

Estradiol levels in HIV-infected pregnant women on dolutegravir-based ART in Botswana

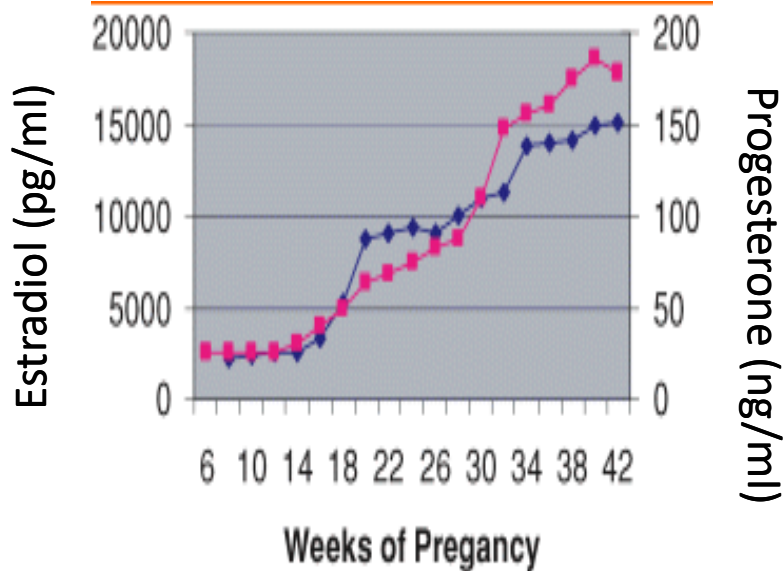
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Background

- Of over 1.4 million pregnant women living with HIV, > 75% are accessing antiretroviral treatment (ART) in pregnancy
- Some antiretrovirals (ARVs) alter maternal hormones important to maintenance of a healthy pregnancy and fetal development
- As newer ARVs are used in pregnancy, it is important to understand the interplay between ARVs and key maternal hormones in pregnancy

Estrogen, Progesterone, and Pregnancy

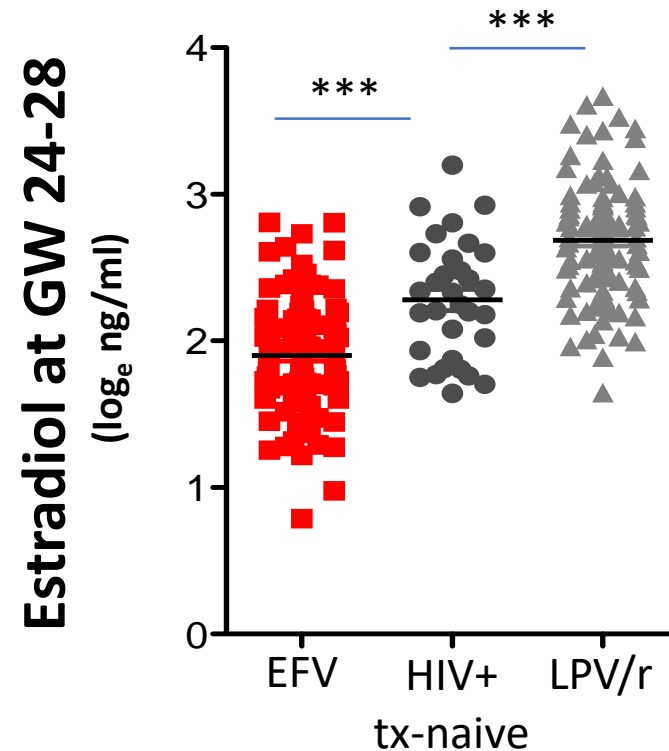


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- Both important in the maintenance and progression of pregnancy
- Low estradiol and progesterone associated with placenta abnormalities, fetal distress, IUGR, and preterm birth
- Play a role in fetal neurodevelopment

PROMOTE Study – Sub-analysis of ARVs and Pregnancy Hormones

- PROMOTE participants randomized to EFV or LPV/r
- Used 326 samples collected between 24-28 gestational weeks (GW) from women enrolled in the PROMOTE study
- Evaluated mean estradiol levels



Dolutegravir in Botswana

- Botswana updates national HIV treatment guidelines in June 2016
 - Dolutegravir/emtricitabine/tenofovir designated as first line regimen for all treatment naïve adolescents and adults living with HIV

Study Objective: To evaluate associations between dolutegravir use in pregnancy, maternal estradiol levels and infant birth anthropometrics.



Study Population

- Pregnant women enrolled in the Tshilo Dikotla cohort
 - Inclusion criteria:
 - ≥ 18 years of age
 - If living with HIV, requirement for dolutegravir/tenofovir/emtricitabine at least 6 weeks prior to delivery
 - Available plasma collected between 24 and 29 weeks gestational age



Outcomes

Primary

- Maternal estradiol and bioavailable estradiol levels between 24-29 weeks gestational age

Secondary

- Infant birth weight and length z-scores



Statistical Methods

- Bioavailable estradiol (bE2) calculated using estradiol and sex hormone binding globulin (SHBG)
 - Student's t-test used to compare mean log-transformed bE2 by maternal exposure to HIV/DTG
 - Linear regression models were fit to assess associations between bE2 and maternal HIV status/DTG use
- Birth weights and lengths converted to z-scores using Intergrowth-21st standards
 - Pearson correlation coefficients calculated between bE2 and birth anthropometric z-scores

Maternal and Infant Characteristics

Maternal Characteristics	HIV-Infected Women (n=47)	HIV-Uninfected Women (n=71)	p-value
Age (years)	27.6 (24.1-32.2)	25.8 (21.1-29.5)	0.02
Gest Age at Blood Draw (weeks)	26.9 (25.0-28.1)	26.9 (25.3-28.1)	0.68
BMI at Blood Draw (kg/m ²)	26.5 (23.2-31.2)	25.5 (22.8-29.7)	0.38
Gravidity	3 (2-4)	1 (1-3)	<0.01
HIV Disease			
% with VL Suppression at Delivery	42 (89%)	NA	NA
Median CD4 Cell Count at Delivery	487 (349-584)	NA	NA
cART from conception	3 (6%)	NA	NA
Median Weeks on cART	11.7 (7.5-15.0)	NA	NA
Infant Characteristics	HIV/ARV-exposed infants (n=41)	HIV/ARV-unexposed (n=56)	p-value
Males	20 (49%)	22 (39%)	0.41
Median Gest Age at Birth (weeks)	39.0 (37.4-40.0)	39.6 (38.3-40.1)	0.38
Preterm Birth (< 37 weeks)	7 (19%)	9 (19%)	1.00
Small for Gestational Age	7 (17%)	6 (11%)	0.38

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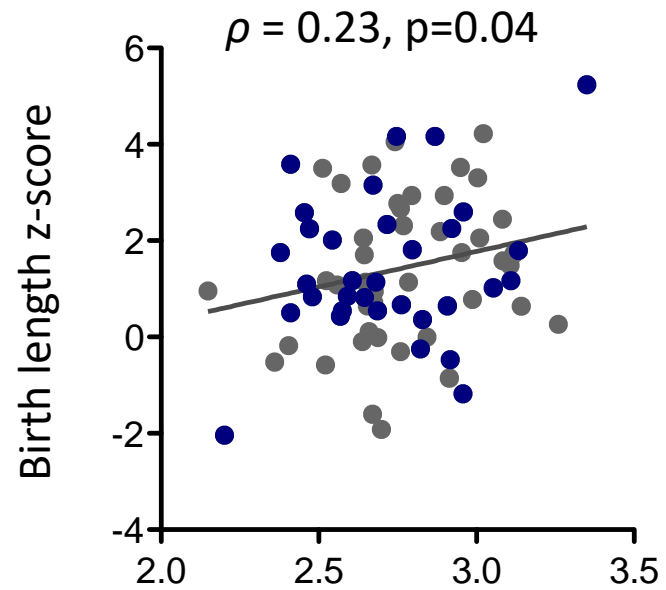
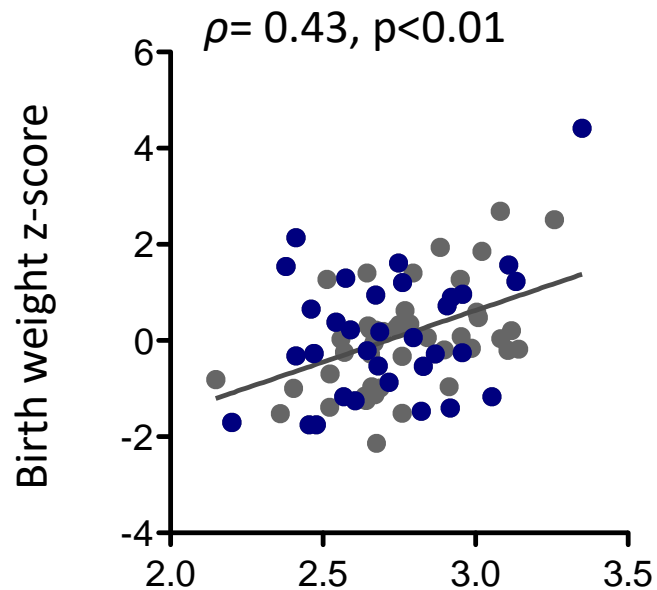
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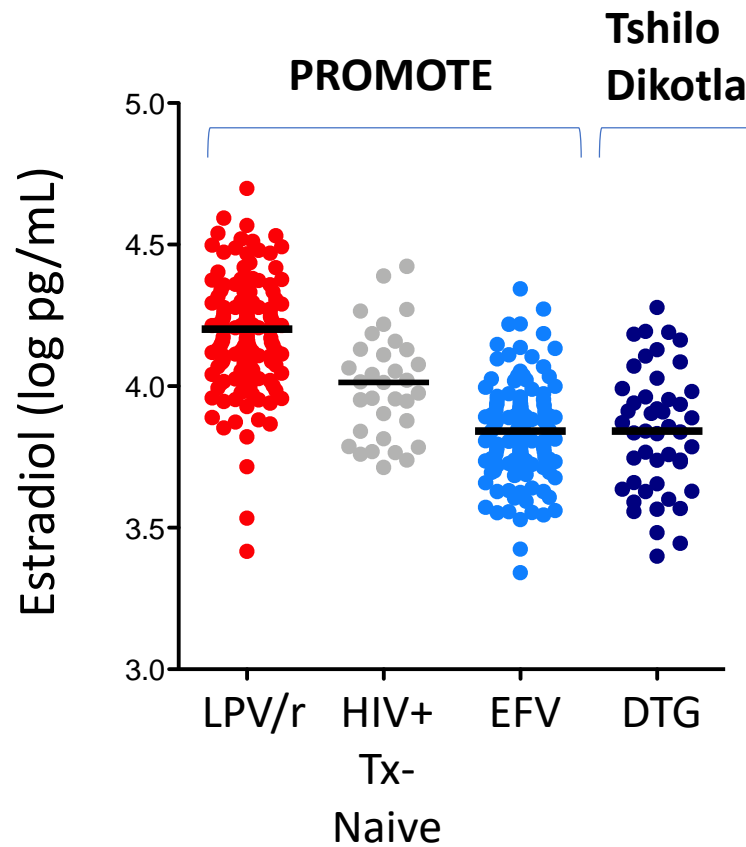
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Bioavailable E2 and Birth Anthropometrics



Bioavailable Estradiol (log pg/mL)

E2 levels in HIV+ women on different cART regimens



Strengths & Limitations

Strengths

- Novel evaluation of DTG use in pregnancy and estradiol
- Comparator group of HIV-uninfected women

Limitations

- Disentangling HIV from DTG
- Few women conceiving on DTG
- Higher attrition prior to delivery among HIV-uninfected women
- Small sample size

Future Studies

- Larger cohorts with comparable groups of women
- Increased proportion of women conceiving on a DTG-containing regimen
- Longer-term follow-up of infants to correlate bE2 in pregnancy with overall health outcomes
- Concurrent work on biological mechanisms associated bE2

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Funders:

