

ANTEPARTUM WEIGHT GAIN AND ADVERSE PREGNANCY OUTCOMES: A MEDIATION ANALYSIS

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BACKGROUND

- Abnormal antepartum weight gain (low or high by IOM guidelines¹) is associated with adverse pregnancy outcomes:
 - Low weight gain (<0.18kg/wk) → small for gestational age infant (SGA), preterm delivery (PTD), and low birth weight (LBW)^{2,3,4}
 - High weight gain (>0.59kg/wk) → macrosomia, hypertensive disorders of pregnancy, gestational diabetes^{4,5}
- IMPAACT 2010 (VESTED): pregnant women with HIV-1 in 9 countries randomized at 14-28 weeks gestational age (GA) to start dolutegravir (DTG)+emtricitabine (FTC)/tenofovir alafenamide fumarate (TAF) vs. DTG+FTC/tenofovir disoproxil fumarate (TDF) vs. efavirenz (EFV)/FTC/TDF
- Previous VESTED analysis → low antepartum weight gain associated with higher risk adverse pregnancy outcomes (vs normal weight gain)
- In this exploratory analysis, we evaluated whether antepartum weight change was a mediator of by-arm differences in adverse pregnancy outcomes.

METHODS

- Composite adverse pregnancy outcome: occurrence of stillbirth (GA ≥20 wks), PTD (GA <37 wks), or SGA (<10th percentile)
- Causal mediation analysis used to separate estimated effect of study arm on risk of the composite pregnancy outcome into two effects:
 - effect mediated through change in weight (indirect effect, modeled continuously), and
 - effect not mediated through weight change (direct effect, modeled as binary outcome) (Figure 1)
- Mediator and outcome models were adjusted for baseline GA, body mass index (BMI), CD4 count, country, age

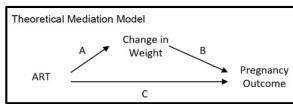


Figure 1: The mediation model depicts the total effect=A+B+C; indirect effect = A+B; and Direct Effect = C

Up to one-third of observed by-arm differences in adverse pregnancy outcomes appear to be mediated by ART-related antepartum weight change.

RESULTS

- 643 participants randomized: 217 in DTG+FTC/TAF, 215 in DTG+FTC/TDF, and 211 in EFV/FTC/TDF arms
- Baseline medians were: GA 21.9 weeks, HIV RNA 903 cp/mL, CD4 count 466 cells/uL, and BMI 25 kg/m²
- Proportion with an adverse pregnancy outcome differed by arm: lower in DTG+FTC/TAF (24%) vs. EFV/FTC/TDF (33%) and DTG+FTC/TDF (33%) arms
- Low weight gain: least common in DTG+FTC/TAF (15%) vs EFV/FTC/TDF (30%) and DTG+FTC/TDF (24%) (Figure 2)
- Low antepartum weight gain (<0.18 kg/week) associated with higher hazard of adverse pregnancy outcomes vs. normal weight gain (HR: 1.4, 95%CI: 1.04, 2.00) (Figure 3)
- For by-arm differences in adverse pregnancy outcomes compared to DTG+FTC/TAF arm: the percent of adverse pregnancy outcome risk differences mediated by weight change was 31% vs EFV/FTC/TDF and 11% vs DTG+FTC/TDF and not significantly different after adjustment. The effect for DTG+FTC/TDF vs EFV/FTC/TDF was small (2%) (Figure 4)

FIGURE 2. Low, Normal, and High Antepartum Weight Gain by Arm

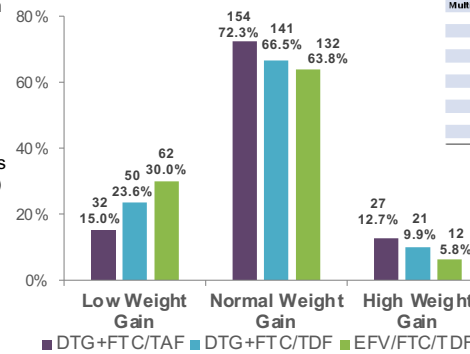


FIGURE 3. Weight Gain and Composite Adverse Pregnancy Outcome by Arm

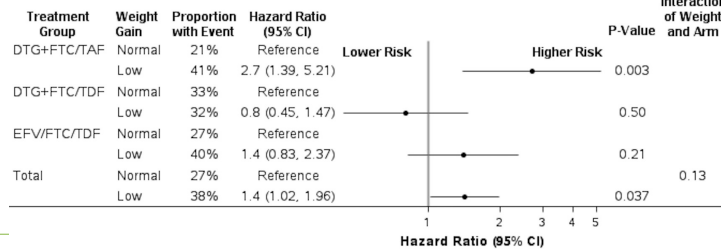
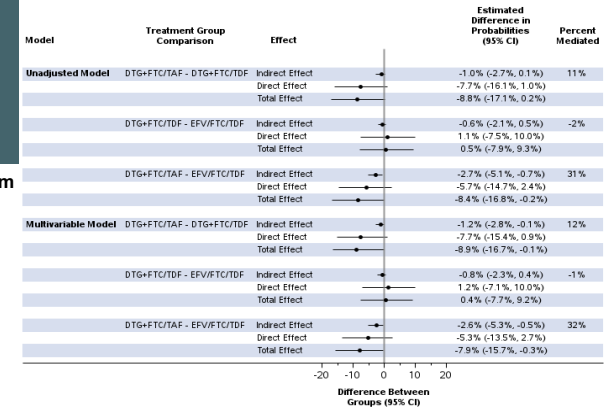


FIGURE 4. Mediation Analysis of Study Arm, Weight Change, and the Composite Adverse Pregnancy Outcome*



*The estimates and confidence intervals were computed using a mediator model with the change in weight as a continuous variable and the adverse composite pregnancy outcome as a binary variable.

CONCLUSIONS

- Low antepartum weight gain was associated with adverse pregnancy outcomes.
- Up to one-third of observed differences in adverse pregnancy outcomes between randomized arms appear to be mediated by ART-related weight change.
- Further study is needed on the role of antepartum weight gain and on ART-related mechanisms associated with adverse pregnancy outcomes in women living with HIV.

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