Validating incident pregnancies among women using contraceptives and antiretrovirals

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BACKGROUND

- Up to two-thirds of pregnancies in sub-Saharan Africa are unintended, including among women living with HIV (WLHIV)[1]
- Effective contraception, including implants, can reduce unintended pregnancies
- Implant effectiveness may be reduced when combined with efavirenz, and validation of pregnancies is required[2]

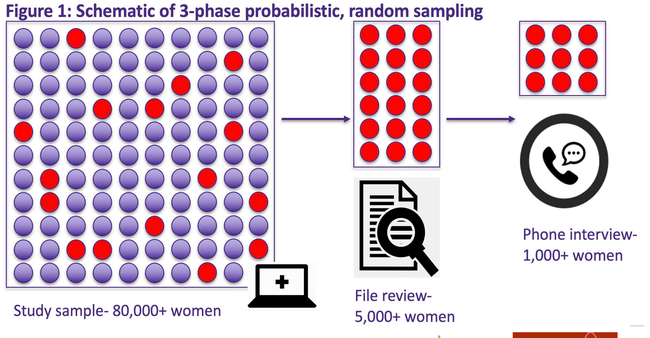
OBJECTIVES

- Replicate prior findings in a larger cohort
- Validate incident pregnancies found in electronic medical records

METHODS

- Retrospective cohort study with prospectively collected electronic medical record data from WLHIV engaged in HIV care in western Kenya
- Validation via 3-phase probabilistic sampling (Figure 1)
- Poisson regression, adjusted for repeated measures, interaction term between contraceptive method and ART regimen, program site, and covariates (e.g. age, parity, WHO clinical stage)
  - 2- and 3-phase estimates via inverse probability weighting and generalized raking
  - Multiple imputations for missing data for covariates

Figure 1: Schematic of 3-phase probabilistic, random sampling



Confirm reduced ***implant*** effectiveness with concomitant ***efavirenz*** use
- chart files and self-reports corroborated electronic medical records
- robust, novel methodology

RESULTS

- The adjusted pregnancy rate ratios (95% CIs) between implant + efavirenz-containing ART vs. implant + nevirapine-containing ART are (Tables 1-5):
  - 1st phase (electronic medical record only): 1.9 (1.6-2.4)
  - 2nd phase (electronic medical record + file review): 2.7 (1.8-4.0)
  - 3rd phase (electronic medical record + file review + phone interview): 4.7 (2.1-10.6)

Table 1: Pregnancy incidence rate and rate ratios, EMR only

Contraceptive method and ART regimen combination	Number of pregnancies/women-years of follow-up	Adjusted pregnancy rate* per 100 women-years (95% CI)	Adjusted pregnancy rate ratio* (95% CI)
Implant			
Nevirapine-based ART	151/5689	1.6 (1.4-1.9)	Ref.
Efavirenz-based ART	187/3296	3.1 (2.7-3.6)	1.9 (1.6-2.4)
No ART	112/2436	2.1 (1.8-2.6)	1.3 (1.0-1.7)
DMPA			1.8 (1.5-2.2)
Nevirapine-based ART	944/10945	5.4 (5.1-5.8)	Ref.
Efavirenz-based ART	515/5101	5.6 (5.2-6.2)	1.0 (0.9-1.2)
No ART	582/5629	4.8 (4.4-5.3)	0.90 (0.8-1.0)

Table 2: Pregnancy incidence rate and rate ratios, file review only

Contraceptive method and ART regimen combination	Number of pregnancies/women-years of follow-up	Adjusted pregnancy rate* per 100 women-years (95% CI)	Adjusted pregnancy rate ratio* (95% CI)
Implant			
Nevirapine-based ART	65/3024	2.1 (1.7-2.7)	Ref.
Efavirenz-based ART	114/2188	4.6 (3.8-5.5)	2.2 (1.6-2.9)
No ART	33/981	2.9 (2.0-4.0)	1.3 (0.9-2.1)
DMPA			
Nevirapine-based ART	156/2025	7.5 (6.4-8.8)	Ref.
Efavirenz-based ART	100/1046	8.3 (6.8-10.0)	1.1 (0.9-1.4)
No ART	118/869	10.5 (8.6-12.7)	1.4 (1.1-1.8)

Table 3: Pregnancy incidence rate and rate ratios, phone interview only

Contraceptive method and ART regimen combination	Number of pregnancies/women-years of follow-up	Adjusted pregnancy rate* per 100 women-years (95% CI)	Adjusted pregnancy rate ratio* (95% CI)
Implant			
Nevirapine-based ART	13/546	2.2 (1.2-3.8)	Ref.
Efavirenz-based ART	31/344	8.5 (5.9-12.2)	3.9 (2.0-7.5)
No ART	27/668	3.5 (2.4-5.0)	1.6 (0.8-3.1)
DMPA			
Nevirapine-based ART	26/255	10.5 (7.2-15.3)	Ref.
Efavirenz-based ART	21/141	14.5 (9.3-22.6)	1.4 (0.8-2.4)
No ART	35/283	11.0 (7.9-15.1)	1.0 (0.6-1.7)

Table 4: Pregnancy incidence rate and rate ratios, EMR + file review

Contraceptive method and ART regimen combination	Number of pregnancies/women-years of follow-up	Adjusted pregnancy rate* per 100 women-years (95% CI)	Adjusted pregnancy rate ratio* (95% CI)
Implant			
Nevirapine-based ART	151/5689	1.5 (1.1-2.0)	Ref.
Efavirenz-based ART	187/3296	4.1 (3.2-5.2)	2.7 (1.8-4.0)
No ART	112/2436	1.9 (1.2-2.9)	1.2 (0.7-2.1)
DMPA			
Nevirapine-based ART	944/10945	5.7 (3.9-8.3)	Ref.
Efavirenz-based ART	515/5101	5.0 (3.6-7.0)	0.9 (0.5-1.5)
No ART	582/5629	5.2 (3.8-7.1)	0.9 (0.6-1.5)

CONCLUSIONS

- Confirm prior findings of reduced implant effectiveness with concomitant efavirenz use
  - Women on efavirenz and implants should be prioritized for switch to dolutegravir (see CROI #129)
- Chart files and self-reports largely corroborated electronic medical records
  - Higher rates in phone interviews from recall bias?→ differential misclassification
- Robust, novel validation methodology
  - Applicable to loss to follow-up studies, Option B+/PMTCT studies
  - Overall data quality ascertainment from electronic medical records-based studies

ADDITIONAL INFORMATION

Citations

1. Hubacher et al. *Contraception* 2008
2. Patel el al. *Lancet HIV* 2015; Perry et al. *AIDS* 2014, Pyra et al. *AIDS* 2015; Vieira et al. *JAIDS* 2014; Scarsi et al. *CID* 2016; Chappell et al. *AIDS* 2017

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Table 5: Pregnancy incidence rate and rate ratios, EMR+file review+phone interview

Contraceptive method and ART regimen combination	Number of pregnancies/women-years of follow-up	Adjusted pregnancy rate* per 100 women-years (95% CI)	Adjusted pregnancy rate ratio* (95% CI)
Implant			
Nevirapine-based ART	151/5689	1.5 (0.7-3.0)	Ref.
Efavirenz-based ART	187/3296	7.0 (4.6-10.8)	4.7 (2.1-10.6)
No ART	112/2436	2.5 (1.6-4.0)	1.7 (0.7-3.9)
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