

November 2013 • VOLUME 39•1 ISSN 1481-8531

# TABLE OF CONTENT

Notes from the Editor	1
Brief — Synopsis of the Human Immunodeficiency Virus (HIV) screening and testing guide	2
Brief - Synopsis of the current evidence on the risk of HIV transmission	
Useful Links	17

# NOTES FROM THE EDITOR

### **CCDR** is changing

PHAC's flagship publication on infectious diseases is being revitalized. During the last few years the Canada Communicable Disease Report (CCDR) has focused on Advisory Committee statements and FluWatch, the Public Health Agency's influenza surveillance report. This year the Agency made revitalizing the CCDR a priority. Over the past few months we have formed an Editorial Office and an Editorial Board.

Our goal is to provide practical and timely information on infectious diseases in Canada for both public health and health care professionals. To date, we've made three changes:

First, we are developing theme issues. Today's edition focuses on HIV/AIDS, in time for World AIDS Day, December 1st. Our theme issues will "tell a story". For example, here we reflect on: What are the best practices for HIV screening now and how have we advanced our understanding of HIV transmission?

Second, CCDR will now feature Briefs. These are short articles that summarize longer, more definitive guidance documents. Our Briefs will give you a quick and useful overview and provide a link to the full document.

Third, we are starting a "Useful Links" section which points to additional information on the Agency website. In this issue, we identify some recent HIV surveillance data in Canada on specific groups of people with HIV/AIDS, namely Aboriginal persons and women.

We are planning 22 biweekly issues for 2014 – with a couple of pauses during the winter holidays and summer break. Sign up for an email subscription.

We have many great upcoming articles and more features planned, so stay tuned. We welcome your feedback.

Patricia Huston MD, MPH Scientific Editor





# BRIEF — SYNOPSIS OF THE HUMAN IMMUNODEFICIENCY VIRUS (HIV) SCREENING AND TESTING GUIDE

GALE-ROWE M, DODDS J, PAQUETTE D, WONG T ON BEHALF OF THE PHAC EXPERT WORKING GROUP\*

KEY WORDS: HIV/AIDS, SCREENING, HIV TESTING

# **Structured Abstract**

### BACKGROUND

The Public Health Agency of Canada (PHAC) estimates that, in 2011, 25% of people living with HIV in Canada were undiagnosed. Hesitation to seek testing may arise from fear, stigma and discrimination associated with the HIV diagnosis and related risk behaviours. This guide is designed to complement existing efforts to support care providers involved in HIV testing, in order to reduce the number of undiagnosed HIV infections in Canada.

### APPROACH

PHAC commissioned a literature review and consulted with provinces and territories, and key stakeholders, including people living with HIV/AIDS, academics, nurses, physicians, professional associations, non-governmental organizations, policy-makers, community workers, and legal and ethical experts. As a result, the recommendations outlined in the guide are based on the most up-to-date evidence and expert opinion.

### SCREENING AND TESTING GUIDE

The consideration and discussion of HIV testing should be made a component of routine periodic medical care. Offering HIV testing routinely can help normalize testing, and address the multiple barriers to reducing the number of undiagnosed cases in Canada. Begin with a brief explanation to the client on how HIV is transmitted: through unprotected sex, the sharing of drug-use equipment, and from a pregnant mother to her child. Clients can then consider their own situation and indicate whether they would like to have an HIV test. Upon request, a risk assessment may be conducted. As with other tests, testing is voluntary and verbal consent is sufficient.

**Negative test results** provide an opportunity to remind clients of those practices that can help them maintain an HIV-negative status. There are a range of referrals and resources available to assist clients in reducing at-risk activities and maintaining a negative status. Those who are part of a couple should be encouraged to discuss HIV testing with their partners so they're not unknowingly involved in a serodiscordant relationship.

**Positive test results** should always be provided in person and ideally by the initial care provider who has information resources and support referrals at the ready. An HIV positive diagnosis can be difficult news; it is important to take the time to discuss the results and answer any questions the client might have. Focus on positive messages by highlighting advances in HIV care, treatment and support. Note that HIV is now considered a chronic illness, and people living with HIV can live long, active and healthy lives. Advise the client about strategies for managing HIV and link them to care. Provide risk reduction information to prevent transmission. Make the client aware that positive test results will be shared confidentially with the local public health

Corresponding author: Margaret.Gale-Rowe@phac-aspc.gc.ca

<sup>\*</sup> Members of the PHAC Expert Working group: D Kirby/H Njoo (Co-Chairs), K Clement, I Culbert, B Dickens, J Gahagan, S Grant, J Greer, L Hanvey, E Jackson, C Kazatchkine, B Larke, R MacLachlan, P MacPherson, M Muchenje, B O'Leary, C Panessa, M Ricketts, G Riehl, RW Smith, M Steben, C Swantee, K Thomas, M Tyhndall, M Yudin.

department, which can assist in notifying previous and current partners of the need to be tested while protecting the client's anonymity and privacy. Strategies for informing past, current and future partners can be reviewed. If not already completed with the HIV test, clients should be tested for other STIs, hepatitis B and C, and tuberculosis.

### Introduction

There is a critical need to optimize opportunities for care providers to offer HIV testing to people living in Canada; undiagnosed cases are missed opportunities to reduce HIV transmission and improve productivity, disease prognosis and quality of life for people living with HIV. The Public Health Agency of Canada estimates that, in 2011, 25% of people living with HIV in Canada were unaware of their infection (1).

There are several benefits to reducing the number of undiagnosed HIV infections. A negative test result is an opportunity for clients to take an active role in remaining HIV negative. Individuals who receive their diagnosis earlier and initiate Highly Active Antiretroviral Therapy (HAART) can have reduced morbidity and mortality associated with HIV infection and disease progression compared with those who do not receive a timely diagnosis (2) Advances in HIV treatment have slowed the progression of the disease to such a degree that HIV infection is now understood to be a chronic, manageable condition enabling more people with HIV to live healthy, long, and active lives.

Those who test positive are more likely to take measures that prevent the onward spread of HIV (3). Emerging evidence is demonstrating that reduced individual viral load as a result of early initiation of HAART, in combination with other prevention supports including consistent condom use, has been associated with a relative reduction of 96% in the number of linked HIV-1 sexual transmissions in certain populations as compared with delayed therapy (4, 5).

In contrast, individuals who are unaware they have HIV infection, are more likely to have increased morbidity and mortality and unknowingly spread the virus.

In spite of the benefits associated with HIV testing, fear of testing positive, and fear of the anticipated discrimination that may come with a diagnosis of HIV can be barriers to testing (6). Reducing the number of undiagnosed HIV infections requires a balance between targeting tests to those most at risk with a less targeted approach directed to populations at "moderate risk" as well. Evidence demonstrates that many individuals who are, or perceived to be, outside of traditional high-risk populations are not being offered HIV testing (7, 8). As such they are sometimes diagnosed late in the progression of HIV disease, in spite of many prior interactions with the health system (8).

This is a summary of the HIV Screening and Testing Guide (9).

# Approach

To inform the development of this guide, the Agency commissioned a literature review and consultations with provinces and territories, and key stakeholders, including people living with HIV/AIDS and other affected populations, academics, nurses, physicians, professional associations, non-governmental organizations, policy-makers, community workers, and legal and ethical experts. As a result, the recommendations outlined in the guide are based on the most up-to-date evidence and expert opinion.

Note, that this guide does not supersede any provincial/territorial legislative, regulatory, policy and practice requirements or professional guidelines that govern and inform the practice of care providers in their respective jurisdictions. As always, care providers should comply with practice requirements and local public health regulations when conducting HIV testing. This guide is designed to provide supplemental guidance in an effort to reduce the number of undiagnosed HIV infections in Canada.

## **Recommendations**

This guide is based on a number of guiding principles. The first is the importance of public health promotion and protection, which includes the need to integrate HIV testing with testing services for other related infections, such as sexually transmitted and blood borne infections and tuberculosis. The second is the importance of human rights, which includes the "3Cs" of HIV testing: counselling, informed consent, and confidentiality. The third is the principle of adaptability which reflects the need to apply recommendations with flexibility depending on the needs of both the client and the care provider.

### NORMALIZE HIV TESTING

It is recommended that the consideration and discussion of HIV testing be made a component of routine periodic medical care. This recommendation is based upon two observations. First, evidence suggests that self-perceived risk does not always accurately reflect actual risk and, when combined with fear, may reduce the likelihood of patient-initiated requests for an HIV test (6). Second, there is good quality evidence demonstrating the benefits associated with normalising HIV testing as a means of overcoming multiple barriers associated with HIV testing (10) (Table 1). The testing process offers all clients with an opportunity to relieve any anxiety about an unknown HIV status and to establish a baseline as part of an individual's overall health care. Individuals involved in high risk behaviours should be offered HIV testing at least annually.

An in-depth comprehensive HIV behavioural risk assessment is not a pre-requisite for offering an HIV test. An assessment that the client understands how HIV is transmitted, the implications of testing (advantages and disadvantages), and how to interpret the test results is sufficient. A provider-initiated offer for HIV testing can begin with a brief explanation to the client on how HIV is transmitted: through unprotected sex, the sharing of drug-use equipment, and from a pregnant mother to her child. Clients can then consider their own situation and indicate whether they would like to have an HIV test.

It is helpful to have print and on-line resources to support client information needs to help inform discussions and decisions around HIV testing. For occasions when clients may not be able to accurately estimate their risk, a review of the clinical indications for HIV testing and risk factors for HIV may be helpful. (Table 2) In rare cases, an in depth behavioural risk assessment may be indicated (9). Advise the client that they have the right to decline the test. HIV testing remains voluntary and based on informed consent. Written consent is not necessary.

To overcome concerns relating to stigmatization, care providers should respect the cultural, sexual and gender diversities of clients by avoiding judgmental language, behaviours and attitudes and use appropriate information resources to reflect these diversities.

Individuals with a risk of HIV exposure, in an ongoing sexual relationship with a regular partner, can benefit from being offered HIV testing as a couple. Evidence indicates that couples who test together and are mutually aware of each other's results are more likely to adopt behaviours that will protect their partners, when compared to those who test alone (11). Couples' testing reduces HIV transmission among serodiscordant couples whose status is unknown to them, and reduces the risk of HIV transmission/acquisition with sexual partners external to the couple.

### PRE-TEST COUNSELLING

It is useful to provide clients with HIV information in the waiting room to help prepare for pre-test discussions. Because clients who test positive are less likely to retain key information of post-test counselling, some post-test information is included as part of the pre-test discussion.

Communicate positive messaging around the benefits associated with the comfort of knowing one's negative HIV status or the benefits of an early diagnosis including available treatments and improved disease prognosis. Explain the window period and, if at risk behaviours have occurred in the previous three months, that follow-up testing may be required. Discuss steps the client can take to avoid acquisition or transmission of HIV and other STBBIs and that such steps should be undertaken until the completion of all testing (a client who continuously engages in risk

behaviours remains in a continuous window period). Assure the testing client that his or her privacy or anonymity will be maintained and how. Explain potential limits to confidentiality including that a positive test result will be shared confidentially with the local public health department. Advise the client of the public health benefits of disclosing their HIV status to current and future partners in the event of a positive test result. Identify the client's post-test support needs. Test results should generally be provided in person, but it may be useful to have an agreed upon alternative to deliver HIV negative results and follow up recommendations, such as via a secure telephone call, letter or email.

### TESTING

Algorithms for HIV testing have been developed to optimize the positive and negative predictive values; a full discussion of the tests goes beyond this guide. For information specific to your area, contact your local public health laboratory. It is important to note however, pre- and post-test counselling needs to be adapted to the generation and type of test. For example, more recent generations of tests have a reduced window period compared to earlier generations. Rapid testing, when compared to lab-based testing, involves an assessment of whether the client is prepared to receive a test result in the same session, and understands the meaning of a non-reactive test, a reactive test and the possibility of a false positive. Health Canada requires that rapid test kits are only to be used in settings where pre- and post-test HIV counselling is available.

### POST-TEST COUNSELLING

Key messages for clients need to be tailored to the result of the HIV test and the individual circumstances. At times, pre- and post-test activities can be combined into a single session. The level of support required in any given testing situation may include information, discussion, counselling and/or referral. All clients should be offered referral service and supports, regardless of their test results, to support risk reduction measures. These services can be found by contacting local public health departments, provincial/territorial health information lines, AIDS hotlines or local crises centres.

#### INDETERMINATE RESULT

When the result is indeterminate, additional testing needs to be completed. Counsel the client to maintain risk reduction practices until all testing is complete. Review pre-test counselling messages.

### NEGATIVE RESULT

For the majority of HIV tests performed, results will be negative. Clients should be made aware of the window period, and if any risk behaviours occurred in the three months prior to the test, follow-up testing is recommended. When negative test results are confirmed, this is an opportunity to remind clients of those practices that can help them maintain an HIV-negative status. Clients testing negative who are part of a couple should be encouraged to discuss HIV testing with their sexual/drug use partners.

#### **POSITIVE RESULT**

An HIV positive test result should always be provided in person and ideally by the initial care provider. Care providers should be prepared in advance by having information resources and support referrals at the ready for the client and be able to spend sufficient time to discuss the results and answer any immediate questions the client might have. Frequently, clients will only hear the positive test result, so it can be helpful to schedule a follow-up appointment within two weeks so further discussions can occur.

Clients should be reassured that their privacy and confidentiality will be protected. Note that with proper care and treatment, people with HIV can live long, healthy and active lives and clients should be made aware that HIV is now considered a chronic manageable condition. Advise the client about strategies for managing HIV and link them to care. If not already completed with the HIV test, the client should be tested for other STIs, hepatitis B and C, and tuberculosis. Baseline testing, such as CD4, plasma viral load, and drug resistance should be ordered. It is imperative that clients be informed about how to prevent the further spread of the virus.

A partner notification plan should be developed with the client so previous and current partners can be notified of their need to be tested. There are several options for notification. With the consent of the client, Public Health services can assist in anonymous notification of potentially exposed sexual and drug-equipment sharing partners who have been identified by the client. Alternatively, the testing provider can assist with anonymous notification or the client may wish to contact his or her partners directly. Some clients may prefer a combination of the above, depending on the contact. In cases where sexual partners have met over the internet or only exchanged an email address or username, web-based tools, such as inSPOT may help increase partner notification. There should be an agreed upon time period for confirming that partners have been notified.

Provide risk reduction information to prevent transmission of the virus as a critical element in post-test procedures. In circumstances where the care provider is not able to offer in-depth risk-reduction information, a referral to risk-reduction services should be provided.

Offer client referrals to specialized counselling services that are equipped to provide newly diagnosed individuals with the specific supports and resources that they need to manage their health and wellness. HIV/AIDS hotlines are available in each province and territory in Canada.

# Conclusion

This guide was designed to support care providers to offer HIV testing routinely and flexibly to detect previously undiagnosed cases of HIV. This can decrease HIV transmission and improve productivity, disease prognosis, and quality of life for people living with HIV. Once the diagnosis is made, supports and ongoing care is critical.

## References

- 1. Public Health Agency of Canada. Summary: Estimates of HIV prevalence and incidence in Canada, 2011. Ottawa, ON: .
- 2. Jain V, Deeks SG. When to start antiretroviral therapy. Current HIV/AIDS Reports. 2010;7(2):60-8.
- Marks G, Crepaz N, Senterfitt JW, Janssen RS. Meta-analysis of high-risk sexual behavior in persons aware and unaware they are infected with HIV in the United States: Implications for HIV prevention programs. J Acquir Immune Defic Syndr. 2005 Aug 1;39(4):446-53.
- 4. Attia S, Egger M, Müller M, Zwahlen M, Low N. Sexual transmission of HIV according to viral load and antiretroviral therapy: Systematic review and meta-analysis. AIDS. 2009;23(11):1397-404.
- Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, et al. Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med. 2011;365(6):493-505.
- 6. Deblonde J, De Koker P, Hamers FF, Fontaine J, Luchters S, Temmerman M. Barriers to HIV testing in Europe: A systematic review. Eur J Public Health. 2010;20(4):422-32.
- 7. Burke RC, Sepkowitz KA, Bernstein KT, Karpati AM, Myers JE, Tsoi BW, et al. Why don't physicians test for HIV? A review of the US literature. AIDS. 2007;21(12):1617-24.
- Girardi E, Sabin CA, Monforte AD. Late diagnosis of HIV infection: Epidemiological features, consequences and strategies to encourage earlier testing. J Acquir Immune Defic Syndr. 2007;46(SUPPL. 1):S3-8.
- 9. Public Health Agency of Canada. Human immunodeficiency virus HIV screening and testing guide. Canada: 2013. http://publications.gc.ca/collections/collection\_2013/aspc-phac/HP40-76-2012-eng.pdf
- 10. European Centre for Disease Prevention and Control. HIV testing: Increasing uptake and effectiveness in the European Union. Stockholm: ECDC; 2010.
- 11. World Health Organization. Guidance on couples HIV testing and counselling including antiretroviral therapy for treatment and prevention in serodiscordant couples: Recommendations for a public health approach. Geneva: WHO; 2012.

## **Acknowledgements**

The Public Health Agency of Canada (PHAC) would like to thank the members of the Communicable and Infectious Disease Steering Committee, Federal/Provincial/Territorial Advisory Committee on AIDS, the Canadian Guidelines on Sexually Transmitted Infections Expert Working Group, the Council of Chief Medical Officers of Health, the Canadian Public Health Laboratory Network and the Canadian Association of HIV Clinical Laboratory Specialists for their input into this Guide. PHAC would also like to acknowledge the many staff of the Centre for Communicable Diseases and Infection Control and the National Microbiology Laboratory who contributed to the development of this document.

# **Conflict of interest statement**

There are no conflicts of interest to declare.

# Funding

This work was supported by the Public Health Agency of Canada.

#### TABLE 1. BARRIERS TO HIV TESTING AND RECOMMENDATIONS IN THE GUIDE TO ADDRESS THEM

Inability to accurately assess levels of risk for exposure to HIV by some clients and providers	Normalise HIV testing; simplify risk assessments; make the consideration of an HIV test part of periodic routine medical care.	
Lack of comfort discussing HIV testing and knowledge about HIV among some clients and providers	Normalise HIV testing; simplify risk assessments; make the consideration of an HIV test a part of periodic routine medical care.	
Provider time constraints for risk assessments and pre- and post-test counselling	Simplify risk assessments; streamline the provision of pre-test information using print, video, mobile and web-based resources; alternate approaches offered to provide negative results.	
Cumbersome consent procedures	Verbal consent for HIV testing, as with other tests, is sufficient; testing remains voluntary.	
Fear of stigma and discrimination associated with risk behaviours and/or testing HIV-positive	Normalise HIV testing and simplify risk assessment to reduce discomfort and stigma and increase uptake of testing; emphasize HIV as a chronic manageable condition and the benefits of treatment to reduce fear of HIV diagnosis.	

#### TABLE 2. CLINICAL INDICATIONS FOR HIV TESTING AND RISK FACTORS FOR HIV INFECTION

#### **CLINICAL INDICATIONS FOR HIV TESTING**

- 1. Individuals requesting an HIV test.
- 2. Individuals with symptoms and signs of HIV infection.
- 3. Individuals with illnesses associated with a weakened immune system or a diagnosis of tuberculosis.
- 4. Unprotected anal or vaginal intercourse or use of shared drug equipment with a partner whose HIV status is known to be positive.
- 5. Pregnant or planning a pregnancy; and their partners as appropriate.
- 6. Victims of sexual assault.

#### FACTORS THAT INCREASE RISK FOR HIV INFECTION

- 1. Sexually active but no history of being tested for HIV.
- 2. Use of shared drug equipment with a partner whose HIV status is unknown.
- 3. Unprotected anal or vaginal intercourse with a partner whose HIV status is unknown.
- 4. Multiple and/or anonymous sexual partnering.
- 5. For men, a history of sex with other men.
- 6. Diagnosis of other STI, hepatitis B or C.
- 7. Sexual activity, sharing of drug-use equipment, or receipt of blood or blood products for people originating from, or who have travelled to, regions where HIV is endemic.
- 8. Receipt of blood or blood products in Canada prior to November 1985.

# BRIEF – SYNOPSIS OF THE CURRENT EVIDENCE ON THE RISK OF HIV TRANSMISSION

PAQUETTE D, DEMERS A, GALE-ROWE M, WONG T

KEY WORDS: HIV/AIDS, TRANSMISSION

## **Structured abstract**

#### BACKGROUND:

Knowledge of the risk of HIV transmission has evolved over the past decade as evidence on the impact of biological and behavioural co-factors, such as viral load, has come to light. We undertook a comprehensive review of the evidence on the risk of HIV transmission.

#### **METHODS:**

A search was conducted for literature published between January 2001 and May 2012. The search focused on systematic, meta-analytic, and narrative reviews. For topics where no reviews existed, primary research studies were included.

#### **RESULTS**:

The risk estimates for the sexual transmission of HIV, per sex act, ranged from 0.5% to 3.38% (with mid-range estimates of 1.4% to 1.69%) for receptive anal intercourse; 0.06% to 0.16% for insertive anal intercourse; 0.08% to 0.19% for receptive vaginal intercourse; and approximately 0.05% to 0.1% for insertive vaginal intercourse. For people who inject drugs, the risk of transmission from a contaminated needle, per injection, was estimated to be between 0.7% and 0.8%. A number of factors impact the risk, including viral load, the presence of other sexually transmitted infections (STIs), and male circumcision.

#### CONCLUSIONS:

Within each route of transmission, estimates of the risk of transmission varied widely, likely due to the role of behavioural and biological co-factors. Viral load appears to be an important predictor of transmission, regardless of the route of transmission. However, the evidence indicates that viral load is not the only determinant and that certain co-factors play a role in increasing (e.g., STIs) or decreasing (e.g., male circumcision) the risk of transmission.

### Introduction

Knowledge of the risk of HIV transmission and the co-factors that impact on risk, particularly viral load and its role in the transmission of HIV, is evolving. This information is valuable to health care professionals conducting risk assessments and counselling. It also provides a foundation for a better understanding of emerging HIV prevention approaches. In 2011, an estimated 84% of new infections were attributed to sexual transmission (47% among men who have sex with men (MSM); 17% heterosexual/endemic exposure; and 20% heterosexual/non-endemic exposure), and 14% of new infections were among people who inject drugs (PWID) (1).

Understanding the biological determinants of HIV transmission is essential for making predictions on the potential spread of HIV infection in a population, directing appropriate prevention strategies, and assessing the risk of infection to an individual who has been exposed to the virus. Our current knowledge of HIV transmission comes from various types of evidence, including animal studies, observational studies, randomized clinical trials (RCTs) and systematic reviews.

This is a summary of the current evidence on sexual transmission and transmission via injection and other drug use, the two most common routes of transmission in Canada. A review of the evidence on the risk of vertical transmission, in addition to a more detailed description of the risk associated with sexual transmission and transmission via drug use, can be found in the full document. (2).

## **Methods**

We searched Scopus, Embase and CINAHL, and limited the search to articles published between 2001 and 2012 in English and French. Systematic reviews were the focus of the search. Where reviews did not exist, we included primary research studies. Key studies or commonly referenced publications outside of the time period were also included.

The following search terms were used: (HIV or "human immunodeficiency virus") and (transmission AND (probability OR rate OR risk)) OR (per AND contact) OR (per AND act) OR infectivity OR infectiousness OR transmissibility, along with key terms specific to each topic covered in this review.

# **Results**

### SEXUAL TRANSMISSION

Although there are challenges in quantifying risk by sex act, anal intercourse has consistently been shown to be a higher risk act than vaginal intercourse, which in turn is a higher risk act than oral intercourse. There is also a higher risk associated with receptive intercourse (both vaginal and anal) compared with insertive intercourse (Table 1).

The risk estimates for the transmission of HIV via anal intercourse, per sex act, ranges from 0.5% to 3.38% for receptive anal intercourse (3-6) and 0.06% to 0.16% for insertive anal intercourse (6-8). While most of these estimates are based on studies of MSM, the risk associated with anal intercourse appears to be similar within heterosexual populations (4).

The risk estimates of HIV transmission from receptive vaginal intercourse (male-to-female) range from 0.08% to 0.19% (5, 6, 9); and 0.05% to 0.1% for insertive vaginal intercourse (female-to-male) (6, 9).

A meta-analysis suggested a low but non-zero transmission probability from unprotected oral intercourse (whether penile-oral or vaginal-oral) (10). The risk of transmission to the receptive partner during oral intercourse increases with ejaculation and in the presence of oral ulcers and oropharyngeal sexually transmitted infections (STIs) (10, 11).

#### VIRAL LOAD

Plasma viral load is the strongest predictor of sexual transmission of HIV (12). For each 10-fold increase in plasma viral load, the relative risk of transmission increases by 2.9 per sexual contact (9). The use of highly active antiretroviral therapy (HAART), which lowers viral load, was associated with a 96% reduction in the number of linked transmissions in an RCT of serodiscordant couples (most of which were heterosexual) (13). It is currently unclear whether there is a viral load threshold under which transmission no longer occurs. Also, little is known about the impact of viral load on the risk of transmission via anal intercourse. It is possible that the degree of risk reduction associated with HAART is not as great for this higher risk route of transmission. The results of ongoing studies (the PARTNER and Opposites Attract studies) will be useful in answering this question.

Plasma viral load likely acts as a surrogate measure for HIV viral load in genital secretions (14), which plays a major role in sexual transmission (15-17). Concurrent STIs have been found to increase genital tract HIV shedding (15-17). Although HAART has been found to suppress HIV replication in the genital tract, non-adherence has been associated with persistent genital shedding of the virus (16). Further, shedding of the virus in the genital tract has been found even among those with undetectable plasma viral load (18, 19). The implications of this finding on the risk of transmission are currently unclear.

Primary (early) and late-stage HIV infections are marked by elevated viral load in plasma and in genital secretions (20, 21). In primary infections, this is due to the high degree of viral replication prior to the development of an immune response (20). Those in the primary stage of infection may also have other risk factors that led to the HIV infection (22). Late-stage infection, despite the elevated viral load, is likely to have a limited contribution to an HIV epidemic, since those with late-stage infection report less frequent sexual intercourse and fewer partners (21).

#### SEXUALLY TRANSMITTED INFECTIONS (STIs)

STIs have consistently been associated with increased susceptibility to HIV in observational studies (23). Several systematic reviews of high quality observational studies found that the presence of STIs increased susceptibility to HIV by a factor of 2 to 4. This effect has been found for both men and women, specifically for herpes simplex virus type 2 (HSV-2); syphilis; gonorrhoea; chlamydia; trichomonas; and also exposure categorized as "any STI," "genital ulcer disease (GUD)," and "non-ulcerative STIs" (24-26). More recent observational studies have also associated the presence of human papillomavirus (HPV) with HIV acquisition among women, heterosexual men, and MSM (27, 28).

Studies indicate that STIs are also associated with increased infectiousness. Much of the evidence for this relationship comes from indirect approaches such as clinical studies that examine the possible biological mechanisms underlying the association. Few observational studies have examined this association (29); however, a systematic review of two studies found that genital ulcers and syphilis significantly increased the risk of HIV transmission 2- to 3-fold (24).

In contrast to the results of observational studies, the results of RCTs examining the impact of STI treatment on the risk of HIV transmission have been equivocal. The results of nine trials have been published to date: six assessed the effects of treating curable STIs, and three examined the impact of herpes suppressive therapy (30). The only trial to find a significant impact was the Mwanza (Tanzania) trial, which found a 40% reduction in HIV incidence following improved STI treatment services (31). The equivocal results may have been due to the type of epidemic within the community (30). In concentrated HIV epidemics, such as in Mwanza, treatable STIs may be an important co-factor in HIV transmission, which might not be the case in generalized epidemics found in the other trials (30, 32). Suboptimal adherence to HSV-suppressive therapy and a lack of power may have led to the inability of HSV treatment trials to demonstrate a significant effect (23, 30).

#### INTACT FORESKIN IN MEN

The three RCTs that studied the effect of male circumcision all found a 50% to 60% reduced risk of HIV acquisition (33). However, there is little epidemiological evidence to suggest that circumcision reduces the risk of transmission to female partners of circumcised men (34) or is effective in the prevention of HIV among MSM, except perhaps for men who report primarily an insertive role (35).

### TRANSMISSION VIA DRUG USE

#### USE OF INJECTION DRUGS

The probability of HIV transmission per injection with a contaminated needle and syringe has been estimated indirectly using mathematical models, due to difficulties with accurately measuring the number of exposures (i.e., number of times a needle and syringe from an HIV-positive individual was shared) and other risk factors (e.g., viral load). Based on these models, the per injection probability of infection from a contaminated needle and syringe was found to be between 0.67% and 0.84% (36, 37). Much like estimates of the risk from sexual transmission, such

summary measures may be misleading as they do not convey the heterogeneity that exists in the risk of transmission per injection (37).

A number of observational studies have examined the risk of sharing, relative to not sharing, needles and syringes, where the HIV status of the injecting partner was unknown. Despite inconsistencies in how sharing needles and syringes was measured, studies have consistently found a positive relationship between the risk of HIV transmission, and needle and syringe sharing. In cohort studies conducted across Canada, those who shared needles and syringes were 1.5 to 5.9 times more likely to seroconvert (38, 39).

Studies suggest that sharing ancillary injecting equipment (e.g., water, cookers or filters) also increases the risk of HIV transmission. In a laboratory study, HIV DNA was detected in injection paraphernalia collected from shooting galleries in Miami (40) and observational studies have shown an epidemiological link between sharing drug preparation equipment and HIV transmission (41, 42).

#### VIRAL LOAD

There are few good quality studies on the association between viral load and the risk of transmission among PWID. For PWID on HAART, the degree of reduction in infectiousness is not known. Higher plasma viral loads have been found during outbreaks of HIV among PWID (43, 44). In addition, the community viral load of PWID was associated with HIV incidence in Vancouver (45). The community viral load is the mean or total of viral load measurements from a population (46). Community viral load is an aggregate measure, thus any association with this group-level measure is subject to ecological fallacy (i.e., an association between aggregate measures does not necessarily reflect a causal relationship at the individual level) (46).

#### SEXUAL TRANSMISSION AMONG PWID

Although the HIV epidemic among PWID is driven primarily by the sharing of injecting equipment, over the past decade the prevalence of syringe sharing has decreased. Studies have shown that after accounting for injecting behaviours, sexual transmission is becoming an important route of transmission in this group (47). HIV seroconversion among PWID has been independently associated with having an HIV-positive sexual partner and engaging in risky sex behaviours (e.g., multiple sexual partners, sex trade work, and inconsistent use of condoms) (48, 49).

#### USE OF NON-INJECTION DRUGS

Use of some non-injection drugs has been reported as an independent risk factor for HIV transmission. Crack smoking (in isolation) and amphetamine use have been identified as independent risk factors for HIV seropositivity, increasing the risk 2- to 3-fold (50, 51). Important limitations with these studies include their dependence on self-reported data and the difficulty of adjusting for confounding factors.

There is limited information on the mechanisms of HIV transmission solely through smoking or snorting. Sharing drug paraphernalia, like straws, banknotes, and crack pipes or stems, has been proposed as a transmission route. Blisters, sores, and cuts on the lips and in the mouths of crack smokers may facilitate oral transmission of HIV (52-54), with the evidence supporting this causal relationship building but still sparse (11).

### Conclusion

An individual's risk of HIV transmission is complex and depends on a number of behavioural and biological cofactors. It remains difficult to accurately quantify the risk of transmission associated with specific acts, however, in sexual transmission, unprotected receptive anal intercourse involves the greatest risk. Across the routes of transmission, plasma viral load appears to be an important predictor of transmission. However, while viral load is a key factor in whether HIV is transmitted, the evidence indicates that it is not the only determinant, and other cofactors play a role in increasing or decreasing the risk of transmission. This review of the evidence points to the growing and evolving nature of our knowledge of HIV transmission risk and the biological and behavioural co-factors that impact on that risk.

### **Acknowledgements**

Many thanks to Chris Archibald, Christopher Boodram, Katherine Dinner, Katie Freer, Brian Gottheil, Ping Yan, and Ameeta Singh for their review and comments on the full document

# **Conflict of interest statement**

There are no conflicts of interest to declare.

## Funding

This work was supported by the Public Health Agency of Canada.

#### TABLE 1. ESTIMATES OF THE PER-SEX-ACT AND PER-INJECTION RISK OF TRANSMISSION

Route of transmission	Transmission probability	References
Receptive anal intercourse	0.5% to 3.38%	(2-5)
Insertive anal intercourse	0.06% to 0.16%	(5-7)
Receptive vaginal intercourse	0.08% to 0.19%	(4,5,8)
Insertive vaginal intercourse	0.05% to 0.1%	(5,8)
Oral intercourse	low but non-zero	(9)
Sharing contaminated needle and syringe	0.67-0.84	(35,36)

### References

- 1. Public Health Agency of Canada. Summary: Estimates of HIV prevalence and incidence in Canada, 2011. Ottawa: Government of Canada 2012.
- 2. Public Health Agency of Canada. HIV transmission risk: A review of the evidence. Ottawa: Government of Canada; 2012. http://publications.gc.ca/site/eng/434865/publication.html
- Powers KA, Poole C, Pettifor AE, Cohen MS. Rethinking the heterosexual infectivity of HIV-1: A systematic review and meta-analysis. Lancet Infect Dis. 2008;8(9):553-63.
- 4. Baggaley RF, White RG, Boily M-. HIV transmission risk through anal intercourse: Systematic review, meta-analysis and implications for HIV prevention. Int J Epidemiol. 2010;39(4):1048-63.
- 5. Boily M-, Baggaley RF, Wang L, Masse B, White RG, Hayes RJ, et al. Heterosexual risk of HIV-1 infection per sexual act: Systematic review and meta-analysis of observational studies. Lancet Infect Dis. 2009;9(2):118-29.
- 6. Fox J, White PJ, Weber J, Garnett GP, Ward H, Fidler S. Quantifying sexual exposure to HIV within an HIVserodiscordant relationship: Development of an algorithm. AIDS. 2011;25(8):1065-82.

- 7. Vittinghoff E, Douglas J, Judson F, McKirnan D, Macqueen K, Buchbinder SR. Per-contact risk of human immunodeficiency virus transmission between male sexual partners. Am J Epidemiol. 1999;150(3):306-11.
- 8. Jin F, Jansson J, Law M, Prestage GP, Zablotska I, Imrie JCG, et al. Per-contact probability of HIV transmission in homosexual men in Sydney in the era of HAART. AIDS. 2010;24(6):907-13.
- 9. Hughes JP, Baeten JM, Lingappa JR, Magaret AS, Wald A, de Bruyn G, et al. Determinants of per-coital-act HIV-1 infectivity among African HIV-1-serodiscordant couples. J Infect Dis. 2012 February 01;205(3):358-65.
- 10. Baggaley RF, White RG, Boily MC. Systematic review of orogenital HIV-1 transmission probabilities. Int J Epidemiol. 2008;37(6):1255-65.
- 11. Campo J, Perea MA, Del Romero J, Cano J, Hernando V, Bascones A. Oral transmission of HIV, reality or fiction? an update. Oral Dis. 2006;12(3):219-28.
- 12. Fox J, Fidler S. Risk of HIV transmission in discordant partners. J HIV Ther. 2007;12(2):48-53.
- 13. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, et al. Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med. 2011;365(6):493-505.
- 14. Cohen MS, Gay C, Kashuba AD, Blower S, Paxton L. Narrative review: Antiretroviral therapy to prevent the sexual transmission of HIV-1. Ann Intern Med. 2007;146(8):591-601.
- Anderson BL, Cu-Uvin S. Determinants of HIV shedding in the lower genital tract of women. Curr Infect Dis Rep. 2008;10(6):505-11.
- 16. Kalichman SC, Di Berto G, Eaton L. Human immunodeficiency virus viral load in blood plasma and semen: Review and implications of empirical findings. Sex Transm Dis. 2008;35(1):55-60.
- 17. Spinillo A, Gardella B, Zanchi S, Roccio M, Preti E. Determinants of genital shedding of human immunodeficiency virus: A review. Curr Women's Health Rev. 2008;4(2):118-23.
- 18. Politch JA, Mayer KH, Welles SL, O'brien WX, Xu C, Bowman FP, et al. Highly active antiretroviral therapy does not completely suppress HIV in semen of sexually active HIV-infected men who have sex with men. AIDS. 2012 Mar 23.
- Cu-Uvin S, DeLong AK, Venkatesh KK, Hogan JW, Ingersoll J, Kurpewski J, et al. Genital tract HIV-1 RNA shedding among women with below detectable plasma viral load. AIDS. 2010;24(16):2489-97.
- 20. Miller WC, Rosenberg NE, Rutstein SE, Powers KA. Role of acute and early HIV infection in the sexual transmission of HIV. Curr Opin HIV AIDS. 2010;5(4):277-82.
- 21. Wawer MJ, Gray RH, Sewankambo NK, Serwadda D, Li X, Laeyendecker O, et al. Rates of HIV-1 transmission per coital act, by stage of HIV-1 infection, in Rakai, Uganda. J Infect Dis. 2005;191(9):1403-9.
- 22. Dosekun O, Fox J. An overview of the relative risks of different sexual behaviours on HIV transmission. Current Opinion in HIV and AIDS. 2010;5(4):291-7.
- Ward H, Rönn M. Contribution of sexually transmitted infections to the sexual transmission of HIV. Current Opinion in HIV and AIDS. 2010;5(4):305-10.
- 24. Røttingen J-, Cameron WD, Garnett GP. A systematic review of the epidemiologic interactions between classic sexually transmitted diseases and HIV: How much really is known? Sex Transm Dis. 2001;28(10):579-97.
- 25. Freeman EE, Weiss HA, Glynn JR, Cross PL, Whitworth JA, Hayes RJ. Herpes simplex virus 2 infection increases HIV acquisition in men and women: Systematic review and meta-analysis of longitudinal studies. AIDS. 2006;20(1):73-83.
- Sexton J, Garnett G, Rottingen JA-. Metaanalysis and metaregression in interpreting study variability in the impact of sexually transmitted diseases on susceptibility to HIV infection. Sex Transm Dis. 2005;32(6):351-7.
- 27. Auvert B, Marais D, Lissouba P, Zarca K, Ramjee G, Williamson AL-. High-risk human papillomavirus is associated with HIV acquisition among South African female sex workers. Infect Dis Obstet Gynecol. 2011;2011:692012.
- Smith JS, Moses S, Hudgens MG, Parker CB, Agot K, Maclean I, et al. Increased risk of HIV acquisition among Kenyan men with human papillomavirus infection. J Infect Dis. 2010;201(11):1677-85.

- 29. Galvin SR, Cohen MS. The role of sexually transmitted diseases in HIV transmission. Nat Rev Microbiol. 2004;2(1):33-42.
- 30. Hayes R, Watson-Jones D, Celum C, van de Wijgert J, Wasserheit J. Treatment of sexually transmitted infections for HIV prevention: End of the road or new beginning? AIDS. 2010;24(SUPPL. 4):S15-26.
- 31. Grosskurth H, Mosha F, Todd J, Mwijarubi E, Klokke A, Senkoro K, et al. Impact of improved treatment of sexually transmitted diseases on HIV infection in rural Tanzania: Randomised controlled trial. Lancet. 1995;346(8974):530-6.
- Barnabas RV, Wasserheit JN. Riddle of the sphinx revisited: The role of STDs in HIV prevention. Sex Transm Dis. 2009;36(6):365-7.
- Siegfried N, Muller M, Deeks JJ, Volmink J. Male circumcision for prevention of heterosexual acquisition of HIV in men. Cochrane Database Syst Rev. 2009(2).
- Weiss HA, Hankins CA, Dickson K. Male circumcision and risk of HIV infection in women: A systematic review and metaanalysis. Lancet Infect Dis. 2009;9(11):669-77.
- 35. Millett GA, Flores SA, Marks G, Reed JB, Herbst JH. Circumcision status and risk of HIV and sexually transmitted infections among men who have sex with men: A meta-analysis. JAMA. 2008;300(14):1674-84.
- Kaplan EH, Heimer R. A model-based estimate of HIV infectivity via needle sharing. J Acquir Immune Defic Syndr. 1992;5(11):1116-8.
- 37. Hudgens MG, Longini Jr. IM, Halloran ME, Choopanya K, Vanichseni S, Kitayaporn D, et al. Estimating the transmission probability of human immunodeficiency virus in injecting drug users in Thailand. Appl Statist. 2001;50(1):1-14.
- Miller CL, Kerr T, Frankish JC, Spittal PM, Li K, Schechter MT, et al. Binge drug use independently predicts HIV seroconversion among injection drug users: Implications for public health strategies. Subst Use Misuse. 2006;41(2):199-210.
- Bruneau, J., Daniel, M., Abrahamowicz, M., Zang, G., Lamothe, F., Vincelette, J. Trends in human immunodeficiency virus incidence and risk behavior among injection drug users in Montreal, Canada: A 16-year longitudinal study. Am J Epidemiol. 2011;173(9):1049-58.
- Shah SM, Shapshak P, Rivers JE, Stewart RV, Weatherby NL, Xin KQ, et al. Detection of HIV-1 DNA in needle/syringes, paraphernalia, and washes from shooting galleries in Miami: A preliminary laboratory report. J Acquir Immune Defic Syndr Hum Retrovirol. 1996 Mar 1;11(3):301-6.
- Brogly SB, Bruneau J, Vincelette J, Lamothe F, Franco EL. Risk behaviour change and HIV infection among injection drug users in Montreal. AIDS. 2000 Nov 10;14(16):2575-82.
- 42. Zhang Y, Shan H, Trizzino J, Ruan Y, Beauchamp G, Mâsse B, et al. Demographic characteristics and risk behaviors associated with HIV positive injecting drug users in Xinjiang, China. J Infect. 2007;54(3):285-90.
- 43. Hu DJ, Subbarao S, Vanichseni S, Mock PA, van Griensven F, Nelson R, et al. Higher viral loads and other risk factors associated with HIV-1 seroconversion during a period of high incidence among injection drug users in Bangkok. J Acquir Immune Defic Syndr. 2002 Jun 1;30(2):240-7.
- 44. Kivelä PS, Krol A, Salminen MO, Geskus RB, Suni JI, Anttila V-, et al. High plasma HIV load in the CRF01-AE outbreak among injecting drug users in Finland. Scand J Infect Dis. 2005;37(4):276-83.
- 45. Wood E, Kerr T, Marshall BD, Li K, Zhang R, Hogg RS, et al. Longitudinal community plasma HIV-1 RNA concentrations and incidence of HIV-1 among injecting drug users: Prospective cohort study. BMJ. 2009;338.
- 46. Castel AD, Befus M, Willis S, Griffin A, West T, Hader S, et al. Use of the community viral load as a population-based biomarker of HIV burden. AIDS. 2012 Jan 28;26(3):345-53.
- 47. Des Jarlais DC, Arasteh K, McKnight C, Hagan H, Perlman DC, Semaan S. Associations between herpes simplex virus type 2 and HCV with HIV among injecting drug users in New York City: The current importance of sexual transmission of HIV. Am J Public Health. 2011;101(7):1277-83.
- Strathdee SA, Galai N, Safaiean M, Celentano DD, Vlahov D, Johnson L, et al. Sex differences in risk factors for HIV seroconversion among injection drug users: A 10-year perspective. Arch Intern Med. 2001 May 28;161(10):1281-8.

- 49. Bacon O, Lum P, Hahn J, Evans J, Davidson P, Moss A, et al. Commercial sex work and risk of HIV infection among young drug-injecting men who have sex with men in San Francisco. Sex Transm Dis. 2006;33(4):228-34.
- 50. McCoy CB, Lai S, Metsch LR, Messiah SE, Zhao W. Injection drug use and crack cocaine smoking: Independent and dual risk behaviors for HIV infection. Ann Epidemiol. 2004 Sep;14(8):535-42.
- 51. DeBeck K, Kerr T, Li K, Fischer B, Buxton J, Montaner J, et al. Smoking of crack cocaine as a risk factor for HIV infection among people who use injection drugs. CMAJ. 2009;181(9):585-9.
- 52. Faruque S, Edlin BR, McCoy CB, Word CO, Larsen SA, Schmid DS, et al. Crack cocaine smoking and oral sores in three inner-city neighborhoods. J Acquir Immune Defic Syndr Hum Retrovirol. 1996 Sep;13(1):87-92.
- Porter J, Bonilla L, Drucker E. Methods of smoking crack as a potential risk factor for HIV infection: Crack smokers' perception and behavior. Contemp Drug Probl. 1997;24:319-48.
- 54. Porter J, Bonilla L. Crack users' cracked lips: An additional HIV risk factor. Am J Public Health. 1993 Oct;83(10):1490-1.

# **USEFUL LINKS**

Here are some resources available on the PHAC website:

- Estimates of HIV Prevalence and Incidence in Canada, 2011
- Population-Specific HIV/AIDS Status Report: Women
- Population-Specific HIV/AIDS Status Report: Aboriginal Peoples