Pregnancy and Neonatal Outcomes Following Prenatal Exposure to Cabotegravir (CAB): Data from The Antiretroviral Pregnancy Registry (APR)

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Disclosures

Dr. Vani Vannappagari is a full-time employee of ViiV Healthcare.

Antiretroviral Pregnancy Registry (APR)

- The APR is an international, prospective exposure-registration cohort study based on voluntary reporting by health-care providers (HCPs), ongoing since 1989
  - Overseen by an independent Advisory Committee
  - Currently 27 sponsoring ARV manufacturers
  - Covers ARVs used for HIV treatment, prevention, and HBV treatment,
  - While the pregnancies reported are predominantly from the US, the APR has received reports from 75 countries
- Designed to assist clinicians and pregnant individuals in weighing potential risks and benefits of ARV use during pregnancy
- Primary Objective:
  - **Monitor prenatal exposures to ARV drugs to detect potential increase in the risk for birth defects and provide early warning signals of major teratogenicity**

13th IAS Conference on HIV Science; July 13-17, 2025; Kigali, Rwanda

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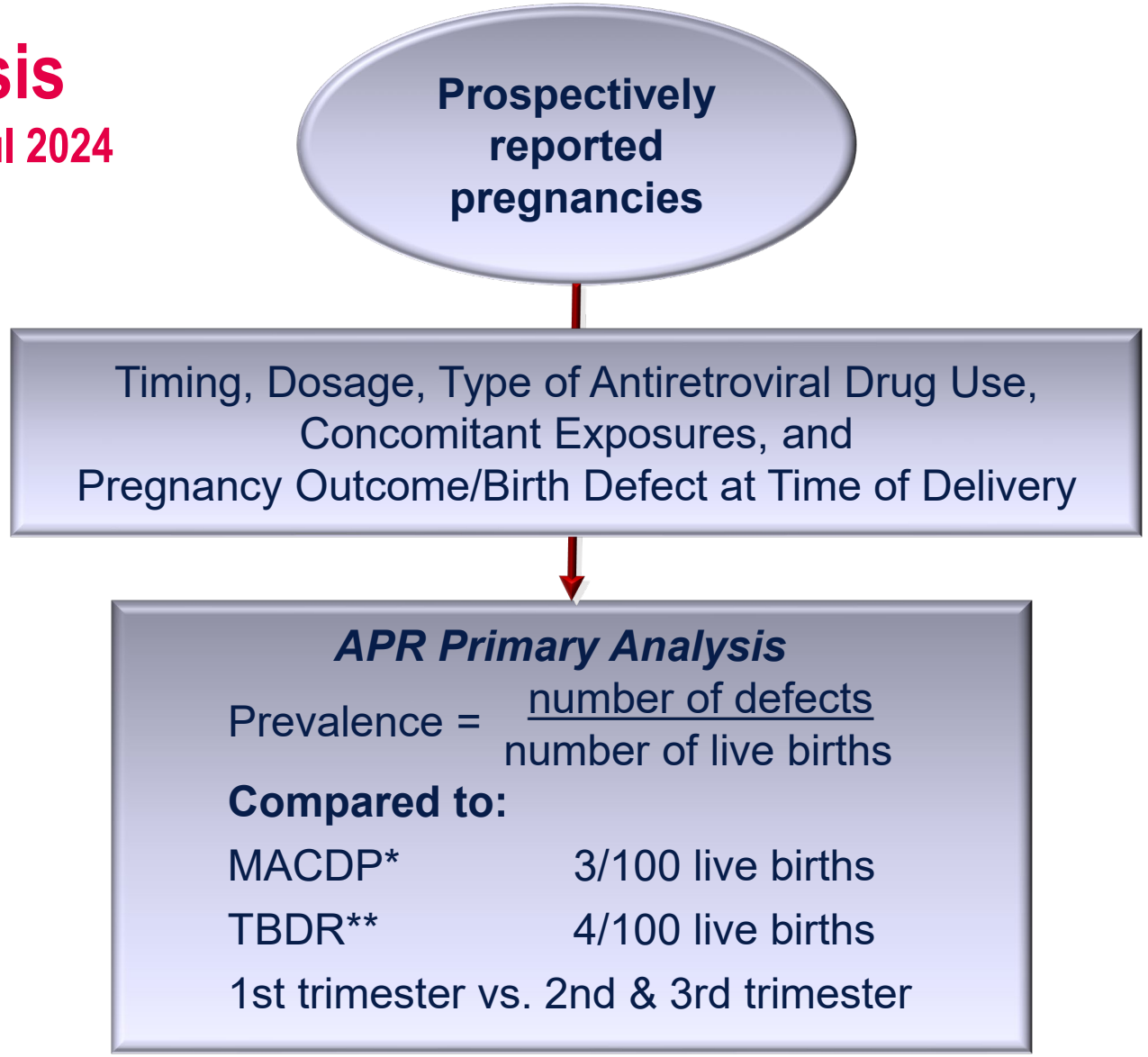
Primary Analysis

APR Data through 31 Jul 2024



** MACDP = Metropolitan Atlanta Congenital Defects Program; TBDR** = Texas Birth Defects Registry*

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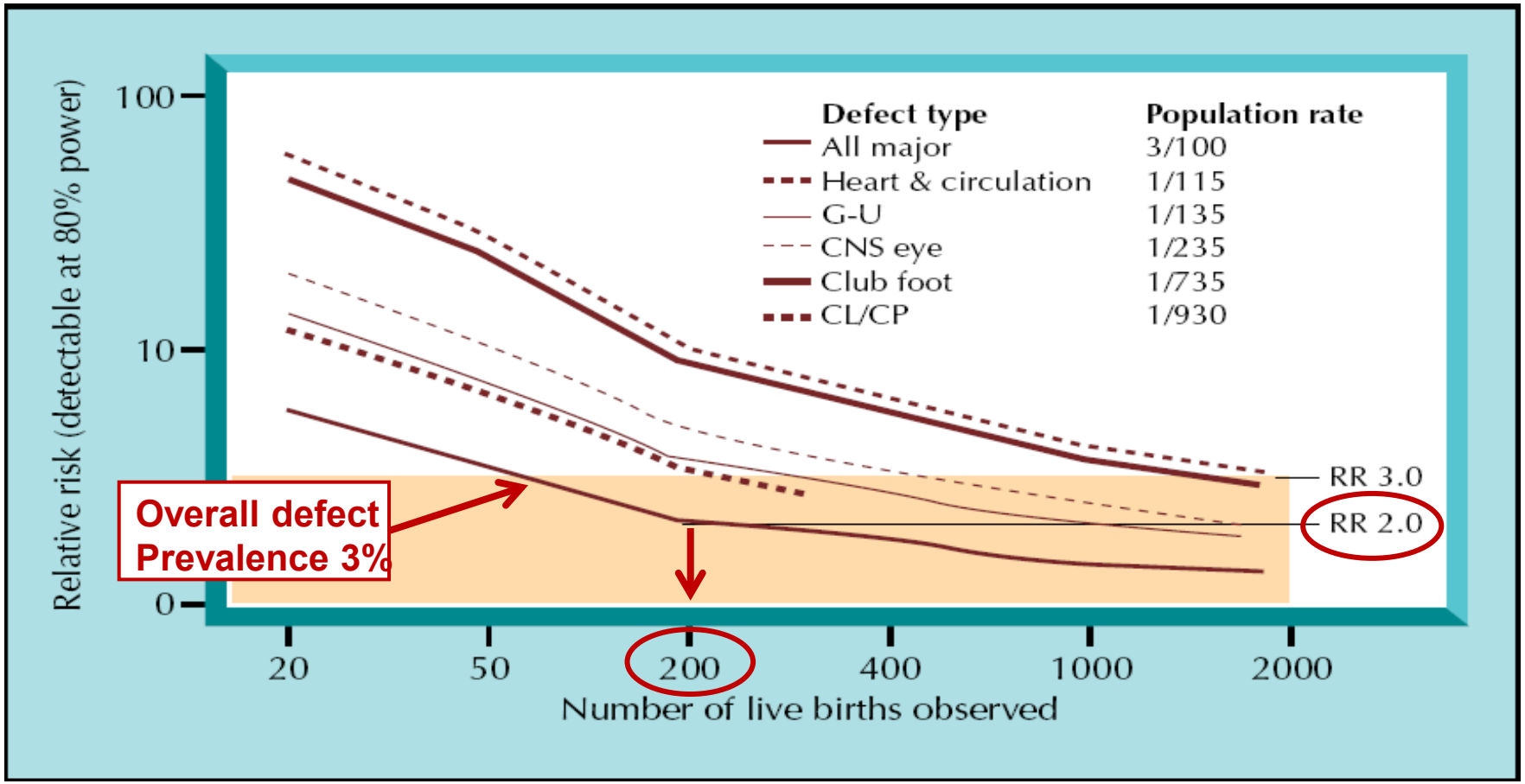
Sample Size is Dependent on Defect Prevalence in General Population

- 200 first trimester exposures are needed to detect a 2-fold ↑ in overall birth defects (prevalence 3%)



Watts DH. Curr HIV/AIDS Rep 2007;4:135-140

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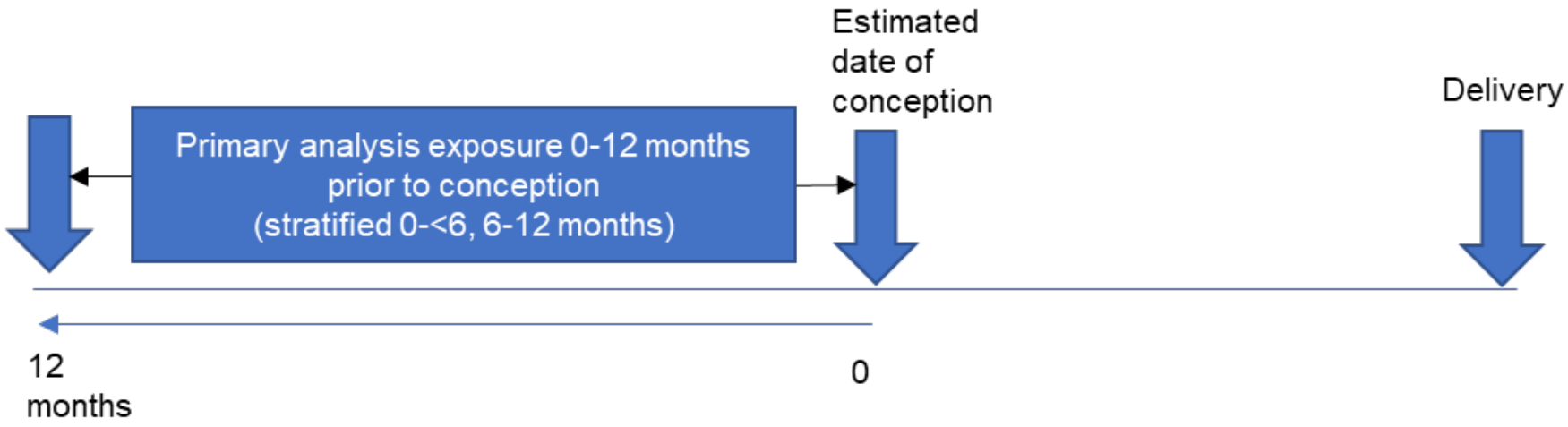
CAB-LA in Pregnancy

- CAB+RPV LA
  - The only complete LA injectable regimen approved for treatment of HIV in virologically suppressed PWH
- CAB LA
  - The first LA agent approved for persons who could benefit from PrEP
- Given long-acting nature of CAB-LA, an individual could have stopped CAB-LA months before getting pregnant but still be “exposed” at conception, complicating collection of exposure data.



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Overall APR Birth Defect Rates

The 24,443 evaluable pregnancies resulted in 24,869 fetal outcomes including 23,129 live birth (including 419 multiple births).

Trimester of Earliest Exposure	Live Births (N)	Birth Defects (N)	Prevalence Ratio	95% CI	Relative Risk (95% CI)
First Trimester	12,853	382	**3.0%**	2.7, 3.3	**1.05** (0.90, 1.21)
Second/Third Trimester	10,273	292	**2.8%**	2.5, 3.2	
Any Trimester	23,129	676	**2.9%**	2.7, 3.1	---

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Demographic Characteristics of Pregnant Individuals Exposed to CAB LA (data through July, 2024)

Total Pregnancies Reported	42
Indication for CAB LA at Start of Pregnancy	
HIV Treatment	32 (76.2%)
HIV Prevention	
Pre-Exposure Prophylaxis (PrEP)	10 (23.8%)
CD4+ T-cell Categories at Start of Pregnancy	
≥ 500 cells/μL	15 (35.7%)
200-499 cells/μL	5 (11.9%)
<200 cells/μL	2 (4.8%)
Missing / Unknown	20 (47.6%)

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Demographic Characteristics of Pregnant Individuals Exposed to CAB LA

Total pregnancies, N	**42**
Maternal age at conception (years)	
Mean	29.5
Median	**29**
Range, min-max	21-39
Country of reporting, n (%)	
USA	21 (50.0%)
Uganda	7 (16.7%)
Kenya	4 (9.5%)
UK	2 (4.8%)
Russia	2 (4.8%)
Spain	2 (4.8%)
South Africa	2 (4.8%)
Canada	1 (2.4%)
Zimbabwe	1 (2.4%)
Timing of earliest exposure to CAB, n (%)	
1st trimester	1 (2.4%)
2nd trimester	1 (2.4%)
3rd trimester	1 (2.4%)
Pre-conception CAB exposure (for those not on CAB at the time of conception)	
0-6 months prior to conception	27 (64.3%)
6-12 months prior to conception	12 (28.6%)

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Pregnancy Outcomes

Total Outcomes, N	**43**
Live births	35* (81.4%) infants
Stillbirths	1 (2.3%)
Spontaneous abortions	3 (7.0%)
Induced abortions	4 (9.3%)

* One twin birth

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Neonatal Outcomes With Prenatal Exposure to CAB (Among Singleton, Live Births Without Defects, N=33)

					With only pre-conception exposure	
	Overall	**1st trimester earliest exposure**	**2nd trimester earliest exposure**	**3rd trimester earliest exposure**	**Earliest exposure 0-6 months prior to conception**	**Earliest exposure 6-12 months prior to conception**
Number of Live, Singleton Newborns Without Defects	33	1	1	1	23	7
Gestational age						
≥37 weeks	27 (81.8)	1 (100)	1 (100)	1 (100)	20 (87.0)	4 (57.1)
<37 weeks (preterm)	**5 (15.2)**	0	0	0	3 (13.0)	2 (28.6)
Missing	1 (3.0)	0	0	0	0	1 (14.3)
Birth weight						
≥2500 grams	22 (66.7)	1 (100)	1 (100)	1 (100)	16 (69.6)	3 (42.9)
<2500 grams (LBW)	**3 (9.1)**	0	0	0	2 (8.7)	1 (14.3)
<1500 grams (VLBW)	**3 (9.1)**	0	0	0	2 (8.7)	1 (14.3)
Missing	5 (15.2)	0	0	0	3 (13.0)	2 (28.6)

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Birth Defect Case – Among live births (n=35)

N=1	Birth Defect	Timing of Earliest Exposure to CAB	Other ARV Drug Exposures/ Timing of Earliest Exposure	Other Exposures	Pregnancy Outcome	Gestational Age/Birth Weight
1	Congenital Ptosis	6-12 months prior to conception	Rilpivirine/prior to conception Darunavir+cobicistat+ emtricitabine+ tenofovir alafenamide/ Unknown	Folic acid	Live birth	37 weeks 2380 grams

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Summary of Results

- 42 pregnancies with exposure to CAB LA resulted in 43 outcomes, including 35 live births
  - 39 had pre-conception exposure to CAB, 1 during the 1st trimester, 1 during the 2nd trimester, and 1 during the 3rd trimester
- Among 35 live births, one birth defect of congenital ptosis was reported
- Among 33 singleton, live births without defects, 5 were preterm, 3 had LBW and 3 had VLBW

Conclusions

- The data, though not definitive, shows no significant concern
  - The limited number of pregnancies warrants cautious interpretation
- These data complement the PK (n=50) and safety data (n=325) reported from pregnancies from the HPTN 084 (Cab LA for PrEP) pregnancy sub-study
- Subsequent reports with further data accrual on CAB usage during pregnancy will allow more detailed analyses of the pregnancy outcomes
- Healthcare providers are encouraged to continue to report pregnancies with ARV exposures prospectively to the APR, especially those involving newer ARVs [www.APRegistry.com]

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Advisory Committee Consensus

We reviewed all reported defects from the prospective registry, informed by clinical studies and retrospective reports of antiretroviral exposure. **We find no significant increases in frequency of birth defects with first trimester exposures when organogenesis occurs compared to second and third trimester exposures. In addition, we have not identified any defect pattern.** While the Registry population exposed and monitored to date is not sufficient to detect an increase in the risk of relatively rare defects, these findings should provide some assurance for patient counseling and formulating patient care plans for pregnant individuals or those considering pregnancy. Potential limitations of registries should be recognized.

The Registry is ongoing. Given the use of new therapies about which data are still accumulating, **health care providers are strongly encouraged to report all eligible people to the Registry** at **SM_APR@APRegistry.com** via the data forms available at **www.APRegistry.com**

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Acknowledgements

- Pregnant individual contributing data to the Registry
- The outstanding efforts of all the HCPs submitting cases to the APR, especially the dedication and participation of our 100% reporting Health Care Providers.
- The valuable contributions of the APR Steering Committee and
- The staff at the Coordinating Center at Syneos Health

Independent Advisory Committee Members

- **Cynthia Holcroft-Argani,** MD, Johns Hopkins Medical Center
- **Martina Badell**, MD, Emory University Hospital Midtown Perinatal Center
- **Karen Beckerman,** MD, Zucker School of Medicine at Hofstra University, Staten Island University Hospital
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- **Andreas Pikis,** MD, Food and Drug Administration
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