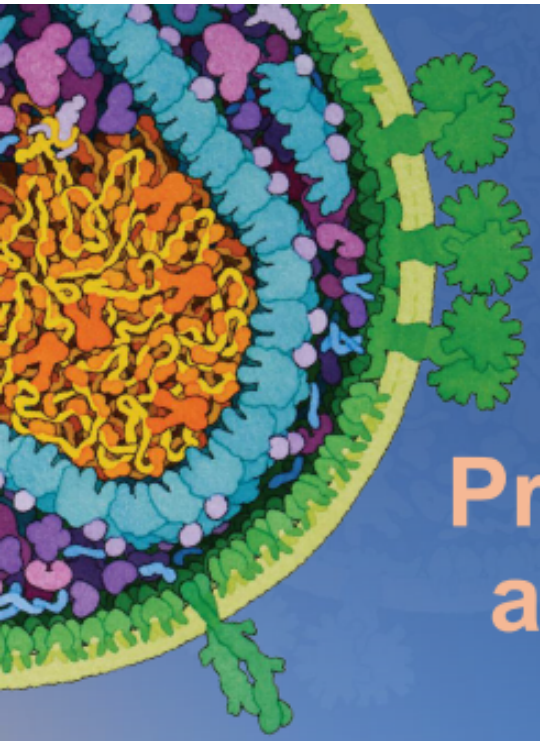


ORAL ABSTRACT

Predicted long-term adverse birth and child health outcomes in the ADVANCE trial

Eva Baxevanidi

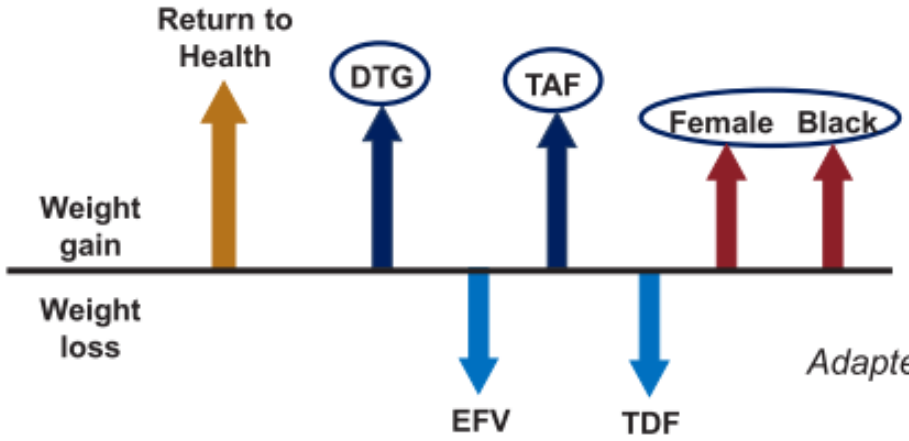
Imperial College London, School of Public Health
London, United Kingdom

Disclosure: None

CROI 2021

Background

- **WHO guidelines**: TDF/XTC/DTG is the recommended first-line regimen for HIV, and TAF/FTC+DTG may be considered for patients with established osteoporosis and/or impaired renal function[1]



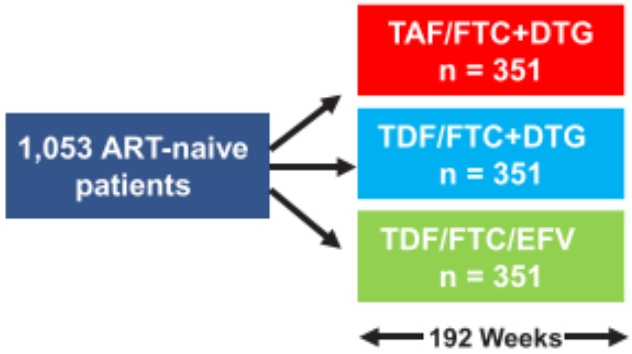
Adapted from Hill et.al, 2019

- DTG is associated with significant weight gain and clinical obesity[2-4]
- Pre-pregnancy obesity (BMI ≥30kg/m^2) increases the risk of adverse pregnancy and child health outcomes[5-7]
- **Aim:** To model the long-term risk of adverse outcomes in pregnancy and child development due to ARV-associated weight gain among HIV-positive pregnant women in the ADVANCE trial over three years (144 weeks)

1. WHO. Interim guidelines. Updated recommendations on first-line and second-line antiretroviral regimens and post-exposure prophylaxis and recommendations on early infant diagnosis of HIV [Internet]. Geneva; 2018. Available from: https://apps.who.int/iris/bitstream/handle/10665/277395/WHO-CDS-HIV-18.51-eng.pdf?ua=1 [Accessed 5 February].
2. Venter W. D. F, Moorhouse M, Sokhela S, Fairlie L, Mashabane N, Masenya M, Serenata C, Akpomiemie G, Qavi A, Chandiwana N, Norris S, Cherish M, Clayden P, Abrams E, Arulappan N, Vos A, McCann K, Simmons B and HA. Dolutegravir plus Two Different Prodrugs of Tenofovir to Treat HIV. The New England Journal of Medicine. 2019;381(9):803–815.
3. Kouanfack C, Mpoudi-Etame M, Bassega P. O, Eymard-Duvernay S, Leroy S, Boyer S, Peeters M, Calmy A and DE. Dolutegravir-Based or Low-Dose Efavirenz–Based Regimen for the Treatment of HIV-1. The New England Journal of Medicine. 2019;381(9):816–826.
4. Mark M. The ADVANCE clinical trial: changes from baseline to week 96 in DXA-assessed body composition in TAF/FTC+DTG compared to TDF/FTC+DTG, and TDF/FTC/EFV Weight Keeps Rising Through 96 Weeks With TAF/FTC+DTG in Black Africans. Natap.org. 2020. 2019. Available from: https://www.natap.org/2019/EACS/EACS_31.htm [Accessed 5 February].
5. Souza RD, Horyn I, Pavalagantharajah S, Zaffar N. Systematic Review Maternal body mass index and pregnancy outcomes : a systematic review and meta-analysis. The American Journal of Obstetrics & Gynaecology MFM. 2019;1(4):1–17.
6. Reilly JRO, Reynolds RM. The risk of maternal obesity to the long-term health of the offspring. Clinical Endocrinology. 2013;78:9–16.
7. Stirrat LI, Reynolds RM. Effects of maternal obesity on early and long-term outcomes for offspring. Research and Reports in Neonatology. 2014;4:43–53.

Methods

I. ADVANCE (2017-2022) – study design[8]
Open label, Phase III trial, South Africa



Study visits: baseline, Weeks 4, 12, 24, 36, 48, 60, 72, 84 and 96 then every 24 weeks

II. Systematic Review of adverse pregnancy and child health outcomes in females with an obese versus normal pre-pregnancy BMI

Medline, EMBASE, Maternal & Infant care and Global Health database searched

Selected **cohort studies** evaluating the impact of maternal obesity on adverse health outcomes in pregnancy

Compared the risk of adverse pregnancy outcomes in women with an **obese versus normal BMI (≥30 kg/m^2 versus 18.5-24.9 kg/m^2)**

25 studies were selected for analysis

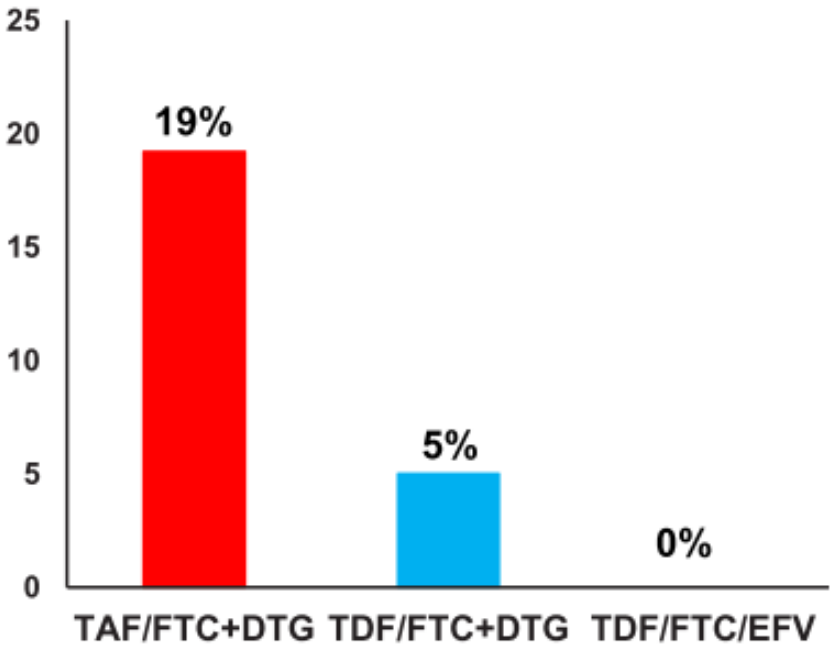
Relative risk for each adverse outcome calculated using Revman 5.3 Software

III. Risk Prediction Analyses - Relative risks of the systematic reviews combined with treatment-associated obesity rates of each treatment group in the ADVANCE trial to predict the number of adverse pregnancy and child health outcomes

8. Venter W.D.F, Moorhouse M, Sokhela S, Fairlie L, Mashabane N, Masenya M, Serenata C, Akpomiemie G, Qavi A, Chandiwana N, Norris S, Chersich M, Clayden P, Abrams E, Arulappan N, Vos A, McCann K, Simmons B and HA. Dolutegravir plus Two Different Prodrugs of Tenofovir to Treat HIV. The New England Journal of Medicine. 2019;381(9):803–815.

Results (1/2)

I. Statistical Analysis: Treatment-associated obesity rates among women in ADVANCE with a normal baseline BMI (18.5-24.9 kg/m^2) – 144 weeks

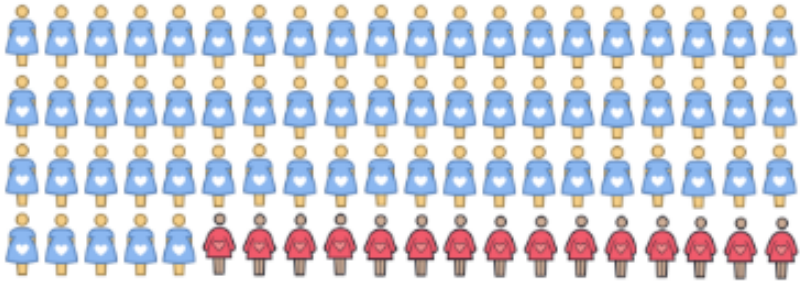


II. Systematic Review: Pre-pregnancy obesity significantly increases the risk of adverse maternal, infant and child health outcomes

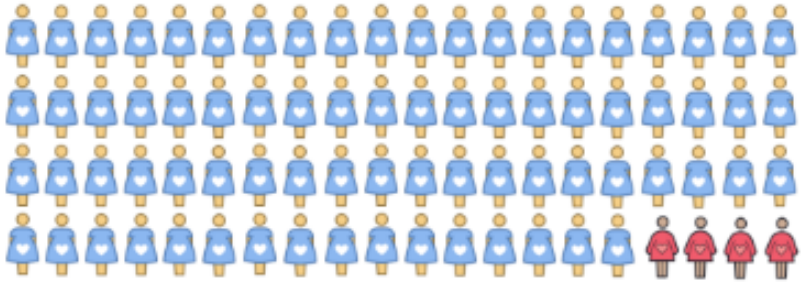
Adverse outcomes	Relative Risk	95% CI	p-values
Gestational hypertension	3.68	[2.97, 4.55]	p<0.00001
Gestational diabetes	4.31	[3.18, 5.85]	p<0.00001
Pre-eclampsia	4.06	[3.09, 5.33]	p<0.00001
Postpartum haemorrhage	1.23	[1.01, 1.50]	p=0.04
Caesarean section	1.64	[1.55, 1.73]	p<0.00001
Large-for-gestational-age	2.04	[1.65, 2.52]	p<0.00001
Macrosomia	2.48	[2.10, 2.93]	p<0.00001
Child overweight and obesity	3.75	[2.41, 5.86]	p<0.001
Child cardiometabolic risk factors	2.59	[1.93, 3.48]	p<0.00001
Child respiratory disorders (asthma)	1.66	[1.14, 2.43]	p=0.009
Child neurodevelopmental disorders	1.93	[1.30, 2.88]	p=0.001

Results (2/2)

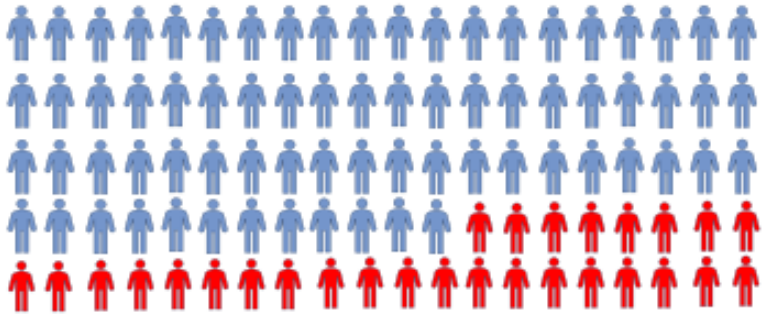
III. Risk Prediction Analyses: Predicted risk of adverse pregnancy and child health outcomes from baseline to Week 144 in ADVANCE



15% additional cases of adverse pregnancy outcomes under TAF/FTC+DTG



4% additional cases of adverse pregnancy outcomes under TDF/FTC+DTG



28% additional cases of adverse child health outcomes under TAF/FTC+DTG

7% additional cases of adverse child health outcomes under TDF/FTC+DTG

Conclusion

- Pre-conception weight gain on antiretrovirals could substantially increase adverse outcomes in pregnancy and child health, especially among women receiving TAF/FTC+DTG.
- For every 100 women becoming pregnant after three years of TAF/FTC+DTG treatment, this analysis predicted 18 additional adverse outcomes.
- New stopping rules may be required to switch women off TAF/FTC+DTG and similar combination treatments, to prevent obesity being the new epidemic among HIV patients.

Acknowledgments

I would like to thank Andrew Hill for designing the research study, and my colleagues for contributing to the data analysis. I would like to thank Ezintsha/Wits RHI for designing the ADVANCE trial, as well as the study participants.

Funding: The ADVANCE study is funded by Unitaid, U.S. Agency for International Development (USAID), the South African Medical Research Council, and ViiV Healthcare, with investigational product provided by ViiV Healthcare and Gilead Sciences.

Imperial College London · University of Liverpool · Ezintsha · Wits RHI · Unitaid Innovation in Global Health · USAID From the American People