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Sexually Transmitted Diseases

JOURNAL OF THE AMERICAN SEXUALLY TRANSMITTED DISEASES ASSOCIATION

“Publishes peer-reviewed, original articles on clinical, laboratory, immunologic, epidemiologic, behavioural, public health, and historical topics pertaining to sexually transmitted diseases and related fields.”

- Official Journal of
  - American Sexually Transmitted Diseases Association
  - International Union Against Sexually Transmitted Infections
- Impact Factor 2.358 (2018)
- Frequency: 12 issues/year
Chemsex Among Men Who Have Sex with Men: a Sexualized Drug Use Survey Among Clients of the Sexually Transmitted Infection Outpatient Clinic and Users of a Gay Dating App in Amsterdam, the Netherlands

Susanne Druckler, MSc et al., Vol 45, No 5, May 2018.

- **Background:** Chemsex (drug use during sex) is practiced by some men who have sex with men (MSM) and is associated with high risk behaviour. In a cross sectional study at the STI clinic of Amsterdam, chemsex practices, risk behaviour and STI prevalence were explored.

- **Methods:** A survey on chemsex was offered to clinic clients during routine STI screening and to Amsterdam users of a gay online dating app. Associations were assessed using chi² tests and multivariable regression.

- **Results:**
  - MSM population n= 4,925. Chemsex reported by 866 (17.6%)
  - Chemsex in MSM visiting the clinic was significantly associated with an STI diagnosis (OR 1.7, 95%; CI, 1.5-2.0)
  - Chemsex was a significant risk factor for bacterial STI in HIV negative MSM visiting the clinic (aOR 1.5; 95% CI, 1.2-1.8) but not in HIV positive MSM.
  - Among gay dating app users, the proportion that reported chemsex use was higher than among MSM visiting the STI clinic (29.3% vs. 17.6%; p < 0.001)
  - A majority practised chemsex once a month or less, and 87% clinic attendees reported sex without drug use in the past month (76.8% in app users: p<.001).

- **Conclusions:** Chemsex is frequently practised by the MSM population and significantly associated with bacterial STI in HIV negative Men but not in HIV positive Men. Prevention strategies should target HIV negative men engaging in chemsex.

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Early Evidence of the Effectiveness of the Human Papillomavirus Vaccination Program Against Anogenital Warts in Manitoba, Canada: A Registry Cohort Study

Karla Willows, MD, FRCS et al., Vol 45, No 4, April 2018.

- **Background:** Changes in incidence of Anogenital warts (AGW) may serve as a useful early indicator of the effectiveness of the HPV vaccination program. This study aimed to assess the effectiveness of the vaccination program in Manitoba, Canada in reducing incident AGW and to what extent effectiveness depends on age at vaccination and number of doses.

- **Methods:** Population based cohorts created by linking Manitoba’s vaccine registry with hospital, physician and prescription claim databases. Participants in the vaccinated cohort were matched on age and area of residence to unvaccinated female participants via the Population registry. Clinical markers of prior sexual activity were a composite measure of pregnancy, previous STI, PAP cytology or contraceptive drug use. Kaplan Meier survival analysis to determine cumulative incidence of AGW. Cox proportional hazard models used to estimate HR for AGW among vaccinated v unvaccinated cohorts.

- **Results:**
  - Study population: n= 31,464 (vaccinated) n= 94,327 (unvaccinated)
  - 18y or less: lower incidence of AGWs compared with their unvaccinated matches (RR 0.6; 95% CI 0.4-0.8)
  - 19y and older: increase in AGW incidence in vaccinated cohort, only statistically significant among those with clinical markers of sexual activity (HR 2.8; 95% CI 2.1-3.7).
  - 18y or less: risk of AGWs was lowest among those who received 3 doses, corresponding to a vaccine effectiveness of 56% (95% CI, 30-70%).
  - 19y and older: those with clinical markers of sexual activity, risk of AGWs was lower after 3 doses of the vaccine (HR 2.5; 95% CI 1.7-3.6) compared with 1 dose (HR 3.7; 95% CI 2.1-6.8). Those without these markers, risk of AGWs remained increased regardless of the number of doses.

- **Conclusions:** Women vaccinated at an older (≥19 years) age may be less protected against AGWs, particularly if sexually active before vaccine administration.
An Exploration of Factors Impacting Preexposure Prophylaxis Eligibility and Access Among Syringe Exchange Users
Alexis M. Roth, PhD, MPH, et al.
Vol 45, No 4, April 2018.

Background: Preexposure prophylaxis has the potential to curb HIV acquisition; however, uptake remains low in PWID. The purpose of the study was to describe PrEP eligibility, willingness to use PrEP and ability to access PrEP among PWID.

Methods: Between July 2015 and Feb 2016, 138 PWID >18yo were recruited from a mobile syringe exchange program (SEP) in Camden, New Jersey. Participants completed a survey assessing sociodemographics and HIV risk and underwent chlamydia and gonorrhoea screening. CDC guidelines were used to assess PrEP eligibility.

Results:
- Study population: n=138 (65 women, 73 men), 78% identified as heterosexual. Median age 32y, most reported white non-Hispanic ethnicity, 75% were homeless, 88.4% considered to have heavy drug dependence.
- PrEP eligibility: 89.9% were considered PrEP eligible using current CDC guidelines.
- Willingness to use PrEP: 79.3% expressed a willingness to take PrEP. Women more likely than men to express willingness (88.9% v 71.0% P<0.02) and also willing to continue taking despite adverse effects (60.5% v 60% P<0.03). Despite high levels of willingness, participants reported they would feel anxious (51.6%) or embarrassed (45%) about taking PrEP, and half (51.4%) indicated that they would not want their sexual partner/s to know they were taking PrEP. These feelings did not vary significantly by sex.
- Ability to access PrEP: 43.8% saw a primary care provider in the last 6 months. 32.9% were uninsured. Most participants (86%) reported they would prefer to access future screening at the SEP versus STI clinics.

Conclusions: Most PWID are eligible for PrEP and find PrEP acceptable but face barriers to accessing it. These include feeling embarrassed or anxious about taking prep, non disclosure to partners, limited engagement with health care providers, lacking health insurance, experiencing severe substance disorder, SEPs are uniquely positioned to promote and provide PrEP.

Rising Chlamydia and Gonorrhoea Incidence and Associated Risk Factors Among Female Sex Workers in Australia: A Retrospective Cohort Study
Denton Callander, PhD, et al.

Background: Recent reports suggest increasing STI diagnoses among female sex workers, warranting closer investigation. Using data from a national surveillance network of sexual health clinics in Australia, a retrospective cohort analysis of HIV and STI incidence among female sex workers was undertaken, with a focus on determining trends and risk factors.

Methods: A retrospective cohort was constructed using repeat testing data extracted from a network of 42 sexual health clinics. Data was collected from 2009-2015. Poisson and Cox regression were used to determine trends in incidence and risk factors for HIV, chlamydia, gonorrhoea and infectious syphilis among female sex workers.

Results:
- Study population: n= 18,475.
- Chlamydia: Overall incidence rate for urogenital CT was 7.7/100 person years (PY) (95% CI, 7.3-8.1). Anorectal CT 0.6/100PY (95% CI 0.4-0.8). Pharyngeal CT overall incidence rate 1.9/100 PY (95% CI, 1.6'-2.2). Risk factors independently associated with increased risk of CT at any site: having ≥2 private partners, inconsistent condom use with private partners, being younger and being born in Australia or NZ.
- Gonorrhoea: Overall incidence rate for urogenital NG was 1.4/100 PY (95% CI, 1.2-1.5). Anorectal NG 0.3/100 PY (95% CI, 0.2-0.6). Pharyngeal NG overall incidence rate was 3.6/100 PY (95% CI, 3.3-4.1). Risk factors for NG at any site: recent injecting drug use and country of birth.
- Infectious syphilis: Overall incidence rate of infectious syphilis was 0.4/100 PY (95% CI, 0.3-0.6). Stable over time. Risk factors: recent injecting drug use, having ≥2 private partners and country of birth.
- HIV: Incident rate of 0.1/100 PY (95% CI, 0.0-0.1). Remains low. Multivariate analysis not conducted.

Conclusions: Although syphilis and HIV remain uncommon in female sex workers attending Australian sexual health clinics the increasing incidence of NG and increasing CT after a period of decline may require enhanced health promotion initiatives. Promotion of pharyngeal testing to both clinicians and sex workers is needed.
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Rapid Increase in Reports of Syphilis Associated with Men Who Have Sex with Women and Women Who Have Sex with Men, Japan, 2012 to 2016

Background: In Japan, syphilis reports have recently increased. However, unlike other developed countries where MSM are often associated with the rise, the increase in Japan has been attributed more to Men who have sex with Women (MSW) and Women who have sex with Men (WSM). This warranted further detailed study.

Methods: Syphilis is a notifiable disease requiring all laboratory confirmed cases to be reported; stage and sex of the partner suspected as the infection source are also reported. The data for this study was gathered from surveillance data in Japan. All reported cases between 2012-2016 included. Main analysis restricted to Primary and secondary syphilis (P&S) cases (i.e. Recently acquired).

Results:
- Study population: n= 10,978 total cases reported. 64% (7040) were P&S.
- The proportion of P&S increased over time (54.5% in 2012 v 69.5% in 2016).
- Among P&S cases, MSW and WSM each surpassed MSM cases in 2016. (1390, 696 and 488 cases respectively).
- Men were older with a wider age distribution (median, 37 years; interquartile range, 28-46 years) relative to women (median, 26 years; interquartile range, 21-34 years). Among those younger than 25 years, the reporting rate per 100,000 was higher in women than in men.
- Small increase in congenital syphilis reports 0.4 in 2012 to 1.4 per 100,000 live births in 2016.
- Tokyo prefecture had the highest reporting rate (3.98 per 100,000 person years).

Conclusions: Reports of P&S syphilis increased yearly among MSW and WSM. Young women seem to be at particular risk. Syphilis prevention and control is currently a public health priority area in Japan.
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Non-Vaccine-Type Human Papillomavirus Prevalence After Vaccine Introduction: No Evidence for Type Replacement but Evidence for Cross-Protection
Monica Saccucci, BS et al. Vol 45, No 4, April 2018.

Aim: To examine non-vaccine type HPV prevalence in a community before and during the first 8 years after vaccine introduction, to assess for (1) type replacement with any non-vaccine type HPV and (2) cross protection with non-vaccine types genetically related to vaccine type HPV among vaccinated and unvaccinated young women.

Methods: Women 13-26yo with a history of sexual contact were recruited from primary care settings for 3 cross sectional studies from 2006-2014. Outcome variables were (1) prevalence of at least 1 of 32 non vaccine type HPVs and (2) prevalence of at least 1 HPV type genetically related to HPV-16 and HPV-18. Changes in proportion of non vaccine type HPV prevalence across the study waves were determined using logistic regression with propensity score inverse probability weighting.

Results:

- Study population: n=1180
- Type replacement:
  - From 2006-2014 no increase in non-vaccine type HPV among vaccinated women (AOR 1.02; 95% CI 0.73-1.42)
  - Increase in non vaccine type HPV in unvaccinated women (AOR, 1.88; 95% CI 1.16-3.04)
- Cross Protection:
  - Decrease in types genetically related to HPV-16 among vaccinated (AOR, 0.57; 95%CI, 0.38-0.88) but not unvaccinated women (AOR, 1.33; 95% CI 0.81-2.17).
  - No significant changes to types genetically related to HPV-18 among vaccinated women

Conclusions: These results may inform cervical cancer screening recommendations, cost effectiveness analyses, education and health policy. Vaccination should continue to be promoted as a preventative health measure.

A Population-Based Study to Compare Treatment Outcomes Among Women with Urogenital Chlamydial Infection in Washington State, 1992 to 2015
Christine M. Khosropour, PhD, MPH et al. Vol 45, No 5, May 2018.

Background:

- Persistent/recurrent urogenital CT is common
- Rectal CT is common among women attending STI clinics and not always associated with a history of anal intercourse
- Doxycycline may be more effective for treatment of rectal CT
- If autoinfection occurs, greater risk of persistent/recurrent urogenital CT in azithromycin treated women, than doxycycline treated women.

Primary goal: to estimate the risk of persistent/recurrent urogenital CT among women treated with azithromycin compared to doxycycline.
A Population-Based Study to Compare Treatment Outcomes Among Women with Urogenital Chlamydial Infection in Washington State, 1992 to 2015

Christine M. Khosropour, PhD, MPH et al. Vol 45, No 5, May 2018.

Methods:
- Washington State surveillance data was used to create a population based retrospective cohort.
- Demographic information, date of diagnosis and treatment, treatment provided, anatomic site, pregnancy status and NG co-infection were obtained.
- Surveillance data don’t include information on the method of testing.
- Urogenital CT- positive lab test from cervix, urethra, urine or vagina.
- Only women who received azithromycin or dox included.
- Persistent/recurrent CT defined as the 1st positive urogenital CT result in the surveillance data that occurred 14 to 180 days after treatment of the initial infection.

Methods:
- Statistical Analysis:
  - Chi² tests used in primary analysis to compare proportion of women with persistent/recurrent urogenital CT.
  - Log binomial regression models used to estimate unadjusted and adjusted relative risk of persistent/recurrent infection after doxycycline v azithromycin treatment.
- 3 secondary analyses:
  - Sensitivity analysis conducted using 2 alternative outcome windows to avoid repeat false positives on repeat testing (21-180 days, 28-180 days)
  - Women with NG coinfection excluded
  - Distribution of reasons for receiving the repeat CT test among women was compared.
A Population-Based Study to Compare Treatment Outcomes Among Women with Urogenital Chlamydial Infection in Washington State, 1992 to 2015

Christine M. Khosropour, PhD, MPH


Results:

- N = 234,733
- 14,382 (6.1%) had persistent/recurrent urogenital CT within 14-180 days after treatment, including 11,242 (6.7%) women treated with azithromycin and 3,140 (4.7%) treated with doxycycline. (P < 0.001)
- Compared with women treated with azithromycin, women treated with doxycycline were more likely to be white, non Hispanic, be symptomatic and be diagnosed before 2006 (P < 0.001)
- Women treated with azithromycin were 41% more likely to have persistent/recurrent CT compared with women treated with doxycycline (RR: 1.41; 95% CI: 1.36-1.47)
- Adjusting for age, race, year of diagnosis, pregnancy status, NG coinfection, reason of initial testing and county where reported, treatment with azithromycin was associated with a 24% higher risk of recurrent/persistent CT (aRR 1.24; 95% CI 1.19-1.30)

<table>
<thead>
<tr>
<th>Characteristic at Time of Initial Diagnosis</th>
<th>Persistent/Recurrent Infection, n/N (%)</th>
<th>aRR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment received</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Azithromycin</td>
<td>12,427/136,350 (9.0)</td>
<td>1.71 (1.61-1.82)</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>11,175/117,647 (9.4)</td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14 - 17</td>
<td>3,739 (9.1)</td>
<td></td>
</tr>
<tr>
<td>18 - 24</td>
<td>1,642 (9.6)</td>
<td></td>
</tr>
<tr>
<td>25 - 29</td>
<td>1,639 (9.6)</td>
<td></td>
</tr>
<tr>
<td>30 - 34</td>
<td>4,555 (9.3)</td>
<td></td>
</tr>
<tr>
<td>65+</td>
<td>1,471 (9.6)</td>
<td></td>
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<tr>
<td>Race/ethnicity</td>
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<tr>
<td>White, NH</td>
<td>6,604 (11.1)</td>
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<tr>
<td>Black, NH</td>
<td>1,338 (7.5)</td>
<td>1.28 (1.22-1.34)</td>
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<tr>
<td>Hispanic</td>
<td>2,060 (9.7)</td>
<td>1.23 (1.17-1.29)</td>
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<tr>
<td>Other, non-Hispanic, NH</td>
<td>1,813 (7.6)</td>
<td>1.20 (1.14-1.26)</td>
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<tr>
<td>Unknown, NH</td>
<td>2,061 (7.9)</td>
<td>1.09 (1.00-1.18)</td>
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<tr>
<td>Concurrent gonorrhea</td>
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<td>Yes</td>
<td>2,345 (6.6)</td>
<td>1.19 (1.16-1.22)</td>
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<tr>
<td>No</td>
<td>2,108 (6.8)</td>
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<tr>
<td>Pregnancy</td>
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<tr>
<td>Yes</td>
<td>508 (6.6)</td>
<td>1.01 (0.92-1.11)</td>
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<tr>
<td>No</td>
<td>2,366 (6.6)</td>
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<td>Unknown</td>
<td>1,150 (6.1)</td>
<td>1.07 (1.02-1.12)</td>
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<tr>
<td>Reason for examination</td>
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<tr>
<td>Symptomatic</td>
<td>5,537 (7.4)</td>
<td>1.33 (1.28-1.38)</td>
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<tr>
<td>Routine examination (no symptoms)</td>
<td>6,455 (11.1)</td>
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<tr>
<td>Exposure to infection</td>
<td>10,361 (7.2)</td>
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<tr>
<td>Missing</td>
<td>1,559 (9.2)</td>
<td>1.04 (0.91-1.19)</td>
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<tr>
<td>Jurisdiction reporting</td>
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<tr>
<td>Pierce County</td>
<td>2,670 (9.3)</td>
<td>0.99 (0.96-1.03)</td>
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<tr>
<td>King County</td>
<td>2,960 (9.7)</td>
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<tr>
<td>Spokane County</td>
<td>1,043 (7.4)</td>
<td>0.84 (0.79-0.90)</td>
</tr>
<tr>
<td>Yakima County</td>
<td>1,092 (7.5)</td>
<td>1.02 (0.95-1.09)</td>
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<tr>
<td>North Sound</td>
<td>1,296 (8.2)</td>
<td>0.79 (0.72-0.87)</td>
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<tr>
<td>Eastern WA</td>
<td>1,781 (9.0)</td>
<td>0.79 (0.72-0.87)</td>
</tr>
<tr>
<td>Western WA</td>
<td>2,503 (8.4)</td>
<td>0.85 (0.81-0.89)</td>
</tr>
<tr>
<td>Year of Diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1992-1995</td>
<td>767 (11.3)</td>
<td>0.92 (0.82-1.04)</td>
</tr>
<tr>
<td>1996-2000</td>
<td>1,550 (9.2)</td>
<td></td>
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<tr>
<td>2001-2005</td>
<td>1,550 (9.2)</td>
<td></td>
</tr>
<tr>
<td>2006-2010</td>
<td>4,510 (9.3)</td>
<td></td>
</tr>
<tr>
<td>2011-2015</td>
<td>2,228 (9.6)</td>
<td></td>
</tr>
</tbody>
</table>
A Population-Based Study to Compare Treatment Outcomes Among Women with Urogenital Chlamydial Infection in Washington State, 1992 to 2015
Christine M. Khosropour, PhD, MPH et al. Vol 45, No 5, May 2018.

Results:

Secondary analyses

Adjustment of retesting window did not alter the primary findings (21-180 days: aRR, 1.24 [95% CI, 1.19-1.30]; 28-180 days: aRR, 1.25 [95% CI, 1.19-1.30])

Excluding women coinfected with NG did not alter primary findings (aRR, 1.24; 95% CI, 1.18-1.29).

Reasons for a repeat CT test—similar proportion of women in the 2 groups reported reexposure (11.1% azithromycin vs. 10.5% doxycycline). Women treated with doxycycline were more likely to receive a repeat test because of symptoms, than those treated with azithromycin (43.9% vs. 33.4%)

Appraisal:

Strengths:

Population based study, >230,000 women
Cases well documented. <6% of cases had incomplete treatment information.
Consolidates existing data about CT
Clear conclusion regarding azithromycin v doxycycline (aRR 1.24)
A Population-Based Study to Compare Treatment Outcomes Among Women with Urogenital Chlamydial Infection in Washington State, 1992 to 2015

**Appraisal:**

- **Weaknesses**
  - Study design
  - Baseline characteristics of azithromycin treated group v doxycycline treated group
  - Use of surveillance data- no active follow up of women
  - Cannot distinguish between persistent and recurrent infection
  - Increasing use of azithromycin coincided with increasing use of NAAT
  - Increasing use of azithromycin coincided with change in CDC guidelines.

- Whether the rectum is a source of persistent/recurrent urogenital CT was not directly studied.
A Population-Based Study to Compare Treatment Outcomes Among Women with Urogenital Chlamydial Infection in Washington State, 1992 to 2015

- Conclusions:
  - Higher risk of persistent/recurrent urogenital CT infection in those treated with azithromycin compared to doxycycline.
  - Reasons for this remain uncertain
  - Role of rectal autoinfection still unclear. An area for future study

Thank you!
HCV infection among gay and bisexual men

Dr Marianne Martinello  |  2 May 2018
Infectious Diseases Staff Specialist | Blacktown Hospital
Lecturer | Viral Hepatitis Research Program, Kirby Institute
Outline

• HCV epidemiology
• Sexual (permucosal) transmission of HCV
  • Heterosexual couples
  • Gay and bisexual men
    • HIV-positive and HIV-negative GBM
• HCV elimination among GBM
  • Treatment as Prevention
  • Reinfection
HCV incidence, 2015

1.75 million new infections in 2015

Injection drug use
Young adult PWID
HIV-positive GBM

Unsafe health-care injection
PWID
HIV-positive GBM

<table>
<thead>
<tr>
<th>WHO region</th>
<th>Incidence rate (per 100 000)</th>
<th>Total number (000)</th>
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<tbody>
<tr>
<td></td>
<td>Best estimate</td>
<td>Uncertainty interval</td>
</tr>
<tr>
<td>African Region</td>
<td>31.0</td>
<td>22.5–54.4</td>
</tr>
<tr>
<td>Region of the Americas</td>
<td>6.4</td>
<td>5.9–7.0</td>
</tr>
<tr>
<td>Eastern Mediterranean Region</td>
<td>62.5</td>
<td>55.6–65.2</td>
</tr>
<tr>
<td>European Region</td>
<td>61.8</td>
<td>50.3–66.0</td>
</tr>
<tr>
<td>South-East Asia Region</td>
<td>14.8</td>
<td>12.5–26.9</td>
</tr>
<tr>
<td>Western Pacific Region</td>
<td>6.0</td>
<td>5.6–6.6</td>
</tr>
<tr>
<td>Global</td>
<td>23.7</td>
<td>21.3–28.7</td>
</tr>
</tbody>
</table>
Australia: Estimated incidence of HCV

Approximately 4500 - 6000 new HCV infections pa
# Under reporting of acute HCV and exposure

Table 2.1.13  Number of diagnoses of newly acquired hepatitis C infection, 2009 – 2013, by exposure category, year and sex

<table>
<thead>
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<tr>
<td>Injecting drug use</td>
<td>167</td>
<td>94</td>
<td>261</td>
<td>159</td>
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<tr>
<td>Sexual contact</td>
<td>7</td>
<td>8</td>
<td>15</td>
<td>7</td>
<td>3</td>
<td>10</td>
<td>4</td>
<td>4</td>
<td>8</td>
<td>3</td>
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<td>9</td>
<td>12</td>
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<td>16</td>
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<tr>
<td>Blood/tissue recipient</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
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<td>2</td>
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<tr>
<td>Skin penetration procedure</td>
<td>4</td>
<td>4</td>
<td>8</td>
<td>5</td>
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<td>2</td>
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<td>Healthcare exposure</td>
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<td>36</td>
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<td>7</td>
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<td>6</td>
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<tr>
<td>Household contact</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
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<td>Other</td>
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<td>16</td>
<td>41</td>
<td>41</td>
<td>41</td>
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<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>244</td>
<td>155</td>
<td>399</td>
<td>223</td>
<td>177</td>
<td>400</td>
<td>284</td>
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<td>127</td>
<td>407</td>
<td>407</td>
<td>407</td>
<td>407</td>
<td></td>
</tr>
</tbody>
</table>

1  Totals include diagnoses in people whose sex was not reported.

Source: National Notifiable Diseases Surveillance System

---

5  HIV, viral hepatitis and sexually transmissible infection in Australia: Annual Surveillance Report Kirby Institute, 2014
Newly acquired HCV notifications, 2007 – 2016

Figure 2.1.12  Newly acquired hepatitis C notification rate per 100,000 population, 2007–2016, by age group

**Highest rate in young PWID**

<table>
<thead>
<tr>
<th>Year</th>
<th>0-14</th>
<th>15-24</th>
<th>25-39</th>
<th>40+</th>
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</thead>
<tbody>
<tr>
<td>2007</td>
<td>0.1</td>
<td>4.4</td>
<td>4.3</td>
<td>0.5</td>
</tr>
<tr>
<td>2008</td>
<td>0.0</td>
<td>4.2</td>
<td>4.2</td>
<td>0.5</td>
</tr>
<tr>
<td>2009</td>
<td>0.2</td>
<td>5.0</td>
<td>4.3</td>
<td>0.4</td>
</tr>
<tr>
<td>2010</td>
<td>0.1</td>
<td>4.3</td>
<td>3.9</td>
<td>0.6</td>
</tr>
<tr>
<td>2011</td>
<td>0.1</td>
<td>6.9</td>
<td>6.4</td>
<td>0.9</td>
</tr>
<tr>
<td>2012</td>
<td>0.1</td>
<td>8.3</td>
<td>7.1</td>
<td>1.0</td>
</tr>
<tr>
<td>2013</td>
<td>0.1</td>
<td>7.8</td>
<td>6.6</td>
<td>0.9</td>
</tr>
<tr>
<td>2014</td>
<td>0.3</td>
<td>7.6</td>
<td>7.1</td>
<td>1.0</td>
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<tr>
<td>2015</td>
<td>0.1</td>
<td>9.0</td>
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<td>1.2</td>
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<tr>
<td>2016</td>
<td>0.1</td>
<td>7.6</td>
<td>6.6</td>
<td>1.2</td>
</tr>
</tbody>
</table>

Source: Australian National Notifiable Diseases Surveillance System.
Sexual (permucosal) transmission of HCV

Who? How? Why?
Sexual transmission of HCV among heterosexual couples is uncommon.
Sexual transmission of HCV in heterosexual couples is uncommon

- Cross-sectional study
- 500 anti–HCV Ab +ve participants + long-term monogamous heterosexual partner
  - Time at risk: 8377 py; median relationship duration: 15 yrs
  - Interviewed separately for lifetime risk factors for HCV, within-couple sexual practices
  - IDU ever: 2.4% of partners
- HCV prevalence among partners, 4% (n = 20)
  - 13/20 HCV RNA +ve; 9/13 concordant genotype/serotype
- HCV isolates in 3 couples (0.6%) = highly related

- Maximum incidence rate HCV sexual transmission: 0.07% per year (95% CI, 0.01–0.13)
- Risk per sexual contact, 1 : 190,000 – 380,000
Potential risk factors for heterosexual partners?

<table>
<thead>
<tr>
<th></th>
<th>Concordant couples</th>
<th>Uninfected couples</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sharing household items</td>
<td>0%</td>
<td>10.1%</td>
<td>1.00</td>
</tr>
<tr>
<td>Vaginal intercourse during menses</td>
<td>100%</td>
<td>65.6%</td>
<td>0.55</td>
</tr>
<tr>
<td>Anal intercourse</td>
<td>66.7%</td>
<td>30.2%</td>
<td>0.22</td>
</tr>
<tr>
<td>Condom use</td>
<td>0%</td>
<td>30.4%</td>
<td>0.56</td>
</tr>
</tbody>
</table>

* 2 of 3 concordant couples had history of either IDU, snorting drug use, or sharing snorting equipment

Drug-use related transmission of HCV not excluded
Potential *over-estimate* of incidence of heterosexual transmission of HCV
In long term heterosexual relationships, <0.1% transmission risk HCV per year

Persons with HCV infection in long-term monogamous relationships need **not** change their sexual practices
### Are any heterosexual couples at higher risk?

**Limited evidence**

<table>
<thead>
<tr>
<th>Group</th>
<th>% anti-HCV Ab positive (average)</th>
<th>Associated factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex workers</td>
<td>1 - 19% (6%)</td>
<td>Number of partners, History of STI, Lack of condom use, Sex with trauma</td>
</tr>
<tr>
<td>MSM</td>
<td>2.9 - 13% (4%)</td>
<td>Risk for IDU &gt; sexual</td>
</tr>
<tr>
<td>Sexual health clinic attendees (incl. IDU)</td>
<td>1.6 - 26% (4%)</td>
<td>Risk for IDU &gt; sexual</td>
</tr>
<tr>
<td>Sexual health clinic attendees (excl. IDU)</td>
<td>1.6 - 7%</td>
<td>Number of partners, High risk sexual contacts, HIV serostatus</td>
</tr>
</tbody>
</table>
Sexual (permucosal) transmission of HCV

Who? How? Why?

- Heterosexual
- GBM
  - HIV +ve
  - HIV -ve
HCV prevalence among GBM by HIV status

Pooled prevalence
HIV –ve GBM
1.5% (95% CI 0.8–2.1)

Pooled prevalence
HIV +ve GBM
8.3% (95% CI 6.7–9.9)
HCV prevalence among GBM who do not inject drugs by *HIV status*

- **HIV-positive GBM**
  - Pooled prevalence: 7.1% (95% CI 5.1-9.0)

- **HIV-negative GBM**
  - Pooled prevalence: 0.9% (95% CI 0-1.8)
HCV prevalence among people living with HIV

People living with HIV/HCV coinfection, 2.3 million (including 1.4 million PWID)
Anti-HCV Ab prevalence among people with HIV, 6.2%

HIV-positive GBM 6.4%  HIV-positive PWID 82.4%

Figure 2: Best estimates of prevalence of hepatitis C virus (HCV) co-infection in four population samples
Acute HCV among HIV-positive GBM

- Matthews 2007
- Matthews 2011
- Lutkemeyer 2006
- Fierer 2008
- Gambotti 2005
- Ghosn 2006
- Gotz 2005
- Vogel 2005
- Browne 2004
- Nishijima 2014
- Sun 2012
- Matthews 2007
- Matthews 2011
HCV incidence among GBM by HIV status

<table>
<thead>
<tr>
<th>Study</th>
<th>Person-years</th>
<th>Incidence (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alsayy et al (2005)</td>
<td>3653</td>
<td>0.38 (0.01, 2.10)</td>
</tr>
<tr>
<td>Richardson et al (2008)</td>
<td>3335</td>
<td>1.50 (0.49, 3.50)</td>
</tr>
<tr>
<td>Jin et al (2010)</td>
<td>4412</td>
<td>1.13 (0.37, 2.64)</td>
</tr>
<tr>
<td>Witt et al (2013)</td>
<td>31780</td>
<td>0.50 (0.29, 0.82)</td>
</tr>
<tr>
<td>Vanhommerig et al (2011)</td>
<td>10888</td>
<td>0.60 (0.00, 3.41)</td>
</tr>
<tr>
<td>Subtotal</td>
<td></td>
<td>0.44 (0.00, 0.88)</td>
</tr>
<tr>
<td>HIV-positive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rauch et al (2005)</td>
<td>3143</td>
<td>4.45 (2.44, 7.46)</td>
</tr>
<tr>
<td>Palacios et al (2009)</td>
<td>5263</td>
<td>1.90 (0.91, 3.49)</td>
</tr>
<tr>
<td>Jin et al (2010)</td>
<td>228</td>
<td>0.00 (0.00, 15.38)</td>
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<tr>
<td>Gamage et al (2011)</td>
<td>4359</td>
<td>8.95 (6.21, 12.21)</td>
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<tr>
<td>Waedelver et al (2012)</td>
<td>23707</td>
<td>4.30 (3.51, 5.22)</td>
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<tr>
<td>Witt et al (2013)</td>
<td>23516</td>
<td>4.21 (3.42, 5.12)</td>
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<td>Kouyos et al (2014)</td>
<td>2300</td>
<td>6.09 (5.27, 10.19)</td>
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<tr>
<td>Nishijima et al (2014)</td>
<td>2246</td>
<td>9.35 (5.80, 14.26)</td>
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<tr>
<td>Vanhommerig et al (2014)</td>
<td>6422</td>
<td>4.52 (3.03, 6.48)</td>
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<tr>
<td>Subtotal</td>
<td></td>
<td>6.25 (4.61, 8.09)</td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td>4.24 (3.01, 5.48)</td>
</tr>
</tbody>
</table>

Pooled incidence HIV –ve GBM 0.04 per 100 py

Pooled incidence HIV +ve GBM 0.64 per 100 py
Increasing HCV incidence among HIV-positive GBM: Swiss HIV Cohort Study

- HET: 0.1 per 100 py
- IDU: 13.9 per 100 py
- MSM: <0.5 per 100 py
- Other: 0.2 per 100 py
Increasing HCV incidence among HIV-positive GBM

- Meta-analysis
- HCV incidence in HIV-positive GBM who denied ever injecting drugs
- Increasing annual incidence
  - 1991: 0.4 per 100 py
  - 2012: 1.3 per 100 py

- Changes to international guidelines promoting HCV screening amongst HIV-positive GBM
Increase in HCV incidence among HIV-positive GBM associated with an increase in sexual risk behaviour and drug use
What drives higher HCV incidence among HIV-positive GBM?

*Behavioural vs biological*
Higher risk behaviour?

Sexual behavior
- Group sex
- ↑ no of partners
- Condom-less AI
- Fisting
- Internet
- Sex toys
- Serosorting
- Bleeding during sex

Drug use
- Snorting drug use
- Shared implements
- PDE-5 use
- Colorectal instrumentation
- Rectal enemas

Chemsex
- GHB, methamphetamine

Increased risk of HCV acquisition
Serosorting and condom-less anal intercourse

Condom-less anal intercourse among GBM in London 1998 - 2008
Increasing sexual risk behaviour and HCV incidence: Swiss HIV Cohort Study

CLAI with CMP

HCV incidence

Rate of initiation of CLAI with CMP
Biological plausibility for sexual transmission?

RAMPT-C: the role of HCV RNA in semen

- N=66
- 43% HCV RNA present in semen
- Median HCV RNA semen: 2.1 log\(_{10}\) (1.8-2.6)
- Median HCV RNA plasma >>>>> semen (by >4 log\(_{10}\))
- No difference by HIV serostatus
- ↑ semen HCV RNA at higher plasma HCV RNA in acute HCV / HIV co-infection

![Graph showing plasma HCV RNA levels in different groups: Acute HIV+, Chronic HIV+, Chronic HIV-]
Semen HCV RNA correlates with blood HCV RNA

33% men had seminal shedding (median $1.49 \log_{10}$ IU/ml)
Average ejaculate contains 50 – 6630 IU
Is mucosal immunity to blame?

HIV induces:
1. Intestinal villous effacement
2. Mucosal CD4 depletion
3. Immune activation and dysregulation

Enhanced susceptibility to permucosal transmission (?)

Ulcereative STI
Syphilis, LGV
Shedding of rectal HCV

![Blood HCV VL (log\textsubscript{10} IU/mL)]

- Not detected (n=23)
- Detected (n=20)

**p < 0.001**
Biological mechanisms: T cell defect?

MACs Cohort, 1984 - 2011

HIV-positive and negative GBM, n=4954

Higher risk in older HIV-positive GBM with lower CD4 count, syphilis and receptive condom-less anal intercourse

<table>
<thead>
<tr>
<th></th>
<th>IRR (all)</th>
<th>P</th>
<th>IRR (HIV)</th>
<th>P</th>
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<tbody>
<tr>
<td>Age</td>
<td>1.40</td>
<td>&lt;0.001</td>
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<td>&lt;0.001</td>
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<tr>
<td>HIV positive</td>
<td>5.98</td>
<td>&lt;0.001</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Ever IDU</td>
<td>4.72</td>
<td>&lt;0.001</td>
<td>4.17</td>
<td>&lt;0.001</td>
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<tr>
<td>Receptive CLAI</td>
<td>3.37</td>
<td>&lt;0.001</td>
<td>3.12</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>multiple partners</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Syphilis</td>
<td>2.95</td>
<td>&lt;0.001</td>
<td>2.75</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CD4 per 100 cells</td>
<td></td>
<td></td>
<td>0.93</td>
<td>0.002</td>
</tr>
<tr>
<td>(in &lt;500 cells)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
In HIV-positive GBM, significant risk of ‘permucosal’ HCV transmission during sexual exposure.

Discuss higher risk behaviours that may lead to HCV transmission.

*Behavioural risk reduction?*

Annual screening (ALT + HCV RNA) recommended; additional testing if potential exposure.
HIV-positive GBM who inject drugs at significantly higher risk of HCV.

Different drug use and sexual behaviours compared with non-GBM PWID populations.
HCV prevalence among GBM who inject drugs

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample size (N)</th>
<th>Prevalence (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-positive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rauah et al (2005)</td>
<td>67</td>
<td>34.33 (23.15, 46.94)</td>
</tr>
<tr>
<td>Kim et al (2008)</td>
<td>89</td>
<td>69.66 (59.01, 79.97)</td>
</tr>
<tr>
<td>Myers et al (2009)</td>
<td>51</td>
<td>23.53 (12.79, 37.49)</td>
</tr>
<tr>
<td>Jin et al (2010)</td>
<td>68</td>
<td>73.53 (44.09, 53.88)</td>
</tr>
<tr>
<td>Raymond et al (2011)</td>
<td>56</td>
<td>25.00 (14.39, 38.37)</td>
</tr>
<tr>
<td>Marangio et al (2012)</td>
<td>10</td>
<td>20.00 (2.52, 55.61)</td>
</tr>
<tr>
<td>Kenyos et al (2014)</td>
<td>162</td>
<td>27.16 (20.48, 34.70)</td>
</tr>
<tr>
<td>Marcellin et al (2014)</td>
<td>59</td>
<td>52.54 (39.12, 65.70)</td>
</tr>
<tr>
<td>Senberg et al (2014)</td>
<td>410</td>
<td>44.15 (39.28, 49.10)</td>
</tr>
<tr>
<td>Urbanus et al (2014)</td>
<td>20</td>
<td>45.00 (23.06, 68.47)</td>
</tr>
<tr>
<td>Subtotal</td>
<td></td>
<td>33.74 (26.92, 35.07)</td>
</tr>
</tbody>
</table>

| HIV-negative      |                 |                     |
| Jin et al (2010)  | 150             | 8.67 (6.70, 10.36)  |
| Marangio et al (2012) | 307        | 43.00 (37.39, 48.74)|
| Senberg et al (2014)| 242            | 40.91 (34.63, 47.39)|
| Subtotal          |                 | 23.52 (18.86, 28.18)|
| Overall           |                 | 31.54 (22.79, 40.30)|

Pooled prevalence HIV +ve GBM + IDU 36% (95% CI 26, 45)
Pooled prevalence HIV -ve GBM + IDU 24% (95% CI 8, 39)
IDU and sexual risk co-exist

Clusters: E1/HVR1 phylogenetic analysis in Australian Trial in Acute Hepatitis C (ATAHC)
Are HIV-negative GBM at greater risk of HCV in the era of HIV PrEP?
Are HIV-negative GBM at greater risk of HCV in the era of HIV PrEP?

AMPrEP: Amsterdam PrEP cohort
N=375; HCV RNA positive, n=15 (4%)

HCV-positive:
- Younger age
- History of STI
- IDU
- rCLAI + multiple partners
- Chemsex

GBM-specific HCV clusters
HIV-positive
HIV-negative
Are HIV-negative GBM at greater risk of HCV in the era of HIV PrEP?

Acute HCV 2014 - 2016
Lyon, France
In HIV-negative GBM without a history of IDU, sexual transmission of HCV remains uncommon. Routine screening is not warranted.

Individualised risk assessment (particularly in relation to HIV serostatus of partners) is suggested.

Screening HIV-negative GBM prior to initiation of HIV pre-exposure prophylaxis (PrEP) should be considered.
HCV elimination among GBM
UN/WHO, May 2016:

Elimination of viral hepatitis as a public health threat by 2030.

• HCV incidence: ↓ 80%
• HCV-related mortality: ↓ 65%
• HCV diagnosis: ↑ 90%
• HCV treatment uptake: ↑ 80%
Targeted DAA scale-up among populations at high risk of transmission, including HIV-positive GBM, could reduce HCV incidence and prevalence.
Modelling: HCV TasP among GBM
Treatment of recent HCV reduces incidence

Martin NK Clin Inf Dis 2016
Modelling: HCV elimination among GBM
The importance of behavioural risk reduction

Increasing HCV incidence + high DAA uptake

Decreasing HCV incidence + lower DAA uptake
Universal access to DAA therapy paves the way for HCV elimination among people with HIV in Australia

- Past HCV infection (HCV RNA negative)
- Current HCV infection, no treatment initiated
- Current HCV infection, treatment initiated

- 2014: 7%
- 2015: 10%
- 2016: 76%
- 2017: 22%

HCV treatment uptake
Universal access to DAA therapy paves the way for HCV elimination among people with HIV in Australia

Impact of DAA scale-up on HCV infection burden

HIV/HCV Ab positive population

Propotion with detectable HCV RNA

0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

2014 2015 2016 2017 2018

82% 80% 77% 27% 18%

HCV RNA positive HCV RNA negative
Declining HCV incidence among HIV-positive GBM in the Netherlands

2014: 93 acute HCV
8290 PYFU
Incidence, 11.2/1000 PY; 95%CI, 9.1–13.7

2016: 49 acute HCV
8961 PYFU
Incidence, 5.5/1000 PY; 95%CI 4.1–7.2
Will HCV reinfection among GBM challenge elimination efforts?
Reinfection: meta-analysis

- **Low risk**: 1%
  - 43 studies
  - n=7,969
  - Avg. FU=3.9 years

- **PWID / prisoner**: 10%
  - 14 studies
  - n=771
  - Avg. FU=2.8 years

- **HIV co-infected**: 15%
  - 4 studies
  - n=309
  - Avg. FU=3.3 years
HCV reinfection after treatment among GBM

• Hagan H et al *AIDS* 2015
  • Meta-analysis
  • HIV-positive GBM who denied IDU
  • Reinfection incidence: 11.4 per 100 py (95%CI 7.4, 17.7)
    • Note, only two retrospective acute HCV cohorts

• Ingiliz P et al *J Hepatol* 2016
  • HIV-positive GBM in western Europe (n = 552)
  • 143 reinfections, 1952 PYFU
  • Reinfection incidence: 7.3 per 100 py (95%CI 6.2, 8.6)
  • Multiple reinfections in some individuals (second reinfection, n = 69; third reinfection, n = 13)
Higher reinfection incidence among people with ongoing high risk drug and sexual behaviour
Risk behaviour and follow-up

Canadian HIV/HCV Cohort (74% PWID)
Combined OST/NSP to prevent primary HCV infection

### High NSP coverage
- Hope, 2011: 0.17 (0.02, 1.54)
- Bruneau, 2015: 0.63 (0.37, 1.07)
- Van Den Berg, 2007: 0.15 (0.06, 0.40)
- Palmateer, 2014: 0.24 (0.10, 0.59)
- Subtotal (I-squared = 64.4%, p = 0.038): **0.29 (0.13, 0.65)**

### Low NSP coverage
- Hope, 2011: 1.08 (0.31, 3.82)
- Van Den Berg, 2007: 1.04 (0.53, 2.05)
- Palmateer, 2014: 0.48 (0.24, 0.95)
- Subtotal (I-squared = 29.6%, p = 0.242): **0.76 (0.44, 1.33)**
- Overall (I-squared = 62.2%, p = 0.014): **0.47 (0.27, 0.80)**

**Note:** Weights are from random effects analysis.
Rapid DAA scale-up is required to limit reinfection
Strategies to reduce HCV (re)infection

- Harm reduction
  - NSP, OST
- Integrated care
  - Mental health assessment
- Education
  - Counselling, peer support
- Post-treatment surveillance
  - Regular HCV RNA testing
- Retreatment of reinfection

Sexual risk behaviour?
Acknowledgements

Kirby Institute, UNSW Sydney:

- A/Prof Gail Matthews
- Prof Greg Dore
- A/Prof Jason Grebely
- Dr Behzad Hajarizadeh
- Dr Tanya Applegate
- Ms Lanni Lin
- Dr Jasmine Skurowski
- Ms Ecaterina Filep
- Ms Pip Marks
ELIMINATION IS THE GOAL

AUSTRALIA - HEP C FREE

Reg M 1
Additional slides
## Enrolment characteristics

<table>
<thead>
<tr>
<th>characteristic</th>
<th>N=402</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>49 (10)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>382 (95)</td>
</tr>
<tr>
<td>Gay and bisexual men, n (%)</td>
<td>322 (80)</td>
</tr>
<tr>
<td>White, n (%)</td>
<td>344 (86)</td>
</tr>
<tr>
<td>Injecting drug use</td>
<td></td>
</tr>
<tr>
<td>Ever</td>
<td>316 (79)</td>
</tr>
<tr>
<td>Current (within 6 months)</td>
<td>146 (36)</td>
</tr>
<tr>
<td>CD4 count (10^6/L), median (IQR)</td>
<td>595 (430,810)</td>
</tr>
<tr>
<td>HIV VL &lt;20 copies/mL, n (%)</td>
<td>286 (69)</td>
</tr>
<tr>
<td>cART, n (%)</td>
<td>386 (94)</td>
</tr>
<tr>
<td>HCV RNA positive, n (%)</td>
<td>290 (72)</td>
</tr>
<tr>
<td>Cirrhosis, n (%)</td>
<td>51 (13)</td>
</tr>
</tbody>
</table>