Maternal Triple Antiretrovirals (mART) and Infant Nevirapine (iNVP) Prophylaxis for the Prevention of Mother-to-Child Transmission (MTCT) of HIV during Breastfeeding (BF)

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IMPAACT
International Maternal Pediatric Adolescent AIDS Clinical Trials Network

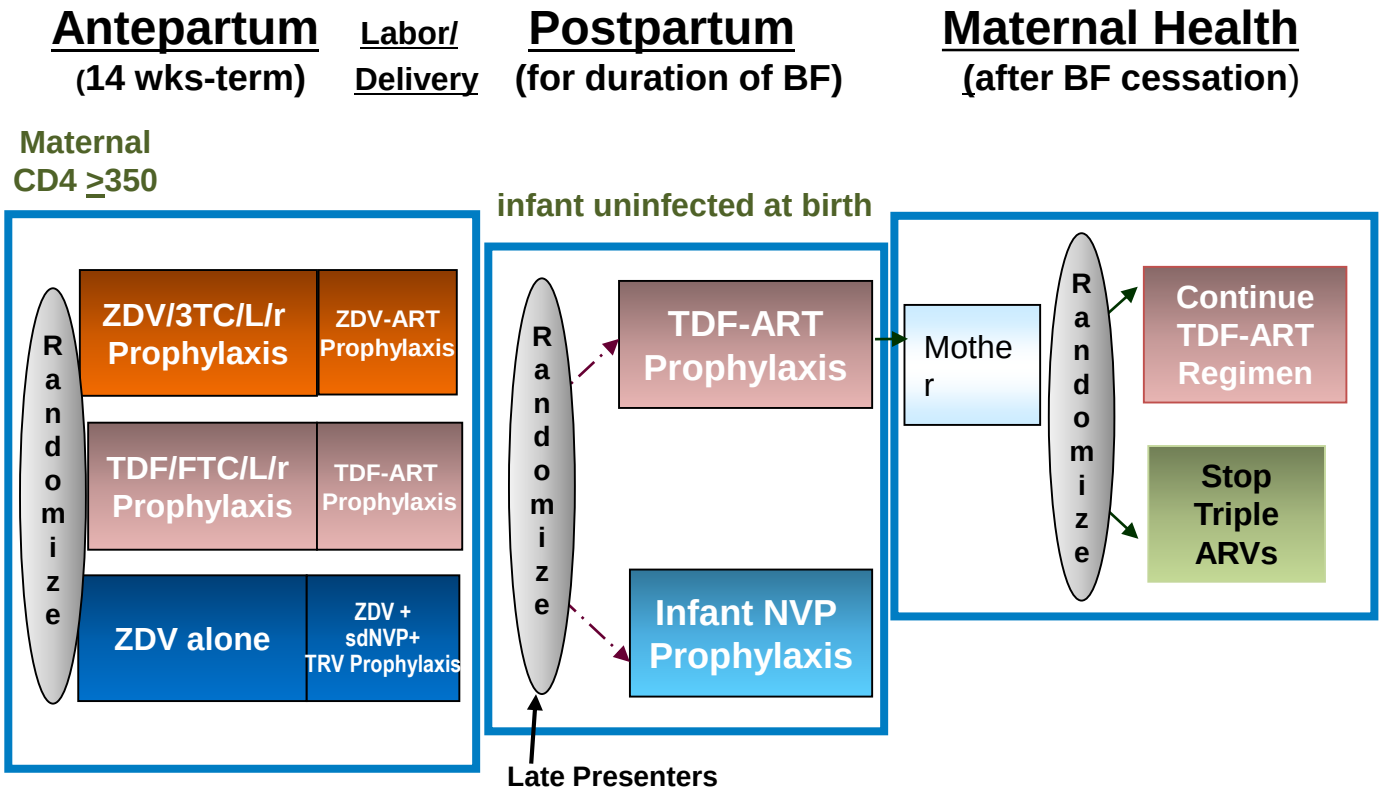
Statement

Dr. Taha has no relevant conflicts.

Background

- Breastfeeding (BF) is crucial to reducing infant morbidity and mortality in developing countries but may result in HIV transmission if the mother is HIV-infected.
- Prior clinical trials showed that both mART and iNVP are effective in PMTCT of HIV. PROMISE is the first randomized trial designed to directly compare the efficacy and safety of these two strategies during extended BF into the second year of life.

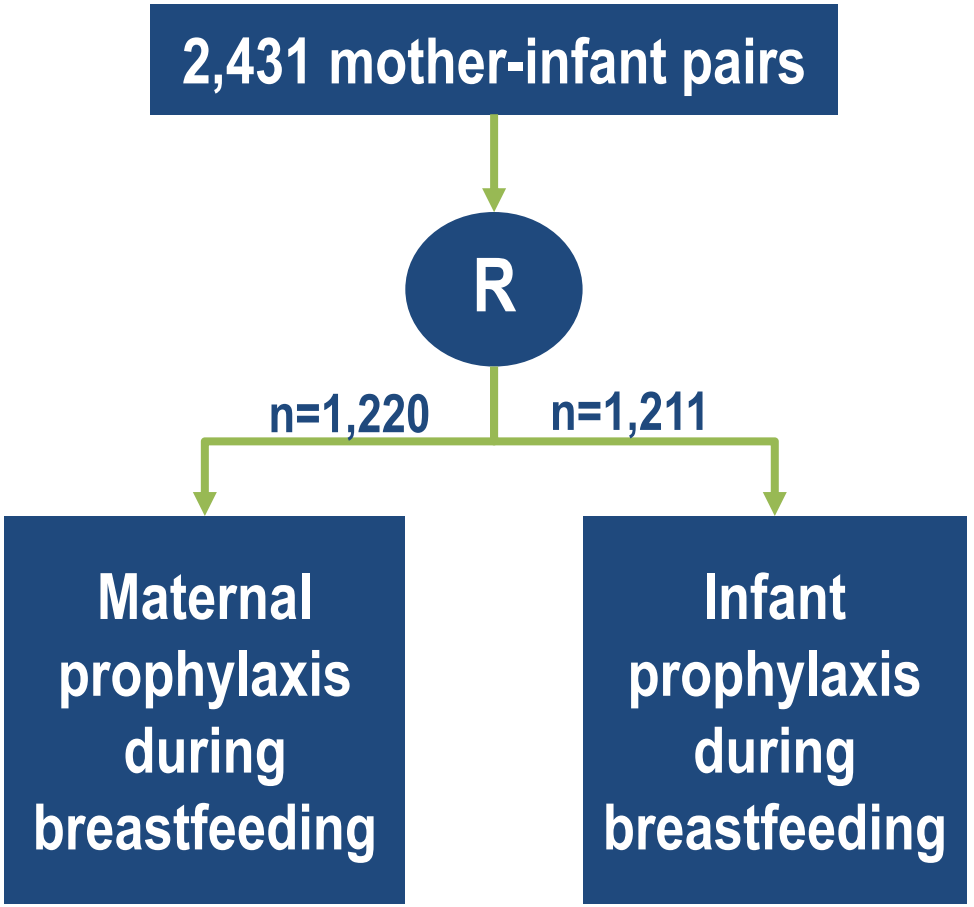
Overall Design of the PROMISE 1077BF Trial: Antepartum, POSTPARTUM and Maternal Health Components



Legend Figure 1A: The 1077BF antepartum component had 3 study arms: in version 2.0, HBV negative women were only randomized to ZDV-ART or ZDV-alone; in version 3.0 antepartum component, all women, regardless of HBV status were randomized to the 3 study arms in a 1:1:1 ratio

Postpartum Component Research Question

Among HIV-infected women who do not meet criteria for initiation of HAART for their own health, **what is the optimal intervention to prevent transmission of HIV to infants during breastfeeding**?



Methods

- The Postpartum Component of PROMISE was conducted in sub-Saharan Africa (13 sites) and India (1 site)
- HIV-infected women with CD4+ ≥ 350 cells/mm^3 (or greater than country-specific guidelines) and their HIV-uninfected newborns were randomized
- Mother-infant pairs were enrolled between June 2011 and October 2014

Methods

- The regimens were continued through 18 months postpartum, through complete cessation of breastfeeding, infant HIV infection, or development of toxicity.
- Kaplan-Meier (K-M) probabilities and incidence rates per 100 person-years were used in primary analyses of efficacy and safety

Results

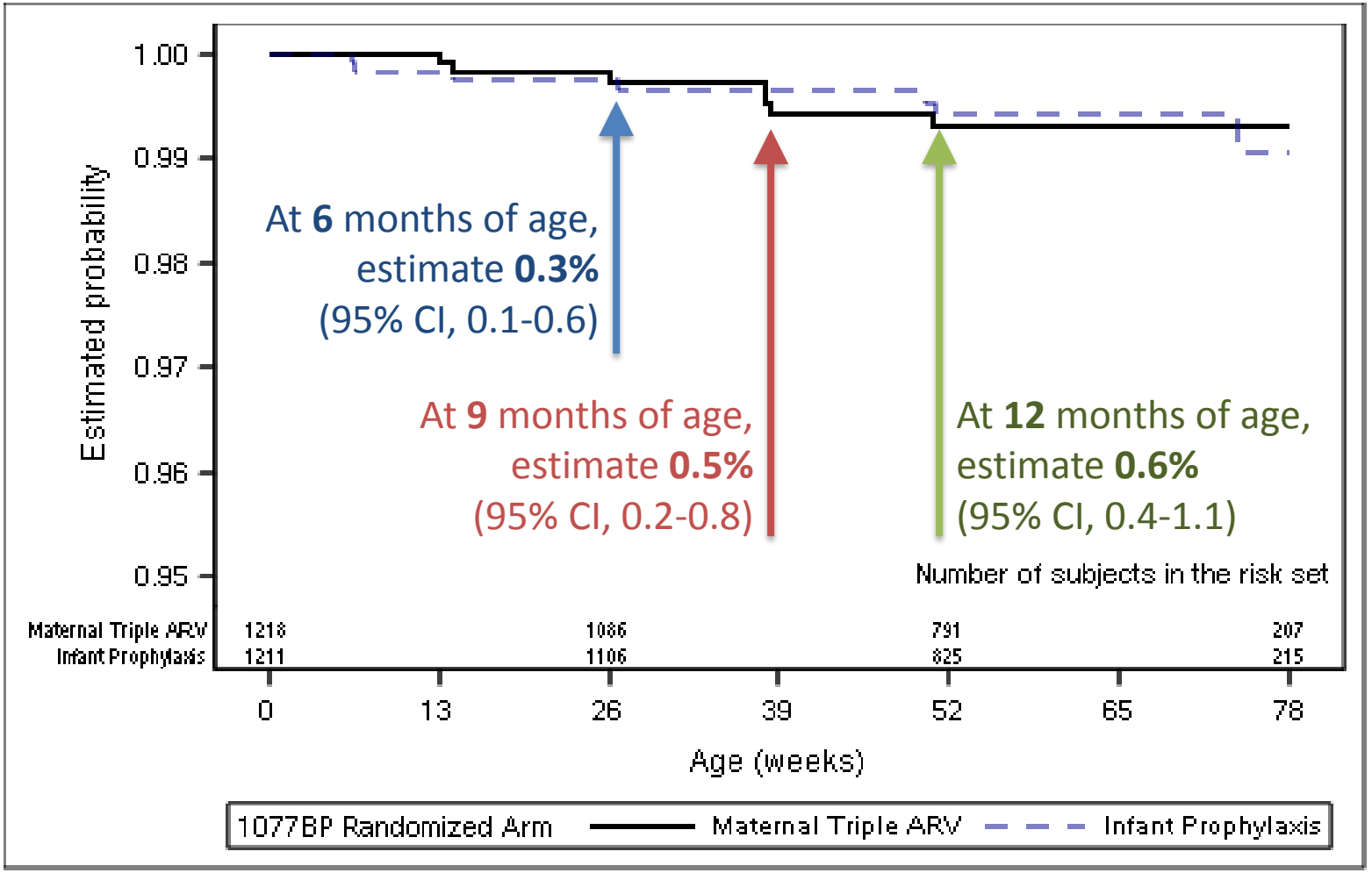
- Overall, women enrolled into the Postpartum Component were asymptomatic
  - Median CD4+ count: 686 cells/mm^3
  - 97% WHO Clinical Stage I
  - Median age of mothers: 26 years old
- Infant's median gestational age and birthweight were 39 weeks and 2.9 kg, respectively and did not differ by study arm.

Results

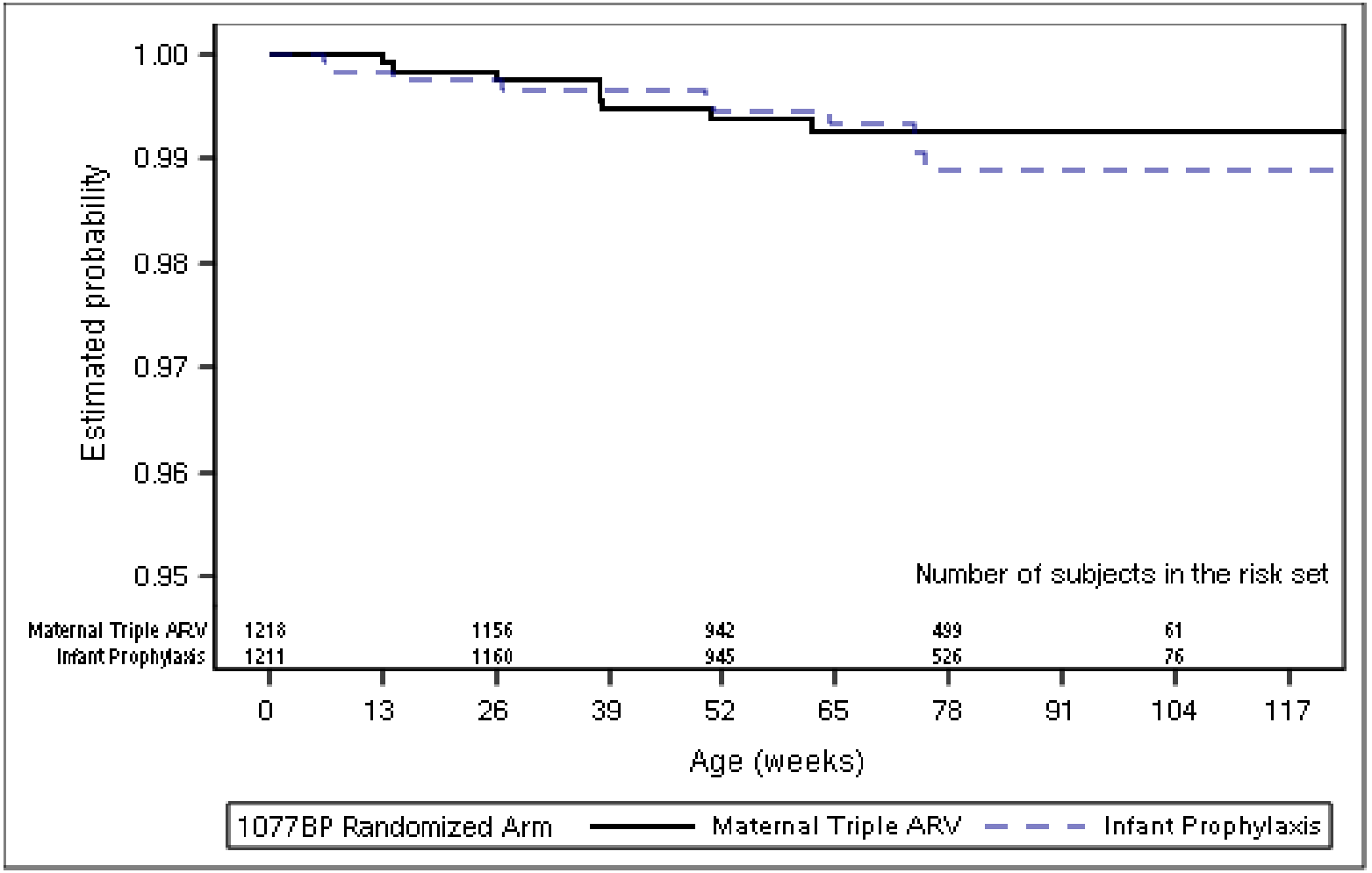
- Maternal and infant baseline characteristics were comparable by study arm.
- Median duration of BF was 15 months and not significantly different by study arm (p=0.85).
- There was no statistically significant difference in probability of MTCT of HIV by study arm (primary and sensitivity analyses) – see Figures.

Results: MTCT of HIV

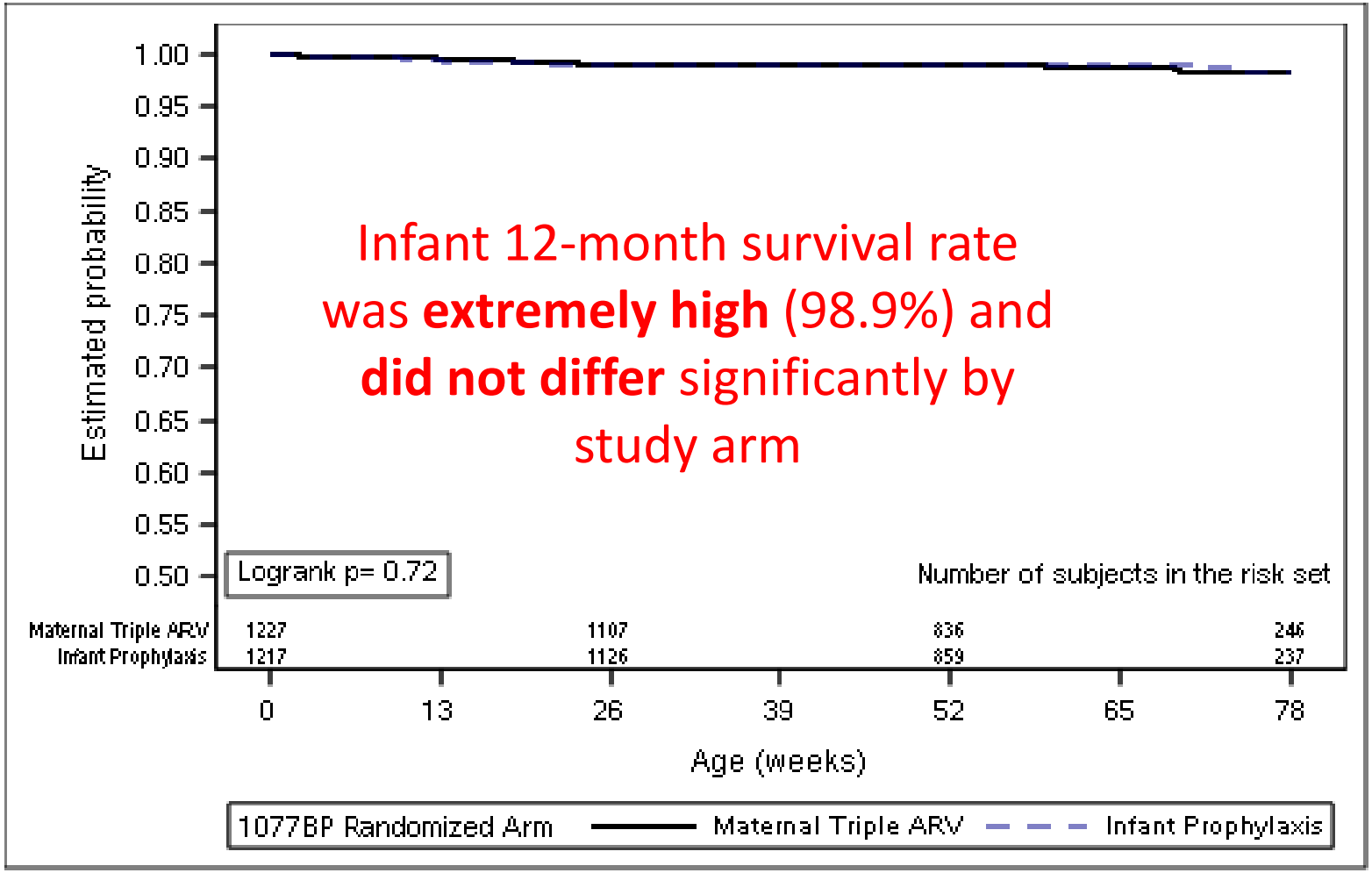
(Primary Analysis)



Results: MTCT of HIV
(Sensitivity Analysis)

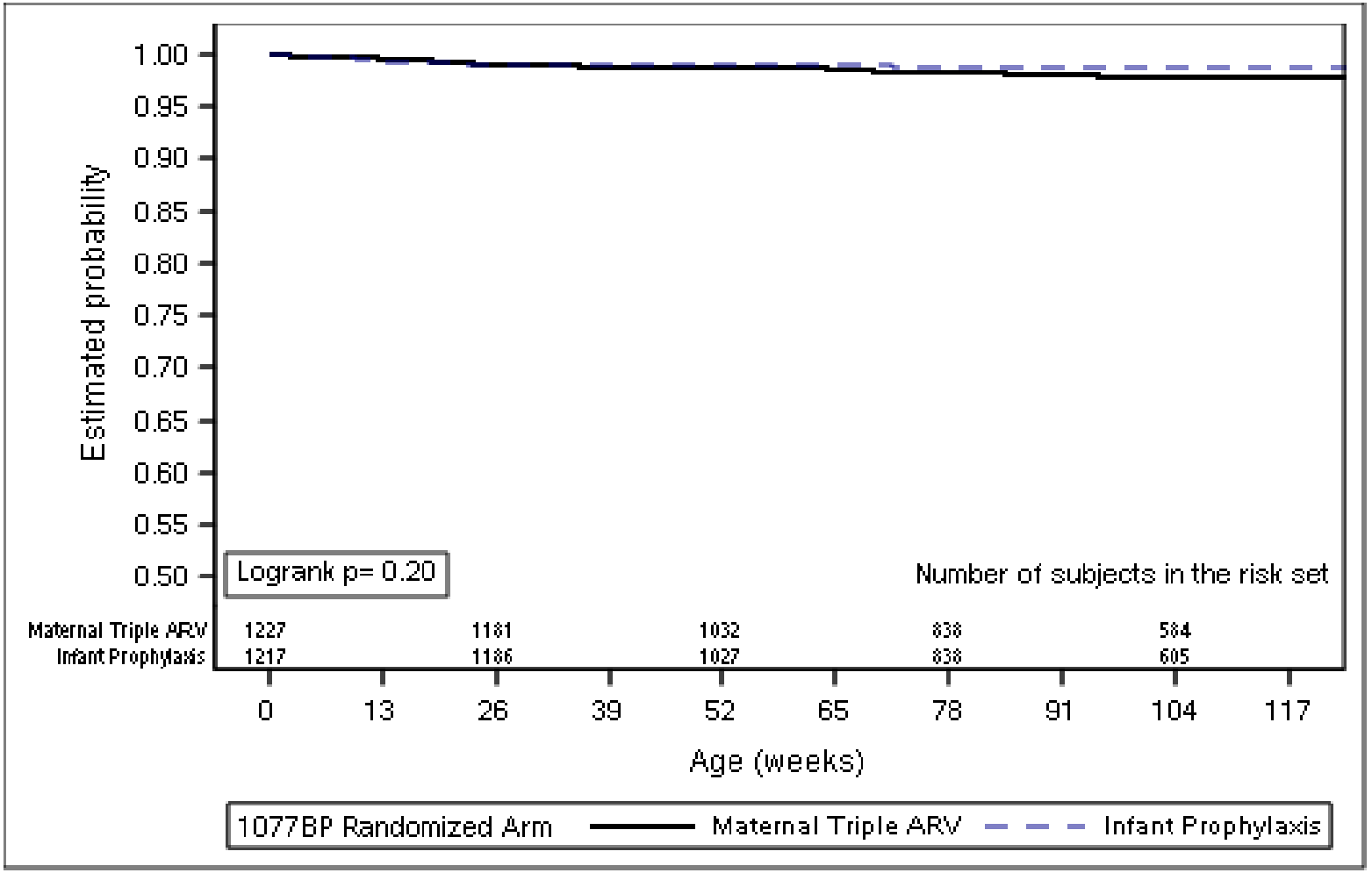


Results: Time to Infant Death (Primary Analysis)



Infant 12-month survival rate was **extremely high** (98.9%) and **did not differ** significantly by study arm

Results: Time to Infant Death (Sensitivity Analysis)



Results

- The incidence rates (per 100 person-years) of maternal and infant safety endpoints did not differ significantly by study arm

Outcome	mARV (N=1220) Rate (95% CI)	iNVP (N=1211) Rate (95% CI)	p-value, K-M log-rank test
Composite maternal safety endpoint (Grade 3/4 signs/symptoms; Grade 2-4 lab events; or maternal death)	14.8 (12.7-17.3)	14.6 (12.5-16.9)	0.99
Composite severe maternal safety endpoint (i.e. excludes Grade 2 Lab events)	5.1 (4.3-6.1)	5.6 (4.8-6.6)	0.61
Composite infant safety endpoint (Grade 3/4 signs/symptoms; Grade 3/4 lab event; or infant death)	44.1 (39.2-49.5)	43.5 (38.7-48.8)	0.95

Conclusions

- Both maternal ART and infant NVP were safe, associated with very low postnatal perinatal transmission rates during extended breastfeeding, and high infant survival rates.
- For mothers who either do not adhere to or tolerate ART, daily infant NVP throughout breastfeeding offers a safe and effective PMTCT alternative during breastfeeding.

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