Communicating risk with serodiscordant couples

CATIE

New Science New Directions in HIV & HCV

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maple leaf medical clinic

WCHH WOMEN'S COLLEGE HOSPITAL Health care for women | REVOLUTIONIZED

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Overview

This presentation will:

1. Review important items to consider when counseling on HIV transmission risk
2. Use case studies to analyze risk & develop strategies for discordant couples
3. Describe the evidence and gaps of the recommendations

Simple format – 1. 2. 3.

- Items to consider for counseling on unprotected intercourse between serodiscordant couples:

1. Purpose: a. Reproduction versus b. Pleasure
   - i.e. number of exposures
2. Heterosexual vs. same-sex male or female couple
   - i.e. vaginal vs. anal vs. oral vs. other exposure
3. HIV-positive partner taking ART with fully suppressed Viral Load (VL)?
   - ART being used? For how long? VL suppressed? For how long?

Complicated items - counseling

- Single partner or both together?
- How long have the partners been together?
- Status of relationship?
- First language?
- Prior knowledge of the issues at hand? – studies to date, criminalization issues
- Knowledge of HIV?

- …. Other issues?

Case #1

- 35 year old HIV-positive woman
- In new heterosexual relationship for 2 months
- Has disclosed all information to new partner:
  - HIV status, being on ART, suppressed VL, meaning/studies to date

- In my office together because new partner wants to know risk of HIV transmission if they have unprotected sex as he feels the risk is not that high

Case #2

- 38 year old HIV-positive man with 40 year old HIV-negative common-law wife
- Looking to get pregnant and have child
  - Wants to get pregnant in next 6 months

- Asking about options for conception to prevent horizontal HIV transmission

Case #3

- 48 year old HIV-positive man recently married to 49 year old HIV-negative man
- HIV-positive partner on ART, fully suppressed VL for 3 years

- In my office for a change of treatment, blood work; and asks by the way - want to know risk of HIV transmission if they have unprotected sex

Case #1

- 35 year old HIV-positive woman in new heterosexual relationship
  1. Purpose: Pleasure -> potential high no. of exposures
  2. Type of exposure: vaginal, anal, and oral
  3. HIV-positive partner is taking ART with fully suppressed VL for 2 years

- Review items to consider for risk
- HPTN 052 results
- My team's Systematic Review results
- International guidelines on the topic

Take approx. 40-60 min.

HPTN 052 Study

Randomized Control Trial

- Compare early (immediate) versus delayed (CD4 < 250) ART for HIV-1 positive patients having 350-550 CD4 and in stable sexual relationship with uninfected partner
  - o Outcome: transmission to uninfected partner (linked)
- 893 couples in Early Therapy Arm; 882 couples in Delayed Therapy Arm
- 28 HIV-transmissions were linked: 27 in Delayed Arm; 1 in Early Arm (occurred at 3 months post-ARVs) (0.1 per 100 person-years) [HR 0.04 (CI 0.01-0.27); p<0.001] = 96% reduction of HIV transmission with ART

Our Systematic Review of Cohort Studies (5) + Controlled Trial (1)

Author (Date)	Study Location	# of Participants	HIV Transmission while on CART
Melo (2008)	Brazil	93	0
Del Romero (2010)	Spain	648	0
Reynolds (2011)	Uganda	250	0
Donnell (2010)	Botswana, Kenya, Rwanda, S. Africa, Tanzania, Uganda, Zambia	3381 analyzed out of 3408 total	1
Apondi (2011)	Uganda	62	1
Cohen (2011)	Botswana, Kenya, Malawi, S. Africa, Zimbabwe, Brazil, India, Thailand, USA	1763 analyzed out of 1775	2

4 Unconfirmed VL Transmissions

Donnell et al. (2010)

•1 case of transmission out of 3381: HIV + woman with steadily declining CD4 counts transmitted the virus to HIV- male partner (confirmed through genetic testing)

•HIV + F was put on antiretroviral therapy 18 days before the 9 month mark of the study

•M tested negative at 9 month mark; however at the 12-month visit, he tested positive for HIV-1

Apondi et al. (2010)

•1 case of transmission out of 62, HIV + woman transmitted to HIV negative male partner (confirmed through genetic testing)

•Seroconversion occurred in the first year but VL not reported at 12 months in this study, only at 36 months

Cohen study et al. (2012)

•Mastro et al.(2011) HIV-1 transmission case occurred within 3 months of partner starting ART

•Eshleman et al. (2011) 1 case of transmission on ART in delayed therapy group; 4 weeks after the start of ART

CONCLUSION

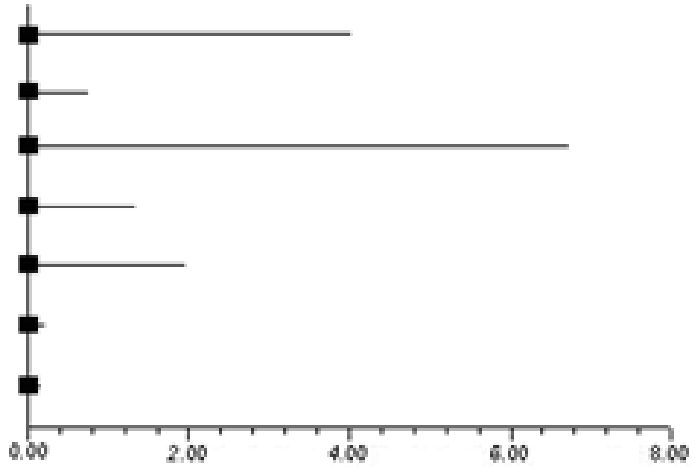
4 transmissions all occurred within 6 months of starting ART; VL likely not suppressed.

These transmissions should be removed via sensitivity analysis

1. Donnell et al. Lancet 2010; 375:2092-2098.
2. Apondi et al. AIDS 2010; 25(10):1317-27.
3. Mastro et al. AIDS 2011; 25: 2049–2051
4. Eshleman et al. J Infect Dis 2011; 1918-1926

Figure 2b. Forest plot of HIV transmission rates per 100 person-years, excluding unconfirmed viral loads

Study name	Event / person years	Rate	Lower limit	Upper limit
Melo 2008	0 / 90	0.00	0.00	4.02
Del Romero 2010	0 / 492	0.00	0.00	0.75
Reynolds 2011	0 / 53	0.00	0.00	6.72
Donnell 2010	0 / 273	0.00	0.00	1.34
Apondi 2011	0 / 185	0.00	0.00	1.97
Cohen 2011	0 / 1755	0.00	0.00	0.21
Total		0.00	0.00	0.01



The transmission rate excluding the 4 transmissions when VL was not confirmed = 0 per 100-person years (95% CI: 0-0.1) – interested in higher 95% CI

1 in 1000 lifetime risk of HIV transmission for each 10 years of a relationship

Case #2

- Serodiscordant couple (HIV-positive male partner) looking to get pregnant and have child
  1. Purpose: Reproduction -> limited no. of exposures
  2. Type of exposure: vaginal
  3. HIV-positive partner is taking ART with fully suppressed VL for 3 years

- Review CHPPG
- Review conception options & risk, cost & success of each

Take approx. 30-45 min.

SOGC CLINICAL PRACTICE GUIDELINE

No. 278, June 2012

Canadian HIV Pregnancy Planning Guidelines

These guidelines have been written and reviewed by the Canadian HIV Pregnancy Planning Guideline Development Team in partnership with the Society of Obstetricians and Gynaecologists of Canada, the Canadian Fertility and Andrology Society and the Canadian HIV/AIDS Trials Network. They were reviewed by the Infectious Diseases Committee and the Reproductive Endocrinology and Infertility Committee of the Society of Obstetricians and Gynaecologists of Canada and by the Canadian HIV Pregnancy Planning Guideline Development Team Core Working Group,* and endorsed by the Executive and Council of the SOGC.

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Disclosure statements have been received from all authors.

Abstract

Objective: Four main clinical issues need to be considered for HIV-positive individuals and couples with respect to pregnancy planning and counselling: (1) pre-conceptional health; (2) transmission from mother to infant, which has been significantly reduced by combined antiretroviral therapy; (3) transmission between partners during conception, which requires different prevention and treatment strategies depending on the status and needs of those involved; and (4) management of infertility issues. The objective of the Canadian HIV Pregnancy Planning Guidelines is to provide clinical information and recommendations for health care providers to assist HIV-positive individuals and couples with their fertility and pregnancy planning decisions. These guidelines are evidence- and community-based and flexible, and they take into account diverse and intersecting local/population needs and the social determinants of health.

Outcomes: Intended outcomes are (1) reduction of risk of vertical transmission and horizontal transmission of HIV, (2) improvement of maternal and infant health outcomes in the presence of HIV, (3) reduction of the stigma associated with pregnancy and HIV, and (4) increased access to pregnancy planning and fertility services.

Evidence: PubMed and Medline were searched for articles published in English or French to December 20, 2010, using the following terms: "HIV" and "pregnancy" or "pregnancy planning" or "fertility" or "reproduction" or "infertility" or "parenthood" or "insemination" or "artificial insemination" or "sperm washing" or "IVF" or "ICSI" or "IUI." Other search terms included "HIV" and "horizontal transmission" or "sexual transmission" or "serodiscordant." The following conference databases were also searched: Conference on Retroviruses and Opportunistic Infections, International AIDS Conference, International AIDS Society, Interscience Conference on Antimicrobial Agents and Chemotherapy, the Canadian Association of HIV/AIDS Research, and the Ontario HIV Treatment Network Research Conference. Finally, a hand search of key journals and conferences was performed, and references of retrieved articles were reviewed for additional citations. Subsequently, abstracts were categorized according to their primary topic (based on an outline of the guidelines) into table format with the following headings: author, title, study purpose, participants, results and general comments. Finally, experts in the field were consulted for their opinions as to whether any articles were missed.

Values: The quality of evidence was rated using the criteria described in the Report of the Canadian Task Force on Preventive Health Care. Recommendations for practice were ranked according to the method described in that report (Table) and through use of the Appraisal of Guidelines Research and Evaluation instrument for the development of clinical guidelines.

Sponsors: The Society of Obstetricians and Gynaecologists of Canada, Women and HIV Research Program, Women's College Research Institute, Women's College Hospital, University of Toronto, Abbott Laboratories Canada, the Ontario HIV Treatment Network, the Canadian Institutes of Health Research, and the Canadian HIV Trials Network.

Key Points and Recommendations

HIV-positive people who are considering pregnancy should be counselled on the following issues so they can make an informed decision.

Key Words: HIV, pregnancy, insemination, fertility, transmission

J Obstet Gynaecol Can 2012;34(6):575–590

Items for counseling from CHPPG

Case Issues	CHPPG Guidance
1. Prevention of Vertical Transmission	▪No risk of transmission since female partner is HIV negative ▪If mother seroconverts in pregnancy→ high risk of transmission
2. Healthy Pre-Conception	▪Counsel on taking folic acid 3 months before pregnancy and during pregnancy
3. Fertility	▪If the individual or couple has infertility guidelines indicate treatment as usual (general population guidelines)
4. Prevention of Horizontal Transmission	▪Review all options & continuum of risk ▪Couple to make informed decision of best choice for them

2) HIV+ man and HIV- woman

Review all different options for insemination & continuum of risk including:

- Unprotected intercourse (on ART, full viral suppression)
- Unprotected intercourse with timed ovulation (on ART, full viral suppression)
- **Sperm washing with IUI (in fertility clinic)**
- Other: IVF, ICSI, sperm donor, adoption

Sperm washing with IUI: typically recommended by HCP due to lowest chance of horizontal transmission; All options after full understanding of risk

PrEP as an option …

PrEP to prevent horizontal transmission in serodiscordant couples in which the man is HIV+ and the woman is HIV-

- **No recommendation in CHPPG**
- **American Statement:**
  - "PrEP use may be one of several options to help protect the HIV-negative partner in discordant couples during attempts to conceive" (CDC, 2012)

One clinical study on topic: Vernazza *et al.* AIDS 2011, 25:2005–2008

In 2011, Vernazza *et al.* (Swiss group)

- HIV-positive males with female partners had VL < 50c/ml on ART and no report of STIs in either partner interested in conception
- PrEP involved 1 dose of tenofovir at LH peak and the morning afterward
- 46/53 couples agreed to use PrEP with unprotected timed intercourse
- Reported 244 documented unprotected events of vaginal intercourse in 53 couples who aimed to conceive
- 75% successful pregnancy rate (after an average of 6 cycles) (out of 53)
- None of the female partners had acquired HIV

Economic analysis

- An economic evaluation of unprotected intercourse with timed ovulation (UIRTO), sperm washing with IUI (SWIUI) and UIRTO-PrEP determined the most cost-effective strategy for male-positive, HIV-discordant couples from the perspective of the Ontario Ministry of Health and Long-term Care
- Cost data from OHIP, CReATE Fertility Centre and the health utilities (preferences) of HIV- women in relationship with HIV+ man were used to calculate the cost per quality-adjusted-life-year (QALY) based on a hypothetical population

- Under circumstances of negligible risk (i.e. Canada), UIRTO-PrEP yields the least costly QALY ($171.69 each), followed by SWIUI (~$4,200.00/QALY), then UIRTO (~$83,000.00/QALY)
- When HIV transmission risk is high, the cost-effective option is SWIUI at $4,101.89 per QALY

*Michelle Letchumanan's MSc in HSR Thesis

Case #3

- 48 year old HIV-positive man recently married to 49 year old HIV-negative man
  1. Purpose: Pleasure -> potential high no. of exposures
  2. Type of exposure: anal and oral
  3. HIV-positive partner is taking ART with fully suppressed VL for 3 years

- Review risk items, HPTN 052 results, our Systematic Review results
- International guidelines on the topic
- Available data for Gay men, heterosexual results are inferred

Take approx. 50-75 min.

Available Data for Gay Men

Swiss Statement

- January 2008, the Swiss National AIDS Commission deemed an HIV-positive individual as "sexually non-infectious" if (3) criteria fulfilled:
  - **(1) Adherence to ART with regular monitoring by physician**
  - **(2) Absence of STIs**
  - **(3) Undetectable plasma VL for 6 months or more**

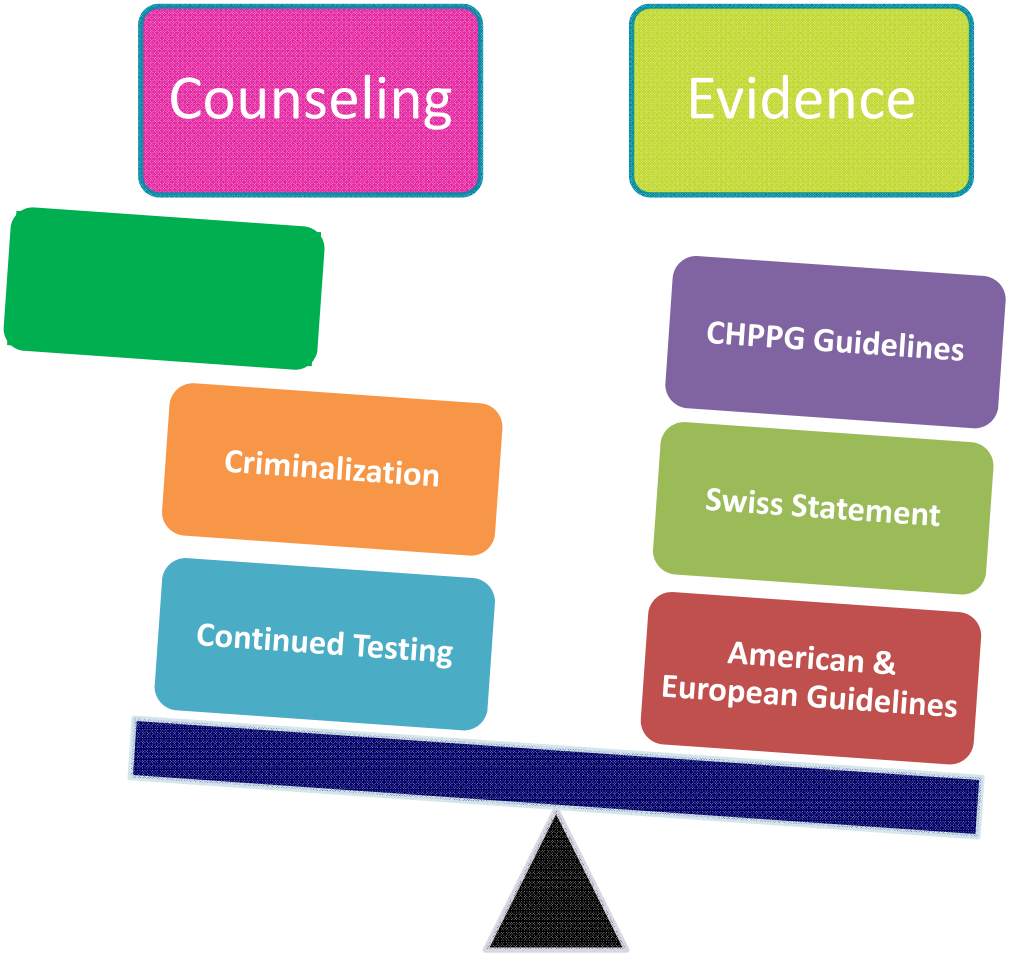
San Francisco Men's Health Study

- HIV-infection incidence per MSM couple 1994 -1996 was 0.12;
- ART has been available since 1996;
- 1996 -1999, HIV-incidence in MSM decreased to 0.048 (not all HIV-infected men were on therapy)

  - **Modeling studies showing reduced transmission**
  - **No equivalent study to HPTN 052, so results from heterosexual studies inferred to same-same couples**

1.Vernazza *et al.* Bulletin des médecins suisses 2008; 89:165-169.
2. UNAIDS/WHO (2008) Statement: Antiretroviral therapy and sexual transmission of HIV

For all cases



Recommendations:

1. Review issues related to criminalization

2. Counsel on HIV testing of the HIV-negative partner every 3 months and if there are symptoms of viral illness (in case of acute seroconversion)

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Thank you!

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