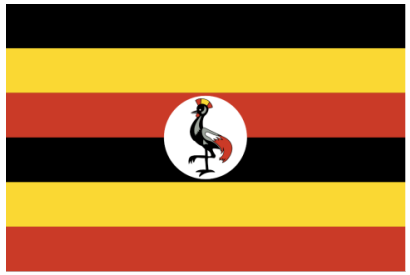
OUTCOMES OF HIV EXPOSED INFANTS BEFORE AND AFTER IMPLEMENTING OPTION B+ PMTCT GUIDELINE IN KAMPALA,UGANDA: A RETROSPECTIVE COHORT STUDY.

***Peter Elyanu*[1], *Addy Kekitiinwa*[2] ,*Rousha Li*[1], *Mary Paul*[3], *LY Hwang*[1]**

1. University of Texas School of Public Health, Houston, Texas

2. Baylor-Uganda, Kampala, Uganda

3. Baylor College of Medicine, Houston, Texas



Background

- In 2012, WHO recommended providing lifelong ART to all HIV-infected pregnant and breastfeeding women, and ARV prophylaxis for their infant for six weeks (Option B+) as part of the strategy to eliminate MTCT.

- Reports show 6 week MTCT rates < 5% *(Maria H Kim et al, 2015, Sebastian et at., 2015, Hierce et al 2015, William Bazeyo et al 2015)*

- However, to date the impact of Option B+ guidelines on 18 month outcomes of HEI from programmatic settings is limited.

- And yet 18 months outcomes measure the success of PMTCT interventions at preventing HIV transmission through breastfeeding, and the impact of child survival intervention.

Objectives

1. To compare HIV exposed infant outcomes (MTCT rate, LTFU and mortality) at 18 months of life, before and after implementing option B+ in Mulago Hospital, Kampala Uganda.

2. To compare cART initiation proportions in Infant who test HIV positive before and after implementing Option B+ in Mulago hospital, Uganda

3. To determine factors associated with MTCT after implementing Option B+ in Mulago hospital, Uganda.

Methods

Study Design: Retrospective Cohort study

Cohort definition:

- HIV exposed Infants born from;
  - July 2010-June 2011 (Option A cohort)
  - July 2013 to June 2014 (Option B+ cohort)

  - Excluded those born from July 2011-June 2013
    - Reduce overlap between the 2 cohorts because of transition of the guidelines

Study setting: Mulago Hospital postnatal clinic

Data collection: Routinely collected patient-level data from the clinic's electronic database.

Objective 1: To compare HIV exposed infant outcomes (MTCT rate, LTFU and mortality) before and after implementing option B+.

Study Population: HEI aged <18 months.

- Attended the Mulago Hosp PNC clinic at least once after birth
- Received 1st HIV test at Mulago Hosp clinic.
- **Excluded:** Transferred in's from other clinics.

Outcomes variables

- HIV infection , Loss to Follow up &Death

Outcome definition

- **HIV infection:** At least, one positive HIV DNA PCR test anytime during the follow-up period or a positive HIV rapid test at 18 months of age.

- **LTFU:** If there were three failed attempts to track the infant after the last clinic visit or if six months elapsed since the infant was last seen at the clinic.

- **HIV Negative:** Negative HIV DNA PCR test -done at least six weeks after cessation of breastfeeding or Negative HIV rapid test at 18 months of age.

- **Transfer out:** The infant transferred care to another health facility before any of the other events occurred.

Statistical analysis

Survival analysis

- Compared 18 month cumulative incidence estimates of outcomes while accounting for competing risks.

Outcome	Time of origin	Competing risk	Censored event
HIV infection	Date of birth	Death HIV negative	Transfer out Loss to follow up
Loss to follow Up	Date of enrolment in care	Death HIV infected HIV negative	Transfer out
Death	Date of Birth	HIV negative HIV infected	Transfer out Loss to follow up

Objective 2: To compare ART initiation proportions of HIV+ Infant before and after implementing Option B+

Study Population: Infants who become HIV infected.

- We used Fisher's exact test to compare cART initiation proportions in HIV-infected infants in the two cohorts.

Objective 3: Determine factors associated MTCT of HIV during Option B+

- Proportional subdistribution hazard regression model for competing risks(Fine and Gray, 1999)
- We used stepwise approach to select the most parsimonious model. Variables with $p<0.2$ at univariable analysis were considered for model selection.

RESULTS

Baseline characteristics- Infants

Characteristic		Option A Cohort N=2203	Option B+ cohort N=1571
Median age in weeks at 1st PCR (IQR)		6.4(6.1,7.3)	6.3(6.0,6.7)
Sex [n (%)]	Male	1131 (51.3%)	788(50.2%)
Median follow up months(IQR)		9.6(3.1, 16.4)	15.3(4.2, 16.5)
Feeding option [n (%)] §	EBF	1962(89.1%)	1447(92.2%)
ARV's for PMTCT [n (%)] ¥	Yes	2150(98.3%)	1542(98.5%)
PMTCT ARV regimen¥			
Daily NVP up to 6 weeks		1113(50.9%)	1529(97.6%)
Daily NVP through BF		897(41.0%)	13(0.8%)
	sd NVP	140(6.4%)	0(0.0%)
	None	36(1.7%)	24(1.5%)
Underweight [N (%)]	Yes	214(10%)	197(12.8%)
Stunted [N (%)]	Yes	162(7.7%)	141(9.6%)

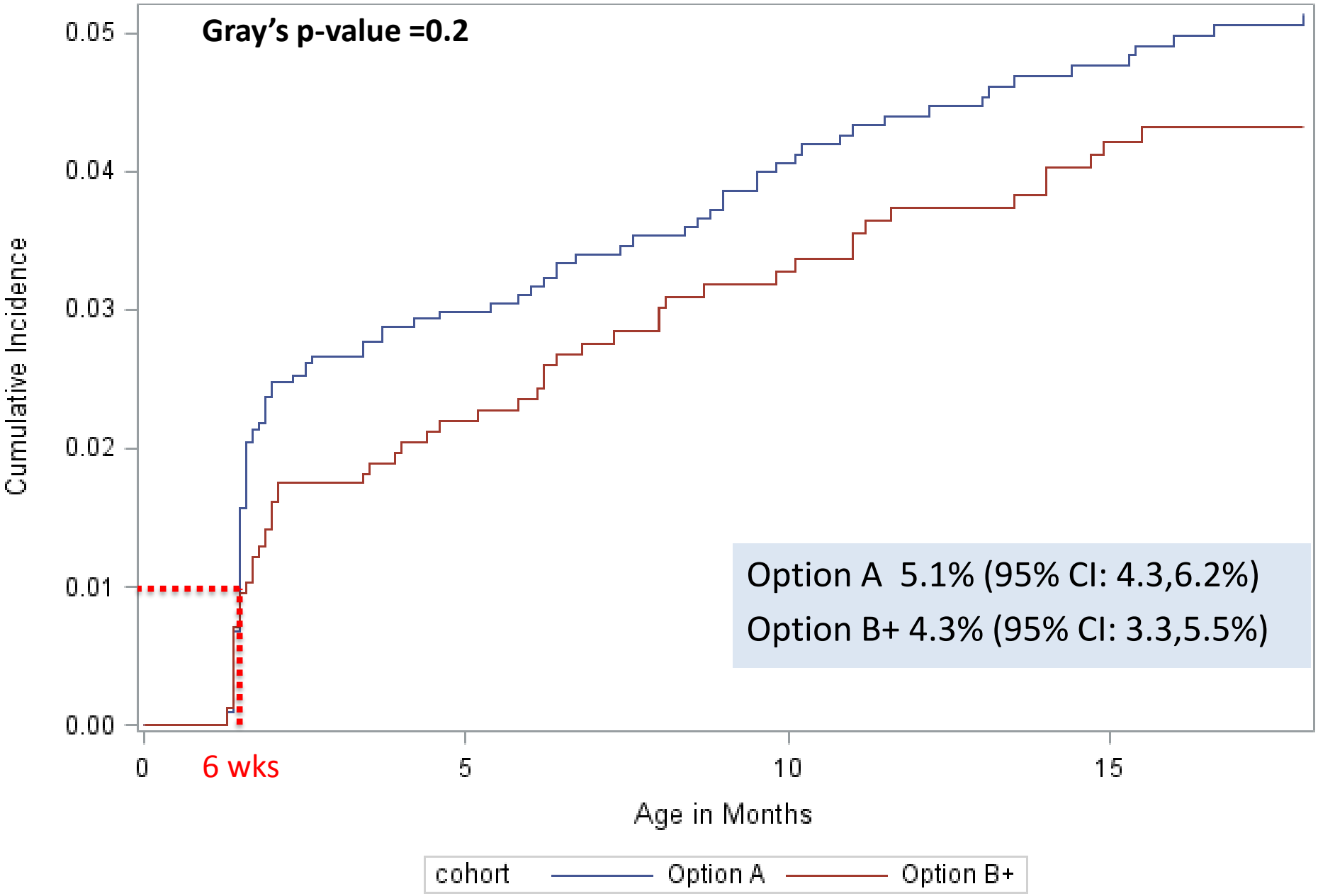
¥ *22 (0.6%) Missing values*

Mothers characteristics at child's enrolment

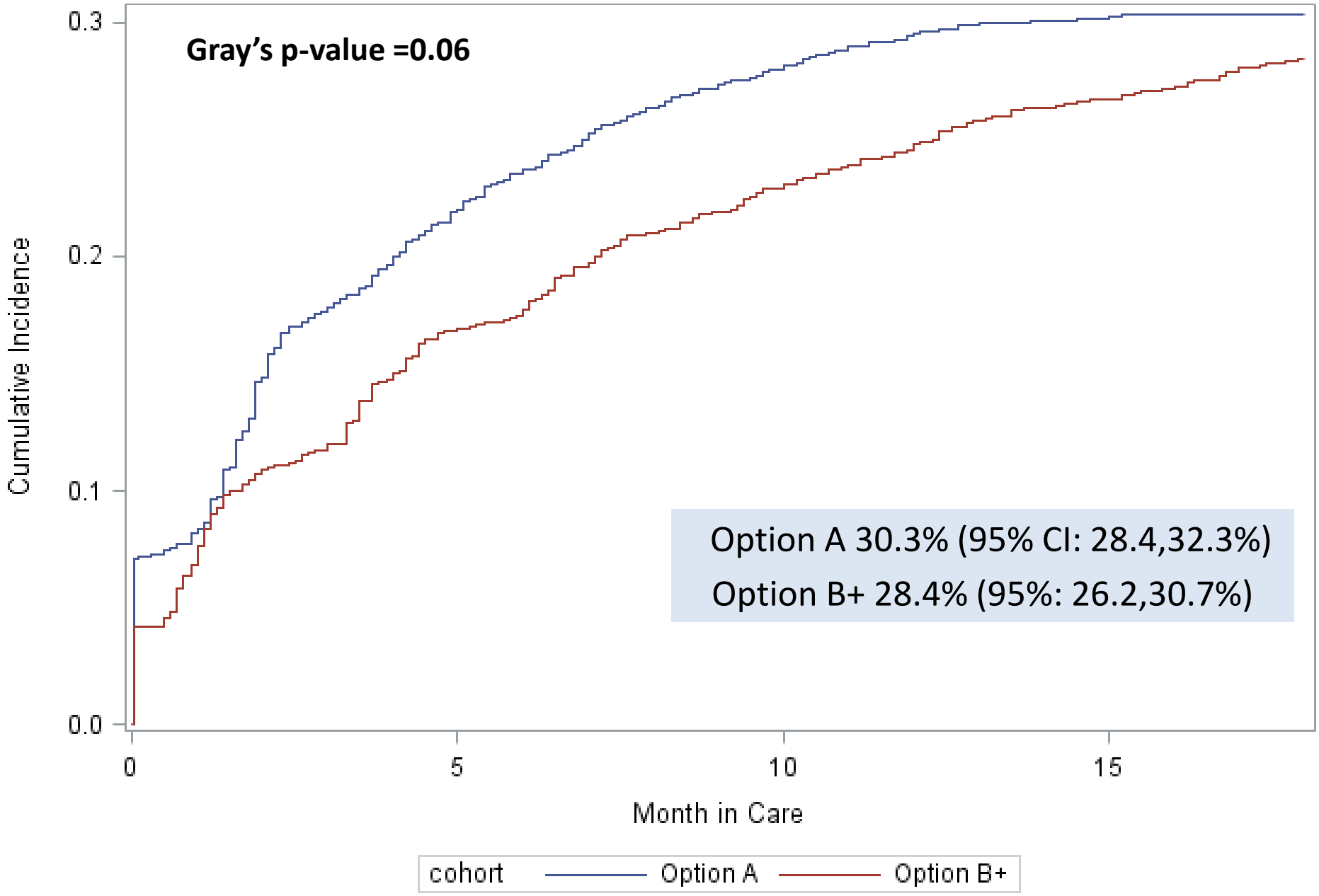
Characteristic	Option A Cohort N=2203	Option B+ cohort N=1571
Mode of delivery [N (%)]		
Vaginal Delivery	1832(83.2%)	1282(81.6%)
Caesarean section	371(16.8%)	289(18.4%)
Place of delivery [N (%)]¥		
Health facility	2148(98.4%)	1545(98.4%)
Home/TBA	34(1.6%)	25(1.6%)
ARV's for PMTCT		
Yes	2118(96.4%)	1517(96.7%)
No	79(3.6%)	52(3.3%)
PMTCT regimen [N (%)]‡		
cART†	1074(48.9%)	1508(96.1%)
AZT+3TC, sdNVP	361(16.4%)	9(0.6%)
AZT, sdNVP	483(22.0%)	0(0%)
sdNVP	200(9.1%)	0(0%)
None	79(3.6%)	52(3.3%)

¥ 22 (0.6%) Missing values; ‡ 8 (0.2%)missing values;† cART Combination antiretroviral therapy.

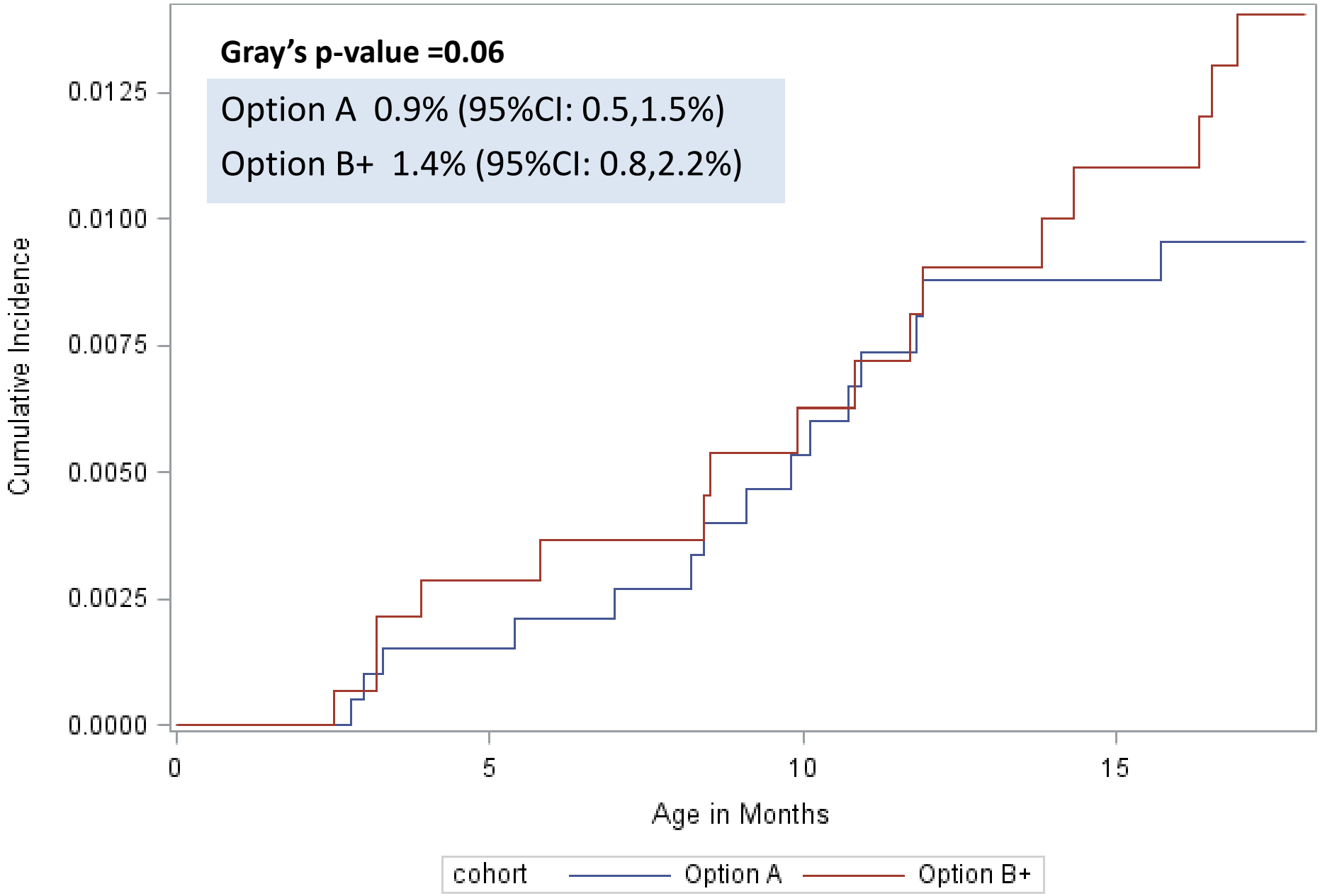
18 month cumulative incidence of HIV infection



18 month cumulative incidence of Loss to follow up



18 month cumulative incidence of mortality



Proportion of HIV infected infants initiated on cART before and after Option B+

Characteristic	Option A Cohort N=97	Option B+ cohort N=58	p-value
Initiated on ART [n (%)]			0.04
Yes	72(74.2%)	51(87.9%)	
No	25(25.8%)	7(12.1%)	
Median age at HIV Diagnosis(months)	1.9(1.5,8.4)	3.7(1.5,8.1)	0.35
Median months from HIV diagnosis to cART initiation(IQR)	2.3(1.6,4.2)	0.6(0.4,0.8)	<0.01

Factors associated with MTCT of HIV during option B+
Final Model

Predictors	Number	%infected	Adjusted HR	
Mother ARV's for PMTCT[a]				
Yes	1517	2.2	Reference	<0.001
No	52	46.2	16.3(7.6,34.6)	
Infant ARV's for PMTCT[b]				
Yes	1542	2.8	Reference	
No	24	14	2.5(1.03,4.95)	0.04

[a] 2 missing values;
[b] 5 missing values

Other variables that were significant at univariable analysis but were eliminated in the final model were; Infant feeding method, age at 1st PCR, place of delivery

Discussion

- We observed similar and low cumulative incidence of HIV infection
  - Half of mothers in Option A cohort received cART
  - The findings may be different from what lower level facilities with different implementation challenges may find.

- CI increased from 1% at 6 wks-4.3% at 18 month.
  - MTCT rates observed at 6wks could double by 18 months(Ciaranello et al., 2011, Schmitz et al., 2013)
  - Highlights the need for countries to report both 6 wk. and 18 months MTCT rates.

- LTFU is high in both cohorts despite robust follow up mechanisms.
  - Referral centre, mother receive care apart from infants and clients may self transfer.

- Estimates of HIV and Mortality are susceptible to bias due to LTFU

  Sensitivity analysis: HIV infection Option B+ lower bound: 3.8% upper bound 31%

Limitation: We studied infants who came for care after delivery. Our results could under-estimate outcomes.

Conclusion

- Outcomes of HIV-exposed infants at 18-months of life Pre and post Option B+ were similar; however, the cART initiation in HIV-infected infants was better during B+ implementation.

- Mothers or infants not receiving ARV's predicted MTCT during Option B+.

- LTFU remains high and should be addressed.

Acknowledge