



Creating a Better Understanding of Pregnancy Outcomes in Sub Saharan Africa: MTN-042B

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DELIVER will provide critical information on the safety and acceptability of HIV prevention products used during pregnancy

Participants who use TRUVADA® oral tablet daily and insert the dapivirine vaginal matrix ring (25 mg) once every 4 weeks **will experience similar distributions of pregnancy outcomes to the general population**

???



Global maternal & neonatal health indicators



MATERNAL, NEWBORN, CHILD & ADOLESCENT HEALTH
Data portal

All Indicators ▶ All Documents ▶

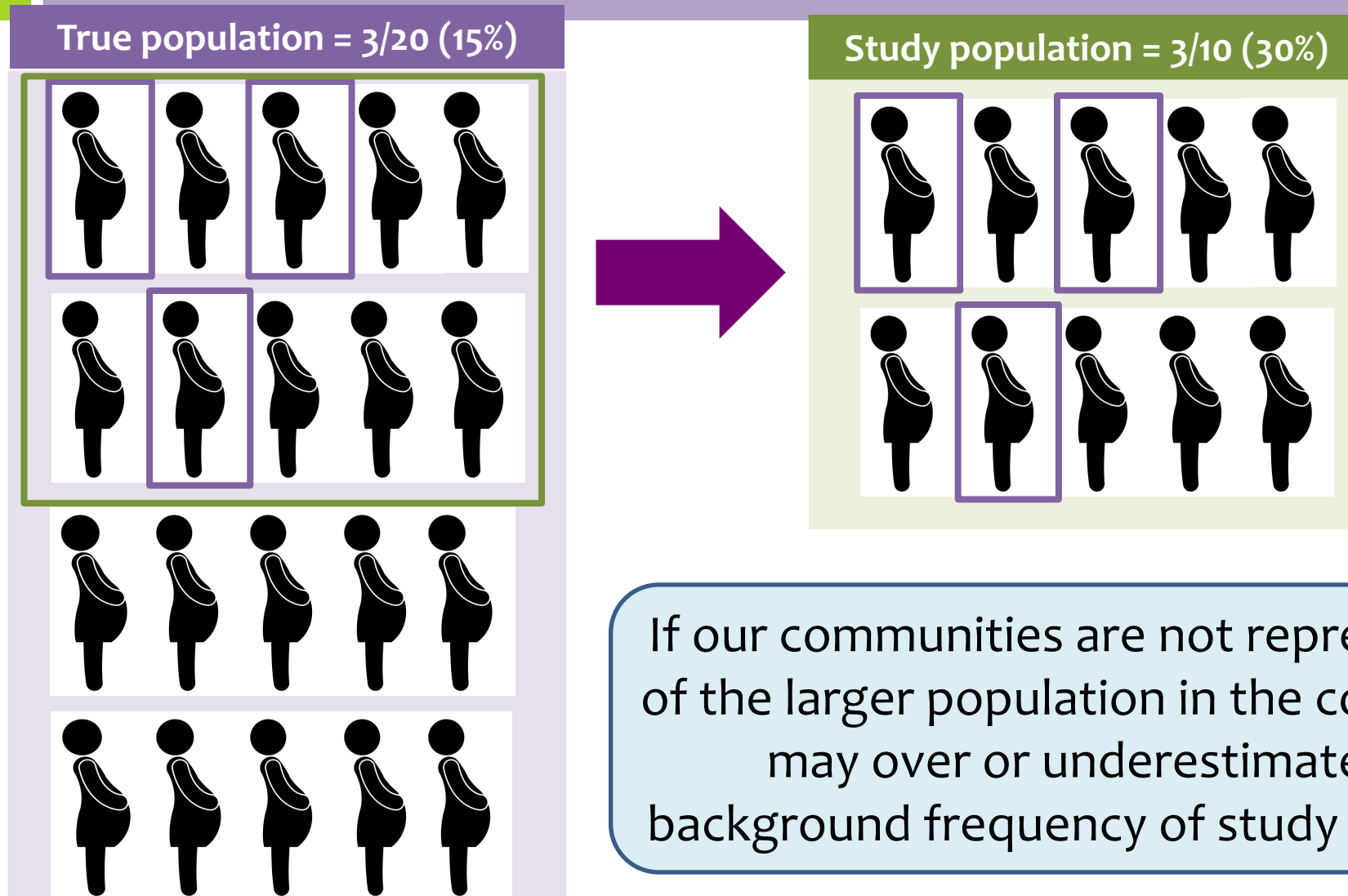
Mother and Newborn Information for Tracking Outcomes and Results (MoNITOR)

The DHS Program

unicef | MICS

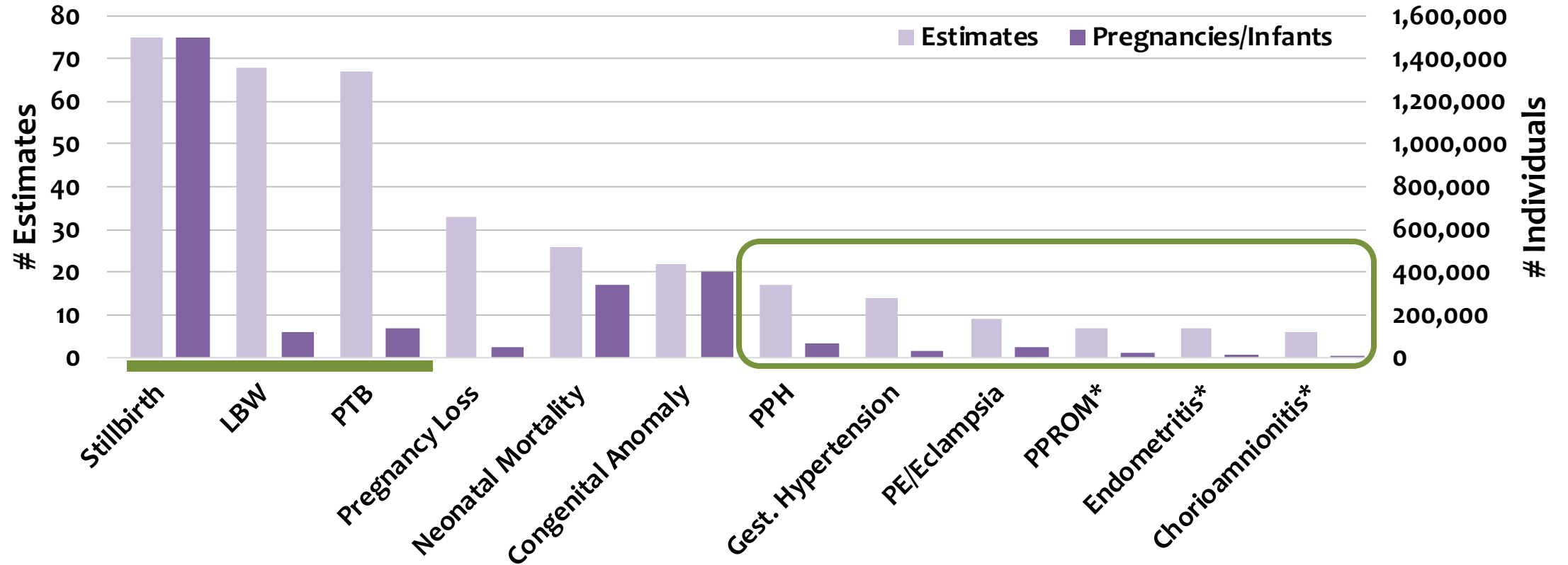
- National data are available on key maternal and neonatal health indicators
 - Maternal mortality
 - Neonatal mortality
 - Low birth weight

While national data are helpful, they may not reflect the prevalence in communities participating in research

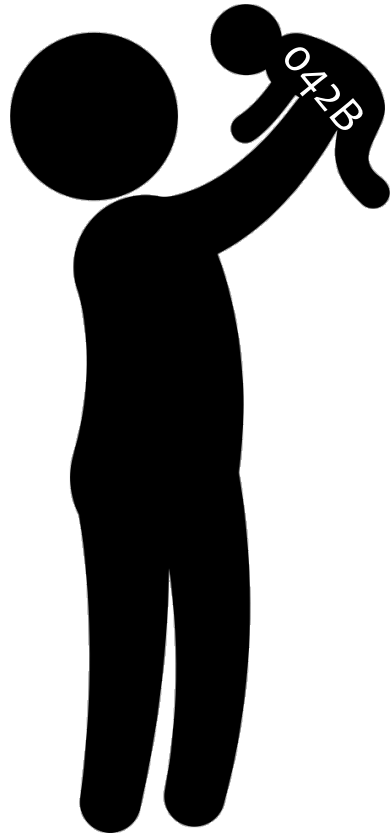


Can published research studies inform estimates of pregnancy outcomes & complications?

Systematic Review - Number of Prevalence Estimates & Individuals



MTN-042B Study Design



- **Study Design:** Multi-site, chart review, cross-sectional study
- **Study Population:** **All women** delivering or receiving immediate postpartum care (within one week of delivery) at one or two facilities affiliated with each of the 4 sites, a primary care facility and a referral facility
- **Duration:** 8 weeks of abstraction at each delivery site

To determine the frequency of...

- Pregnancy & maternal outcomes

- Full term live birth (≥ 37 weeks)
- Premature live birth (< 37 weeks)
- Stillbirth/intrauterine fetal demise (≥ 20 weeks)
- Maternal death

- Pregnancy complications

- Fever of unclear etiology
- Chorioamnionitis
- Postpartum endometritis
- Postpartum hemorrhage
- Gestational hypertensive disorder (gestational hypertension, pre-eclampsia, eclampsia)

- Infant outcomes & complications

- Neonatal death (after delivery, before mother is discharged)
- Neonatal ICU admission
- Congenital malformations

The heroes of MTN-042B

Blantyre



Chimwemwe Khonjera, Lonjezo Jemi, Hawah Mbali, pictured with Noel Kayange, Bonus Makanani, Frank Taulo

MU-JHU-Kampala



Birungi Harriet Mawanda, Kemigisa Everlyn, Atwebembire Prossy, Mirembe Ritah, Ekel Irene, Amanyana Spincious, Oloo Keziron Eric, Atukunda Mediaas, Naluggwa Abisagi, Helen Agoile Unzia, Annett Miwanda

WRHI - Shandukani



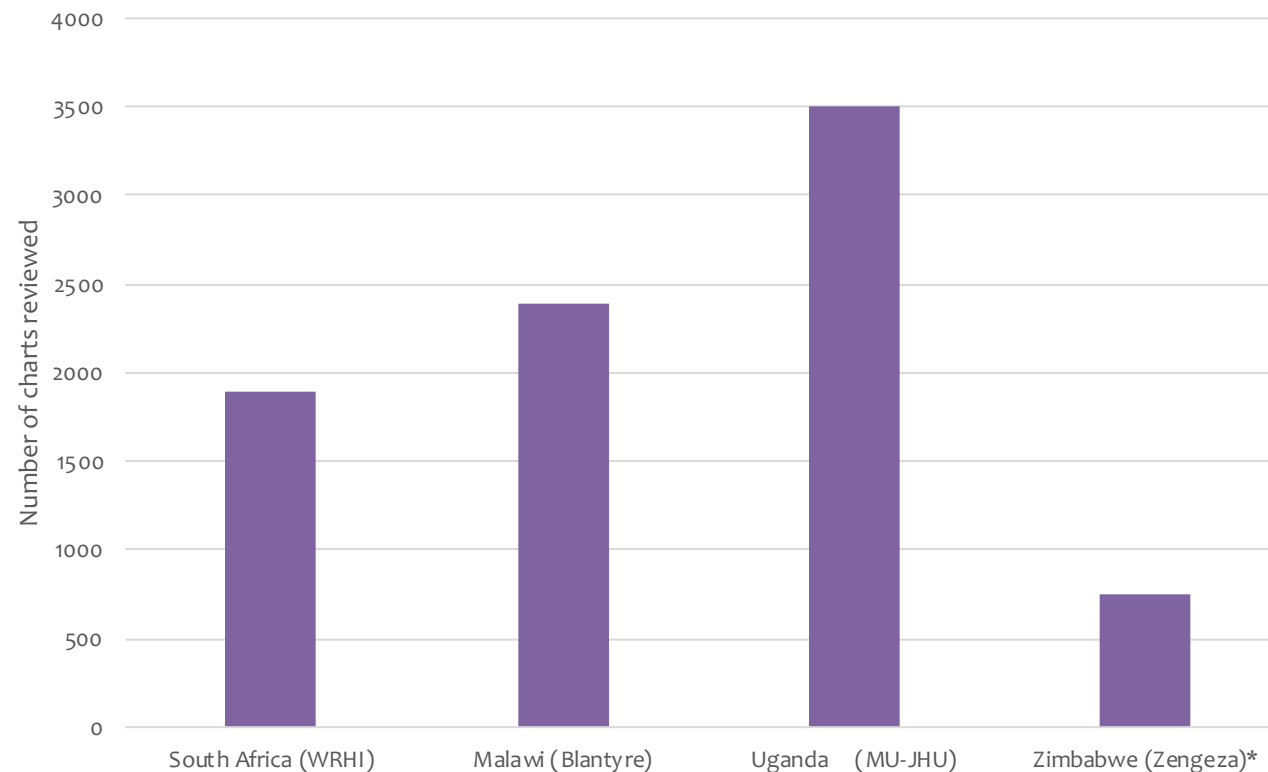
Zinhle Tshabalala, Sarah Whittaker, Megan Dempster, Jean Leroux, Caroline Vika, Karabo Kongoane

UZCHS Zengeza



Fungai Murewa, Grecenia Ndhlovu, Tsitsi Zinyengere, Vannessa Gatsi, Mary Mudavanhu, Moleen Matimbira

Chart abstraction progress



**7,345 charts
abstracted**

**Final data for Malawi
and Uganda**

**Data from South
Africa and Zimbabwe
through November
2019 and do not
represent final
estimates**

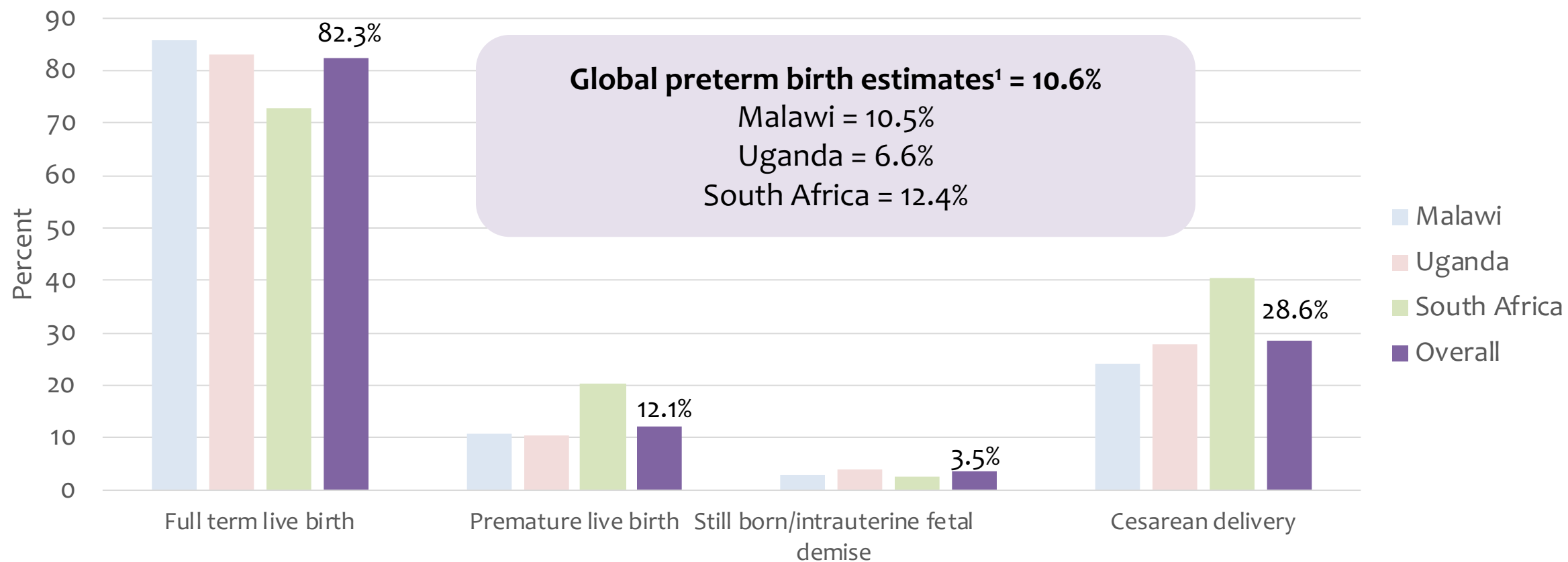
Data abstraction teams meticulously reviewed charts and abstracted data for deliveries occurring within the past 7 days

Demographic characteristics by country

	Malawi	Uganda	South Africa	Overall*
	N=2384	N=3505	N=1117	N=7345
Maternal age (mean ± SD)	25.7±6.7	25.5±5.6	28.7±6.2	26.1±6.2
Gravidity (mean ± SD)	2.5±1.6	2.6±1.7	2.6±1.3	2.6±1.6
Parity (mean ± SD)	1.4±1.5	1.4±1.6	1.3±1.1	1.4±1.5
Attended 4+ antenatal care visits	1070 (46.7%)	540 (38.9%)	772 (72.1%)	2501 (49.6%)
HIV status				
Negative	2008 (84.2%)	3013 (86.0%)	841 (75.3%)	6149 (83.7%)
Positive	311 (13.0%)	368 (10.5%)	273 (24.4%)	981 (13.4%)
Unknown or not documented	65 (2.7%)	124 (3.6%)	3 (0.3%)	215 (2.9%)
Number of infants at delivery				
1	2327 (97.6%)	3387 (96.8%)	1089 (97.5%)	7134 (97.2%)
>1	57 (2.3%)	112 (3.2%)	28 (2.5%)	205 (2.7%)

*Overall includes data from Zimbabwe where data collection is still in progress

Pregnancy outcomes & delivery mode



Pregnancy outcomes not documented for 2.1% of outcomes

¹Chawanpaiboon et al. Lancet Global Health (2018)

Serious maternal & infant outcomes

Maternal deaths:
7 (0.1%)

Neonatal deaths:
123 (1.7%)

	MTN-042B Maternal deaths*	DHS Maternal death rate ¹	MTN-042B Neonatal deaths*	DHS Perinatal death rate ²
Malawi	n=7 (293 per 100,000)	439 per 100,000	n=61 (26 per 1,000)	31 per 1,000
Uganda	0	368 per 100,000	n=43 (13 per 1,000)	32 per 1,000
South Africa	0	47 per 100,000	n=12 (11 per 1,000)	29 per 1,000

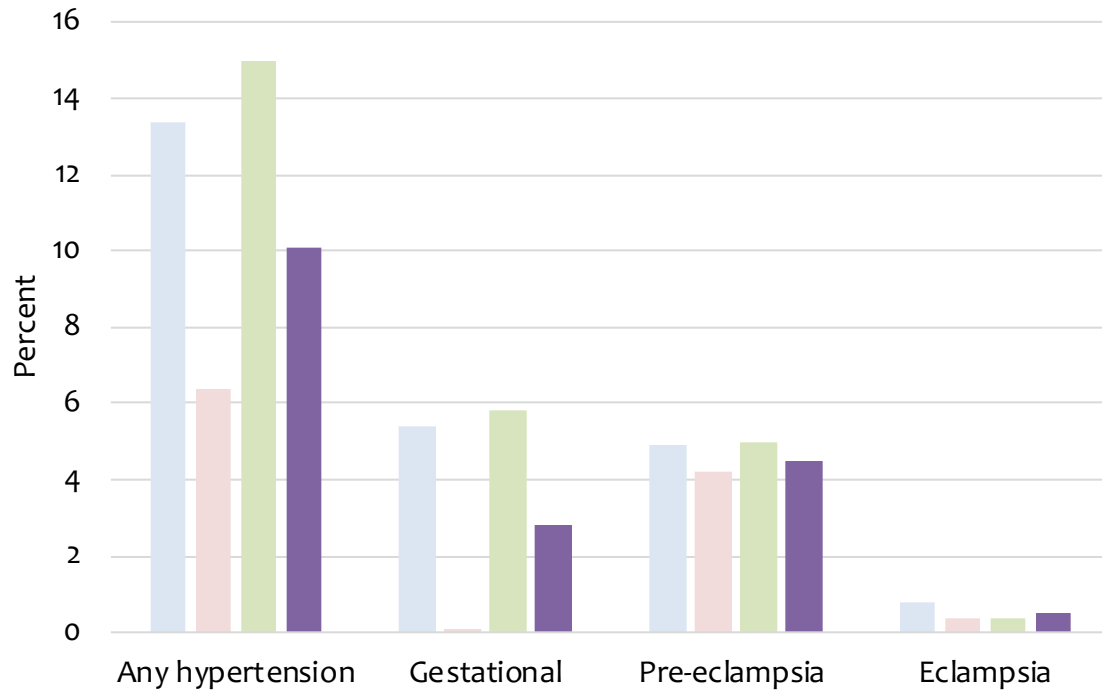
*Data presented are not rates but prevalence in MTN-042B and transformed for comparability

¹Data from DHS reports 2015 and 2016; includes deaths within 42 days from delivery

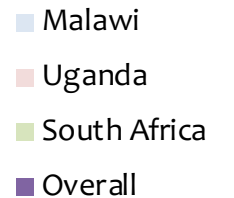
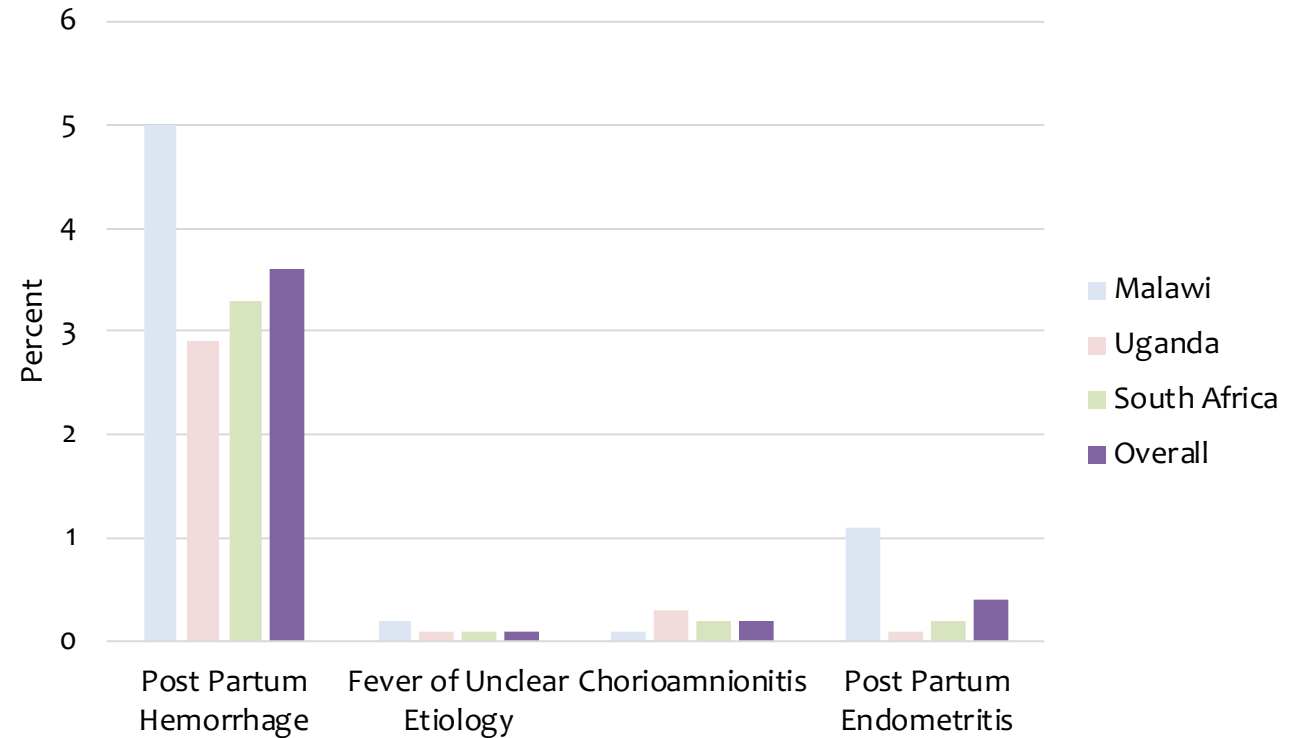
²For women 20-29, perinatal death rate includes stillbirths and deaths within 7 days of birth

Maternal complications

Hypertension-related complications



Other complications

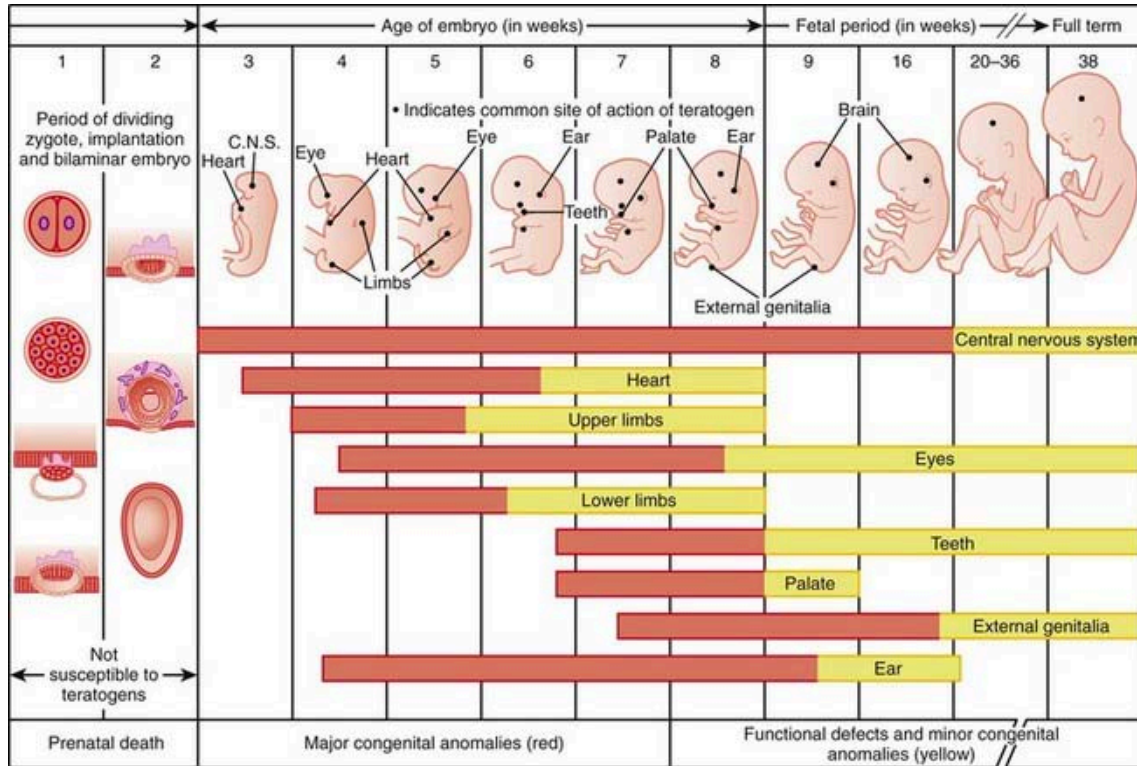


Information not documented for <1% of outcomes

Congenital anomalies

	Malawi	Uganda	South Africa	Overall*
Total number of records	N=2442	N=3614	N=1146	N=7549
Any malformation identified at delivery	33 (1.4)	23 (0.6)	18 (1.6)	78 (1.0)
Polydactyly	16 (0.7)	2 (0.1)	7 (0.6)	25 (0.3)
Musculoskeletal including clubfoot	6 (0.2)	1 (<0.1)	1 (0.1)	9 (0.1)
Cleft Lip and/or Palate	2 (0.1)	3 (0.1)	1 (0.1)	6 (0.1)
Umbilical Hernia	3 (0.1)	1 (<0.1)	2 (0.2)	6 (0.1)
Neural tube defects and/or Hydrocephalus	3 (0.1)	1 (<0.1)	0 (0)	4 (0.1)
Esophageal, gastrointestinal, or anorectal	1 (<0.1)	0 (0)	0 (0)	3 (<0.1)
Genitourinary	1 (<0.1)	1 (<0.1)	0 (0)	2 (<0.1)
Natal Tooth	0 (0)	0 (0)	1 (0.1)	1 (<0.1)
Other	5 (0.2)	12 (0.3)	7 (0.6)	25 (0.3)

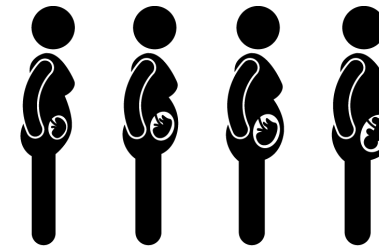
Congenital anomalies: timing is everything



Red indicates highly sensitive periods when teratogens may induce major anomalies.

That vast majority of congenital anomalies attributed to a teratogen occur with exposure prior to 12 weeks gestation

DELIVER will assess the safety of at different time points in pregnancy



12 weeks – delivery

- Data on congenital anomalies will be collected in all DELIVER cohorts
- Data from cohorts 1 through 3 will provide additional data on the background rate of congenital anomalies in our study population

Congenital anomalies: Data in Context

- ~3% prevalence of any birth defect/congenital anomaly in the US and Europe¹
- Congenital anomalies in ASPIRE:
 - 8 (7%) suspected anomalies reported, 4 in each arm²
 - Inguinal/umbilical hernia (5) most commonly reported

TABLE 3. Additional Details on Reported Congenital Anomalies

Participant	Study Arm	Pregnancy Outcome	Anomaly
1	Dapivirine	Full-term live birth	Umbilical hernia that was reducible
2	Dapivirine	Full-term live birth	Micrognathia and epicanthic folds
3	Dapivirine	Full-term live birth	Inguinal hernia that was repaired
4	Dapivirine	Full-term live birth	Craniofacial (structural) right frontal skull depression positional plagiocephaly
5	Placebo	Full-term live birth	Reducible umbilical hernia, approximately 4 cm in diameter
6	Placebo	Full-term live birth	Umbilical hernia, uncomplicated
7	Placebo	Full-term live birth	Umbilical hernia noted, 1.8 by 2 cm, reducible and nontender
8	Placebo	Full-term live birth	Polydactyly both hands (bilateral)

¹Moorthie et al. *J Com Gen* (2018); <https://www.cdc.gov/ncbddd/birthdefects/data.html>

²Makanani & Balkus et al. *JAIDS* (2018)

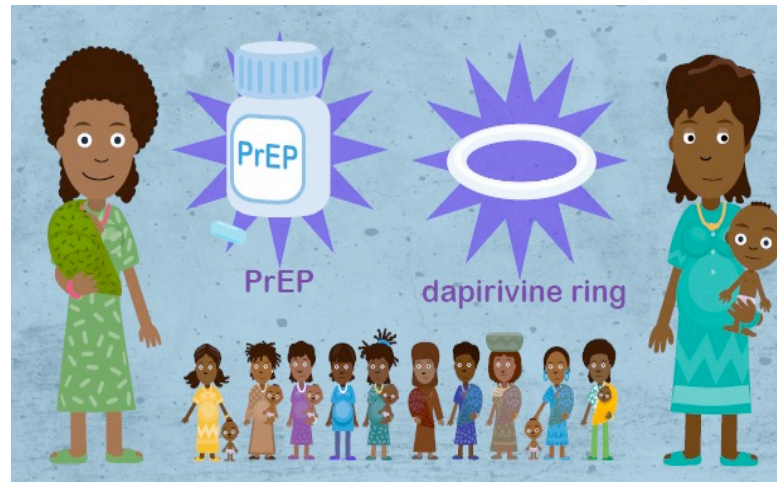
Congenital anomalies: Data in Context

MTN-042B

- Included a very short window of infant evaluation (within 7 days of delivery)
- Passive ascertainment of congenital anomalies (i.e. what was written in the chart)

DELIVER*

- Infants followed for 12 months
- Active ascertainment of congenital anomalies (CRF questions about potential anomalies)
- External expert reviews by a geneticist

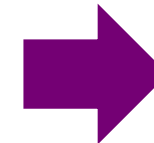


**Similar processes were implemented for ASPIRE and MTN-016*

How the data will be used by the DELIVER team?

Participants who use TRUVADA® oral tablet daily and insert the dapivirine vaginal matrix ring (25 mg) once every 4 weeks **will experience similar distributions of pregnancy outcomes to the general population**

Prevalence of outcomes in populations where DELIVER will be conducted¹



Observed frequency of outcomes in DELIVER



¹Data from MTN-042B and systematic review will be used to generate the “target”

Summary

- Chart abstraction is not as easy as it sounds and requires dedicated teams, clear communication, and the ability to accept potentially “imperfect data”
- Data on key DELIVER outcomes were available for the majority of charts abstracted (<1% missing data)
- Site estimates of certain outcomes differed somewhat from other national data sources
 - Underlying differences in the study catchment area?
 - Differences due to the type of facilities included in MTN-042B?
- **MTN-042B data will play a critical role in the conduct of DELIVER and will be a valuable resource for future studies conducted at participating sites that evaluate investigational products in pregnancy**

THANK YOU!



**MTN-042B protocol chairs &
management team**
MTN-042B site teams
Tanya Harrell, SCHARP
Moni Neradilek, SCHARP
Danny Szydlo, SCHARP
Elizabeth Brown, SCHARP
Ashley Mayo, FHI360
Rachel Scheckter, FHI360
Tara McClure, FHI360
Erica Lokken, UW



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