

The incidence of tuberculosis among HIV-infected children in a large observational cohort in Western Kenya



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BACKGROUND

The true burden of childhood TB is unknown due to a lack of adequate diagnostics to confirm TB in children. HIV complicates this problem further by:

- a) increasing vulnerability to acquiring TB infection;
- b) making it more likely that the child will develop active disease;
- c) collapsing the timeline from acquisition to death, thereby limiting the diagnostic window of opportunity; and
- d) increasing the probability of both death and TB relapse compared to mono-infected children.

OBJECTIVE

To calculate the incidence of, and factors associated with, tuberculosis in children by using the initiation of tuberculosis treatment as a proxy measure of clinically diagnosed disease.

METHODS

- The Academic Model for the Prevention and Treatment of HIV/AIDS (AMPATH) is Kenya's largest HIV/AIDS care system, with 65,000+ patients ever enrolled at 19 clinics around western Kenya.
- Patients were aged 0-13 years, confirmed HIV-infected, and had no evidence of tuberculosis at enrolment.
- Tuberculosis was diagnosed using a modified scoring system for children under 15 years recommended by WHO that includes chronic cough (>2 weeks), fever, night sweats, failure to thrive, anorexia, weight loss, history of contact with adults with smear-positive pulmonary TB, no response to standard broad-spectrum antibiotic treatment, one or more sputum smear positive for acid-fast bacilli, culture positive for *Mycobacterium*, and/or radiographic abnormalities consistent with active TB. A score of ≥ 5 triggers TB treatment initiation.
- Statistics: included descriptive statistics, Kaplan-Meier and Cox Proportional Hazards analysis.
- Age *a priori* not included in multivariable analysis because of its known predictive value, and its collinearity with school attendance and orphan status.
- Incidence rates (IR) and 95% confidence intervals (CI) were calculated per 100 person-years (PY) of follow-up.

RESULTS

- There were 6535 HIV-infected children aged 0-13 years eligible for analysis, 50.1% female, with a mean age of 2.9 years (s.d. 3.4). Of these, 234 (3.6%) had TB at enrolment and were subsequently excluded.
- Among the remainder, there were 765 new tuberculosis events in 4368.0 person-years of follow-up
 - **Incidence rate: 17.5 (16.3-18.8)/100py.**

Table 1. Factors associated with incident TB

Variable	Incident TB n (%)	No Incident TB n (%)	P-value
Gender			
Male	407 (51%)	2678 (49%)	0.205
Female	390 (49%)	2825 (51%)	
Age at enrolment			
Median(IQR) years	4.5 (2.0-7.8)	0.81 (0.2-3.9)	<0.001
Urban/rural clinic			
Urban	379 (59%)	2566 (54%)	0.007
Rural	259 (41%)	2206 (46%)	
Ever attended school			
Yes	304 (46%)	855 (20%)	<0.001
No	355 (54%)	3,449 (80%)	
Orphan status			
Orphan	302 (38%)	989 (18%)	<0.001
Non-orphan	495 (62%)	4515 (82%)	
Weight for height (z)			
≤ 3	208 (28%)	902 (17%)	<0.001
> 3	548 (72%)	4347 (83%)	
CD4% at enrolment			
Median (IQR)			
Age ≤ 18 months	17 (10-22)	22 (14-32)	<0.001
Age 18 mths-5yrs	16 (10-24)	20 (14-29)	<0.001
Age ≥ 5 yrs	15 (7-23)	18 (11-26)	<0.001
On ARVs at TB Dx			
Yes	130 (16%)	1054 (19%)	0.055
No	667 (84%)	4450 (81%)	

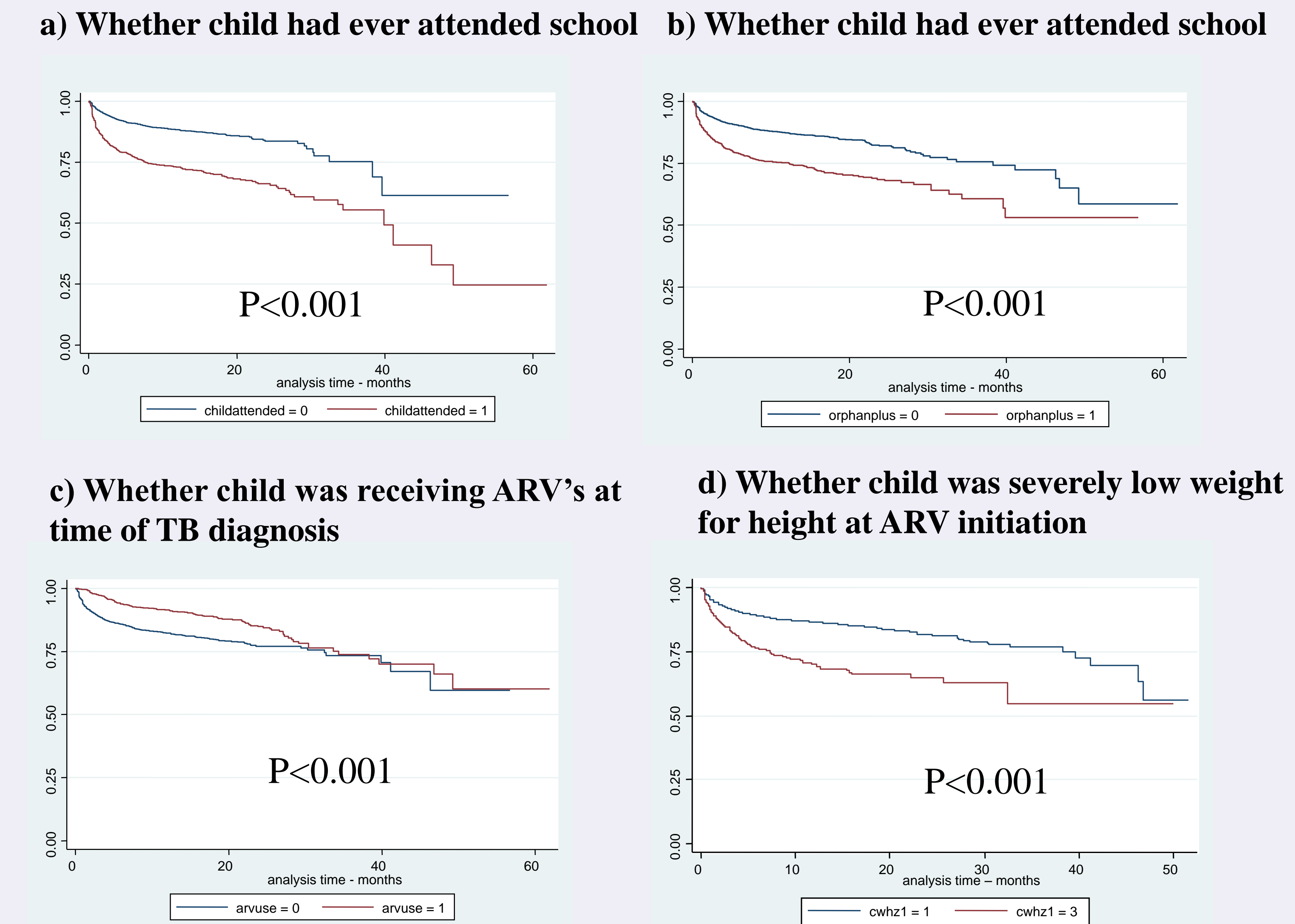
Table 2. Multivariate factors associated with incident TB

	Unadjusted HR (95%CI)	Adjusted HR (95% CI)
Ever in school* (yes vs. no)	2.61 (2.23-3.04)	2.43 (1.96-3.02)
Orphan* (orphan vs. non-orphan)	2.13 (1.84-2.47)	1.48 (1.21-1.82)
CD4 percent* (Per category of age- dependent definition of immune suppression)	1.70 (1.61-1.80)	1.89 (1.72-2.06)
Weight for height* (severely low vs. moderately low/normal)	1.51 (1.39-1.64)	1.50 (1.35-1.66)
On ARVs at TB diagnosis (yes vs. no)	0.53 (0.44-0.64)	0.16 (0.12-0.21)
Urban clinic* (urban vs. rural)	1.18 (1.00-1.39)	1.36 (1.14-1.63)

*: at ARV initiation

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Figure 1. Time to incident TB from initiation of ARV's by whether a) child had ever attended school, b) child was an orphan, c) child was receiving antiretroviral treatment at the time of the TB diagnosis, and d) severely low weight for height at ARV initiation.



CONCLUSIONS

- There is a high burden of tuberculosis among these HIV-infected children in Western Kenya.
- Although it requires controlled validation, TB treatment initiation can serve as a proxy for measuring disease burden in this situation.
- Children who have ever attended school, orphaned children, and those severely undernourished are at much higher risk of presumed TB disease requiring treatment.
- Children receiving antiretroviral treatment are at greatly reduced risk of active TB disease.
- These data suggest that screening for TB in places of congregation such as schools, and targeting efforts among orphans and children of low weight for height may reduce TB incidence in high prevalence areas.
- These data further suggest that the use of ARV treatment among HIV-infected children may significantly reduce their risk of developing active TB disease, similarly to HIV-infected adults.