



# Evidence for optimal HIV screening and testing intervals in HIV-negative individuals from various risk groups: A systematic review

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## Abstract

**Background:** Human immunodeficiency virus (HIV) testing plays a crucial role in Canada's HIV prevention and treatment efforts and is the first step to achieving the Joint United Nations Programme on HIV/AIDS (UNAIDS) 90-90-90 targets; however, how often Canadians, including populations at increased risk of HIV exposure, should be tested is unclear. We conducted a systematic literature review to determine the optimal HIV screening and testing intervals.

**Objective:** To examine the current evidence on HIV testing intervals in HIV-negative individuals from various risk groups and to assess the potential harms and patients' values and preferences associated with different testing frequencies.

**Methods:** We searched MEDLINE/PubMed, Scopus, Embase, the Cochrane Library, PsychINFO and EconLit for studies on different frequencies of HIV testing published between January 2000 and September 2016. An additional search was conducted for grey literature published between January 2000 and October 2016. Data extraction included study characteristics, participants, exposure, outcomes and economic variables. The quality of the studies was assessed and results summarized.

**Results:** Of the 2,702 articles identified from the searches, 27 met the inclusion criteria for review. This included assessments of HIV testing intervals among the general population, men who have sex with men, people who use injection drugs and sex workers. Optimal testing intervals across risk groups ranged from one-time testing to every three months. Data from modelling studies may not be representative of the Canadian context. Few studies identified potential harms of increased screening, specifically an increase in both false positive and false negative results. There were only two studies that addressed patient values and preferences concerning HIV screening, which suggested that the majority of participants were amenable to routine screening through their primary care provider.

**Conclusion:** There was insufficient evidence to support optimal HIV screening and testing intervals for different populations. Context-specific factors, such as budget allocation, human resources, local epidemiology, socioeconomic factors and risk behaviours, along with clinical judgement, inform whom and how often to screen, suggesting the need for research specific to Canada. Research on patient preferences as well as the benefits and harms of more frequent screening are also indicated.

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**Keywords:** HIV screening, HIV testing intervals, men who have sex with men, sex workers, high risk populations



## Introduction

Human immunodeficiency virus (HIV) screening is essential to HIV prevention and treatment efforts, as early detection allows people living with HIV to access appropriate care and treatment that can help improve their health and prevent onward transmission (1–3). For this reason, the Joint United Nations Programme on HIV/AIDS (UNAIDS) 90-90-90 global strategy ambitiously aims to have 90% of all people living with HIV diagnosed and 90% of those diagnosed consistently receiving antiretroviral therapy by 2020, with 90% of those receiving treatment achieving viral suppression (4). Canada has committed to achieving these targets.

In 2016, an estimated 14% of the 63,110 Canadians living with HIV were unaware of their infection (5). HIV infection is concentrated in specific sub-groups, such as men who have sex with men (MSM), persons who inject drugs (PWID) and Indigenous populations (accounting for 49.3%, 15.3% and 9.1% of people living with HIV in 2014, respectively) (6–8). The 2012 Public Health Agency of Canada's *HIV Screening and Testing Guide* suggests that individuals involved in high risk practices should be screened for HIV infection at least annually (1). At the time of publication of this guide, insufficient evidence was available to provide recommendations on the optimal testing frequency for specific risk populations.

Evidence-informed guidance on testing frequencies for populations with distinct risk profiles may optimize and promote testing among healthcare providers; however, only one systematic review has been conducted on HIV screening and testing intervals specifically among MSM (9) and none has been published on other populations. To inform potential revisions to the *HIV Screening and Testing Guide*, we decided to conduct a systematic review to assess evidence for different HIV screening and testing intervals among various populations. Patient harms, values and preferences were also examined to understand whether increased HIV screening intervals would be feasible and acceptable in at risk populations.

The objectives of the systematic review were to examine and synthesize the current evidence on different HIV testing intervals in HIV-negative individuals from various risk groups, and, if possible, to include information on potential harms and patient values and preferences regarding screening intervals.

## Methods

The systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) statement (10). It follows a peer-reviewed *a priori* protocol registered with the International Prospective Register of Systematic Reviews (PROSPERO; registration number CRD42016046575) and published in the Canada Communicable Disease Report (11,12). Some amendments to the protocol were made following publication

(primarily related to quality assessment) and are reflected in the revised PROSPERO entry.

## Search strategy

A comprehensive search strategy was developed with the assistance of a Health Canada research librarian and peer-reviewed by an external research librarian prior to execution. The full search strategy is available in the previously published protocol (12).

We searched the MEDLINE/PubMed, Scopus, Embase, Cochrane Library, PsycINFO and EconLit databases, as well as Open Grey, ClinicalTrials.gov and relevant sources from the CADTH Grey Matters checklist (13). Searches were conducted for quantitative and qualitative studies published in English and French between January 2000 and September 2016. A search for grey literature for reports published between January 2000 and October 2016. Studies were eligible for inclusion if they investigated the frequency of HIV screening and testing among persons of unknown or previously-confirmed negative serostatus. Case studies, narrative summaries and commentaries were excluded. There were no restrictions on the country of study.

## Study selection, data collection and quality assessment

Two reviewers (MW and PB) independently performed title/abstract and full-text screening using standardized, piloted forms on the systematic review software, DistillerSR (Evidence Partners Incorporated, Ottawa, ON). Disagreements were resolved by a third reviewer (KT or GT).

Data extraction was carried out by one reviewer (PB) and quality assessments were completed by two reviewers (MW and PB). Data extraction was verified by two reviewers (TA and SH) and disagreements were resolved by a third reviewer (KT). Data extraction included the following: study characteristics (e.g., study design, setting); type of participants (e.g., risk group); exposure (e.g., testing intervals being compared, type of HIV test used); outcomes (e.g., number of new HIV diagnoses, average CD4 cell count and/or viral load at diagnosis, number of new HIV diagnoses, and change in number/percent of individuals with undiagnosed HIV infection); and economic variables (e.g., time horizon, currency) as appropriate. The quality of the descriptive studies was assessed using the *Public Health Agency of Canada's Infection Prevention and Control Guidelines: Critical Appraisal Tool Kit* (14,15). The quality of the economic modelling studies was assessed using a unique checklist that combined key items from the *British Medical Journal checklist for economic evaluations* and the *Eddy checklist on mathematical models* (16,17). These quality appraisal tools were selected in light of the systematic review findings and were judged appropriate for the types of studies identified (13). Although we intended to use the GRADE methodology to rate the certainty of evidence, the majority of the studies included in this review were modelling studies so it was not feasible to apply GRADE. In addition, the

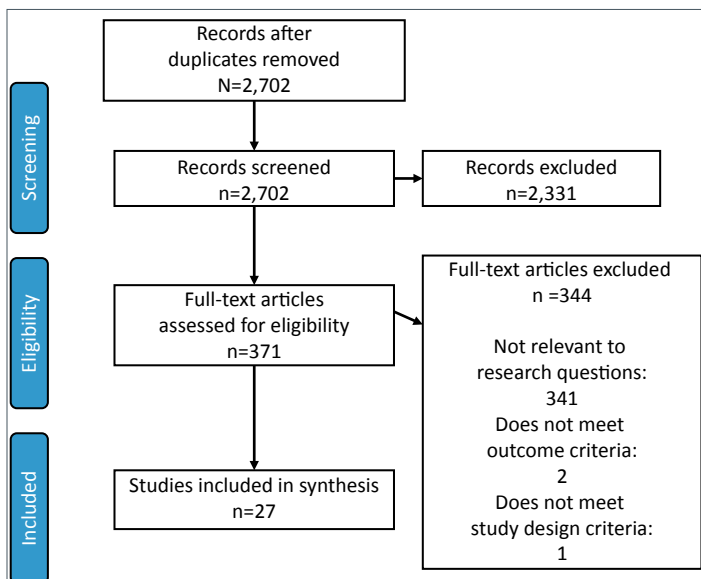


wide range of assumptions and inputs in the modelling studies lead to heterogeneity of findings, so meta-analysis was also not possible. For these reasons, we summarized the conclusions of the studies regarding the optimal testing frequency. For details on the protocol amendment, refer to the PROSPERO record (11). As *a priori*, we qualitatively summarized outcomes on patient harms, values and preferences to represent the descriptive nature of the data.

## Results

The literature search initially identified 2,702 articles (after the removal of duplicates), of which 27 met the systematic review inclusion criteria (Figure 1). A total of 344 studies were excluded after full-text review; mostly because they did not concern the topic of the systematic review (n=341). Two additional studies did not meet the outcome criteria and one study did not meet the study design criteria.

**Figure 1: PRISMA flow chart**



Abbreviations: n, number; N, total number; PRISMA, Preferred Reporting Items for Systematic Review and Meta-Analyses

The majority of the evidence came from 20 modelling studies (18-37). There was one descriptive study (38); three non-economic modelling studies (39-41); one cohort study (42); one cross-sectional study (43); and one mixed-methods study (descriptive and modelling) (44). The included studies were conducted in various countries, including 14 in the United States (US), three in Australia and two in the United Kingdom (UK). Third and fourth generation enzyme-linked immunosorbent assays (ELISA) were the most commonly-used tests in the studies.

## Optimal HIV testing frequency by population group

### General population

Thirteen studies, all of which were cost-effectiveness models, addressed optimal testing frequencies in the general population considered at low risk for HIV, with incidence ranging from 0.0084% to 4% per year (20,23,24,27-30,32-34,36,37,45). Recommended testing frequencies ranged from a one-time test to annual testing, with the largest proportion (n=5) advocating for a one-time test (23,24,30,36,37).

Sanders et al. proposed an economic model set in the US (30). They concluded that routine screening would be cost-effective if the prevalence of undiagnosed HIV infection were as low as 0.05%. Similarly, Long et al. reported that one-time screening of low risk populations coupled with annual screening of high risk populations would result in a low incremental cost-effectiveness ratio (ICER) and 2,555 HIV infections averted over 10 years (24). They concluded that one-time screening was the optimal testing frequency for a population with an HIV prevalence of 0.033% rather than the status quo of targeted risk-based testing (24). Special consideration was placed on the other variables that affect screening effectiveness, such as reduction in risk behaviors, with authors stating that the ICERs and HIV infections averted were contingent upon concurrent reduction of overall risk behaviors by 25%, even amongst low risk populations.

Nine studies were considered to be of high quality (23,24, 27-30,32,37,45), with thorough backgrounds and rationales, robust methods and data collection procedures, and strong justifications for the analysis plans. In addition, one study was deemed moderate/high quality (46), two studies were considered moderate quality (23,34) and one was low/moderate quality (20). Of the studies that were assessed as low/moderate quality, some variables (e.g., discount rates) were not reported and some studies did not provide justification for the selection of variables.

### Men who have sex with men

The search identified 14 studies that addressed the optimal HIV screening interval among MSM. Eight studies were economic modelling studies (19,20,22-25,32,37) and five were modelling studies without economic inputs (38,40-42,44). Recommended testing frequencies ranged from one-time only, to annually and to once every three months.

In the economic modelling studies from France and the UK (23,37), screening one-time and/or annually was found to be cost-effective. Among MSM in France (incidence: 0.99%/ person-year), one-time screening was the most cost-effective strategy compared with risk-based screening; annual screening was also considered cost-effective in this population with a lower ICER (37).



Among the modelling studies on MSM, the majority (n=8) were assessed as high quality (19,22,24,32,36,37,44,45). Three studies were rated as moderate quality (23,40,41) and one was low/moderate quality (20). Modelling studies that scored low/moderate quality did not provide strong rationales for the background and analysis. The study by Baker et al. reported the only descriptive study and it received only a moderate score due to the lack of generalizability to the target population, data collection sources and methods used, analysis plan and strength of study design (38).

**People who inject drugs**

Nine economic modelling studies (18,19,22–24,32,36,37,46) investigated the cost-effectiveness of HIV testing intervals among PWID. The majority of studies (n=6) stated that annual screening of PWID (usually coupled with less frequent screening of the general population) was economically justifiable (22–24,32,36, 37). Of note, Yazdanpanah et al. found that one-time, every three years, every five years and annual screenings of PWID were comparably cost-effective screening strategies in France (incidence: 0.17%/person-year) (36,37); however, three US studies recommended semi-annual testing versus annual testing (18,19,46).

Among the studies with PWID, seven studies were rated as high quality (18,19,22,24,32,36,37). In addition, one study was rated as moderate/high quality (46) and one as moderate quality (23); these two studies scored moderate quality due to the strength of the rationale and lack of clarity around the data collection methods.

**Sex workers**

Four of the included studies discussed the optimal frequency of HIV testing among sex workers operating in various

settings (21,22,32,35). Kaplan and Satten (21) explored HIV screening intervals among legal commercial sex workers using mathematical modelling and found the optimal screening frequency is every month when the annual cost of infection is \$360,000. Another study assessed HIV testing intervals among sex workers in jurisdictions where sex work was legal (35). The cost-effectiveness analysis of HIV testing intervals of legal commercial sex workers in Victoria, Australia (incidence rate of 0.1% HIV cases per person-year) concluded that implementing the current approach (testing once every three months) costs over \$4,000,000 AUD for every HIV infection averted (35) and for HIV testing to be cost-effective among these Australian sex workers, there should be at least 42 weeks between HIV tests. Moreover, Wilson et al. found that decreasing the frequency of testing to once a year did not greatly impact the likelihood of transmission, as the expected number of HIV cases remained less than one (35). Studies set in China (22) and India (32) also concluded that annual testing would be the most cost-effective testing interval for sex workers.

These four studies varied in quality: two were assessed as high quality (22,32), one as moderate quality (35) and one as low quality (21). The two studies that received moderate and low ratings scored low in multiple domains (e.g., data collection, analysis and results) due to lack of details around price adjustments or currency conversions and clarity around justification of variables used.

**Table 1** summarizes the economic modelling studies on optimal HIV testing and their quality scores.

**Table 1: Optimal HIV testing frequencies of included studies**

| First author, year (ref) | Population | Model input parameters; HIV prevalence/ incidence | Testing frequencies considered  | Optimal HIV screening frequency (conclusion)   |
|--------------------------|------------|---|---|--|
| <b>HIGH QUALITY</b>      |            |   |   |  |
| Cipriano, 2012 (18)      | PWID       | Prevalence:<br>Overall: 0.47%<br>PWID: 6.5%       | Ab test with or without confirmatory RNA testing: <ul style="list-style-type: none"> <li>Once upon entry to ORT program</li> <li>Once on entry followed by annually</li> <li>Once on entry followed by every six months</li> <li>Once on entry followed by every three months</li> </ul> No screening | Using Ab test and confirmatory RNA screening, testing once upon entry to ORT program and every six months among those in the ORT program was most cost-effective   |
| Gray, 2013 (44)          | MSM        | N/A   | Testing frequencies: <ul style="list-style-type: none"> <li>One-time</li> <li>Annually</li> <li>Twice a year</li> <li>Four times a year</li> </ul>  | Increasing HIV testing frequency results in a 13.8% reduction in HIV infections (or 208.7 infections averted) over 10 years if the 55–75% of men who test at least annually start testing every three months |
| Hutchinson, 2016 (19)    | MSM, PWID  | Prevalence:<br>MSM: 1.27%<br>PWID: 0.62%          | Ag/Ab or rapid test: <ul style="list-style-type: none"> <li>Every three months</li> <li>Every six months</li> <li>Annually</li> </ul>   | Testing every three or six months using either an Ag/Ab or rapid test is cost-effective for MSM. Testing greater than annually using an Ag/Ab test is cost-effective for PWID                                |



Table 1 (continued): Optimal HIV testing frequencies of included studies

| First author, year (ref)        | Population   | Model input parameters; HIV prevalence/ incidence   | Testing frequencies considered   | Optimal HIV screening frequency (conclusion)  |
|---------------------------------|--|---|--|---|
| <b>HIGH QUALITY (continued)</b> |  |   |  |   |
| Li, 2012 (22)                   | MSM, PWID, sex workers, clients of sex workers, low-risk women | Prevalence:<br>Male PWID: 9.3%<br>Female PWID: 9.3%<br>MSM: 5%<br>Female sex workers: 0.6%<br>Clients of female sex workers: 0.4%<br>Low-risk men: 0.025%<br>Low-risk women: 0.025% | Ab testing/confirmatory western blot: <ul style="list-style-type: none"> <li>One time low-risk and annual high-risk</li> <li>Low-risk every three years and annual high-risk</li> <li>Everyone screened every three years</li> <li>Everyone screened annually</li> <li>The above interventions with expanded ART and harm reduction access</li> </ul> Current annual testing rates of 37% for high-risk groups and 2% for low-risk groups with an ART utilization rate of 30% and without harm reduction programming | Low-risk groups: one-time screening<br>High-risk groups: annually   |
| Long, 2010 (24)                 | MSM, PWID, general population                                  | Prevalence:<br>MSM:12.6%<br>MSM/PWID:18.8%<br>Male PWID: 12.9%<br>Female PWID: 17.3%<br>Low-risk men: 0.10%<br>Low-risk women: 0.22%  | ELISA and confirmatory western blot: <ul style="list-style-type: none"> <li>Low risk individuals once, high-risk annually</li> <li>Low risk every three years, high risk annually</li> <li>Everyone screened every three years</li> <li>Everyone screened annually</li> <li>The above interventions in combination with increased ART utilization from 50% at CD4 &gt;350 cells/mL to 75%</li> </ul> No screening  | One-time HIV screening of low-risk individuals coupled with annual screening of high-risk individuals   |
| Lucas, 2013 (46)                | General population   | Incidence:<br>Low-risk: 0.01%/year<br>Medium-risk: 0.1%/year<br>High-risk: 1%/year  | Ab tests over varied HIV screening intervals (from 0–8 years)  | Low risk groups: Every 2.4 years;,<br>Moderate-risk groups: every nine months;<br>High risk groups: every three months  |
| Martin, 2010 (27)               | General population   | Incidence: 0.09%/year   | ELISA or rapid test: <ul style="list-style-type: none"> <li>Every five years</li> <li>Every 10 years</li> </ul>  | Testing every 10 years is more cost-effective than an expanded HIV screening program (testing every five years)   |
| Paltiel, 2005 (29)              | General population, high-risk                                  | Incidence:<br>High-risk: 1.20%/year<br>CDC threshold population: 0.12%/year<br>General population: 0.01%/year   | Testing intervals: <ul style="list-style-type: none"> <li>Current practice (five years to the detection of HIV on average) (29)</li> <li>Current practice and one-time ELISA</li> <li>Current practice and ELISA every five years</li> <li>Current practice and ELISA every three years</li> <li>Current practice and annual ELISA</li> </ul>  | Screening every 3–5 years is cost-effective among “all but the lowest-risk populations”   |
| Paltiel, 2006 (28)              | General population   | Incidence:<br>Baseline population: 1.0%/year<br>US general population: 0.10%/year<br>Low-risk population: 0.0084%/year  | Rapid test: <ul style="list-style-type: none"> <li>One-time</li> <li>Every five years</li> <li>Every three years</li> <li>Annually</li> </ul> No specific screening program  | One-time screening is the most cost-effective in all settings where the HIV prevalence was <0.20%   |
| Sanders, 2005 (30)              | General population   | Incidence: 0.03%/year   | ELISA and confirmatory western blot: <ul style="list-style-type: none"> <li>One-time</li> <li>Every five years</li> <li>No screening</li> </ul>  | One-time screening is the most cost-effective strategy in a population with a 1% prevalence of unidentified HIV infections. Screening every five years may be more appropriate in settings with high infection incidences |
| Soorapanth, 2006 (31)           | Infants  | Prevalence among pregnant women: 29.5%<br>Incidence during pregnancy: 2.3%/year   | Rapid test: <ul style="list-style-type: none"> <li>At 20 and 28 weeks gestation</li> <li>At 20 and 34 weeks gestation</li> <li>At 20 and 36 weeks gestation</li> <li>Only at 20 weeks gestation</li> </ul>   | The minimum time interval between the initial and repeat screens should be from three to 18 weeks, depending on prophylactic and treatment regimens, for HIV rescreening to be cost saving                                |





Table 1 (continued): Optimal HIV testing frequencies of included studies

| First author, year (ref)        | Population   | Model input parameters; HIV prevalence/ incidence  | Testing frequencies considered   | Optimal HIV screening frequency (conclusion)   |
|---------------------------------|--|--|--|--|
| <b>HIGH QUALITY (continued)</b> |  |  |  |  |
| Venkatesh, 2013 (32)            | MSM, PWID, general population, migrants, from HIV + country, sex workers | National population:<br>Prevalence: 0.29%<br>Incidence: 0.032%/year<br><br>High prevalence districts:<br>Prevalence: 0.8%<br>Incidence: 0.088%/year<br><br>High-risk groups:<br>Prevalence: 5.0%<br>Incidence: 0.552%/year | Testing intervals: <ul style="list-style-type: none"> <li>One-time</li> <li>Every five years</li> <li>Annually</li> </ul>  | Screening the national population every five years and people in high-risk groups and high prevalence districts annually is cost-effective   |
| Walensky, 2011 (33)             | General population   | Prevalence: 16.9%<br>Incidence: 1.3%/year  | Rapid test: <ul style="list-style-type: none"> <li>One-time at age 33 years</li> <li>Every five years</li> <li>Annually</li> <li>Every 10 years as well as upon presentation with an AIDS-defining</li> </ul>                        | Annual testing is the most cost-effective strategy   |
| Yazdanpanah, 2010 (37)          | MSM, PWID, general population  | Incidence:<br>General population: 0.01%/year<br>PWID: 0.17%/year<br>French Guyana: 0.35%/year<br>MSM: 0.99%/year<br>Heterosexual population: 0.01%/year  | ELISA: <ul style="list-style-type: none"> <li>One-time plus risk-based screening</li> <li>Every five years plus risk-based screening</li> <li>Annually plus risk-based screening</li> <li>Risk-based screening only</li> </ul>       | One-time screening is recommended in addition to risk-based screening; however, more frequent screening in higher-risk subpopulations is justified   |
| Yazdanpanah, 2013 (36)          | MSM, PWID, general population  | Incidence:<br>National population: 0.03%/year<br>PWID: 1.08%/year<br>MSM: 0.43%/year   | Rapid test: <ul style="list-style-type: none"> <li>One-time plus risk-based screening</li> <li>Every three years plus risk-based screening</li> <li>Annually plus risk-based screening</li> <li>Risk-based screening only</li> </ul> | One-time screening is recommended in addition to risk-based screening; however, more frequent screening in higher-risk subpopulations is justified   |
| <b>MODERATE QUALITY</b>         |  |  |  |  |
| Baker, 2013 (38)                | MSM  | N/A  | Testing intervals: <ul style="list-style-type: none"> <li>every three months</li> <li>every six months</li> </ul>  | Screening high risk groups every three months is associated with an increase in the potential for earlier HIV diagnoses  |
| Brown, 2008 (39)                | Infants  | N/A  | Comparing assays at three, six, nine, and 12 months of age to the current practice of assays at birth, at 4–8 weeks, 15–18 months of age   | Testing one month after weaning or 12 months of age (whichever comes first), identified 81% of those infected during the late postnatal period (after 4–8 weeks) through breastfeeding<br><br>HIV-1 diagnostic testing should be performed at 4–8 weeks of age to capture early HIV-1 transmission, AND at the first of one month after weaning or 12 months of age to capture late postnatal transmission |
| Delaney, 2015 (40)              | MSM  | N/A  | Testing intervals: <ul style="list-style-type: none"> <li>Annual testing</li> <li>every three months</li> </ul>  | Current practice (testing “almost annually”) is sufficient   |
| Katz, 2014 (41)                 | MSM  | N/A  | Home-based testing <ul style="list-style-type: none"> <li>Annual testing</li> <li>2.9 times a year</li> </ul>  | Home-based testing resulted in increased HIV testing and HIV prevalence  |



Table 1 (continued): Optimal HIV testing frequencies of included studies

| First author, year (ref) | Population   | Model input parameters; HIV prevalence/ incidence  | Testing frequencies considered  | Optimal HIV screening frequency (conclusion)   |
|--------------------------|--|--|---|--|
| <b>MODERATE QUALITY</b>  |  |  |   |  |
| Long, 2011 (25)          | MSM, PWID, low-risk  | Prevalence:<br>Male PWID: 12.9%<br>MSM: 12.6%<br>MSM/PWID: 18.8%<br>Male other: 0.10%<br>Female PWID: 17.3%<br>Female other: 0.22%                             | Ag/Ab or Ab test (alone or with pooled NAAT):<br><ul style="list-style-type: none"> <li>• Every three months</li> <li>• Every six months</li> <li>• Annually</li> </ul> Current annual testing rates of 23% for high-risk groups and 10% for low-risk groups  | Testing every six months using the Ag/Ab test is more cost-effective than annual pooled NAAT screening   |
| Long, 2014 (23)          | MSM, PWID, general population, migrants from HIV + country | Prevalence:<br>Men from endemic countries: 2.5%<br>Women from endemic countries: 5.0%<br>PWID: 1.2%<br>MSM: 5.0%<br>Male other: 0.033%<br>Female other: 0.033% | Testing intervals:<br><ul style="list-style-type: none"> <li>• All adults tested every one, two, or three years</li> <li>• MSM, PWID, and people from endemic countries are tested annually, with other adults being tested either one-time or every two years</li> <li>• Annual testing</li> </ul> | High-risk groups: annual testing<br>Low-risk groups: one-time  |
| Waters, 2011 (34)        | General population   | Incidence: 0.8, 1.3, or 4.0%/year  | Testing intervals:<br><ul style="list-style-type: none"> <li>• Every three and six months</li> <li>• Every 1, 2, 3, 4.29, 5, 6, 7.5, 10 or 15 years</li> <li>• One-time 30 years from model start</li> </ul>  | "Accounting for secondary infections averted, the most cost-effective testing frequency was every 7.5 years for 0.8% incidence, every five years for 1.3% incidence, and every two years for 4.0% incidence"                     |
| Wilkinson, 2015 (42)     | Sex workers  | Incidence: 0.1%/year   | ELISA over varied HIV screening intervals (from 0–55 weeks)<br><ul style="list-style-type: none"> <li>• Testing every 12 weeks is the comparator interval</li> </ul>  | "At an assumed willingness to pay of \$50 000 AUS per QALY gained, HIV testing should not be conducted less than approximately every 40 weeks[...]"  |
| Wilson, 2010 (35)        | Sex workers  | Incidence: 0.1%/year   | ELISA over varied HIV screening intervals (from 0–55 weeks)<br><ul style="list-style-type: none"> <li>• Testing every 12 weeks is the comparator interval</li> </ul>  | "At an assumed willingness to pay of \$50 000 AUS per QALY gained, HIV testing should not be conducted less than approximately every 40 weeks [...]"   |
| <b>LOWER QUALITY</b>     |  |  |   |  |
| Hutchinson, 2010 (20)    | General population, MSM, high risk                         | Prevalence: 1.0-1.8%<br>Incidence: 0.01-0.21%/year   | Ab or rapid test with NAAT:<br><ul style="list-style-type: none"> <li>• HIV diagnosis one year after infection</li> <li>• HIV diagnosis six months after infection</li> <li>• HIV diagnosis five years after infection</li> </ul>   | "NAAT screening was cost-effective in targeted to settings with very high HIV incidence, such as the community clinic, where it remained cost-effective compared with retesting for HIV antibody as often as every three months" |
| Kaplan, 2000 (21)        | Sex workers, active duty soldiers                          | Incidence:<br>Sex workers: 0.004/year<br>Soldiers: 0.0003/year   | ELISA over varied HIV screening intervals (from 0–4 months)   | Sex workers: every month when the annual cost of infection is \$360,000.W<br>Soldiers: every 1.4 years when the annual cost of infection is \$8,570  |

Abbreviations: Ab, antibody; Ag, antigen; ART, antiretroviral therapy; \$ AUS, Australian dollar; CDC, Centers for Disease Control and Prevention; ELISA, enzyme-linked immunosorbent assay; HIV + country, HIV endemic country; MSM, gay, bisexual, and other men who have sex with men; NAAT, nucleic acid amplification testing; N/A, not applicable; ORT, opioid replacement therapy; PWID, persons who inject drugs; QALY, quality-adjusted life year; ref, reference; RNA, ribonucleic acid; US, United States; <, inferior to; >, superior to

## Potential harms, patient values and preferences

Two studies identified the potential harms associated with HIV screening intervals (23,24). Both studies found that the implementation of more frequent screening (within the general population, MSM, PWID and migrants from HIV-endemic country

population groups) resulted in an increase in the number of false positive and negative results. However, it was reported that the number of false positive/negative results decreased as fewer people remain undiagnosed (23,24). No studies reported on the other outcomes of interest for harms (e.g., psychosocial harms, stigmatization, etc.). One study was assessed as high quality (24) and the other was assessed as moderate quality (23) due to a



lack of specificity and reporting of the rationale, data collection and method of analysis.

Two studies examined patients' values and preferences associated with HIV testing intervals (43,44). In an Australian study, the authors surveyed self-identified MSM living in New South Wales and found that 25% were "very likely" to accept more frequent (i.e., every three months) HIV testing (44). The setting of the second study was in American primary care clinics in underserved and low-income neighbourhoods. The authors reported that 86% of African American and Latino respondents value HIV testing on a regular basis, with 77% of respondents expressing interest in annual or semi-annual testing and 80% of respondents indicating a preference to have the HIV test performed by their primary care provider rather than an HIV-specific counsellor. One was assessed as moderate quality (44) and the other assessed with a lower quality (43) due to concerns about the data collection methods.

Table 2 summarizes the findings from descriptive studies of optimal HIV testing frequency and related findings.

Table 2: Results on potential harms, patient values and preferences of included studies

| First author, year | Population                    | Objective  | Potential harms, patient values and preferences   | Rating |
|--------------------|-------------------------------|--|---|--------|
| Gray, 2013 (44)    | MSM                           | Assess whether increases in HIV testing would be acceptable to gay men in New South Wales and model the potential impact of increases in testing coverage and/or frequency | Increasing HIV testing would be acceptable if testing was more convenient.<br><br>Only 25% of men surveyed were 'very likely' to increase their level of HIV testing                      | High   |
| Long, 2010 (24)    | MSM, PWID, general population | To evaluate the effects of expanded ART, HIV screening, or interventions to reduce risk behavior   | Annual screening in high risk populations and one-time screening in the general population will result in false-positive and false-negative diagnoses. These will decrease over 20 years. | High   |

Table 2 (continued): Results on potential harms, patient values and preferences of included studies

| First author, year | Population   | Objective   | Potential harms, patient values and preferences   | Rating |
|--------------------|--|---|---|--------|
| Long, 2014 (23)    | MSM, PWID, general population, migrants from HIV endemic countries | Estimate the effectiveness and cost-effectiveness of HIV testing in the United Kingdom        | False-positives and false-negatives would occur with annual high-risk screening and one-time low risk screening. Over time, the occurrences will decrease.  | Mod    |
| Simmons, 2005 (43) | General population (African Americans and Latinos)                 | Determine the attitudes of patients who attend urban primary-care clinics towards HIV testing | 77% of study participants said that they wanted to be tested annually or semi-annually for HIV.<br><br>Participants also indicated their desire to be tested for HIV routinely by their primary care provider, as opposed to an HIV counsellor. | Low    |

Abbreviations: ART, antiretroviral therapy; Mod, moderate; MSM, men who have sex with men; PWID, persons who inject drugs; HIV, Human immunodeficiency virus

### Discussion

This systematic review of 27 studies found there was insufficient high quality evidence and a lack of consistency in the findings to identify an optimal HIV testing interval for specific risk populations. Optimal screening and testing frequencies ranged widely from once in a lifetime for the general population to every three months for high-risk populations, depending on the type of study and the population studied. There were only two studies addressing potential harms that identified the risk of false positives or negatives. In addition, there were limited data on patients' values and preferences, although it appeared in high risk groups that more frequent testing would be acceptable.

The results of our systematic review are consistent with those of a recent review conducted by the Centers for Disease Control and Prevention (CDC) on HIV screening for gay, bisexual and other MSM. The CDC concluded that the evidence, programmatic experiences and expert opinions did not warrant changing the recommendations for HIV testing in MSM from once per year to more frequent intervals.





## Strengths and limitations

This is the first review to assess HIV screening and testing intervals in risk populations other than MSM and to summarize potential harms and patient preferences. Other strengths of this study include the comprehensiveness of the review, the robustness of the search strategy and the systematic nature of the analysis.

There are some limitations to consider. Although this study included 20 modelling studies, they were difficult to interpret for a Canadian population. Although some of the studies had an overall high quality and modelling studies may be useful for supporting the development of clinical guidelines in the absence of experimental evidence (47), the modelling studies examined included numerous assumptions that were not directly applicable to Canada. In addition, there was an absence of studies for other high-risk groups, such as Indigenous and incarcerated populations (6,7,48) and very little data on patients' values and preferences. In all the studies, it was difficult to control for context-specific factors such as budget allocation, human resources, local epidemiology and socioeconomic factors.

## Conclusion

Determining the optimal screening intervals for HIV in different risk populations is challenging due to the paucity of applicable, consistent, high quality evidence. In light of the inconsistency of findings and the limitations of modelling studies, population-based experimental studies could be done for different risk populations and Canadian-specific modelling studies may be helpful.

## Authors' statement

KT – Conceptualisation, methodology, investigation, writing – review and editing, supervision, project administration  
 MW – Investigation, writing – original draft, writing – review and editing, visualisation  
 GT – Conceptualisation, methodology, investigation, writing – review and editing  
 PP – Investigation, writing – original draft, writing – review and editing, visualisation  
 TA – Conceptualisation, methodology, investigation, writing – reviewing and editing  
 SH – Conceptualisation, methodology, writing – review and editing  
 BA – Investigation, writing – review and editing

## Conflict of interest

None.

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