Women’s Health and Fertility
AWACC 28 September 2013
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What to consider

• Does HIV affect fertility success?
• Does HIV affect fertility desire?
• Avoiding un-intended pregnancies
• Does a desire for fertility affect ‘HIV risk’ behaviour?
• Managing conception among the HIV affected couple – a missing PMTCT prong
• Resource considerations
Fertility success

• Demographic Health Surveys conducted across 13 countries compared fertility rates among HIV infected and uninfected women
• Controlled for age, employment, education, behaviour
• Looked at number of births in the last year and last 5 years

Fertility success

<table>
<thead>
<tr>
<th></th>
<th>Number of births last year OLS (1)</th>
<th>Number of births last year OLS (2)</th>
<th>Number of births last year OLS (3)</th>
<th>Number of births last 5 years OLS (4)</th>
<th>Number of births last 5 years OLS (5)</th>
<th>Number of births last 5 years OLS (6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive HIV status</td>
<td>-0.043* (0.007)</td>
<td>-0.042* (0.007)</td>
<td>-0.032* (0.007)</td>
<td>-0.177* (0.015)</td>
<td>-0.176* (0.015)</td>
<td>-0.145* (0.014)</td>
</tr>
<tr>
<td>N</td>
<td>64,056</td>
<td>64,056</td>
<td>64,056</td>
<td>64,056</td>
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<td>64,056</td>
</tr>
<tr>
<td>Mean HIV-Positive</td>
<td>0.127</td>
<td>0.127</td>
<td>0.127</td>
<td>0.616</td>
<td>0.616</td>
<td>0.616</td>
</tr>
<tr>
<td>Mean HIV-Negative</td>
<td>0.167</td>
<td>0.167</td>
<td>0.167</td>
<td>0.722</td>
<td>0.722</td>
<td>0.722</td>
</tr>
</tbody>
</table>
• Found that HIV disease significantly lowers an infected woman’s fertility.
• Being infected with HIV reduces ‘births last year’ by 20–25 %, depending on whether we control for marital status.
• Impact is small
• For example, in Lesotho, with an HIV prevalence of 26.4%, the total fertility rate would be 0.15–0.3 (4-8%) children higher in the absence of HIV.
Reasons for reduced fertility

• Women who are infected may be widowed, separated, or divorced, (associated lower birth rates).
• Lower fecundity or the individual may be too sick to be sexually active.
• Higher rates of miscarriage and stillbirth
• Co-infection with other sexually transmitted infections with resultant tubal disease
• Menstrual dysfunctions
• Weight loss leading to amenorrhoea

Zaba and Gregson 1998; Fabiani et al. 2006
Taulo F et al 2009 AIDS Behv
Fertility intentions
Fertility intentions
The Fertility Intentions & Incidence Study

• Among 850 HIV+ women (18 – 35 years) on ART in Johannesburg

• Conducted in 4 PEPFAR supported ART sites in inner city Johannesburg, September 2009 – March 2011

• 18-month clinical cohort study investigating
  – Fertility intentions amongst 850 women on ART
  – Contraceptive use, method preference and barriers
  – Incidence of planned and unplanned pregnancies
  – Hormonal contraceptive failures
  – Issues related to ART regimens and pregnancy

Schwartz, S et al AIDS Behav 2011
Fertility intentions

At baseline

– 12% of the women were actively trying to conceive
– 36% had intentions to conceive within the next 12 months.
– 75% indicated that they had plans of conceiving at some point in the future
– partner cohabitation/marital status and number of children with current partner are strong predictors of current fertility intentions

Schwartz, S et al AIDS Behav 2011
Results: Contraceptive Use amongst those not trying to conceive (n=748)

HC: 32%
Consistent Condoms: 54%
Dual Use: 15%
Unmet Need: 29%

Schwartz, S et al AIDS Behav 2011
Patient-provider communication

“What is it, boy? Want to go outside?”
Enrolment and follow up

907 Consented for enrollment

57 Were not enrolled
- 38 Tested pregnant at time of consent
- 14 ≥36 years
- 4 Not receiving regular care at study site
- 1 Sterilized

850 Enrolled for follow-up

28 No follow-up visits

822 Had ≥1 follow-up visit

670 No recorded pregnancies
- 6 confirmed deaths
- 1 sterilization

161 Incident pregnancies
- 170 Total pregnancies
- 7 women with two pregnancies
- 1 woman with three pregnancies
Incidence of pregnancy in a cohort of South African women August 2009 – March 2011

<table>
<thead>
<tr>
<th>Pregnancy</th>
<th>Time at Risk</th>
<th>Number of women who conceived</th>
<th>Incidence Rate / 100 PY (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unplanned</td>
<td>602.1</td>
<td>97 (60%)</td>
<td>16.1 (13.2-19.7)</td>
</tr>
<tr>
<td>Planned</td>
<td>143.2</td>
<td>64 (40%)</td>
<td>44.7 (35.0-57.1)</td>
</tr>
<tr>
<td>Total</td>
<td>745.2</td>
<td>161</td>
<td>21.6 (18.5-25.2)</td>
</tr>
</tbody>
</table>
Incidence of unplanned pregnancy according to baseline need for contraception

Cumulative Incidence

log-rank p < 0.0001

Unmet need

Met need

Months since enrollment

Number at risk

Baseline met need 519
Baseline unmet need 181

421
123
371
113
40
10
Incidence of unplanned pregnancy according to time-varying contraceptive use

Cumulative Incidence

- No reliable method
- Condoms only
- HC & HC+condoms

log-rank p<0.0001

Number at risk
- No reliable method 76
- Condoms alone 416
- HC & HC+condoms 208

Months since enrollment
Outcomes

• 170 pregnancies among 161 women
• 105 (62%) of pregnancies were unplanned, of these 38 women elected a termination of pregnancy, 19 had a spontaneous abortion and there was 1 still birth
• 8 pregnancies occurred while participants were on hormonal contraception (4.3/100py vs 0.3/100py)
Special Group: Perinatally Infected Women/Youth

- UK Ireland cohort of 252 women >12 year
- 42 pregnancies among 30 women
- Median age 18 (14-22 years)
- 81% unplanned
- >50% of partners unaware of HIV status
- 36% elected termination of pregnancy
- 33% had detectable VL
- 1/21 infants infected with HIV

Poor uptake of contraception

• Studies of unintended pregnancies in HIV infected women in sSA
  – 84% among PMTCT clients in South Africa
  – 51% among women in Cote d’Ivoire
  – 99% among women in an ART program in Uganda
  – 62% among women on ART in South Africa

• Newly HIV-diagnosed women in Malawi have 46% contraceptive use at 12 months post-diagnosis.

Rochat et al; JAMA 2006
Desgrées-du-Loû et al., Int J STD AIDS 2002
Smart, T. Aidsmap. 2006.
Schwarts, S et, al, al AIDS behav 2011
Perceptions of Contraception

• When choosing contraception women consider side effects, convenience and protection against STIs.
• Condoms often preferred - lack of side effects and protection against STIs.
• Drawbacks to condoms - fear of breakage and need of male participation.
• The pill not liked because of burden of having to remember to take it daily
• Injectable liked for convenience and their secrecy.
• Other methods of contraception (e.g., tubal ligation, the loop) were largely unknown
Discontinuation of Contraception

Qualitative research of HIV infected women identified reasons for discontinuation and included:

- Need for follow-up (the pill)
- Side effects
- Changing physical appearance
- Concern about amenorrhea and vaginal wetness
- Interaction with ART
- Fertility desire

Laher F et al AIDS Behav 2009
Todd CS et al AIDS Behav 2011
WHO Hormonal Contraception and HIV

- Women at high risk of HIV can continue to use all existing hormonal contraceptive methods without restriction.
- Women living with HIV can continue to use all existing hormonal contraceptive methods without restriction.
- Consistent and correct use of condoms, male or female, is critical for prevention of HIV transmission.
- Voluntary use of contraception by HIV-positive women is an important strategy for PMTCT.

WHO Technical Statement. 2012
Communication: family planning and contraception provision

• Above highlights the need for improved HCW and patient communication

• Integration of contraceptive service provision within ART clinics

• FP integration should address providers’ concerns over condom substitution and patient perceptions
Do you want to conceive?

Bill Frymire
Different approaches to HIV infected couples

HIV Infected woman → HIV Uninfected man

HIV Uninfected woman ← HIV Infected man

HIV Infected woman ← HIV Infected man

Remember: adherence is the responsibility of the infected partner and the risk is to the uninfected partner.
Pre-conception counselling

• Disclosure of status
• Reproductive options: including risks, risk reduction, costs and chances of success
• Balance the risk of natural conception with established risk-reduction methods
• Consequences of failure to prevent transmission to partner and child and importance of regular testing
Reduce risk of HIV sexual transmission at an individual level

• Risk per event is low, but not eliminated

• Reduce risk of HIV transmission at an individual level:
  – Viral load
  – Mucosal integrity
  – Frequency of exposure

• Reduce risk of HIV acquisition
  – Post exposure prophylaxis
  – Mucosal integrity
  – Frequency of exposure
  – Circumcision
Minimum pre-conception medical assessment

• Exclude STI’s through syphilis serology and clinical assessment
• Clinically and immunologically should not have AIDS: Medical exam and CD4 cell count
• Those on ART should have an undetectable VL
• Screen for infertility through history
• Pregnancy: RH, haemoglobin
Medical management

• Optimise medical condition
• Treat any current infection
• Treat co-morbid illnesses
• Prevent infections as appropriate
• Determine ovulatory cycle
Fertility and HIV

• The infected partner should ideally be on ART and have suppressed viral load
• Pre-exposure prophylaxis for the uninfected partner, not sure of additional benefit if VL suppressed.
Assisted reproduction

• Assisted techniques for discordant couples
  – IUI, IVF, ICSI
  – Sperm washing with VL check

• Most studies have looked at HIV - infected males, but a few have looked at infected women

• Expensive and not routinely available

• Lowest risk of horizontal transmission

Chadwick RJ, Topics in Antiviral Med, 2011
Fertility and HIV

• Self insemination

• Sperm collection with self-insemination at the time of ovulation (avoiding spermicide-containing condoms)
  – Man ejaculates in clean receptacle
  – Semen drawn up into a large syringe (10 - 20ml)
  – Syringe placed about 4 – 6 cm in woman’s vagina in prone position and semen pushed out of the syringe
  – Can be done at home or in clinic.

• No studies published on self insemination
Natural Conception

- The couple practice safe sex for most of the woman’s cycle using condoms.
- Use ovulatory method and have sex without condom on alternate days during ovulation.
- Increasingly being accepted for concordantly infected couples, starting to be accepted for discordant couples.
- Limited research of natural conception among discordant couples.
- Big concern that safe sex messaging will be compromised.

Natural Conception

• Extrapolation from studies of HIV discordant couples in stable relationships

• A meta-analysis of 11 cohorts with 5021 couples, there was no horizontal transmission if infected partner was on ART and VL <400

• In Spain, 393 couples followed for 12 years there was not transmission among those on ART

Attia S et al. AIDS, 2009
Sastilla J et al. IJAIDS, 2005
Natural Conception

• In Uganda, 174 discordant couples followed for 4 years linked transmission to VL

<table>
<thead>
<tr>
<th>Transmission/coital act</th>
<th>VL copies/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0001</td>
<td>&lt;1 700</td>
</tr>
<tr>
<td>0.0023</td>
<td>~ 38 500</td>
</tr>
<tr>
<td>0.041</td>
<td>With herpes</td>
</tr>
</tbody>
</table>

• HPTN 052 96% risk of 0.37/100 person years
Natural Conception

• Among 3 studies of natural conception among discordant couples (variable ART use)
• 168 couples – 3 horizontal and 1 vertical infection.
• All horizontal transmissions occurred in pregnancy (months after conception)

Criteria for natural conception

- HIV positive partner on ART for 6 months or longer
- Viral load undetectable on PCR (< 50 copies/ml)
- Perfect adherence to treatment and regular medical follow-up
- Mutually faithful relationship
- No concomitant sexually transmitted infections
- Limited to 6 months during ovulation period only
- Condoms should be used at all other times

Barreiro, Human Reproduction 2007
Unsuccessful

• After attempting 6 ovulation cycles and the couple are unsuccessful in conceiving, consider reduced fertility and risk of continuing naturally may be more harmful than successful
• Council and if appropriate refer for further work-up
• Repeat HIV testing of exposed partner
Successful
• Repeated HIV antibody testing for exposed partners

• If woman seroconverts during pregnancy, provide ART as soon as possible as seroconversion is associated with high rates of mother-to-child transmission

• Test infant at birth and 6 weeks if positive start ART
Important to protect partner after conception

Increased Risk of HIV-1 transmission in pregnancy: Prospective study among Africa serodiscordant couples

- HIV viral load in genital secretions during pregnancy is increased
- Increased risk of transmission of HIV from a pregnant woman to her sexual partner

Mulago NR et al, AIDS 2011
PMTCT

- If woman HIV infected, ideally she was on ART prior to conception. She should continue ART throughout pregnancy.

- If the woman was not on ART, provide ART if feasible (guideline limitations in some settings), else provide PMTCT as per local guidelines.
Thank you