IT'S ALL ABOUT SAFETY!
DELIVER and B-PROTECTED Studies

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MTN
microbicide trials network

Ensuring Safe HIV Prevention Methods for Pregnant and Breastfeeding Women

Harare, Zimbabwe – 29 January 2020

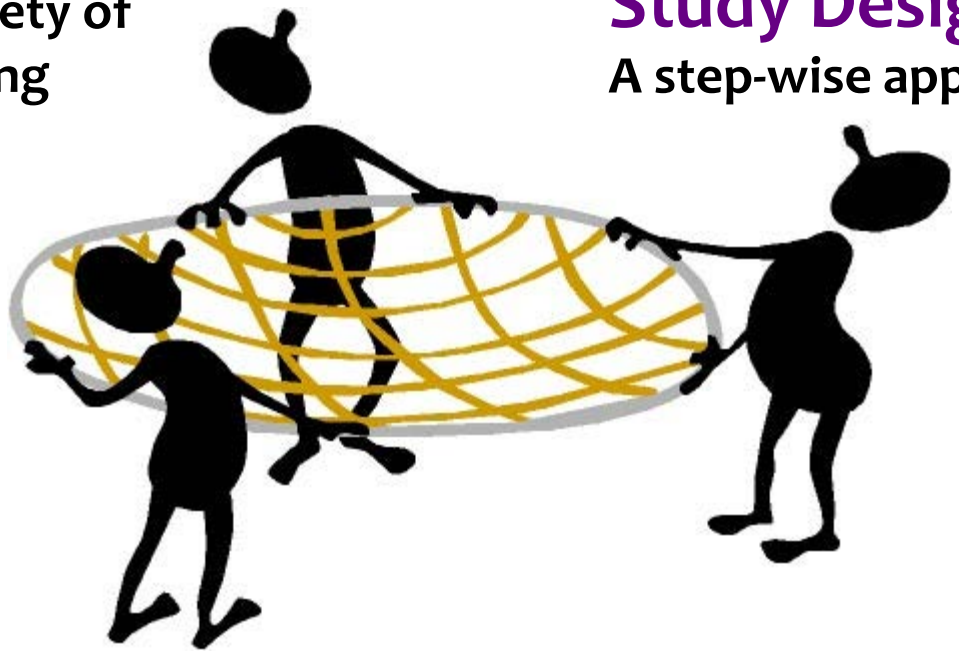
MTN-042: A Three-Way Safety Net for Two

Study Objective

Understanding the safety of PrEP and the ring during pregnancy

Study Design

A step-wise approach



Study Conduct

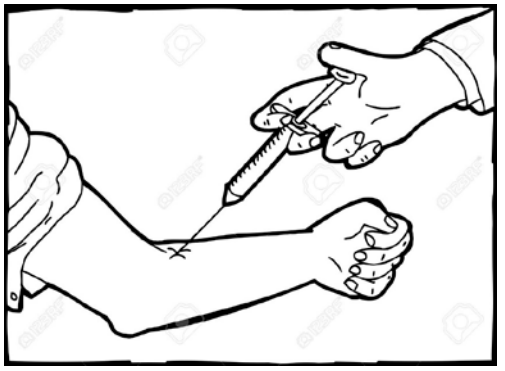
Multiple measures to ensure safe participation

So that women can be protected against HIV at all times, including during pregnancy, with methods that are safe for them and their babies

Study Objective

Study objective

- The goal of the study is to see whether the two study products are safe for baby and mom
- This starts at the site level



- Participants will be seen every 1-4 weeks depending on how far along in the pregnancy they are until 6 weeks after delivery
- Infants will be seen for a year

Primary goal: Birth Outcome

- In addition to collecting information about problems women might have while in the study we will follow women through delivery
- We will know how the pregnancy ended- "the outcome"
  - Was it a normal delivery of a fully developed baby? (full term birth)
  - Was it an early delivery- more than three weeks before expected? (preterm birth)
  - Was it a delivery of a baby that was dead when it came out? (still birth)
  - Was it an early loss of the baby- less than 5 months? (pregnancy loss)

How do we know whether oral PrEP or ring affect birth outcomes?

- At the end of the study, we will compare how often women and babies had serious problems AND how often moms had bad pregnancy outcomes

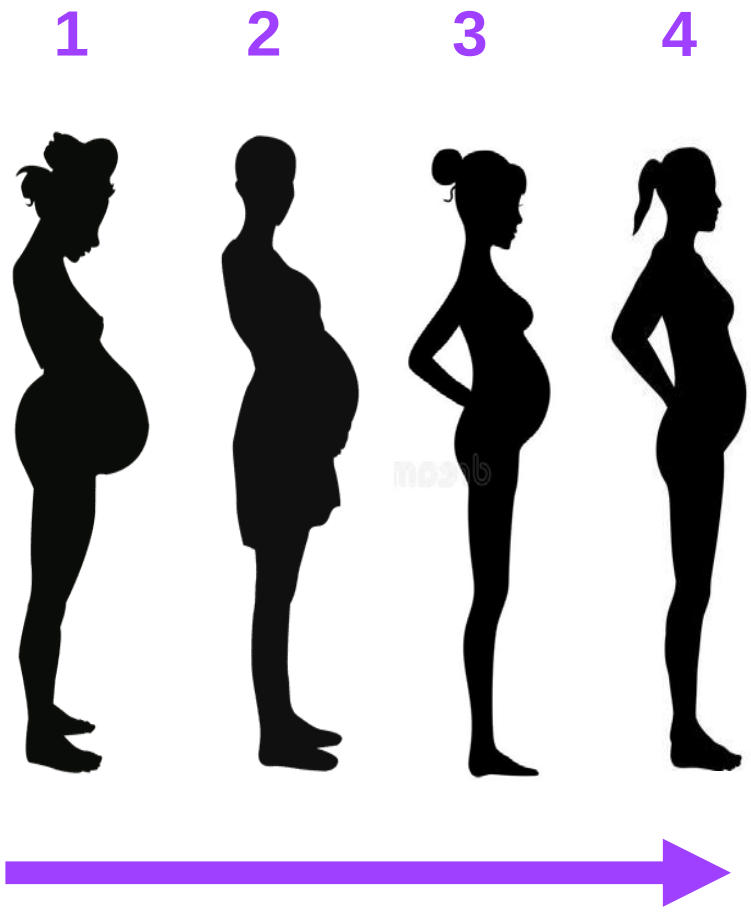
- We can compare what happens to women in our study to women delivering at our hospitals who were not part of the study

Other important safety information which will be measured

- High blood pressure (hypertensive disorders of pregnancy)
- Infection of the womb (chorioamnionitis or endometritis)
- Infection in the blood (Puerperal sepsis)
- Dangerous bleeding (Hemorrhage)
- Water around the baby breaking too early (Preterm premature rupture of membranes)
- Fever

Study Design

Study design



- Remember there are four groups
- The first group is farthest in pregnancy

Experts will review outcomes before the next group is enrolled

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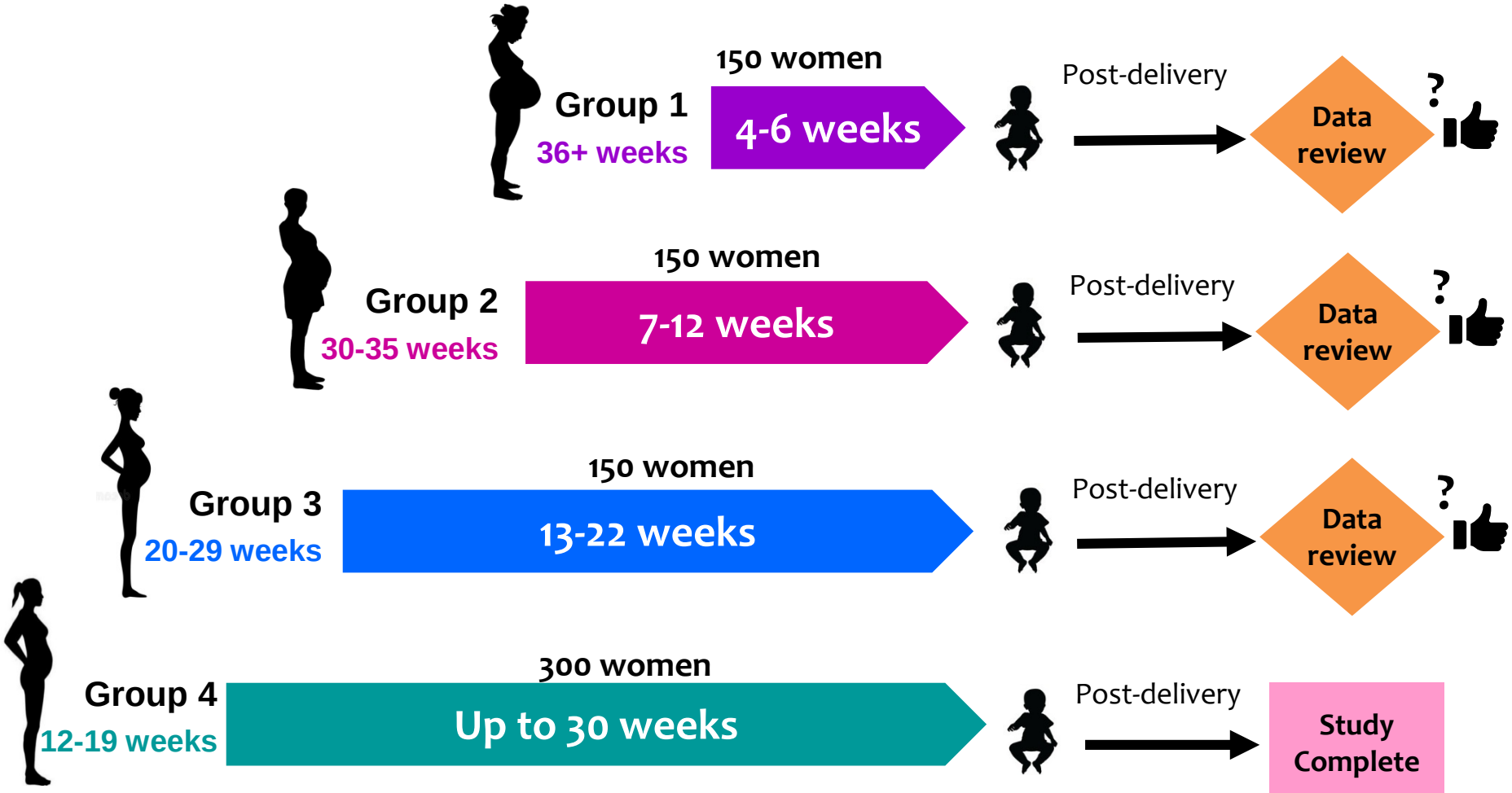
The importance of design

- Most of the study information will come from the last group of enrolled participants
  - They will use the product for the longest time

- Instead of starting with the last and biggest group, we start with the women farthest in pregnancy to be sure the products are safe

A stepwise approach with interim reviews



The experts in the interim review panel

- Our 7 person dream team:
  - 2 obstetrics care provider from Sub-Saharan Africa
    - Physician and midwife
  - 1 obstetrics care provider from the United States
  - 1 pediatrician from Sub-Saharan Africa
  - 1 ethicist
  - 1 biostatistician
  - 1 maternal-child health expert from the public health sector
- They cannot have any connection to the study so that we know that they speak truthfully

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Each group will use the ring or PrEP a longer time

		number	Ring or PrEP?	Approximately how long?
Group 1 **36+ weeks**		150	100 will use the ring 50 will use PrEP	4-6 weeks
Group 2 **30-35 weeks**		150	100 will use the ring 50 will use PrEP	7-12 weeks
Group 3 **20-29 weeks**		150	100 will use the ring 50 will use PrEP	13-22 weeks
Group 4 **12-19 weeks**		300	200 will use the ring 100 will use PrEP	Up to 30 weeks

What will the review group see?

- Rates of pregnancy and infant outcomes for the PrEP and dapivirine ring groups
- Rates of the same outcomes in the population of women from the same hospitals but not in our study as well as published data from studies of pregnancy outcomes from the same regions
- Summary of the safety data from all study participants

The process

- Safety physicians from the study and study statisticians will be there to answer questions put forward by the safety review panel but will not vote on whether or not the study will proceed
- At least 5 of 7 members will have to vote “yes” in order for the study to move forward to the next group
- The decision of the interim safety review panel will be communicated to the study team, the IRB, the participants and the community

Study Conduct

Ensuring safety at several levels

- Site clinicians will monitor the safety and well-being of participants at each visit
  - Deliver has its own safety review team led by safety physicians who will review routine safety data every month and more serious issues in real time
- Ongoing oversight by local IRBs/ECs
- Study outcomes will be reviewed by an external Interim Safety Review Panel at the conclusion of each group and determine whether the next cohort can be enrolled

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When there is a problem

- This will be detected by the site team
- First and foremost, the site will treat the problem or refer to the hospital if necessary
- If serious and related to the ring or PrEP, the woman will stop using the product
  - This is expected to be rare. It did not happen in ASPIRE or the Ring Study. It was rare in PrEP studies
- Second, the site notifies the larger study team, who follows problems across all four sites

The site is committed to providing the best care possible to its participants

Acknowledgements

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