

# Antibiotic usage in the first year of life in HIV-exposed, uninfected infants in Malawi: Results from the Breastfeeding, Antiretrovirals and Nutrition (BAN) Study

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## BACKGROUND

HIV-exposed, uninfected (HEU) infants in sub-Saharan Africa are a growing population at especially high risk for infectious diseases and resulting morbidity. Their antibiotic usage needs to be better studied to improve our understanding of their health care needs and to glean the magnitude of antibiotic use in such populations in under-resourced settings.

## OBJECTIVES

1. Describe the prevalence of antibiotic use, according to clinical indication and antibiotic category in HEU infants
2. Identify factors associated with increased hazard of antibiotic use in HEU infants

## METHODS

- Data are from the Breastfeeding, Antiretrovirals and Nutrition (BAN) study in Lilongwe, Malawi from 2004-2010
- Mother-infant pairs were randomly assigned to an ARV intervention arm (infant nevirapine, maternal triple-drug ARV regimen or neither) at birth and continued for 28 weeks or until breastfeeding cessation, if earlier.
- Enrollment criteria:
  - Mothers: CD4 count  $\geq 250$  cells/ $\mu\text{L}$  ( $\geq 200$  cells/ $\mu\text{L}$  before July 24, 2006)
  - Infants: birthweight  $\geq 2$  kg
- All infants and mothers received 7 days of zidovudine/lamivudine and infants received a single dose of nevirapine at birth
- Due to evidence of intervention effectiveness, control arm ceased after enrolling 668 mother-infant pairs
- Data on prescriptions were abstracted from study pharmacy records
- Outcomes in this analysis comprised prescriptions for antibacterial agents. Other prescriptions, including anti-malarial and anti-parasitic medications were excluded.
- Cotrimoxazole preventive therapy (CPT) was initiated study-wide for women and infants on June 13, 2006.
- Time analyzed: follow-up from 2 to 48 weeks of age
- Categorical proportions of exposures, covariables and total antibiotic prescriptions were compared using chi-square tests and continuous variables were assessed using the Kruskal-Wallis test.
- Cox proportional hazards models with recurrent events modeled as a counting process, was used to assess the hazards of antibiotic prescription by baseline and time-varying covariates (malaria season, infant age and cotrimoxazole exposure).

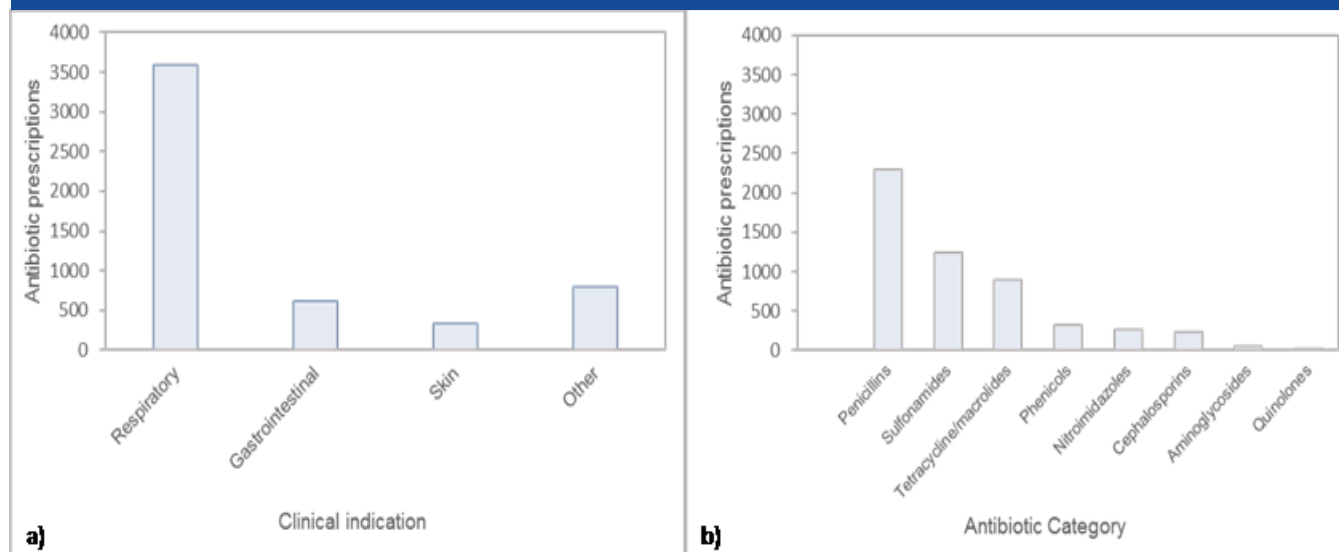
**Table 1. Baseline Characteristics of HIV-exposed, uninfected infants (at the 6-week post birth visit) in the Breastfeeding, Antiretrovirals and Nutrition (BAN) Study, Malawi, 2004-2010, overall and according to baseline visit timing relative to cotrimoxazole prophylaxis (CPT) guideline implementation (June, 2006)**

	Total	pre-CPT Total	post-CPT Total	p*
n	2152	692 (32.16)	1460 (67.84)	
Maternal education				1.0
None (%)	245 (11.4)	81 (11.7)	164 (11.3)	
Primary (%)	1153 (53.7)	369 (53.3)	784 (53.8)	
Secondary (%)	730 (34.0)	236 (34.1)	494 (33.9)	
Tertiary (%)	21 (1.0)	6 (0.9)	15 (1.0)	
Maternal CD4, cells/ $\mu\text{L}$ **	440 (330, 582)	437 (328, 596.5)	441 (330, 578)	0.8
Maternal HIV viral load during pregnancy, copies/mL**	16045 (4462, 48857)	51274	15281 (4339, 48192)	0.2
Maternal age at delivery, years**	<b>26 (22, 29)</b>	<b>25 (22, 29)</b>	<b>26 (23, 29)</b>	<b>0.047</b>
Male (%)	1088 (50.6)	358 (51.7)	730 (50.0)	0.5
Birth weight, g**	3000 (2700, 3300)	3000 (2700, 3300)	3000 (2700, 3300)	0.7
ARV treatment arm				<b>0.002</b>
Control (%)	<b>597 (27.7)</b>	<b>227 (32.8)</b>	<b>370 (25.3)</b>	
Maternal ARV (%)	<b>766 (35.6)</b>	<b>229 (33.1)</b>	<b>537 (36.8)</b>	
Infant nevirapine (%)	<b>789 (36.7)</b>	<b>236 (34.1)</b>	<b>553 (37.9)</b>	
Nutrition arm (%)	1076 (50.0)	345 (49.9)	731 (50.1)	0.9

\*P-values based on Kruskal-Wallis test for continuous variables. P-values for categorical variables based on Pearson's chi-square test

\*\*Median (interquartile range)

**Figure 1. Antibiotic prescriptions by clinical indication (panel A) and antibiotic category (panel B), among HIV exposed, uninfected infants in the Breastfeeding, Antiretrovirals and Nutrition (BAN) study, Malawi, 2004-2010.**



**Table 2. Hazard ratio estimates for associations between antibiotic prescriptions and other variables in the Breastfeeding, Antiretrovirals and Nutrition (BAN) study, Malawi 2004-2010, Cox proportional hazards models\***

Factor	Hazard Ratio (95% confidence interval)
Cotrimoxazole Preventive Therapy	0.57 (0.52, 0.61)
Treatment arm	
Maternal antiretrovirals	0.85 (0.78, 0.93)
Infant nevirapine	0.90 (0.82, 0.98)
Nutritional supplement	1.05 (0.98, 1.12)
Maternal HIV viral load during pregnancy, log(copies/mL)	1.02 (1.003, 1.04)
Male sex	1.09 (1.02, 1.17)
Birth weight, kg	1.17 (1.06, 1.28)
Age category (reference: Birth-1 month)	
1-3 months	0.80 (0.67, 0.95)
3-6 months	0.63 (0.53, 0.76)
6-12 months	0.48 (0.40, 0.58)

\*Only covariates with significant hazard ratios shown. Model also adjusted for malaria season (October-April, nutritional supplement arm, maternal CD4+ count, maternal age and maternal education).

## DISCUSSION & CONCLUSIONS

HEU infants in the BAN study were prescribed antibiotics frequently, primarily to treat respiratory infections, and there was a strong association between CPT and lower hazard of antibiotic prescription.

With the expansion of life-long ART and CPT coverage in Malawi and other areas of high HIV and other infectious disease burden, HEU infants may experience decreased infectious morbidity and a resulting decrease in antibiotic use. Our study provides a useful reference point for measuring antibiotic usage among infants at high risk of infectious disease morbidity in a low-income country, and for assessing the effects of programs to improve the health of HEU infants in Malawi.

## CONTACT INFO

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