



ADJUSTED ANALYSIS OF THE EFFECT OF ISONIAZID PREVENTATIVE THERAPY ON ADVERSE PREGNANCY OUTCOMES IN WOMEN WITH HIV

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BACKGROUND

Recently, the TB APPRISE (IMPAACT P1078) double-blind placebo-controlled trial associated isoniazid preventive therapy (IPT) started in pregnancy with increased risk of a composite adverse pregnancy outcome compared to when IPT was deferred to 3 months postpartum (23.6% vs 17%, $p < 0.01$)¹. Since there are many potential factors that affect pregnancy outcome, **we conducted an analysis adjusting for other risk factors that impact pregnancy outcomes.**

METHODS

- 925 HIV-infected pregnant women from 8 high TB incidence countries with observed pregnancy outcomes
- Randomized to 28 weeks of IPT initiated during pregnancy (**Immediate INH**) or at 12 weeks postpartum (**Deferred INH**)
- Adverse pregnancy outcomes: **Preterm delivery** (PTD <37 week gestation); **Low birth weight** (LBW <2500g); **Perinatal death 1** – fetal demise or neonatal death (<28 days); **Perinatal death 2** – fetal demise or early neonatal death (<7 days); **Composite outcome 1** – PTD, LBW, congenital anomalies, spontaneous abortion (<20 week gestation), stillbirth (≥ 20 week gestation); **Composite outcome 2** – excluding congenital anomalies, including neonatal death; **Composite outcome 3** – excluding congenital anomalies, including early neonatal death.

STATISTICAL ANALYSIS

- Logistic regression models were fit to assess the association of each composite outcome with study arm, stratified by gestational age (14 to <24 weeks vs. 24 to 34 weeks) and adjusted for important outcome-specific risk factors ($p < 0.15$ in univariate analysis).*
- Interaction of study arm with each factor was tested.

*Maternal age, ARV regimen, timing of ARV initiation, CD4 count, plasma HIV RNA, HBsAG status, hepatitis C serology, interferon-gamma release assay status, mid-upper arm circumference, twin pregnancy, current smoker, food insecurity, non-infectious pregnancy complication, infectious pregnancy complication, and maternal hospitalization.

Initiating INH during pregnancy carries an independent $\cong 1.6$ fold increased odds of composite adverse pregnancy outcome compared to postpartum initiation

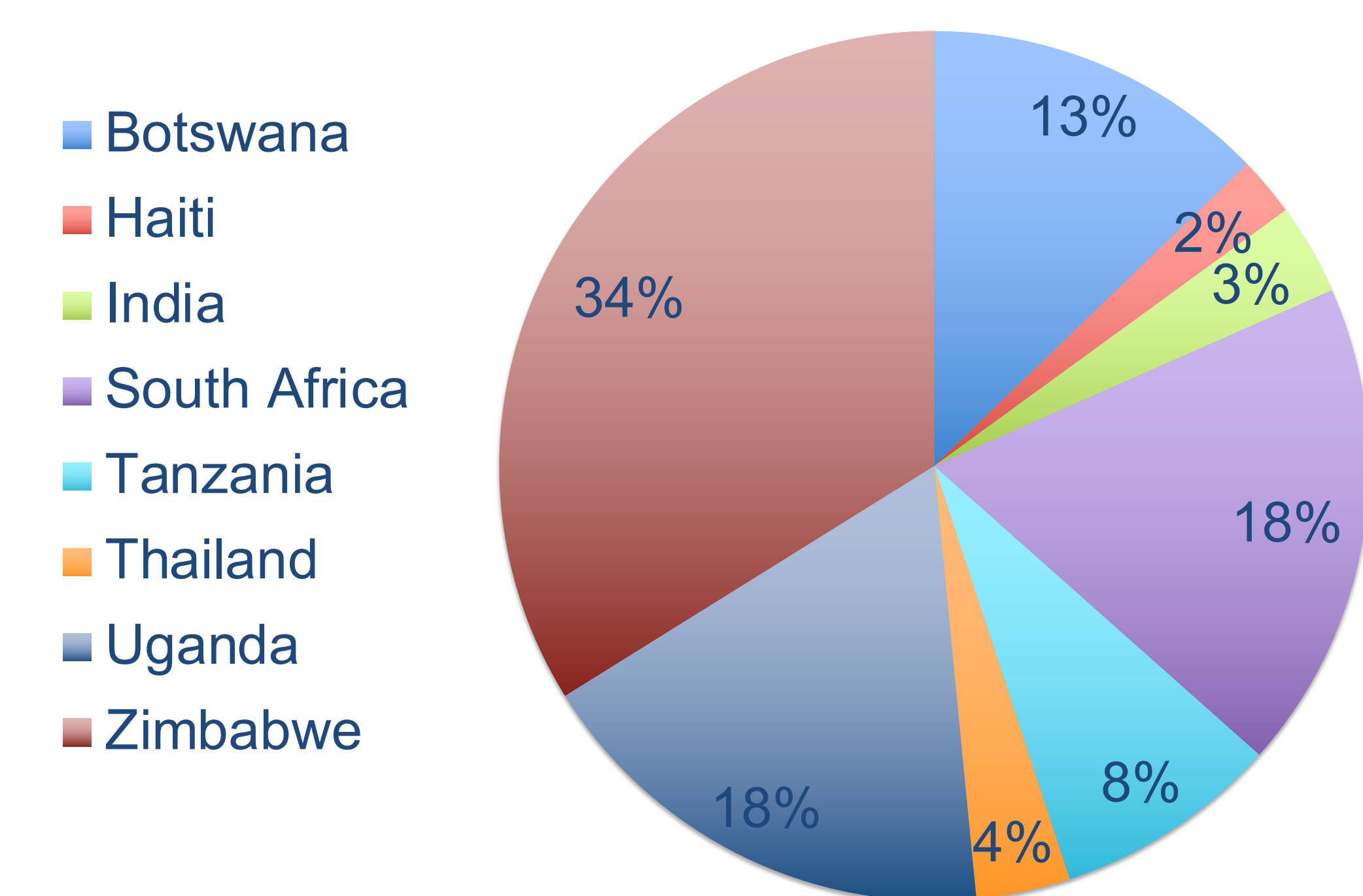
RESULTS

TABLE 1. Participant Characteristics

Characteristic	Overall, N=925
Immediate INH	459 (49.5%)
Deferred INH	466 (50.4%)
ART contains Efavirenz*	784 (84.8%)
ART contains Nevirapine*	121 (13.1%)
Median maternal age at delivery, y (IQR)	30 (25 – 34)
Median mid-upper arm circumference, cm (IQR)	28 (26 – 31)
Singleton pregnancy	914 (98.8%)
Current smoker	17 (1.8%)
Food insecurity	118 (12.8%)
Non-infectious pregnancy complication	170 (18.4%)
Infectious pregnancy complication	70 (7.6%)
Hospitalized	53 (5.7%)

*All women were on ART at enrollment

FIGURE 1. Proportion of study population by country



Summary of Birth Outcomes

- The majority (~97%) of pregnancies resulted in a live birth, irrespective of study group.
- Stillbirth was the most common form of fetal demise observed, occurring in ~2% of pregnancies.
- There was one case of spontaneous abortion and one case of induced abortion. Both were singleton pregnancies of women randomized to the Immediate INH group.
- There was one case of discordant twin birth outcome (one live birth/one stillbirth) in the Deferred INH group.

FIGURE 2. Timing of ART initiation

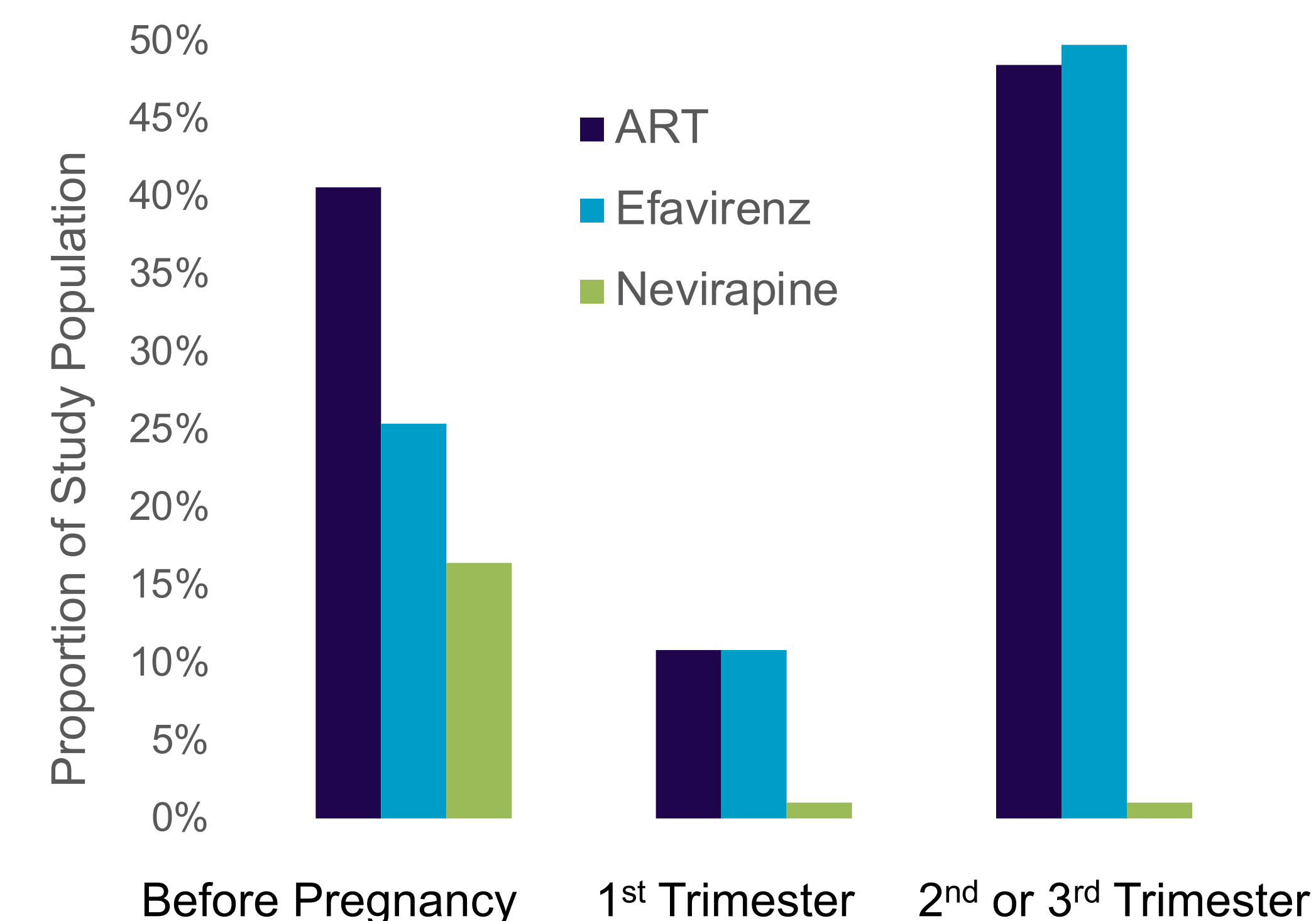


TABLE 2. Pregnancy outcomes by study group and adjusted odds ratios

Outcome	Immediate INH	Deferred INH	aOR (95% CI)
Preterm delivery	48/442 (10.9%)	40/458 (8.7%)	1.40 (0.89-2.21)
Low birth weight	62/430 (14.4%)	46/446 (10.3%)	1.68 (1.10-2.59)
Perinatal death 1	23/459 (5.0%)	20/459 (4.4%)	1.18 (0.63-2.22)
Perinatal death 2	21/459 (4.6%)	13/459 (2.8%)	1.73 (0.84-3.57)
Composite 1	106/449 (23.6%)	78/460 (17.0%)	1.68 (1.19-2.38)
Composite 2	105/450 (23.3%)	78/459 (17.0%)	1.59 (1.12-2.26)
Composite 3	105/450 (23.3%)	73/459 (15.9%)	1.70 (1.20-2.42)

ADDITIONAL KEY INFORMATION

- Mid-upper arm circumference, non-infectious pregnancy complications, and twin pregnancy were important risk factors in at least one of the pregnancy outcomes studied.
- Chronic Hepatitis B (HBsAG positive) was an important risk factor for Composite outcome 1.

CONCLUSIONS

- Composite adverse pregnancy outcomes 1, 2 and 3 were significantly higher in the immediate IPT group compared to the deferred IPT group.
- Initiating IPT during pregnancy is independently associated with higher risk of adverse pregnancy outcomes after adjusting for known risk factors.

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