Timing of dolutegravir initiation and birth outcomes among pregnant women living with HIV in Kenya

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BACKGROUND

- The effect of antiretroviral therapy (ART) initiation before conception and at different stages of gestation on adverse perinatal outcomes remains uncertain; existing studies yield conflicting results.
- Few studies evaluate how the timing of dolutegravir (DTG)-based ART initiation during pregnancy affects perinatal outcomes.

OJBECTIVE

To evaluate the association between timing of maternal DTG initiation and adverse birth outcomes

METHODS

- **Study population:** Pregnant women living with HIV (WLHIV) on first-line DTG-ART in an ongoing cohort study at 8 public antenatal clinics in Western Kenya
- **Exposure:** Timing of DTG initiation: Pre-conception (reference), 1st (<14 weeks gestation) and 2nd trimester (14-28 weeks gestation).
- **Outcome:** Composite adverse outcome (PTD, SGA, or stillbirth)
  - Stillbirth (≥20 weeks), Preterm delivery (<37 weeks), Small-for-gestational-age (<10th percentile)
- **Statistics:** Log-binomial regression models to estimate risk ratios
  - Adjusted for primigravidity, ART adherence, and maternal age apriori
  - Multiple pregnancies and loss of pregnancies < 20 weeks were excluded

ACKNOWLEDGEMENTS

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1st trimester DTG-initiation was associated with 2x higher risk of adverse perinatal outcomes compared to pre-conception DTG-initiation.

RESULTS

Figure 1. Adverse perinatal outcomes

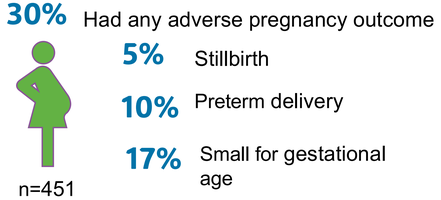
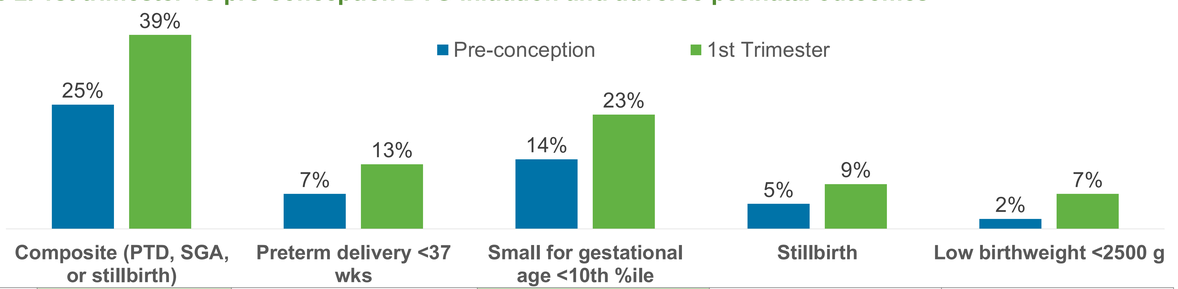


Table 2. Timing of DTG initiation

	n	Median (IQR)
		Months since DTG initiation
Preconception	156	36 months (20-46)
		Gestational age at DTG initiation
1st trimester	147	10 weeks (6-12)
2nd trimester	156	20 weeks (17-23)

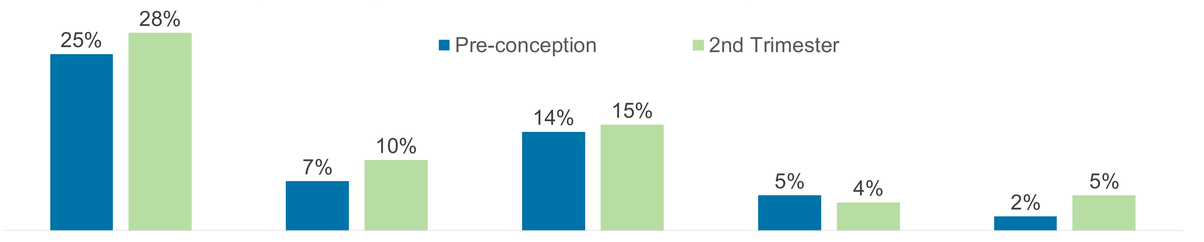
Figure 2. 1st trimester vs pre-conception DTG initiation and adverse perinatal outcomes



	Composite (PTD, SGA, or stillbirth)	Preterm delivery <37 wks	Small for gestational age <10th %ile	Stillbirth	Low birthweight <2500 g
Adj RR (95% CI)*	2.03 (1.38, 2.99)	2.72 (0.92, 8.06)	2.25 (1.60, 3.16)	1.76 (0.83, 3.76)	5.97 (0.58, 61.71)
P-value	<0.001	0.07	<0.001	0.14	0.13

*Adjusted by maternal age, primigravida, ART adherence during pregnancy, and clustered by site

Figure 3. 2nd trimester vs pre-conception DTG initiation and adverse perinatal outcomes



	Composite (PTD, SGA, or stillbirth)	Preterm delivery <37 wks	Small for gestational age <10th %ile	Stillbirth	Low birthweight <2500 g
Adj RR (95% CI)*	1.14 (0.60, 2.14)	1.40 (0.16, 12.58)	1.59 (0.86, 2.94)	0.18 (0.02, 1.36)	3.03 (0.53, 17.48)
P-value	0.69	0.76	0.14	0.10	0.21

*Adjusted by maternal age, primigravida, ART adherence during pregnancy, and clustered by site

Table 1. Baseline characteristics

Characteristic	% or Median (IQR) N = 454
Maternal age, years	28 (24-31)
Gestational age, weeks	21 (14, 26)
Currently married	82%
Only primary school education	58%
Household crowding (≥ 3 people/ room)	23%
No regular employment	83%
Primigravida	16%
Any prior pregnancy loss or stillbirth	17%

CONCLUSIONS

- **Findings:** 1st trimester DTG-initiation was associated with higher risk of adverse perinatal outcomes compared to pre-conception initiation
- **Limitations:** Associations may reflect delayed diagnosis and immune reconstitution during early pregnancy, rather than DTG exposure itself, however the lack of association with 2nd trimester initiation suggests viral non-suppression alone may not fully account for observed differences.
- **Implications:** Findings reinforce the importance of early HIV diagnosis and timely ART initiation, ideally prior to conception, to improve perinatal outcomes.
- **Next steps:** Analyze growth and neurodevelopment by DTG-initiation through 36-months.
  - Estimate DTG exposure in-utero and via breastmilk among WLHIV and their infants

PLAIN LANGUAGE SUMMARY

In this cohort of WLHIV in Kenya, 1st trimester DTG-initiation was associated with higher risk of poor birth outcomes compared to pre-conception DTG-initiation. Poor birth outcomes did not differ between WLHIV who initiated DTG in the 2nd trimester compared to pre-conception. These findings support current guidelines for early HIV testing and ART initiation, ideally prior to conception.