ART outcomes in perinatally-infected adolescents attending QECH, Blantyre, Malawi: Statistical analysis plan

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ART outcomes in adolescents

QECH is a tertiary referral hospital for the southern region of Malawi, but the clinic also provides primary care to the local population. All patients are managed according to the Malawian ART guidelines.

Type of study

This will be a retrospective cohort analysis using routinely collected clinical and outcome data from an electronic managements system (EMS) in use at the ART clinic of QECH.

Study population

The study will include data for all patients who were commenced on ART since the start of the program in June 2004 to December 2011 regardless of age. Data for all patients who started ART at other clinics then transferred to QECH ART clinic will be excluded from the analysis. Age will be categorized as follows: Children (0-<10 years), adolescents (10-19), adults (≥ 20 years).

Anonymized data will be obtained from the EMS from Baobab health. For each patient the following data will be extracted from the routine database: date of birth, age at start of ART, date of starting ART, starting ART regimen, gender, WHO staging and staging defining condition, baseline CD4 (if available), weight and height at start of ART, whether the patient was a PTB suspect at initiation of ART, past PTB treatment, PTB treatment at registration, new initiation of PTB treatment, occurrence and date of changing to second line ART, and ART outcome (ART stop, alive on ART, died, loss to follow up, and transfer out) as defined below.

Definitions of ART outcomes

The following are used by the national ART programme to define ART outcomes, with all patient cards reviewed once every 3 months by an external supervisor.

- **Loss to follow up:** is defined as when a patient failed to returned 8 weeks after his/her due appointment without known transfer out to another health facility.
- **ART stop:** when a patient or clinician decides to stop ART for whatever reason.

- **Died**: the patient has reportedly died.
- **Alive on ART**: the patient or registered guardian has attended his/her last appointment and collected medication.
- **Transfer out**: the patient has requested and been granted transfer out to another clinic

Analysis plan

All analyses will be conducted using Stata (version 12; Stata Corporation, College station, Texas, USA).

The key exposure variable of interest will be age group, categorized as: children (0-<10 years), adolescents (10-19), adults (≥ 20 years).

The study outcomes will include:

- Rates of each unfavourable ART outcome (death, loss to follow up, stopping ART, transferring out).
- Proportion lost to follow up at 12, 24, 36, 48 months after treatment initiation.
- Proportion that have died at 12, 24, 36, 48 months after treatment initiation.
- Distribution of WHO stage at registration (Table 13).
- Proportion on second-line ART (Table 13).
- The proportion of individuals with suspected PTB or with a history of PTB treatment on the first ART visit (Table 13).

Table 1: characteristics of study participants

Variable	Child (0-<10 years)	Adolescent (10-19 years)	Adult (≥20 years)	P value
Male				
CD4 count (cells/μL) <50 50-99 100-199 200-299 ≥300				
WHO stage Stage I or II Stage III Stage IV				
Death (overall) 12 months 24 months 36 months 48 months				
Loss to follow up 12 months 24 months 36 months				

48 months				
Transfer out				
Stop ART				
Second line ART				
Stunted				
Suspected or PTB history				
Period on ART (years) 1 2 3 4 ≥5				

For each outcome, data will be summarised both overall and by age group. Categorical outcomes will be compared between age groups using Pearson chi-squared test statistics and logistic regression. For the rate outcomes, age will be considered as a time-dependent variable (i.e. continuously updated throughout the follow up period). Kaplan–Meier survival curves will be generated to describe time to death and loss to follow up. Survival curves will be compared using the log-rank test, and hazard ratios will be calculated using Cox proportional hazard models**.**

The same techniques will be used to investigate other risk factors of death (Table 14) and loss to follow up (Table 15) in the different age-groups, including CD4 count, sex, WHO stage as specified *a priori* risk factors and other variables as identified through backwards stepwise Cox regression. The effect of these potential confounders on the relationship between age group and rates of death and loss to follow up will be assessed using multivariable Cox regression. Statistical significance will be defined as p-value of <0.05 for 2-sided comparisons.

Table 2: Multivariable analysis of risk of death

Variable	Unadjusted (95%CI)	P value	Adjusted (95% CI)	P value
Age group (years) 10-19 0-9 ≥20				
Sex Male Female				
CD4 count (cells/µL) <50 50-99 100-199 200-299 ≥300				
WHO stage Stage I or II Stage III Stage IV				
Period on ART (years) 1 2 3 4 ≥5				

Table 3: Multivariable analysis of risk of loss to follow up

Variable	Unadjusted (95%CI)	P value	Adjusted (95% CI)	P value
Age group (years) 10-19 0-9 ≥20				
Sex Male Female				
CD4 count (cells/µL) <50 50-99 100-199 200-299 ≥300				
WHO stage Stage I or II Stage III Stage IV				
Period on ART (years) 1 2 3 4 ≥5				