The feasibility of retention of subsequent pregnancies in clinical trials: The incidence of subsequent pregnancies in women enrolled in the DolPHIN-2 studies.

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BACKGROUND

Inadequate safety and efficacy data for medications during pregnancy often result from **excluding pregnant and postpartum women** from clinical trials.

Despite global efforts, challenges persist in achieving fair inclusion of this group in research.

In the context of antiretroviral therapy (ART), the transition from efavirenz (EFV) to dolutegravir (DTG) as the World Health Organization's recommended **first-line regimen occurred with limited pregnancy data.**

In some clinical trials, **becoming pregnant resulted in withdrawal**, and there is a lack of long-term follow-up beyond trial durations.

This secondary analysis aims **to address this gap by retaining women who have subsequent pregnancies** and obtaining comprehensive pregnancy data from ongoing trials.

However, evidence on the **incidence of subsequent pregnancies** among women in these trials remains limited.

METHODS

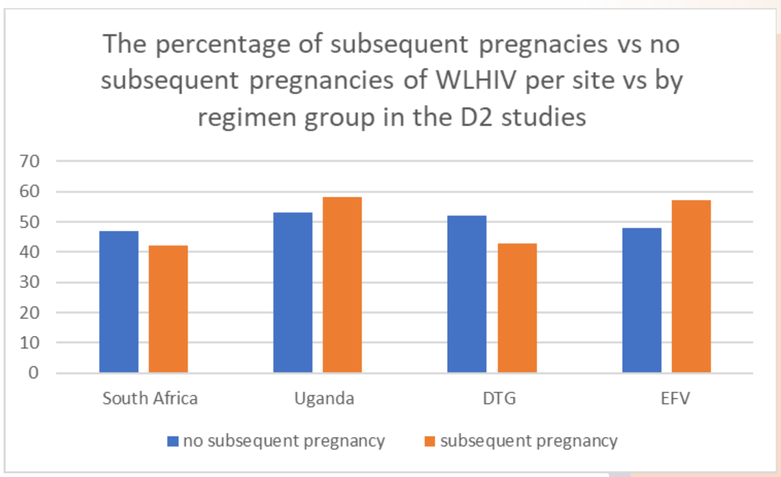
The study explores the incidence of subsequent pregnancies in women enrolled in the **DolPHIN-2 randomized trial and its observational extension, D2 TRIO.**

This secondary analysis utilized data from 250 women (**South Africa n=114, Uganda n=135**) who met intention-to-treat (ITT) criteria in the DolPHIN-2 study and were followed for **192 weeks.**

The trial investigated the safety and efficacy of DTG in pregnant women aged ≥18 years presenting late (≥28 weeks gestational age) for antenatal care.

Descriptive statistics were used to summarise baseline socio-demographic and clinical characteristics of the women with **subsequent pregnancies** as well as the subsequent infant and birth outcomes.

Statistical tests, including the Shapiro-Wilk test, Mann-Whitney U-test, and chi-square analysis, were used to compare women with and without subsequent pregnancies, with p-values reported.

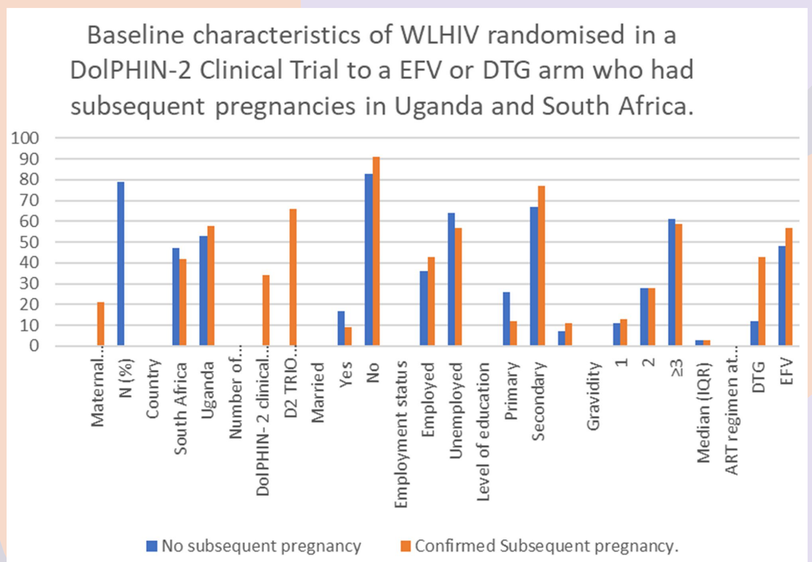


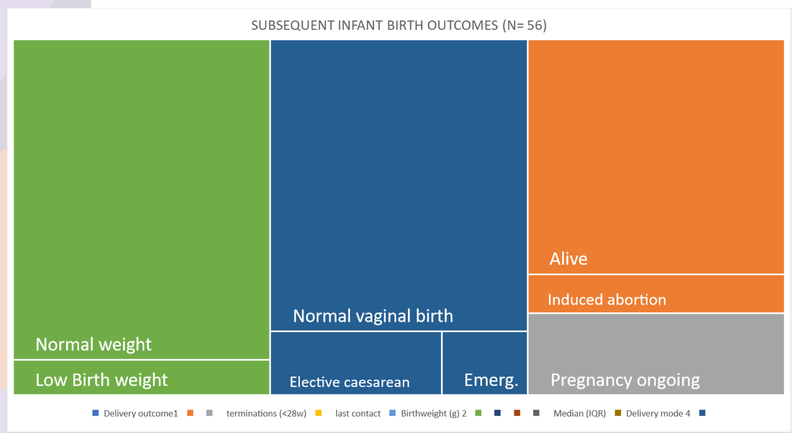
RESULTS

Of all women enrolled in the clinical trial 21% (n=53) experienced at least one subsequent pregnancy.

During the DolPHIN-2 trial 7% (n=18) of subsequent pregnancies occurred during the clinical trial and 14% (n=34) during the D2 TRIO observational study.

A higher proportion of subsequent pregnancies occurred inthe EFV arm (57%, n=30) and at the Uganda site (58%, n=31) compared to South Africa (42%, n=22).





Characteristics of women with subsequent pregnancies:
Multigravida (87%, n=46)
Unmarried (90%, n=40)
High school education (70%, n=33),
Unemployed (57%, n=25)

Birth outcomes:
Live births: 66% (n=23)
Pregnancy termination: 11% (n=4)
normal birth weight (≥2.5 kg) (90%, n=19).

Conclusion

This analysis highlights that a significant proportion (21%) of women enrolled in a clinical trial had a subsequent pregnancy underscoring the need for their **inclusion** and **retention** in trials to enhance medication safety and efficacy data

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