logistics of the test – how test will be conducted, time taken for results to be available, and mode of delivery of results

*\*There is evidence from a number of studies that a course of anti-retroviral medications commenced within 72 hours of high-risk exposure to HIV and continued for 28 days can reduce the risk of a chronic HIV infection. A detailed discussion of HIV PEP is outside the scope of this article. Clinicians inexperienced in PEP initiation should always refer and adhere to the most recent PEP protocols and seek appropriate advice from experts or refer cases to colleagues who are familiar with the administration of PEP.*

**Table 1**

Type of exposure with known-HIV source who is NOT on ART	ASHM <sup>†</sup>	BHIVA <sup>#</sup>
Receptive anal intercourse with ejaculation	1/70	1/65
Receptive anal intercourse without ejaculation	1/155	1/170
Insertive anal intercourse uncircumcised	1/160	1/161
Insertive anal intercourse circumcised	1/900	1/909
Receptive vaginal intercourse	1/1,250	1/1,000
Insertive vaginal intercourse	1/2,500	1/1,219
Receptive or insertive oral intercourse	Unable to estimate risk – extremely low	<1/10,000

Source:

<sup>†</sup>ASHM – Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine (ASHM). Australian National Guidelines (Second Edition). Post-Exposure Prophylaxis after Non-occupational and Occupational Exposure to HIV. Available online at: <http://www.pep.guidelines.org.au/index.php/assessment-of-the-risk-of-hiv-transmission/what-is-the-hiv-transmission-risk->



exposure#table1 [Accessed 6 July 2021]

#BHIVA – British HIV Association. UK Guideline for the use of HIV Post-Exposure Prophylaxis 2021. Available online at: <https://www.bhiva.org/file/6074031a87755/PEPSE-guide-lines.pdf> [Accessed 6 July 2021]

## POST-TEST COUNSELLING

Physicians and providers of HIV testing must ensure that protocols are in place to inform individuals of their test results. Individuals with HIV-negative test results may be counselled without direct personal contact between physicians/providers and individuals.

If the test is negative:

- Explain the negative test results and window period
- Arrange for a follow up visit for re-testing if required
- Prevention counselling\*
- Consider vaccination for Hepatitis B, Hepatitis A, and Human Papilloma Virus
- Discuss testing for other STIs
- Reinforce the utility of regular HIV testing and arrange for a follow-up visit for HIV test
- Reassure confidentiality

*\*Patients who test negative for HIV but continue to be at risk should be advised on strategies available to mitigate their risk of acquiring HIV infection. Abstinence and being in a mutually monogamous relationship with a HIV-negative partner protect against HIV. The correct and consistent use of condoms for anal and vaginal sex reduces the risk of HIV transmission.*

*HIV Pre-Exposure Prophylaxis (PrEP) is an effective strategy in preventing HIV infection. HIV PrEP involves taking HIV anti-retroviral medication prior to potential HIV exposure. It is highly effective in preventing sexual transmission of HIV. A detailed discussion of HIV PrEP is outside the scope of this document. Physicians are advised to refer to NCID Guidance Document on PrEP.<sup>24</sup>*

If the test is positive:

A positive HIV test result should always be given in person. Providers should be prepared in advance by having information resources and support referrals at the ready. Providers should be able to spend sufficient time in discussing the result with the patient.

Some patients may be better prepared to receive positive test results than others. The emotional impact of hearing these results may prevent patients from clearly understanding information in the post-test counselling session and further follow-up sessions may be required.

If the patient is deemed to be at risk of committing suicide or self-harm, the assistance of a mental health professional should be sought immediately.<sup>16</sup>

Providers should note the following when conveying a positive result:

- Ensure privacy and that the consultation is not interrupted
- Avoid information overload
- Listen and respond to needs
- Given clear instructions on immediate plans and support
- Assess support requirements and link up with available services (refer to **Table 2**)
- Reinforce that someone who recently acquired a HIV infection is highly infectious due to high HIV viral loads and strategies to prevent onward transmission of HIV
- Reassure the patient that HIV is manageable chronic disease with a normal life expectancy when treated early and effectively
- Reinforce that the patient's diagnosis and identity will remain private and explain potential limits to confidentiality (see pre-test counselling)

**Table 2**

Institution	Contact Information
National Centre for Infectious Diseases (NCID)	National Centre for Infectious Diseases, Level 1 16 Jalan Tan Tock Seng Singapore 308442 Tel: 6357 7900 (NCID Clinic J)
National University Hospital	National University Hospital 5 Kent Ridge Road Singapore 119074 Tel: 6772 2002 (13b Medicine Clinic)
Action for AIDS Singapore	AfA Support Group for PLHIV Tel: 6254 0212 Email: <a href="mailto:info@afa.org.sg">info@afa.org.sg</a>
Oogachaga	Counselling Services WhatsApp: 8592 0609 Email: <a href="mailto:CARE@oogachaga.com">CARE@oogachaga.com</a>

## ADDITIONAL PRE- AND POST-TEST COUNSELLING FOR POC TESTS

For patients undergoing POC HIV tests, the following additional topics should be covered during pre- and post-test counselling:

- Reactive, inconclusive, or erroneous results on POC tests must be followed up with a venous sample sent to a diagnostic laboratory for confirmatory testing
- Patients are to provide reliable contact information to receive the results of the confirmatory test

- Not having a confirmed HIV status can be a great source of mental and emotional stress for the patient. If necessary, the assistance of mental health professionals should be sought. Minimally, the patient should be provided with the contact information of support and counselling services and encouraged to get in touch with them
- Counsel the patient to maintain risk reduction practices and to inform any potential sexual partners on the risk of contracting HIV and the partner must accept the risk voluntarily prior to engaging in any sexual activity until all testing is complete

## LINKAGE TO CARE

All patients with confirmed HIV infection should be immediately referred to an Infectious Disease Physician. Patients should be given clear, preferably written, instructions on the details of the appointment. There is overwhelming evidence that rapid initiation of anti-retroviral therapy, regardless of the stage of the disease, leads to better patient outcomes.<sup>8</sup>

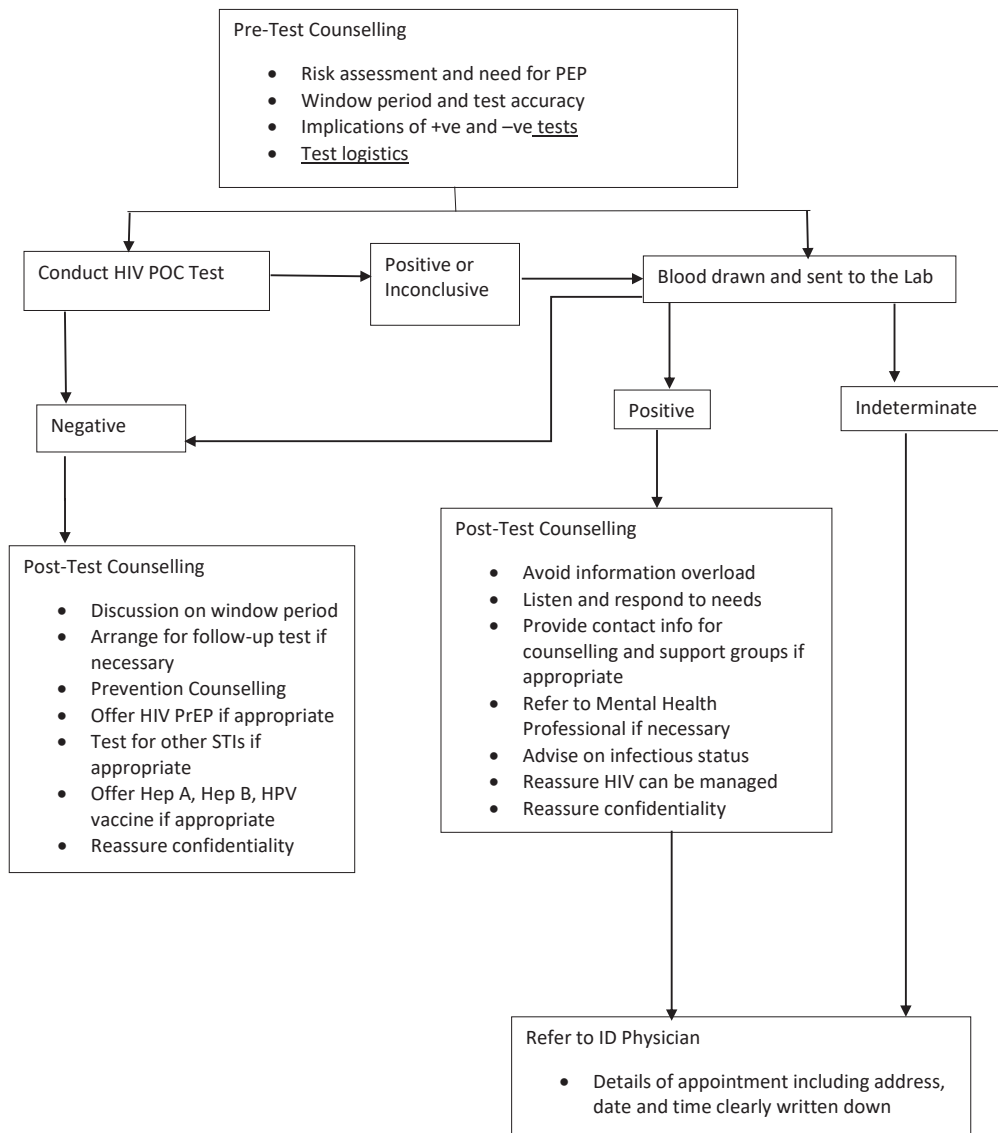
The benefits of ART include:

- Reduces HIV-related morbidity and mortality at all stages of infection
- Improves the duration and quality of life of PLHIV
- Prevents HIV transmission (U=U)
- Prevents or delays drug resistance
- Decreases immunological responses and inflammation responsible for cardiovascular and other end-organ damage reported in PLHIV

The patient should also be linked to other support and counselling services if this is assessed to be required.

Antiretroviral medications used in the treatment of HIV have been added to the Standard Drug List and Medication Assistance Fund and are subsidised by the Ministry of Health, thus minimising financial barriers to treatment. This means that all subsidised PLHIV will now receive either a 50 or 75 percent subsidy, depending on their means-test status, when they buy any of the ART drugs on the list.

**Figure 2. Suggested Workflow for HIV testing in a GP Clinic**



## STIGMA AND DISCRIMINATION AS BARRIERS TO CARE

Stigma and discrimination are powerful social processes where individuals are given negative labels and stereotypes and mistreated because of their associations to a particular (often minority) group. Stigma is especially compounded for HIV/AIDS as patients are often deemed culpable for their condition and may have multiple characteristics that are subject to discrimination. Stigma and discrimination are recognised as significant barriers to healthcare.<sup>25-33</sup>

Clinics can be places of particular stress for patients because in order to attain services such as HIV testing or HIV PrEP, they would have to disclose private information such as their sexual orientation or sexual practices, which may trigger discriminatory actions from healthcare workers. This can then result in marginalisation and disengagement from services and support networks. Experiencing stigma and discrimination also increases the risks of major depressive disorder, schizophrenia, bipolar disorder, and addiction.<sup>30</sup>

Providers are encouraged to recognise stigma and make stigma reduction a routine part of healthcare delivery.<sup>32,33</sup>

## CONCLUSION

GPs and family physicians are uniquely qualified to provide HIV testing services. This document aims to provide a consolidated source of pertinent information for GPs to initiate or expand upon HIV testing in their clinics, with the objectives of increasing HIV testing, identifying patients with HIV infection, and reducing the risk to patients who are currently uninfected.

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