HIV and Contraception, Preconception and Reproductive Health

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Statewide Clinical HIV Update
June 17, 2016
Disclosure

- No relevant financial disclosures
Objectives

- Review options for ART for reproductive capable HIV infected women.
- Describe contraceptive options for women living with HIV.
- Explain specific consideration related to hormonal contraception and antiretroviral treatment
- Discuss reproductive strategies for HIV-infected individuals including pre-exposure prophylaxis (PrEP).
- Discuss issues with postpartum retention in HIV care.
Case 1- Sheila

- 27 yo female newly diagnosed with HIV after testing at STD clinic
- CD4 586, PVL 21,000 copies/mL
- No children, active with one sexual partner, occasional condom use.
Do you discuss pregnancy plans with HIV(+) women in your care?

1. At intake only
2. Once a year
3. Only if patient initiates
4. At every visit
5. Never
Do you discuss pregnancy plans with HIV(+) men in your care?

1. At intake only
2. Once a year
3. At every visit
4. Only if patient initiates
5. Never
# Introduction

Recommendations in these guidelines are based on scientific evidence and expert opinion and are rated using the system below:

<table>
<thead>
<tr>
<th>Strength of Recommendation</th>
<th>Quality of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A: Strong</strong></td>
<td>I: One or more randomized trials with clinical outcomes and/or validated laboratory end points</td>
</tr>
<tr>
<td><strong>B: Moderate</strong></td>
<td>II: One or more well-designed, nonrandomized trials or observational studies with long-term clinical outcomes</td>
</tr>
<tr>
<td><strong>C: Optional</strong></td>
<td>III: Expert opinion</td>
</tr>
</tbody>
</table>
Science: There is evidence that individual components of preconception care work:

- Rubella vaccination
- HIV/AIDS screening
- Management and control of:
  - Diabetes
  - Hypothyroidism
  - PKU
  - Obesity
- Folic acid supplements
- Avoiding teratogens:
  - Smoking
  - Alcohol
  - Oral anticoagulants
  - Accutane
Preconception Counseling and Care

**Purpose:**

- Prevention of unintended pregnancies.
- Optimization of maternal health prior to pregnancy.
- Prevention of perinatal transmission.
- Prevention of HIV transmission to an uninfected partner while trying to conceive.
ART for HIV-infected women of childbearing age

- A regimen’s effectiveness.
- A woman’s hepatitis B status.
- Teratogenic potential of the drugs in the cART regimen. (Efavirenz* -pregnancy testing)
- Possible adverse outcomes for the mother and fetus.
Case 2—Roberta

- 30 year-old woman tested HIV+ positive during her recent pregnancy and started HIV treatment with Complera (tdf/ftc/rilpivirine)
- CD4 (T-cells) have improved on treatment and her viral load is undetectable
- Infant is 4 months old and HIV-uninfected

Plan:
- Renew medications today, check labs before she returns for a check up in 3 months.
- Encourage adherence
- Remind to use condoms
Case 2—Roberta...

☐ You ask about contraception.

☐ She previously used oral contraceptives and asks about restarting them.

☐ How do you counsel her?
Preconception Counseling and Care

Recommendations

- Discuss childbearing intentions with all women of childbearing age on an ongoing basis throughout the course of their care (AIII).

- Provide information about effective and appropriate contraceptive methods to reduce the likelihood of unintended pregnancy (AI).
HIV infection does not preclude the use of any contraceptive method (AII). However, drug-drug interactions between hormonal contraceptives and cART should be taken into account.

- Interactions between some ARVs and hormonal contraceptives may lower contraceptive efficacy.
Condoms

- The one method that protects against STDs and provides contraception
- How do your patients feel about using male condoms? Female condoms?
Condoms

- However, 15% failure rate in preventing pregnancy
- Many couples (even serodiscordant couples=one partner HIV+ and one partner HIV-) use condoms off and on, rather than always
- So, a second method is recommended
Hormonal Contraceptives

- Combined oral contraceptive pills (COCs)
- Progestin-only oral contraceptive pills (POPs)
- Injectables (Depo-Provera/DMPA)
- Implants (Norplant, Jadelle, Sinoplant, Implanon)
# Drug Interactions between ARVs and Hormonal Contraceptives (CIII)

## NNRTIs: See Guidelines Table 3

<table>
<thead>
<tr>
<th>ARV Drug</th>
<th>Recommendation for Combined Hormonal Methods and Progestin-Only Pills</th>
<th>Recommendation for DMPA</th>
<th>Recommendation for Etonogestrel Implants</th>
</tr>
</thead>
<tbody>
<tr>
<td>EFV</td>
<td>Use alternative or additional contraception</td>
<td>No additional contraceptive needed</td>
<td>Use alternative or additional contraception</td>
</tr>
<tr>
<td>ETR</td>
<td>No additional contraceptive needed</td>
<td>No additional contraceptive needed</td>
<td>No additional contraceptive needed</td>
</tr>
<tr>
<td>NVP</td>
<td>Consider alternative contraceptive, or barrier + oral hormonal methods</td>
<td>No additional contraceptive needed</td>
<td>Consider alternative contraceptive, or barrier + implant</td>
</tr>
<tr>
<td>RPV</td>
<td>No additional contraceptive needed</td>
<td>No additional contraceptive needed</td>
<td>No additional contraceptive needed</td>
</tr>
</tbody>
</table>
Drug Interactions between ARVs and Hormonal Contraceptives (CIII)

RTV-Boosted PIs: See Guidelines Table 3

<table>
<thead>
<tr>
<th>ARV Drug</th>
<th>Recommendation for Combined Hormonal Methods and Progestin-Only Pills</th>
<th>Recommendation for DMPA</th>
<th>Recommendation for Etonogestrel Implants</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATV/r</td>
<td>Use alternative or additional contraception</td>
<td>No additional contraceptive needed</td>
<td>Consider alternative contraceptive, or barrier + implant</td>
</tr>
<tr>
<td>DRV/r</td>
<td>Use alternative or additional contraception</td>
<td>No additional contraceptive needed</td>
<td>No additional contraceptive needed</td>
</tr>
<tr>
<td>FPV/r</td>
<td>Use alternative or additional contraception</td>
<td>No additional contraceptive needed</td>
<td>Consider alternative contraceptive, or barrier + implant</td>
</tr>
<tr>
<td>LPV/r</td>
<td>Use alternative or additional contraception</td>
<td>No additional contraceptive needed</td>
<td>Consider alternative contraceptive, or barrier + implant</td>
</tr>
</tbody>
</table>
Drug Interactions between ARVs and Hormonal Contraceptives (CIII)

**PIs without RTV:** See Guidelines Table 3

<table>
<thead>
<tr>
<th>ARV Drug</th>
<th>Recommendation for Combined Hormonal Methods and Progestin-Only Pills</th>
<th>Recommendation for DMPA</th>
<th>Recommendation for Etonogestrel Implants</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATV</td>
<td>No additional contraceptive needed • OC should contain ≤30 μg ethinyl estradiol (EE), or use alternative method • No data on OCs with &lt;25 μg EE or progestins other than norethindrone or norgestimate</td>
<td>No additional contraceptive needed</td>
<td>No additional contraceptive needed</td>
</tr>
<tr>
<td>FPV</td>
<td>Use alternative contraception (use with estradiol/norethindrone may cause virologic failure)</td>
<td>No additional contraceptive needed</td>
<td>Use alternative or additional contraception</td>
</tr>
</tbody>
</table>
Drug Interactions between ARVs and Hormonal Contraceptives (CIII) (6)

**Integrase Inhibitors:** See Guidelines Table 3

<table>
<thead>
<tr>
<th>ARV Drug</th>
<th>Recommendation for Combined Hormonal Methods and Progestin-Only Pills</th>
<th>Recommendation for DMPA</th>
<th>Recommendation for Etonogestrel Implants</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAL</td>
<td>No additional contraceptive needed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DTG</td>
<td>No additional contraceptive needed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EVG/COBI</td>
<td>No additional contraceptive needed</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**CCR5 Antagonist:** See Guidelines Table 3

<table>
<thead>
<tr>
<th>ARV Drug</th>
<th>Recommendation for Combined Hormonal Methods and Progestin-Only Pills</th>
<th>Recommendation for DMPA</th>
<th>Recommendation for Etonogestrel Implants</th>
</tr>
</thead>
<tbody>
<tr>
<td>MVC</td>
<td>No additional contraceptive needed</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Other hormonal options

- Patch (Ortho Evra), vaginal ring (Nuva Ring), and transdermal implant (Implanon)
  - Warnings are similar to OCPs regarding drug-drug interactions
  - However, in theory, they avoid the “first pass” effect of liver metabolism that may occur with oral agents and should not be subject to the same limitations as OCPs
Intrauterine devices (IUDs)

- No known drug interactions
- No increase in shedding of HIV
- 2 types
  - Copper (Paragard) works for 10 years, may be associated with heavier menses, periods regular
  - Levonorgestrel IUD (Mirena) works for 5 years, reduces menstrual blood loss (is FDA-approved as a treatment for menorrhagia), periods scant and not regular
Effectiveness of Contraception for HIV-Infected Women using Antiretroviral Therapy

Maria Pyra\textsuperscript{a,b}, Renee Heffron\textsuperscript{a,b}, Nelly R. Mugo\textsuperscript{b,d,e}, Kavita Nanda\textsuperscript{f}, Katherine K. Thomas\textsuperscript{a}, Connie Celum\textsuperscript{a,b,c}, Athena P. Kourtis\textsuperscript{g}, Jared M. Baeten\textsuperscript{a,b,c}

for the Partners in Prevention HSV/HIV Transmission Study and Partners PrEP Study Teams

\textsuperscript{a} Department of Epidemiology, \textsuperscript{b} Department of Global Health, \textsuperscript{c} Department of Medicine, University of Washington, Seattle, Washington, USA; \textsuperscript{d} Department of Obstetrics & Gynaecology, University of Nairobi, \textsuperscript{e} Sexual, Reproductive, Adolescent and Child Health Research Program, Kenya Medical Research Institute, Nairobi, Kenya; \textsuperscript{f} FHI 360, Integrated Health Sciences, Research Triangle Park, North Carolina, USA; \textsuperscript{g} Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia, USA
**Question:** Does effectiveness of hormonal contraception (implant, injectable, oral pill) differ by ART use?

**Sample:** 5,153 women (1,376 pregnancies) in serodiscordant couples from 3 prospective studies in Africa
- Partners in Prevention HSV/HIV Transmission Study
- Couples Observation Study
- Partners PrEP Study

**Characteristics:**
- Young (median age 29), healthy (51% CD4>500), and ART naïve at enrollment
- Median follow-up 1.8 years
- 24% became pregnant and 31% ever took ART

**Analysis:** Cox proportional hazard models with repeated outcomes (pregnancy)
- Tested interactions between ART use and contraceptive method
Results

For all three methods of hormonal contraception, there were no significant differences in the adjusted hazard ratios by ART use. However, when different estrogen pills were used, effectiveness rates were 57% for implants, 71% for injectables, and 14% for OC. Data on real-world hormonal contraception effectiveness are important in determining family planning guidelines for women with HIV.

Note: Arrows represent adjusted hazard ratios.
CONCEPTION
Fertility desires among HIV+ adults

1998
US HIV Cost & Services Utilization Survey
2,864 HIV+ in care:
29% wanted to have children

2007
Cross-sectional US data; HIV(+) women on HAART:
61% felt could bear children with appropriate medical care
What if both partners are HIV-positive?

- When a couple is not attempting conception, we recommend condoms to avoid superinfection and sharing of antiretroviral resistant virus.

- If pregnancy desired: Ovulation predictor kit, maintaining an undetectable viral load, and once monthly unprotected sex is a reasonable approach.
Reproductive Options for HIV-Concordant (both positive) and Serodiscordant Couples

- Expert consultation is recommended so that approaches can be tailored to specific needs (AIII).

- Partners should be screened and treated for genital tract infections before attempting to conceive (AII).

- The HIV-infected partner should attain maximum viral suppression before attempting conception (AIII).
Ovulation predictor kits

These replace the old basal body temperature charts
The Serodiscordant Couple
Serodiscordant Heterosexual Couples US 2006

- 1.2 million HIV-infected in US
- 240,000 heterosexuals of reproductive age
- >140,000 serodiscordant couples
- Estimated > 70,000 desire children
Case 3-- Elizabeth

- Julia is 31, HIV+, diagnosed 1 year ago after ending a relationship with an HIV-infected partner
- No history of HIV-related illness
- Not on HIV medications
- CD4 in the 600's
- VL is 8,000
- New partner is HIV-uninfected
- Seems anxious and upset

Plan:
- Discuss pros and cons of starting HIV treatment
- Recommend HIV testing for partner
- Reinforce the importance of using condoms.
- Refer to a support group
- Re-check her VL and CD4 in 3 months.
- Continue to evaluate for and discuss HIV treatment
Case 3—Elizabeth...

- You ask Elizabeth if she wants to have another child.
  - She says, “Yes.”
  - You ask, “When?”
  - She says, “Now.”

- How do you counsel her?
Preconception counseling

- If a woman is not on ARVs, consider starting them prior to attempting conception
- If a woman is on ARVs and is considering pregnancy
  - Substitute other ARVs for efavirenz (Sustiva) because of possible risk of neural tube defects (NTDs)
  - Recommend folate or prenatal vitamins preconceptionally to reduce chance of NTDs
Discordant couples with HIV-infected women, HIV- man:

- The safest conception option is artificial insemination, including the option of self-insemination with a partner’s sperm during the periovulatory period (AIII).
Serodiscordant couples

- If the woman is HIV+ and the man is HIV-, discuss the options of:
  - Ovulation predictor kits
  - Home insemination (“turkey baster method”)
When the time is right, the choices are:

- Home insemination with partner’s semen

  The “turkey baster” method
  
  * A needle-less syringe works fine
20% of couples seeking Assisted Reproduction Services reported engaging in unprotected intercourse to achieve pregnancy at some point in the past.

Barreiro et al AIDS Rev 2006
Periconception Prep

- Very few data to date on periconception PrEP; studies under way.
- Infected partner should be on ART with fully suppressed HIV viral load.
- **Once daily tenofovir/emtricitabine is currently FDA approved for PrEP; CDC recommends 1 month before and 1 month after conception attempted.**
- Couples should use condoms at all times except during periovulatory intercourse.
- No reported increase in congenital anomalies for children whose mothers were exposed to tenofovir or emtricitabine during first trimester.
Case 4—Davis

☐ 32 year old HIV-positive male diagnosed with HIV 3 years ago,

☐ On ARVs. CD4 882 and VL<20 (undetectable)

☐ Excited about plans to get married next month to a woman he’s been dating for a year

☐ Plan:
  ■ Refill medications
  ■ Counsel on use of condoms
  ■ Return in 6 months
Case 4—Davis

- You ask Davis whether his fiancee has been tested for HIV
  - He says, “Yes, and she is HIV-negative.”
- You ask whether they are thinking about having children
  - He tells you, “Yes, sooner rather than later.”

How do you counsel him?
If the infected male has an undetectable plasma viral load, timed unprotected intercourse in order to conceive does not pose a risk to the negative female partner

1. TRUE
2. FALSE
Discordance of Genital and Plasma HVL

- Well-documented evidence that HIV RNA can be detected in genital secretions despite undetectable plasma HVL
- Prospective study, 25 men starting HAART, despite undetectable HVL plasma, 48% had intermittent shedding, no STIs
- 5% of 145 men on HAART seeking ART services found to have detectable genital HIV despite negative plasma HVL x 6 months, no documented STIs

(Sheth et al AIDS 2009; Marcelin et al AIDS 2008)
Discordant couples with HIV-infected men, HIV- woman:

- The use of donor sperm from an HIV-uninfected male with artificial insemination is the safest option (AIII).
- When the use of donor sperm is unacceptable, the use of sperm preparation techniques coupled with either intrauterine insemination or in vitro fertilization should be considered (AII).
- Semen analysis is recommended for HIV-infected males before conception is attempted to prevent unnecessary exposure to infectious genital fluid when the likelihood of getting pregnant is low because of semen abnormalities (AIII).
Barriers to Assisted Reproduction Services

Accessibility

Prohibitive Advisories/Regulations

Cost Limitations
Nearly each state in the US has a fertility clinic that offers assisted reproduction services to HIV serodiscordant couples

1. TRUE
2. FALSE
Barriers to Assisted Reproduction Services

- **Accessibility**
  - 80% US Fertility Clinics NOT supporting services for HIV-affected couples (estimated 70,000 couples in US)
  - Per Perinatal HIV Hotline only 6 fertility clinics in US offering sperm wash-IUI
Barriers to Assisted Reproduction Services

Accessibility

Prohibitive Advisories/Regulations
• In 1990, CDC advised against sperm wash due to one isolated case of transmission when current standard sperm wash protocol not employed
• As of 2006 ASRM “endorses” sperm wash; reversing 1994 advisory against sperm wash
• As of 2014, DHHS Guidelines support use of sperm wash
• Some states still have prohibitive legislation; criminal penalties for using HIV-infected semen

Cost Limitations
Barriers to Assisted Reproduction Services

Accessibility

Prohibitive Advisories/Regulations

Cost Limitations
Reproductive Options Comparison

<table>
<thead>
<tr>
<th>Variable</th>
<th>IUI with SW</th>
<th>IVF with SW</th>
<th>ICSI with SW</th>
<th>Self-insemination</th>
<th>Intercourse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average number of cycles</td>
<td>2.8</td>
<td>1.4</td>
<td>0.6</td>
<td>5.5</td>
<td>5.5</td>
</tr>
<tr>
<td>Average cost/cycle</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without PrEP</td>
<td>$1,265</td>
<td>$12,513</td>
<td>$15,128</td>
<td>$30 (kit)</td>
<td>$0</td>
</tr>
<tr>
<td>With PrEP</td>
<td>$2,195</td>
<td>$13,443</td>
<td>$16,058</td>
<td>$960</td>
<td>$930</td>
</tr>
<tr>
<td>Average cost/live birth</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without PrEP</td>
<td>$12,635</td>
<td>$41,132</td>
<td>$46,256</td>
<td>$30</td>
<td>$0</td>
</tr>
<tr>
<td>With PrEP</td>
<td>$16,835</td>
<td>$42,062</td>
<td>$47,156</td>
<td>$5,145</td>
<td>$5,115</td>
</tr>
<tr>
<td>Pregnancy rate/procedure</td>
<td>19%</td>
<td>38.1%</td>
<td>23%</td>
<td>20%</td>
<td>20%</td>
</tr>
<tr>
<td>Risk of HIV transmission</td>
<td>0.1-0.5%</td>
<td>0-0.4%</td>
<td>0-0.09%</td>
<td>0.03-0.14%</td>
<td>0.03-0.14%</td>
</tr>
</tbody>
</table>
Preexposure prophylaxis and timed intercourse for HIV-discordant couples willing to conceive a child

Pietro L. Vernazza\textsuperscript{a}, Irma Graf\textsuperscript{b}, Ulrike Sonnenberg-Schwan\textsuperscript{c}, Maria Geit\textsuperscript{d} and Anja Meurer\textsuperscript{c}

Many HIV-discordant couples express a strong wish to conceive a child. Insemination with processed semen is offered to these couples in many countries. Given the very low level of transmission risk during fully suppressive antiretroviral therapy, we offered timed intercourse combined with preexposure prophylaxis to further reduce the transmission risk. In 53 cases, natural conception was attempted using the proposed method. Pregnancy rates were high and reached a plateau of 75\% after six cycles. Advanced age in the female partner was a predictor for infertility in these couples.

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Prep and Timed Intercourse for Conception

- Male partner on HAART with undetectable HIV-RNA in plasma (<50 copies/ml)
- No current symptoms of genital infections
- Urine LH-test to determine the optimal time of conception (36 h after LH-peak)
- Administration of PrEP (tenofovir po), First dose at LH-peak-Second 24 hours later
- After 6 unsuccessful attempts, fertility evaluation recommended

(Vernazza et al, AIDS 2011)
PrEP for Conception

- Outcomes: March 2004 – 2007
  - 46 serodiscordant couples
  - 75% became pregnant: 50% after 3 or fewer attempts
  - 0 seroconversions or adverse events

Periconception Prep

– Very few data to date on periconception PrEP; studies under way.
– Infected partner should be on ART with fully suppressed HIV viral load.
– **Once daily tenofovir/emtricitabine is currently FDA approved for PrEP; CDC recommends 1 month before and 1 month after conception attempted.**
– Couples should use condoms at all times except during periovulatory intercourse.
– No reported increase in congenital anomalies for children whose mothers were exposed to tenofovir or emtricitabine during first trimester.
ART DURING PREGNANCY
Principles of ARV Use during Pregnancy

- Coordination of services among prenatal care providers, primary care and HIV specialty care providers, and when appropriate, mental health and drug abuse treatment services, and public assistance programs, is essential to ensure that infected women adhere to their ARV drug regimens (AIII).
General Principles of Drug Selection

- Guidelines for use of cART for maternal health during pregnancy generally are the same as for women who are not pregnant.
  - Some modifications based on concerns about specific ARVs during pregnancy and limited experience during pregnancy with newer ARVs.

- Ensure that at least 1 NRTI with high placental transfer is included in cART regimen for sufficient infant preexposure prophylaxis.

- Counsel women on the importance of close adherence to ARV regimen.
  - Offer support services, mental health services, smoking cessation, and drug abuse treatment plans as indicated.

- Coordinate between HIV and OB specialists.
# Initial ART for ARV-Naive Pregnant Women (1)

## Preferred 2-NRTI Backbone Regimens

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Comments</th>
</tr>
</thead>
</table>
| ABC/3TC        | • Available as FDC, can be given once daily  
• Potential HSR: ABC should not be used in patients who test positive for HLA-B*5701 because of risk of hypersensitivity reaction  
• Not recommended with ATV/r or with EFV if pretreatment HIV RNA >100,000 copies/mL |
| TDF/FTC or TDF + 3TC | • Available as FDC, can be given once daily  
• TDF has potential renal toxicity, use with caution in patients with renal insufficiency |
| ZDV/3TC        | • Most experience for use during pregnancy  
• Available as FDC. Twice-daily administration  
• Higher risk of hematologic toxicity |
### Preferred PI Regimens

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATV/r + preferred 2-NRTI backbone</td>
<td>• Once daily administration</td>
</tr>
<tr>
<td></td>
<td>• Extensive experience in pregnancy</td>
</tr>
<tr>
<td></td>
<td>• Maternal hyperbilirubinemia</td>
</tr>
<tr>
<td>DRV/r + preferred 2-NRTI backbone</td>
<td>• Better tolerated than LPV/r.</td>
</tr>
<tr>
<td></td>
<td>• PK data available. Increasing experience in pregnancy</td>
</tr>
<tr>
<td></td>
<td>• Must be used twice-daily in pregnancy.</td>
</tr>
</tbody>
</table>
Initial ART for ARV-Naive Pregnant Women (3)

## Preferred NNRTI Regimen

<table>
<thead>
<tr>
<th>EFV + preferred 2-NRTI backbone</th>
<th>Comments</th>
</tr>
</thead>
</table>
| **Note:** May be initiated after the first 8 weeks of pregnancy | • Birth defects in primates; risk in humans is unclear.  
• Postpartum contraception must be ensured.  
• Preferred regimen in women requiring coadministration of drugs with significant interactions with PIs or the convenience of co-formulated, single-tablet, once-daily regimen. |
Initial ART for ARV-Naive Pregnant Women (3)

## Preferred Integrase Inhibitor Regimen

<table>
<thead>
<tr>
<th>RAL + preferred 2-NRTI backbone</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• PK data available and increasing experience in pregnancy.</td>
</tr>
<tr>
<td></td>
<td>• Rapid viral load reduction.</td>
</tr>
<tr>
<td></td>
<td>• Useful when drug interactions with PI regimens are a concern.</td>
</tr>
<tr>
<td></td>
<td>• Twice-daily dosing required.</td>
</tr>
</tbody>
</table>

August 2015
Initial ART for ARV-Naive Pregnant Women (5)

### Alternative PI Regimens

<table>
<thead>
<tr>
<th>LPV/r + preferred 2-NRTI backbone</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Abundant experience and established PK in pregnancy.</td>
</tr>
<tr>
<td></td>
<td>• More nausea than preferred agents.</td>
</tr>
<tr>
<td></td>
<td>• Twice-daily administration. Once-daily LPV/r is not recommended for use in pregnant women.</td>
</tr>
</tbody>
</table>

August 2015
### Initial ART for ARV-Naive Pregnant Women (6)

#### Alternative NNRTI Regimen

<table>
<thead>
<tr>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>RPV + preferred 2-NRTI backbone</td>
</tr>
<tr>
<td>• RPV not recommended with pretreatment HIV RNA (&gt;100,000) copies/mL or CD4 cell count (&lt;200) cells/mm(^3).</td>
</tr>
<tr>
<td>• Do not use with PPIs.</td>
</tr>
<tr>
<td>• PK data available in pregnancy but relatively little experience with use in pregnancy.</td>
</tr>
<tr>
<td>• Available in co-formulated single-pill once daily regimen.</td>
</tr>
</tbody>
</table>
## Initial ART for ARV-Naive Pregnant Women

### Insufficient Data to Recommend Routine Use
- DTG
- EVG/COBI/TDF/FTC FDC
- FPV
- MVC
- RPV

### Not Recommended
- ABC/3TC/ZDV | SQV
- d4T | ETR
- ddI | NVP
- IDV/r | T-20
- NFV | TPV/r
- RTV as single PI

*August 2015*
HIV-Infected Pregnant Women Who Are Currently Receiving Antiretroviral Therapy (1)

- In general, HIV-infected pregnant women receiving cART who present for care in the 1st trimester should continue treatment during pregnancy, assuming the regimen is tolerated and effective in suppressing viral replication (HIV-1 viral load less than lower limits of detection of the assay) (AII).

- It is recommended that efavirenz be continued in pregnant women receiving efavirenz-based cART who present for antenatal care in the first trimester provided the regimen is achieving virologic suppression (CIII).
Monitor HIV RNA:
- At the initial visit (AI)
- 2-4 weeks after initiating or changing ARV drug regimens (BI)
- Monthly until HIV RNA is undetectable (BIII)
- At least every 3 months during pregnancy (BIII)
- HIV RNA should also be assessed at approximately 34-36 weeks’ gestation to inform decisions about mode of delivery and about infant ARV prophylaxis (AIII).
POSTPARTUM CARE
Postpartum Care

Because the immediate postpartum period poses unique challenges to antiretroviral adherence, arrangements for new or continued supportive services should be made before hospital discharge for women continuing cART (AII).

– Counsel women about the challenge of adherence in the postpartum period.

– Remain vigilant for signs of depression, intimate partner violence, and drug or alcohol use.

– Consider simplifying cART regimens to improve adherence.
Background

- Postpartum HIV-infected women face challenges with treatment adherence.
- Women in the deep South may experience greater difficulties with care engagement due to poor access to care, stigma, lack of social support, and mistrust in the health care system.

2. Watts DH et al. Progression of HIV disease among women following delivery. JAIDS 2003; 33:585–93
4. Sex, race, and geographic region influence clinical outcomes following primary HIV-1 infection. JID Feb 15 2011;203(4):442-451
Background

- A growing number of HIV-infected women are giving birth every year.

- Pregnancy provides a unique opportunity to impact the HIV Treatment Adherence Cascade


HIV in Mississippi, 2013

- PLWH: 10,473
  - 68% men, 32% women
- HIV Incidence: 536
  - 24.8% female (82% HS, 16% IDU)
  - AA women case rate 9x White women
- 9 Ryan White Funded Clinics

Mississippi Public Health Districts I-IX
Objectives

- Retrospective analysis of all HIV-infected women ≥16 years who delivered in Mississippi from January 1, 2002 to Dec 31, 2014.

- Focus on health care utilization and outcomes:
  - Death/Progression to AIDS
  - Engaged in care in 2015 (one medical visit or CD4/PVL in 2015)
  - HIV-1 Plasma Viral Load <200 copies/mL in 2015
Methods

- Clinical data from all 9 federally funded Ryan White clinics in Mississippi (Careware)
  - Statewide implementation in 2005-2006

- Mississippi Department of Health (MSDH) Enhanced HIV/AIDS Reporting System (eHARS)
  - Mandatory CD4/HIV Viral Load reporting to MSDH started Jan 2013
## Demographics

<table>
<thead>
<tr>
<th>Category</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Women</strong></td>
<td>548</td>
</tr>
<tr>
<td><strong>Total number of deliveries</strong></td>
<td>685</td>
</tr>
<tr>
<td><strong>Median Age at First Delivery (IQR)</strong></td>
<td>26 (23,31)</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>474 (86.5%)</td>
</tr>
<tr>
<td>White</td>
<td>57 (10.4%)</td>
</tr>
<tr>
<td>Multiple</td>
<td>4 (0.7%)</td>
</tr>
<tr>
<td>AI/AN</td>
<td>3 (0.5%)</td>
</tr>
<tr>
<td>Not reported</td>
<td>10 (1.8%)</td>
</tr>
<tr>
<td><strong>Hispanic</strong></td>
<td>15 (2.7%)</td>
</tr>
<tr>
<td><strong>Median Annual Income (IQR) (n=208)</strong></td>
<td>$9780 ($4116, $15570)</td>
</tr>
<tr>
<td><strong>Insurance</strong></td>
<td></td>
</tr>
<tr>
<td>Medicaid*</td>
<td>123 (22.4%)</td>
</tr>
<tr>
<td>Uninsured</td>
<td>65 (11.8%)</td>
</tr>
<tr>
<td>Private</td>
<td>20 (3.6%)</td>
</tr>
<tr>
<td>Medicare</td>
<td>9 (1.6%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>217 (39.6%)</td>
</tr>
<tr>
<td><strong>Housing Status</strong></td>
<td></td>
</tr>
<tr>
<td>Stable/Permanent</td>
<td>192 (35%)</td>
</tr>
<tr>
<td>Temporary/Unstable</td>
<td>23 (4.2%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>215 (39.2%)</td>
</tr>
<tr>
<td>Health District (N=300)</td>
<td></td>
</tr>
<tr>
<td>------------------------</td>
<td>-------</td>
</tr>
<tr>
<td>I</td>
<td>10 (3.3%)</td>
</tr>
<tr>
<td>II</td>
<td>6 (2%)</td>
</tr>
<tr>
<td>III</td>
<td>36 (12%)</td>
</tr>
<tr>
<td>IV*</td>
<td>12 (4%)</td>
</tr>
<tr>
<td>V</td>
<td>134 (44.7%)</td>
</tr>
<tr>
<td>VI*</td>
<td>27 (9%)</td>
</tr>
<tr>
<td>VII</td>
<td>23 (7.7%)</td>
</tr>
<tr>
<td>VIII</td>
<td>31 (10.3%)</td>
</tr>
<tr>
<td>IX</td>
<td>21 (7%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Current State of Residence eHARS (N=415)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mississippi</td>
</tr>
</tbody>
</table>

* No Ryan White HIV Provider in District
| **HIV** |
|-----------------|------------------|
| **Median Age at HIV Dx (IQR) (n=548)** | 22 (19, 27) |
| **HIV Risk** | |
| Heterosexual | 395 (72.1%) |
| Perinatal | 15 (2.7%) |
| IDU | 13 (2.4%) |
| Unknown | 125 (22.8%) |
| **HIV dx around pregnancy** | 206 (37%) |
| **AIDS Diagnosis** | 268 (48.9%) |
| **Median Age at AIDS (IQR) (n=268)** | 28 (23, 32) |
| **AIDS within 1 year of HIV dx** | 68 (13%) |
| **Median Time HIV to AIDS, years (n=268)** | 4.67 (.91, 8.3) |
| **Median Last available CD4 cells/µL (IQR)** | 494 (305, 695) |
| **Most recent HIV-1 PVL** | |
| <200 copies/mL | 146 (26.7%) |
| >200 copies/mL | 228 (41.6%) |
| Missing | 174 (31.8%) |
| **Perinatal Transmission** | 9 (1.3%) |
Engagement in 2015

*Any CD4/HIV PVL (eHARS) or medical visit in CAREWARE in 2015*
Outcomes by Health District in 2015

- % in care in 2015
- % with VL <200 in 2015

District I  District II  District III  District IV  District V  District VI  District VII  District VIII  District IX

% in care: 40  83  53  58  54  63  56  42  38
% VL <200: 20  83  25  17  23  33  35  42  38
## Mortality

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of Deaths</strong></td>
<td>67 (12.2%)</td>
</tr>
<tr>
<td><strong>Median Age at death (IQR)</strong></td>
<td>32.4 (28.1, 36.7)</td>
</tr>
<tr>
<td><strong>Median Time from HIV dx to death, years (IQR)</strong></td>
<td>9.3 (6, 14.7)</td>
</tr>
<tr>
<td><strong>Median Time from AIDS dx to death, years</strong></td>
<td>4.5 (2.1-7.9)</td>
</tr>
<tr>
<td><strong>Median time from last delivery to death, years (IQR)</strong></td>
<td>5.35 (3.0, 7.0)</td>
</tr>
<tr>
<td><strong>Median last available CD4 cells/µL (IQR) n=60</strong></td>
<td>38 (9, 133)</td>
</tr>
<tr>
<td><strong>Median last available HIV PVL copies/mL (IQR) n=58</strong></td>
<td>59220 (7713, 195137)</td>
</tr>
</tbody>
</table>
Conclusions

- Young, HIV infected women in Mississippi experience low rates of retention and viral suppression, and significant morbidity and mortality following delivery.
- Systems based and innovative interventions initiated during pregnancy and continued through postpartum phase to support engagement with care may improve longitudinal treatment adherence and health outcomes.
- Interventions should be developed in collaboration with target health districts with lowest rates of care engagement.
Next Steps

- Analysis of predictors of retention, viral suppression and AIDS/mortality
- Cause of death
- GIS mapping (census tract data, health districts)
- Prospective study of HIV-infected pregnant and postpartum women
  - Followed longitudinally over 2 year period
  - Assessments of structural and behavioral barriers to care
Websites to Access the Guidelines

- http://www.aidsetc.org
QUESTIONS??