



# Epidemiology of hepatitis C virus infection among men who have sex with men

## ? Question

- What is the epidemiology of hepatitis C virus infection among men who have sex with men in high-income settings?

## 🔑 Key Take-Home Messages

- HCV prevalence and incidence are low among HIV-negative men who have sex with men without a history of injection drug use (1-5) and insufficient evidence exists to warrant routine screening in this population (3).
- Since 2000, incidence and prevalence of HCV have increased dramatically among HIV-positive men who have sex with men (1-7).
- HIV-positive men who have sex with men are more than four times more likely to acquire HCV than HIV-negative men who have sex with men (3).
- Factors associated with potential sexual transmission of HCV among men who have sex with men include: co-infection with HIV; unprotected anal intercourse and inconsistent condom use; use of recreational drugs; sexually transmitted infection(s); serosorting; multiple, anonymous, or casual sex partners and group sex; and sexual practices that result in bleeding or tissue damage (1-13).
- HCV reinfection rates are high among HIV-positive men who have sex with men (8;10;14).
- HIV-positive men who have sex with men would benefit from routine screening for HCV in (3;7) and more extensive risk behaviour counselling and targeted HCV prevention services (3;8).

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## The Issue and Why It's Important

The first cases of sexually transmitted hepatitis C virus (HCV) in men who have sex with men were described in the mid-1990s (15). By the mid-2000s, more articles reported similar findings among HIV-positive men who have sex with men (8;16-18). Localized epidemics of HCV in HIV-positive men occurred in large European cities (19-22) as well as in the U.S. (23;24) and Australia (25). Previous HCV epidemics were in people with a history of injection drug use, however, this was not the case in most HIV-positive men who have sex with men diagnosed with HCV (16-18).

Over the past two decades, new patterns of HCV incidence and prevalence emerged in men who have sex with men, including high incidence in HIV-positive men, but no apparent increased risk among HIV-negative men. Spontaneous clearance rates of HCV are almost twice as low in HIV-positive than HIV-negative men (26). HIV and HCV co-infection increases the risk of advanced liver fibrosis two-fold, and HIV treatment is complicated in the presence of hepatitis-related liver damage (10;27). As a result, liver disease and hepatocellular carcinoma have become leading causes of death in people with HIV (10;28;29). Furthermore, the risk of hepatocellular carcinoma is three to eight times higher among people who are HIV-HCV co-infected versus those who are HCV-mono-infected (10;30).

To develop sexual health promotion and disease prevention programs for men who have sex with men – and avoid these negative health outcomes -- it is important to understand the epidemiology of HCV in this population as well as the behavioural and environmental factors that affect HCV risk.

## What We Found

HCV can be transmitted via three routes:

- Intravenous drug use or blood product transfusion (parenterally)
- Sexually (permucosally)
- Mother-to-child (vertically) (7).

The most efficient means of HCV transmission is parenteral exposure to blood. HCV is 10 times more likely than HIV to be transmitted through intravenous drug use (6).

### Heterosexual transmission of HCV

Heterosexual transmission of HCV is widely considered to be inefficient (1). Prospective studies of heterosexual monogamous couples (where one partner was HCV-infected) reported incident

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transmission rates of up to 0.6% per year (31-33). A literature review found no increased risk of sexual transmission of HCV among heterosexual couples in monogamous relationships (13).

## Homosexual transmission of HCV

Over the last decade, there has been an increase in the HCV incidence rate among men who have sex with men (9;17;19;23;34). The importance of homosexual transmission of HCV is highlighted through data from the Swiss HIV Cohort Study, which show that the incidence of HCV was greater in men who have sex with men than in heterosexuals who inject drugs (22). Many other studies also found associations between sexual risk behaviour and HCV infection among men who have sex with men (4;19;35-37). The use of molecular epidemiology has defined HCV transmission clusters within networks of men who have sex with men (1;19;20;34;35;38-40).

## HCV transmission among HIV-negative men who have sex with men

Prevalence and incidence of HCV is low among HIV-negative men who have sex with men who do not have a history of injection drug use (1;41-45). Although there have been some reports of sexually acquired HCV infection among HIV-negative men (2;46;47), the evidence suggests that HIV-negative gay men remain largely unaffected and are not at higher risk of acquiring HCV (5;8;20;45). In a recent Zurich-based serological survey of over 800 HIV-negative men who have sex with men and who had a median of six sexual partners a year, the prevalence of anti-HCV antibodies was 0.4% and only one patient had a replicating HCV infection (48). These data suggest HCV prevalence is no higher in HIV-negative men who have sex with men than in the general population (2) despite the large proportion of these men reporting unprotected anal intercourse. The few cases of HCV infection detected among HIV-negative men who have sex with men have been generally among those who have engaged in high-risk sexual activities with HIV-positive male partners (6;20;35;41;47).

These findings are consistent with other evaluations in European, Australian and American cities and with a recent systematic review, which concluded that systematic screening of HCV in HIV-negative men who have sex with men is not recommended (3), except on a case-by-case basis, such as when high-risk sexual behaviours are reported (3).

## HCV transmission among HIV-positive men who have sex with men

On the other hand, there is strong evidence that HCV infection is a rapidly growing problem among HIV-positive men who have

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sex with men (1;14;16;23;24;49). According to a systematic review and meta-analysis of 25 studies (3) undertaken to investigate the incidence of HCV in HIV-positive and HIV-negative men who have sex with men and assess the need for routine screening and targeted prevention, the HIV-positive men had a 4.1 times higher risk of acquiring HCV (6.1/1000 person-years -- 95% CI 5.2 to 7.0). A review of 80 reports on the evidence related to sexual transmission of HCV had similar findings (13): HIV-positive men who have sex with men have a much higher risk than HIV-negative men of acquiring HCV (adjusted odds ratio 4.1-5.7). One large cross-sectional study from Amsterdam reported that HIV-positive men were almost 43 times (95% CI 8.5 to 215.1) more likely to acquire HCV infection than HIV-uninfected men (36).

The incidence of HCV in HIV-positive men who have sex with men is high and it appears to be rapidly increasing over time. It is now approaching the rates currently seen in some populations of people who inject drugs (3):

- In 2012, a comprehensive analysis of HCV seroconversions in a Swiss HIV Cohort Study showed an 18-fold increase in HCV incidence in HIV-positive men who have sex with men between 1998 and 2011 (with the annual incidence of transmission approaching 2-4%). Over the same period, the incidence of HCV among people who inject drugs decreased steadily (22).
- According to data from 12 cohorts within the CASCADE collaboration, which reported HCV incidence in HIV-positive men who have sex with men from 1990 to 2007 (41), the incidence of HCV (per 1000 person years) increased substantially from 0.9 to 2.2 in 1990 to 5.5-8.1 in 1995. to 16.8 to 30.0 in 2005 and 23.4 to 51.1 in 2007. Of all the transmission events in the study, about 63% occurred after 2000 (4;41).

As a result of this higher risk for acute HCV infection among HIV-positive men, researchers recommended that they be routinely screened for HCV (3).

## HCV reinfection among HIV-positive men who have sex with men

HIV-positive men who have sex with men are at higher risk of HCV infection; they are also more likely to be re-infected (14;50;51). In a study of 145 HIV-positive men who have sex with men with a documented primary HCV infection at a large hospital in London, the reinfection rate was 8.0 per 100 person-years over a median follow-up time of 2.1 years (52). In another study from Amsterdam, the incidence of reinfection was even higher: an estimated 15.2 per 100 person-years (51). In fact, reinfection rates are much higher among HIV-positive men who have sex with men than in people

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who inject drugs, where reinfections are rare even in the context of on-going injection drug use (53).

These findings reinforce the need for more extensive risk behaviour counselling and prevention for HIV-positive men who have sex with men (8) -- although few public health efforts have been proven effective to date (12). On a positive note, recent advent of new directly acting antiviral drugs will significantly improve HCV treatment strategies and outcomes (2), however access continues to be an issue.

## Factors associated with sexual transmission of HCV among HIV-positive men who have sex with men

Many studies, including two large case-control studies, have examined transmission factors comparing HIV-positive people with acute HCV (i.e. cases) to HIV-positive but HCV-negative people (i.e. controls) (19;54). Reasons for increased sexual transmission of HCV in HIV-positive men who have sex with men is complex (6) and likely due to the interplay between a number of different factors (8), including:

- increased biological vulnerability due to the presence of HIV (5;36)
- increased biological vulnerability due to the presence of other STIs. Increase in sexually transmitted infections (both current or previous), especially ulcerative infections (13) including lymphogranuloma venereum proctitis, syphilis, and herpes has been associated with increased HCV transmission (1;9;16-18;20;22;23;35;46;55-57). For example, a recent Canadian cohort study estimated that the risk for HCV seroconversion was elevated among men who had ever had syphilis (adjusted hazard ratio 2.5, 95% CI 1.1 to 5.5) and men who had acute syphilis infection in the previous 18 months - adjusted hazard ratio 2.8 (95% CI 1.0 to 7.9) (55), but this study was not able to determine if syphilis was simply a marker for high-risk sexual behaviour or networks, or whether it potentiated sexual HCV transmission among individuals with HIV (55).
- increases in risk behaviours, including:
  - › **unprotected sex.** The steady increase in HCV in HIV-positive men since 1996 coincides with the expanded availability of highly active antiretroviral therapy (HAART) (5;6;39). With treatment some HIV-positive men may perceive unprotected sex to be less risky (6;58). In recent years, condom use has decreased among HIV-positive individuals with an undetectable HIV viral load (8;22;59). Multiple studies have identified unprotected anal intercourse as a factor in potential

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sexual transmission of HCV among men who have sex with men, especially for the receptive partner (18;19;38;56;60-62).

- › **serosorting.** Seroadaptive behaviour (engaging in unprotected sexual activity with individuals with the same HIV status, also known as serosorting) is increasingly common in HIV-positive men who have sex with men, leading to an increase in unprotected sex (5;6;8;9;63-65). In practice, the assumptions and lack of communication that often accompanies serosorting makes it an unreliable HIV prevention strategy as it does not prevent other sexually transmitted infections, including HCV (5).
- › **traumatic sexual practices** (such as fisting and use of shared sex toys). These practices may increase bleeding during sexual activity thereby increasing the risk of HCV transmission (1;6;9;13;17-19;36;54;61;62).
- › **multiple partners.** Multiple or anonymous as well as casual sex partners also increase HCV risk (1;13;18;19;38;62).
- › **group sex.** In group sex settings, different risk factors can converge including serosorting, recreational drug use and sexual practices that cause trauma to mucosal surfaces and rectal bleeding (1;10;19;20;36;39;54).
- › **recreational drug use,** as well as drug use during sex. Drugs such as GHB (gamma hydroxy butyrate) (7;36), cocaine (7;36;54), crystal methamphetamine (7;12;54;60), ketamine (54) and poppers (7) have been linked to higher risk of HCV transmission (36;51;54;60;62). The interaction between sex and drugs is complex, and many of these factors are highly correlated and difficult to disentangle (5). Sharing equipment for intranasal and rectal drug use may increase risk of HCV transmission; however, it is more likely that the association with drug use reflects sexual risk behaviour due to disinhibition and sexual arousal (5;7;19;54).

The HCV epidemic in HIV-positive men who have sex with men is mainly driven by a combination of biological vulnerability and behavioural risk factors. Reducing the risk of HCV infection among men who have sex with men will require the combined efforts of public health specialists, clinicians, policymakers and men living with HIV (7).

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## Factors That May Impact Local Applicability

All studies cited in this review were conducted in high-income countries in Western Europe (U.K., Switzerland, Germany, Netherlands and France) as well as in the U.S., Canada and Australia. Because of the similarities of HIV and HCV epidemics among men who have sex with men in these countries, the review findings are highly relevant and transferable to the Canadian context.



## What We Did

We searched Medline using a combination of (text terms Hepatitis C or MeSH terms Hepatitis C or Hepatitis C, Chronic) AND (text terms gay or men who have sex or homosexual\* or bisexual\* or transgender or MSM or transsexual\* or queer or LGBT or MeSH terms Homosexuality or Homosexuality, Male). Reference lists of identified literature reviews and systematic reviews were also searched. All searches were conducted on December 15, 2015 and results limited to English articles published from 2005 to present in high income countries. The search yielded 388 references from which 65 studies were included. Sample sizes of primary studies ranged from 159 to 42,983.

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### Rapid Response: Evidence into Action

The OHTN Rapid Response Service offers quick access to research evidence to help inform decision making, service delivery and advocacy. In response to a question from the field, the Rapid Response Team reviews the scientific and grey literature, consults with experts, and prepares a brief fact sheet summarizing the current evidence and its implications for policy and practice.

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