A Target Trial of Pre-conception Switch from Nevirapine- to Dolutegravir-based ART on Birth Outcomes

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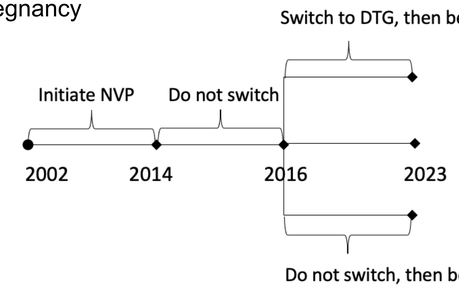
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BACKGROUND

- Antiretroviral regimens have differential effects on adverse birth outcomes
- Nevirapine (NVP) has been associated with particularly high risk of adverse birth outcomes compared with newer ART like dolutegravir (DTG)
- DTG became first-line ART in Botswana in 2016, and thereafter individuals on NVP were switched to DTG
- **Objective**: To emulate a hypothetical randomized trial (a target trial) of pre-conception switch from NVP to DTG to evaluate whether switching from high-risk to low-risk regimens prior to pregnancy can favorably impact birth outcomes.

METHODS

- **The Tsepamo Study** has been conducting birth outcomes surveillance at government delivery sites in Botswana since 2014 (up to 18 delivery sites, >250,000 deliveries to date).
- **Eligibility Criteria:** Individuals who initiated NVP from 2002-2014 and remained on NVP in 2016.
- **Treatment Strategies:** We compared those who switched to DTG with those who did not switch from NVP prior to pregnancy



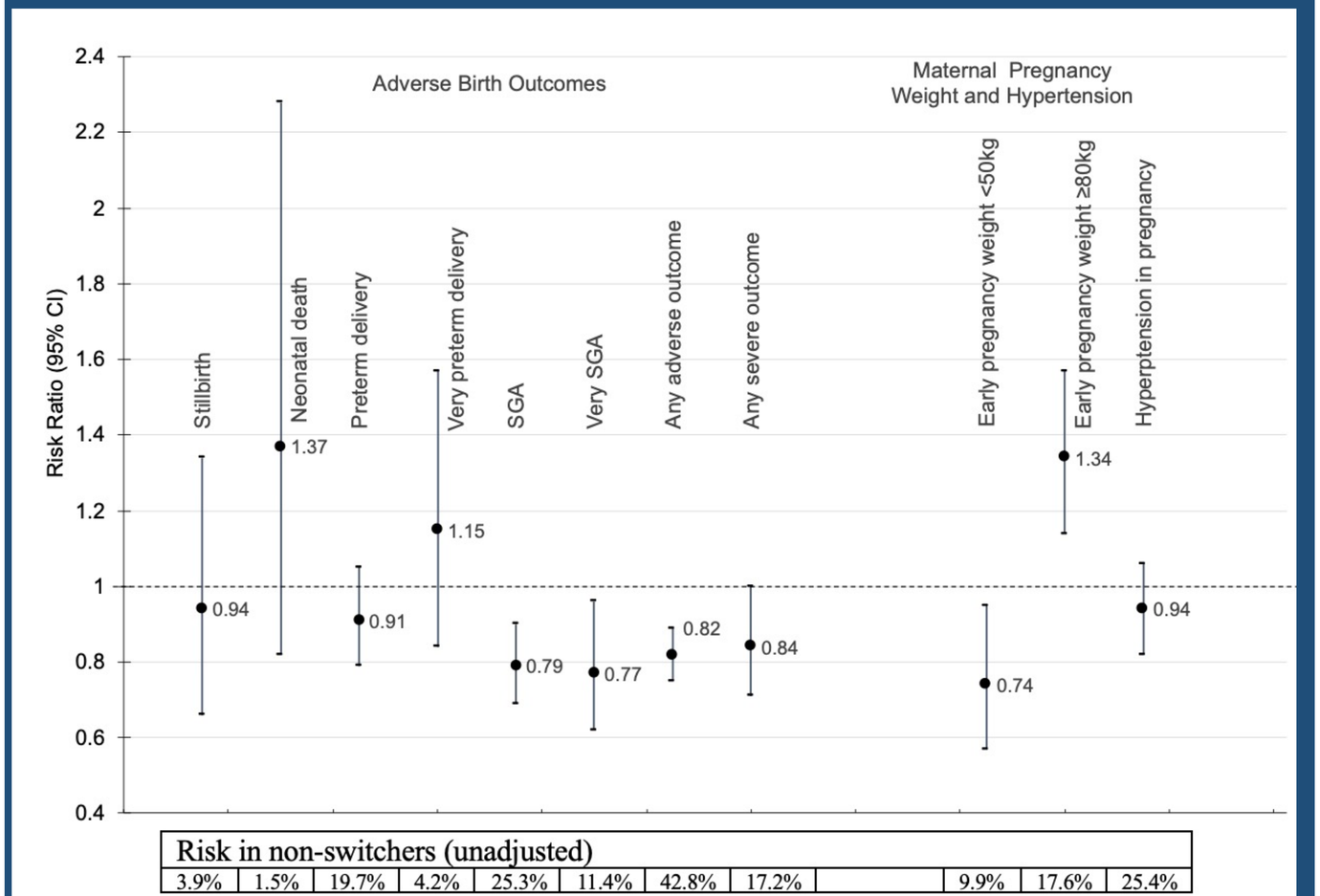
- **Outcomes:** **Infant outcomes:** Stillbirth, in hospital neonatal death (<28 days), preterm delivery (<37 weeks), very preterm delivery (<32 weeks), small-for-gestational-age (SGA) (<10%tile), very SGA (<3%tile), and combined endpoints of any adverse or severe adverse outcome. **Maternal outcomes:** Low (<50kg) and high (≥80kg) early pregnancy weight (before 24 weeks) and hypertension in pregnancy (SBP≥140 or DBP≥90 mm/Hg)
- **Analysis:** Log-binomial models to estimate adjusted risk ratios and 95% confidence intervals

RESULTS

Characteristics of study population:

- **4,265 eligible individuals: 1,102 (26%) switched** from NVP to DTG and **3,163 (74%) did not switch** pre-pregnancy
- Median (IQR) **age in pregnancy**: 36 (32, 39) years
- Common **backbones during pregnancy**: For switchers: TDF/3TC (90%) and TDF/FTC (8%); Non-switchers: ZDV/3TC (60%) and TDF/FTC (39%)

Figure: Adjusted risk ratios and 95% confidence intervals for adverse birth outcomes (Left Panel) and maternal pregnancy weight and hypertension (Right Panel), comparing pre-conception switchers (NVP to DTG) to non-switchers (NVP), in the Tsepamo Study.



Sensitivity Analyses:

- Little evidence for time-trends in birth outcomes over the study period in sensitivity analyses
- Results were similar when excluding ZDV backbones

Main Findings:

- Comparing **switchers with non-switchers**, RRs were **0.82 (0.75, 0.89)** for **any adverse birth outcome** and **0.84 (0.71, 1.00)** for **any severe adverse birth outcome**
- Differences were driven by SGA and very SGA **(Figure, Left Panel)**
- Switchers were less likely to have low and more likely to have high early pregnancy weight **(Figure, Right Panel)**

CONCLUSIONS

- **Switching from legacy NVP-based regimens to DTG/TDF/XTC prior to pregnancy may reduce the risk of low maternal weight in early pregnancy and fetal growth restriction**
- **This study provides further evidence that specific regimens impact birth outcomes, and that switching from legacy regimens prior to conception can improve birth outcomes**

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