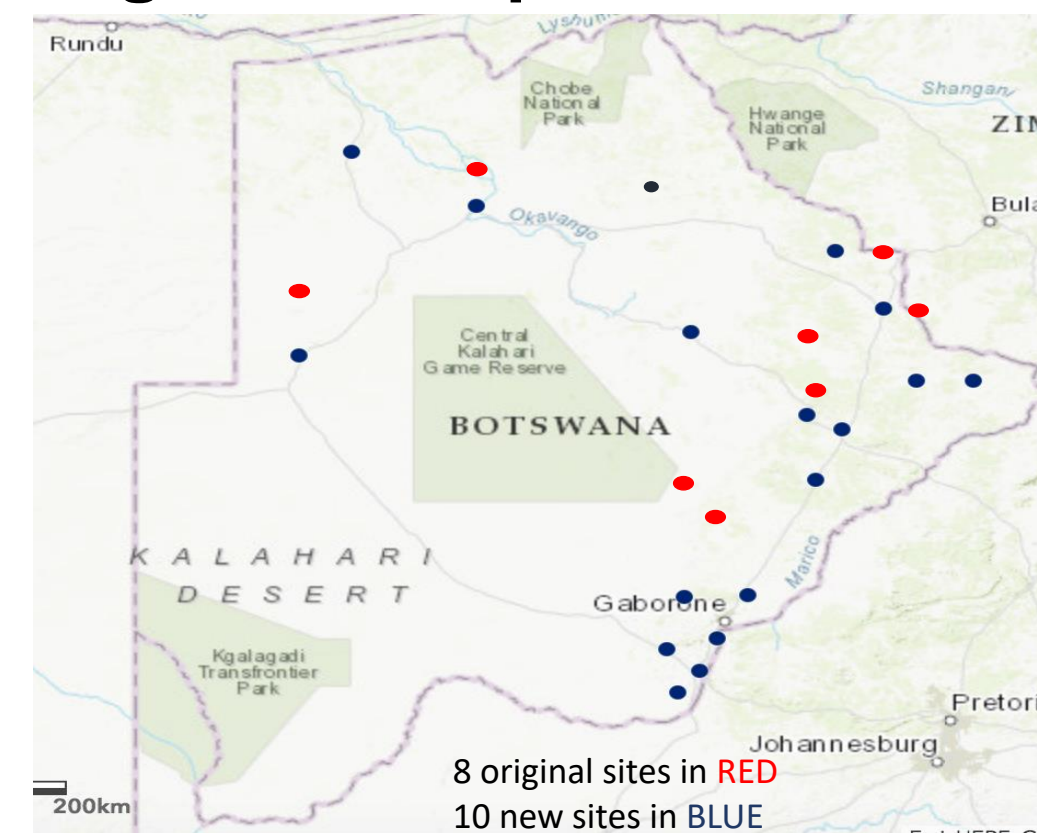


Update on Neural Tube Defects with Antiretroviral Exposure in the Tsepamo Study, Botswana

BACKGROUND

- Botswana began using Dolutegravir (DTG) as first-line antiretroviral treatment (ART) in 2016. In May 2018, the Tsepamo Study first reported a possible safety signal for neural tube defects (NTDs) associated with DTG exposure at conception.
- Original signal: 0.94% NTDs for conception DTG (N=426) vs. 0.12% for other ART (N=11,300)
- With additional DTG exposure data, the signal declined.
- March 2021: 0.15% NTDs for conception DTG (N=5,860) vs. 0.10% (22,475)
- We now report updated data collected in Tsepamo through March 2022.**

Figure 1. Tsepamo Sites



METHODS

- We conducted birth outcomes surveillance at government hospitals in Botswana, currently covering ~70% of all births in the country (Figure 1)
- Midwives perform surface examinations of all live births and stillbirths and described abnormalities.
- Research assistants photographed major abnormalities after maternal consent, which were reviewed by a birth defects expert blinded to exposures
- Prevalence of NTDs was determined by maternal HIV and antiretroviral exposure status (95%CI by Wilson method) and the primary analysis evaluated prevalence differences by exposure status (95%CI by Newcombe method).

STUDY POPULATION

- Between Aug 15, 2014 and March 31, 2022, 224,251 deliveries occurred at study sites. This analysis includes 223,797 (99.8%) with an evaluable infant surface exam.
 - 9,460 were exposed to DTG from conception
 - 23,664 were exposed to non-DTG ART from conception (14,432 specifically to EFV)
 - 6,551 started DTG during pregnancy
 - 170,723 were born to women without HIV

Figure 2. Trends in NTD Prevalence (and 95% CI) with a) Dolutegravir (DTG) at conception, b) non-DTG ART at conception, c) EFV at conception and d) women without HIV March 2021-March 2022

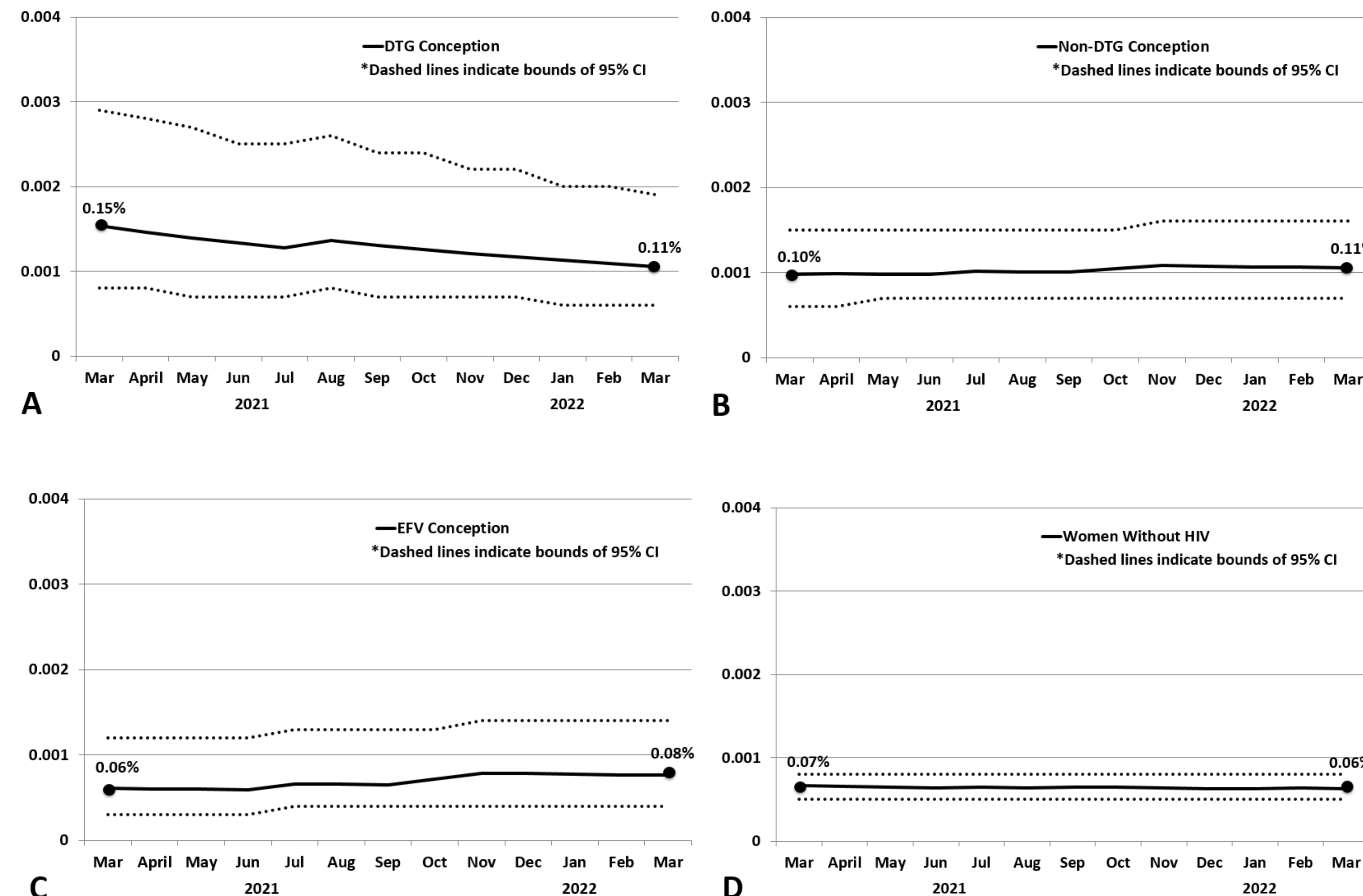


Table 1. Prevalence Difference of Neural Tube Defects by ARV and HIV Exposure Categories

Exposure group vs. Comparison group	Prevalence Difference (%) (95% CI)
DTG at conception vs. Non-DTG at conception	0.00 (-0.07, 0.10)
DTG at conception vs. EFV at conception	0.03 (-0.05, 0.12)
DTG at conception vs. DTG started in pregnancy	0.04 (-0.06, 0.14)
DTG at conception vs. Women without HIV	0.04 (-0.01, 0.13)

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RESULTS

- Since March 2021 (last Tsepamo update) (Figure 2)**
 - 32,819 additional births were recorded, including 3,600 additional DTG conception exposures.
 - 16 additional NTDs were identified:
 - 1 with DTG-conception exposure
 - 3 with non-DTG conception exposure
 - 1 with DTG started during pregnancy
 - 11 among women without HIV
 - The additional NTD with DTG-conception exposure was anencephaly (no photo)
- Since August 2014 (entire study)**
 - In total:** 156 (0.07%, 95% CI 0.06%, 0.08%) NTDs identified (100 with photo, 56 by description only).
 - DTG at conception:** 10 NTDs among 9,460 exposures (0.11%; 95%CI 0.06%, 0.19%)
 - Non-DTG ART at conception:** 25 NTDs among 23,664 exposures (0.11%; 95%CI 0.07%, 0.16%)
 - EFV at conception:** 11 NTDs among 14,432 exposures (0.08%; 95%CI 0.04%, 0.14%)
 - DTG during pregnancy:** 4 NTDs among 6,551 exposures (0.06%; 95%CI 0.02%, 0.16%)
 - Women without HIV:** 108 NTDs among 170,723 exposures (0.07%; 95%CI 0.05, 0.08%)

CONCLUSIONS

- The prevalence of NTDs among infants born to women on dolutegravir at conception has declined slightly to 0.11% and does not substantially differ from other exposure groups.
- These data support existing WHO guidelines that recommend DTG as first-line for use in all adults, regardless of reproductive potential