IMPAAACT 2009
Different Pieces of the Puzzle
Lynda Stranix-Chibanda
for the protocol team
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HIV Prevention Puzzle –
How to prevent new HIV infections?

Prevention Scientific Committee

- HIV prevention strategies that are
  - Effective
  - Safe
  - Throughout the life-course
  - Don’t jeopardise treatment
  - Global scale
  - Variety of health settings

- We don’t have all the pieces

https://impaactnetwork.org/
Many pieces in place for infants

- 70% reduction in new child infections since 2000 due to life-long ART for women

In 2017, still 180,000 new HIV infections U15s

2020 goal <20,000
Many pieces in place for infants
1º prevention in pregnancy
The pieces we do have

- 6-29% reproductive years spent pregnant and breastfeeding
- Substantial risk of new HIV infection
  - Incidence 5.37 / 100py
- Peaks in late pregnancy
- Increased risk per act vs. non-pregnant state
  - 4.97 (95%CI 2.95, 8.38)

World Bank; Thomson KA, et al. J Inf Dis 2018
The pieces we do have

- Mothers are young
  - Adolescent birth rate 109/1000 women aged 15-19yrs
The pieces we **do** have

- Women aged 15-24 years make up 19% of new HIV infections
  - Sub Saharan Africa bears the greatest burden
The pieces we do have

• Adolescent and young women face particular challenges
  – Accessing health care
    • HIV services
    • Sexual reproductive health services
  – Gender based violence
  – Unplanned pregnancy
  – Pregnancy complications

http://www.who.int/news-room/fact-sheets/detail/adolescents-health-risks-and-solutions
The pieces we do have

- PrEP is effective in this population
- May need specific support to adhere to medication
  - PrEP
  - ART
  - Oral tablets
  - Other product formulations
The pieces we *do* have

- Tenofovir/Emtricitabine safety profile in pregnancy established
  - HIV
  - Hepatitis B

- Pharmacology studied
  - HIV-infected women (pregnant and non-pregnant)
  - HIV-exposed infants
  - HIV-uninfected men
  - HIV-uninfected non-pregnant women in the US
The pieces we do have

Based on the available safety data, WHO considers that PrEP should not be discontinued during pregnancy and breastfeeding for women who continue to be at substantial risk of HIV infection. PrEP can also be considered as an additional prevention choice for HIV-negative pregnant women who are at substantial of HIV infection, as part of a comprehensive PMTCT package.
More safety data needed

• Adverse pregnancy outcomes
• Effects of *in utero* and breastmilk ARV exposure on infant bone development and growth
• Effects of TDF use on maternal bone mineral density
• Adolescents will require more adherence support and enhanced comprehensive SRH information
Now to put them all together for pregnant women
Pharmacokinetics, Feasibility, Acceptability, and Safety of Oral Pre-Exposure Prophylaxis for Primary HIV Prevention during Pregnancy and Breast Feeding in Adolescents and Young Women

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What will 2009 add to current knowledge?

• At this time of particular risk for new HIV infection in young women
  
  – PK in pregnancy
  
  – Deeper understanding of adherence
  
  – Safety information to inform the risk:benefit ratio
IMPAAACT 2009 Study Sites

Kampala, Uganda:
- Baylor CRS & Makerere University - JHU CRS

Blantyre, Malawi (JHU)

Harare, Zimbabwe:
- Harare Family Care Center, Saint Mary’s & Seke North

Johannesburg, South Africa:
- Shandukani WRHI
Pharmacokinetic (PK) Component
PK Component Procedures

• 12 weeks of PK monitoring, with weekly DBS specimens for drug levels
  – Followed by an observational period to 6 weeks postpartum

• Intensive monitoring of drug adherence
  – This may include
    – directly observed therapy (DOT) at the clinic,
    – DOT at the home, via community health workers, or
    – “real-time” video-based monitoring via smartphone, tablet, or computer.
PK Component Outcome

• Concentration of tenofovir diphosphate (TFV-DP) associated with adequate adherence to TDF/FTC among women observed ingesting daily oral PrEP during pregnancy and postpartum.

• Compare TFV-DP concentrations pre- and post-delivery.
PrEP Comparison Component
Study Design

• Observational cohort study for HIV-uninfected healthy pregnant women aged 16-24 years with EGA <32 weeks
  – 200 pregnant women who choose PrEP
  – 100 pregnant women who decline PrEP

• Followed ~monthly in pregnancy, at L&D, then weeks 6, 14 and 26 postdelivery
  – Acceptability
  – Adherence
  – Safety
Adherence Intervention

• *integrated Next Step Counseling (iNSC).*
  – All maternal participants in both cohorts.

• *Drug level monitoring with feedback.*
  – Starting at Week 4 visit

• *SMS Adherence Support.*
  – 1-way personalized stage-based messages to support maternal and child healthcare (e.g. MAMA platform); *also* receive weekly 2-way text messages that provide general adherence support (i.e., “are you doing OK?”).
Primary Objectives

• To characterize PrEP adherence among HIV-uninfected women aged 16-24 years who initiate once-daily TDF/FTC in pregnancy

• To compare maternal and infant adverse events (including pregnancy outcomes) between women who initiate PrEP and those who decline PrEP
Secondary Objectives

- To identify individual, social, and structural barriers and facilitators to PrEP uptake during pregnancy
- To compare between the PrEP and non-PrEP cohorts:
  - Reported sexual risk behavior and incidence of STIs
  - HIV incidence
  - HIV drug resistance among HIV-infected mothers and infants
## Outcome measures

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<thead>
<tr>
<th>Objective</th>
<th>Outcome Measures</th>
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<tr>
<td>2.3.1 PrEP adherence: TFV-DP drug concentration level in Dried Blood Spots (DBS)</td>
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<td>2.3.2 Maternal Adverse Events:</td>
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<td>Maternal Grade 3 or higher adverse events (signs, symptoms, labs, and diagnoses)</td>
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<td>Maternal Grade 2 or higher chemistry abnormalities</td>
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<td>2.3.2 Adverse Pregnancy Outcomes:</td>
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<td></td>
<td>Composite outcome of</td>
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<td>Spontaneous abortion (occurring at &lt;20 weeks gestation)</td>
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<td>Stillbirth (occurring at ≥20 weeks gestation)</td>
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<td>Preterm delivery (&lt;37 completed weeks’ gestation)</td>
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<td>Small for gestational age (&lt;10th percentile using WHO norms for weight-for-age and ultrasound derived gestational age at delivery)</td>
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<td>Infant Safety:</td>
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<td>Infant death within the first 26 weeks of life</td>
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<td>Infant Grade 3 or higher adverse events (signs, symptoms, labs, diagnoses) reported between birth and exit</td>
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<td>Infant bone mineral content based on DXA scan of the whole body (WB-BMC) at birth and lumbar spine (LS-BMC) at birth and 26 weeks postpartum</td>
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<td>Infant creatinine and CrCl rate at birth and 26 weeks postpartum</td>
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<td>Infant length for age z-score at birth and exit</td>
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MTN – 042 vs IMPAACT 2009

- Similar overarching goal to prevent HIV acquisition among pregnant and breastfeeding women in SSA
- Different agents being evaluated
- Slightly different approach and focus
- Opportunity to exchange ideas and experience
Thank you
Tatenda