Implant vs Injectable Contraceptive Effectiveness During Efavirenz Use Varies by Breastfeeding

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BACKGROUND

- Breastfeeding (**BF**), especially exclusive BF in the 6 months post-delivery (**PD**), may prevent ovulation and provide layered protection for imperfect contraception.
- Efavirenz (**EFV**) can reduce levonorgestrel (**LNG**) levels, and in depot medroxyprogesterone acetate (**DMPA**) users may increase MPA clearance, creating potential for contraceptive failure.
- Previously, we reported for women with HIV (**WHIV**) on EFV, typical-use contraceptive effectiveness of LNG implant *vs.* DMPA injectable overall was similar in the initial 1–2yrs of use.[1]
- Herein, we evaluate effectiveness of LNG implant *vs.* DMPA injectable by BF status at initiation among WHIV on EFV-based antiretroviral treatment (**ART**).

METHODS

- We analyzed a prospective observational study of WHIV on ART who initiated LNG implant or DMPA.
- Study Population: WHIV aged 18–40 years in Malawi, within 28 days of starting LNG implant or DMPA. At entry, reported no desire of pregnancy for 4+ years.
- **Breastfeeding groups at enrollment**:
  - BF for ≤6mo PD | BF for >6mo PD | Not BF
- **Outcome**: 1st incident pregnancy. Urine pregnancy tests at entry, wk4, and every 24 weeks thereafter.
- **Analysis cohort**: those receiving EFV (600mg) at enrollment, with follow-up censored at the earliest of: LNG/DMPA discontinuation (d/c), tubal ligation, last visit, 28 days after EFV d/c.
- **Within BF groups**, we estimated 48- and 96-wk pregnancy risks and risk differences (RDs) for LNG *vs.* DMPA using the Kaplan-Meier method with inverse probability weighting (**IPW**) for exposure and censoring. Bootstrap 95% CIs were constructed.
- **Covariates in IPW models:** age, gravidity, coital frequency, facility type, time since HIV diagnosis, education, roof material, plans for future children, time since last pregnancy (non-BF group). Censoring weights only: enrollment contraceptive (LNG/DMPA), *time-varying:* pregnancy intent, follow-up (24-wk bins).

Contraceptive studies should carefully consider that breastfeeding (BF), particularly exclusive BF, can provide layered protection from incident pregnancy.

RESULTS

We analyzed 1,178 participants:

463 BF ≤6mo PD | 281 BF >6mo PD | 434 not BF

Enrollment period: Aug 2017–Mar 2020.

At entry, median age: 30 (*IQR:* 26, 34), gravidity: 3 (2, 4), 63% were BF, 45% planned for no future children.

At entry, report of coitus in the past week varied by BF status: *BF ≤6mo PD*: 39%, *BF >6mo PD*: 55%, *not BF*: 59%, chi-square p<.001.

Baseline features were mostly balanced between LNG and DMPA users and were addressed via IPW.

Initially, pregnancy risk was low among BF women (**Figure**).

At 48 weeks, LNG implant was associated with lower pregnancy risk than DMPA in 2 of 3 BF groups (**Table**).

At 96 weeks, pregnancy risks appeared similar for the implant and DMPA within each BF group (**Table**).

Figure. IPW Kaplan-Meier estimates, by BF group

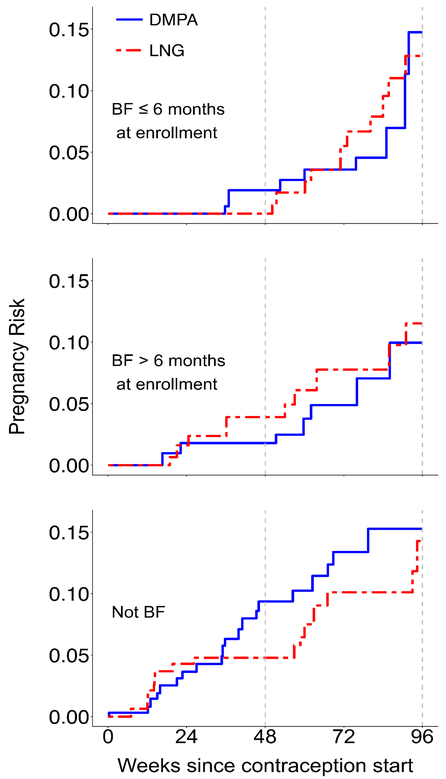
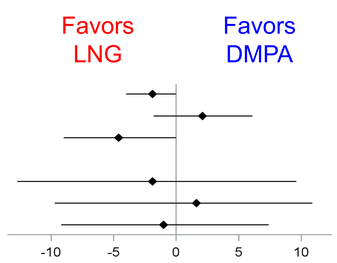


Table. Contraceptive effectiveness for WHIV on efavirenz, by breastfeeding group

	Crude: Pregnancies / Sample Size		*IPW* Pregnancy Risk Estimate		*IPW* Risk Difference [95% CI]
Time Period *BF group*	LNG	DMPA	LNG	DMPA	LNG - DMPA
48-weeks					
BF ≤6mo PD	0 / 211	2 / 252	0.0%	1.9%	-1.9% [-4.0, 0.0%]
BF >6mo PD	4 / 168	2 / 113	3.9%	1.8%	2.1% [-1.8, 6.1%]
Not BF	9 / 212	15 / 222	4.8%	9.4%	-4.6% [-9.0, 0.0%]
96-weeks					
BF ≤6mo PD	11 / 211	8 / 252	12.8%	14.8%	-1.9% [-12.7, 9.6%]
BF >6mo PD	9 / 168	7 / 113	11.5%	10.0%	1.6% [-9.7, 10.9%]
Not BF	16 / 212	20 / 222	14.3%	15.3%	-1.0% [-9.2, 7.4%]

Risk differences, by BF group



CONCLUSIONS

- Within BF subgroups, 48-week pregnancy risk was lower for LNG implant *vs.* DMPA in those BF ≤6mo PD and those not BF at entry, whereas 96-week risk was comparable for LNG vs. DMPA across BF groups.
- Contraceptive effectiveness studies should account for the impact of enrolling women in the first 6 months post delivery, when we observed low pregnancy incidence and less sexual activity.

REFERENCES

1. Mollan KR et al. Effectiveness of levonorgestrel implant and depot medroxyprogesterone acetate injectable for women with HIV on efavirenz. *AIDS*. 2025 Jul 15;39(9):1197-1203

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PLAIN LANGUAGE SUMMARY

For women on efavirenz and seeking the DMPA injectable or LNG implant, contraceptive effectiveness during typical use varied by breastfeeding status at DMPA/LNG initiation. Those who were not breastfeeding were at higher risk of contraceptive failure.

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