



SOUTHERN AFRICAN HIV CLINICIANS SOCIETY

# Tsepamo: DTG Exposure at Conception Associated With Small but Stabilizing Elevation in Neural Tube Defect Prevalence in Analysis Through April 2020



## Tsepamo Update (April 2020): Background

- Tsepamo study: birth outcomes surveillance study performed at government maternity sites in Botswana since August 2014, with primary aim of evaluating NTD prevalence associated with ARV exposure at conception<sup>[1]</sup>
- In May 2018, an unplanned analysis of the Tsepamo study observed increased NTD prevalence among infants born to women receiving DTG at conception<sup>[1]</sup>
  - NTD prevalence with DTG vs non-DTG ART at conception: 0.94% vs 0.12%
- Updated analysis of data through April 2019 reported a lower NTD prevalence among women who received DTG at conception, but still higher than in other exposure groups<sup>[2]</sup>
  - NTD prevalence with DTG vs non-DTG ART: 0.30% vs 0.10%; prevalence difference: 0.20% (95% CI: 0.01% to 0.59%)
- Current report presents analysis of data collected through April 30, 2020, for the Tsepamo study<sup>[3]</sup>

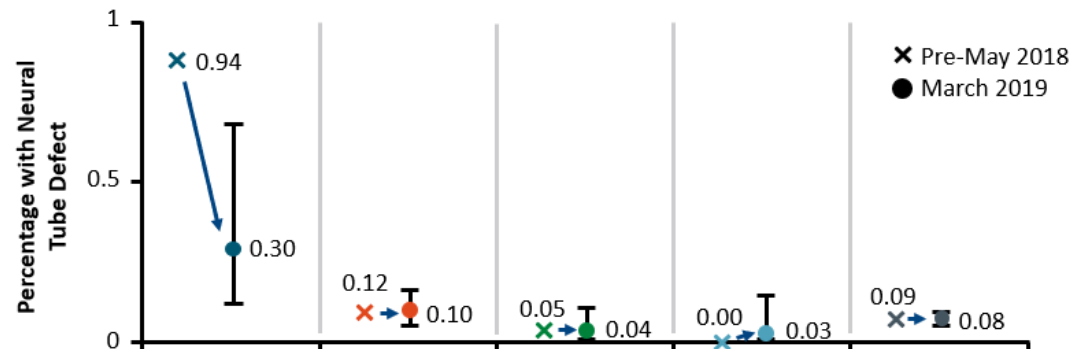


## Tsepamo Update (April 2020): Study Design

- Birth outcomes surveillance study among Botswanan women  $\pm$  HIV infection; initiated August 2014<sup>[1,2]</sup>
  - Original plan: assess NTD prevalence in live-born infants/stillbirths among women receiving EFV at conception
  - Comparative analysis expanded to include DTG in response to (1) 2016 update to Botswana adult first-line ART guidelines recommending DTG vs EFV (both plus FTC/TDF), and (2) 2018 WHO HIV guidelines committee request for preliminary data on pregnancy outcomes in women initiating DTG before pregnancy
- Data abstracted from obstetric cards of all in-hospital deliveries<sup>[1,2]</sup>
  - Government midwives trained to assess congenital abnormalities performed infant surface exams; abnormalities photographed with maternal consent and reviewed by external medical geneticist (blinded to drug exposure history)
  - From July to September 2018, surveillance area expanded from 8 to 18 hospitals to capture  $\sim$  72% of all births in Botswana; from September 2019, 16 surveillance sites maintained, capturing  $\sim$  70% of all births
- Current analysis assesses prevalence of NTDs with DTG exposure at conception vs other ART exposure groups using data collected through April 30, 2020<sup>[3]</sup>



# Prevalence of NTDs by ARV Exposure in Earlier Analyses of Tsepamo Study



	Conception			Pregnancy	HIV Negative (n = 89,372)
	DTG (n = 1683)	Non-DTG (n = 14,792)	EFV (n = 7959)	DTG (n = 3840)	
Total NTDs per exposures, n/N	5/1683	15/14792	3/7959	1/3840	70/89372
Prevalence difference, % (95% CI)	Ref	0.20 (0.01-0.59)	0.26 (0.07-0.66)	0.27 (0.06-0.67)	0.22 (0.05-0.62)
NTDs per exposures after May 2018, n/N	1/1275	1/3492	0/2172	1/1028	9/23,315



## Tsepamo Update (April 2020): Additional NTDs and ARV Exposures From April 1, 2019, to April 30, 2020

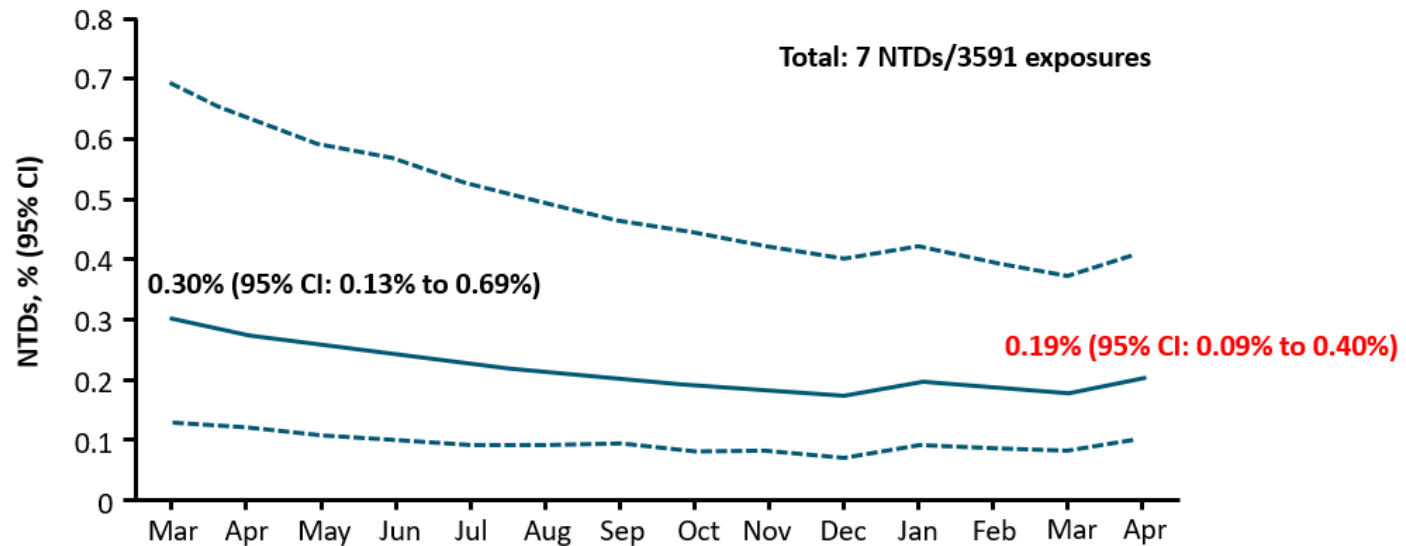
Additional NTDs and Exposures, n	NTDs	Exposures
Total	28	39,200
DTG conception	2	1908
Non-DTG conception	6	4569
EFV conception	5	2999
DTG started in pregnancy	1	741
Women without HIV	17	30,258

- 2 new NTD cases observed with exposure to DTG at conception, each with photo
  - Both infants born to women with no other medications at conception, no preconception folate, no medical history

Characteristics	New NTD Cases With DTG Conception Exposure	
	Case 1	Case 2
NTD	Lumbosacral myelomeningocele (spina bifida)	Encephalocele
Maternal age, yrs	32	27
Maternal weight	107 kg (at 21 wks gestational age)	58 kg (at 13 wks gestational age)
Gravidity/parity	G3P2	G3P2
DTG start date	June 1, 2018	June 24, 2016
LMP	April 19, 2019	July 13, 2019
Delivery date	January 16, 2020	April 20, 2020

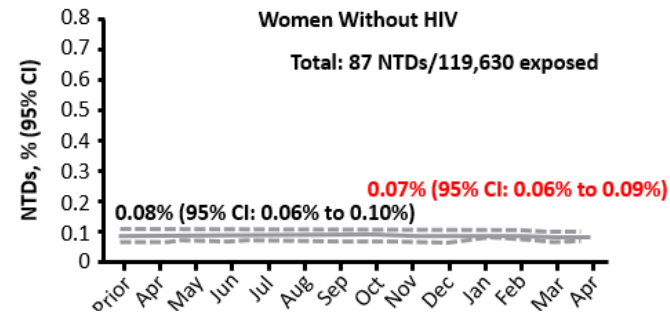
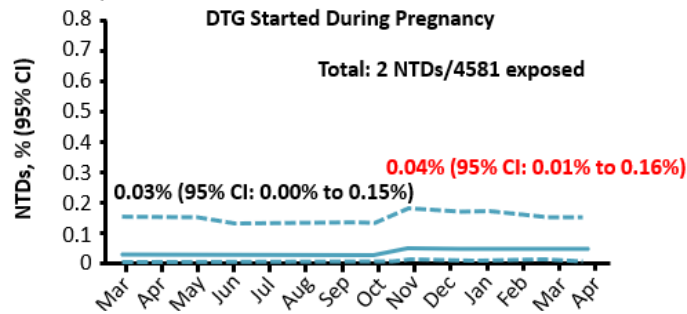
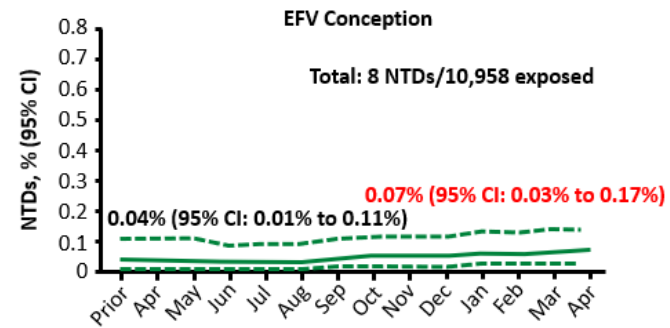
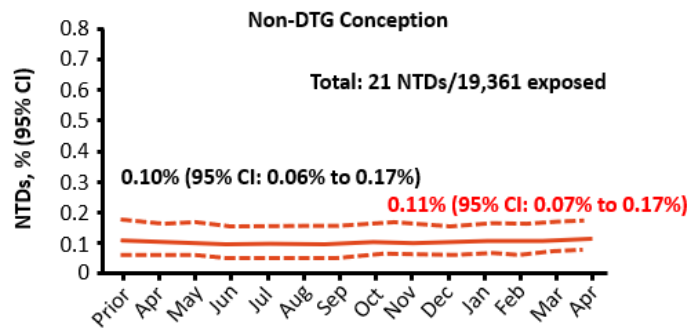


## Tsepamo Update (April 2020): NTD Prevalence With DTG at Conception From April 1, 2019, to April 30, 2020





# Tsepamo Update (April 2020): NTD Prevalence by Exposure From April 1, 2019, to April 30, 2020





## Tsepamo Update (April 2020): Prevalence Difference of NTDs by ARV Exposure

NTD Outcome by Analysis, % (95% CI)	Conception			Pregnancy	HIV Negative
	DTG	Non-DTG	EFV	DTG	
<b>Results as of March 2019</b>	n = 1683	n = 14,792	n = 7959	n = 3840	n = 89,372
▪ NTD prevalence	0.30 (0.13-0.69)	0.10 (0.06-0.17)	0.04 (0.01-0.11)	0.03 (0-0.15)	0.08 (0.06-0.10)
▪ Prevalence difference	Ref	0.20 (0.01-0.59)	0.26 (0.07-0.66)	0.27 (0.06-0.67)	0.22 (0.05-0.62)
<b>Results as of April 2020</b>	n = 3591	n = 19,361	n = 10,958	n = 4581	n = 119,630
▪ NTD prevalence	0.19 (0.09-0.40)	0.11 (0.07-0.17)	0.07 (0.03-0.17)	0.04 (0.01-0.16)	0.07 (0.06-0.09)
▪ Prevalence difference	Ref	0.09 (-0.03 to 0.30)	0.12 (0-0.32)	0.15 (0-0.36)	0.12 (0.01-0.32)





## Tsepamo Update (April 2020): Conclusions

In this current analysis of the Tsepamo birth outcomes surveillance study with data collected through April 30, 2020, the observed NTD prevalence among infants born to women with DTG exposure at conception appears to be stabilizing at ~ 2 cases per 1000 after decreasing from the initial analysis in May 2018

- Initial analysis (May 2018): DTG vs non-DTG ART at conception, 0.94% vs 0.12%
- Updated analysis (April 2019): 0.30% vs 0.10%; prevalence difference: 0.20% (95% CI: 0.01% to 0.59%)
- Current analysis (April 30, 2020): 0.19% vs 0.11%; prevalence difference: 0.09% (95% CI: -0.03% to 0.30%)