

Treatment outcomes and tolerability of the revised WHO antituberculous drug dosages among children living in high HIV prevalence settings

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BACKGROUND

- In 2010, WHO revised the dosages of antituberculous drugs for children increasing rifampicin (R) to 15mg/Kg, isoniazid (H) to 10mg/Kg and pyrazinamide (Z) to 35mg/Kg.
- We assessed the treatment outcomes and safety, particularly liver toxicity of children treated with the new recommendations in Mbarara, Uganda.

OBJECTIVES

- To describe the end of treatment outcomes and the one year TB recurrence rate
- To identify factors associated with death
- To describe the occurrence of adverse events

METHODS

Eligibility criteria

- Aged 1 month to 14 years AND suspicion of tuberculosis based on:
 - At least one clinical sign suggestive of TB, OR
 - Referred with a CXR suggestive of TB, OR
 - Asymptomatic child with a recent TB contact history and abnormal chest X-ray
- Excluded if on TB treatment or had completed treatment within the past 6 months.

Study design

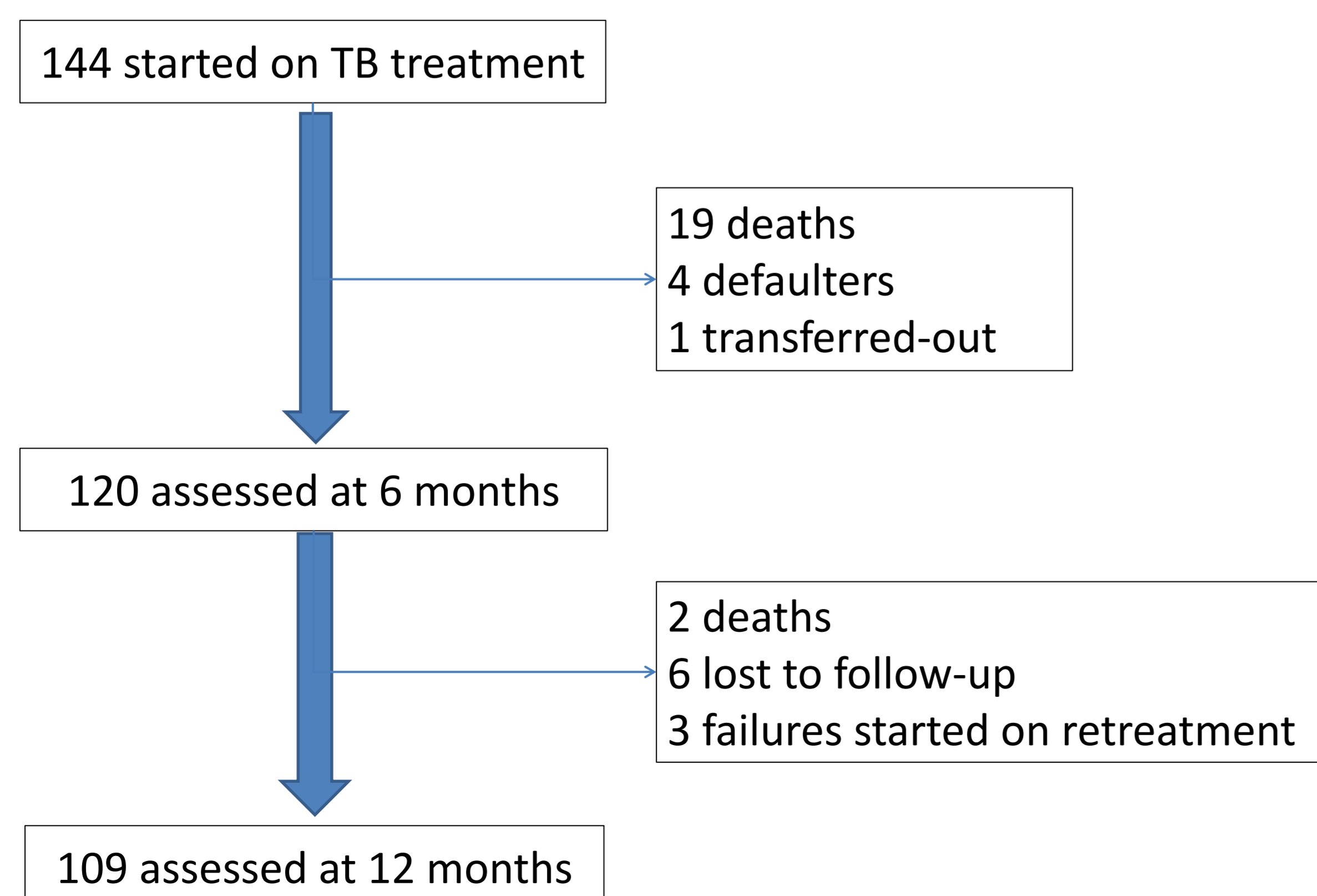
Prospective cohort

Procedures

- Diagnosis of TB :
 - Clinical assessment by a medical doctor
 - Antero-posterior and lateral chest X-ray
 - Sputum or induced sputum: smear, Xpert and culture
- Treatment of TB :
 - 2HRZ 4 HR
 - Addition of ethambutol (E) in HIV infected children or extensive disease or smear positive or suspicion of H resistance
 - WHO dosages-R 15mg/kg, H-10mg/kg, Z-35mg/kg and E-20mg/kg
- Bi-weekly follow up visits for intensive phase and monthly for continuation phase
- Alanine aminotransferase (ALT) monitoring at weeks 2, 4 and 8 of treatment
- Six months follow-up visit after completion of treatment

RESULTS

Study profile



Children Characteristics

- 106 (72.2%) were <5 years and 64 (60.4%) of these were <2 years.
- 56.3% males
- 48 (33.3%) HIV infected
- Malnutrition (weight for height Z score): 33.3% moderately to severely (<-2SD)
- 20 (13.9%) microbiologically confirmed
- Of the 124 empirically treated for TB, 100 (80.6%) had CXR suggestive of TB and 11(8.9%) had CXR abnormal non-suggestive of TB

TB Treatment Outcomes, N=144

Outcomes	Success	Failure	Default	Death	Transferred out
N (%)	117 (81.3%)	3 (2.1%)	4 (2.8%)	19 (13.2%)	1 (0.7%)

Median time between treatment initiation and death was 12 days IQR(8-39)

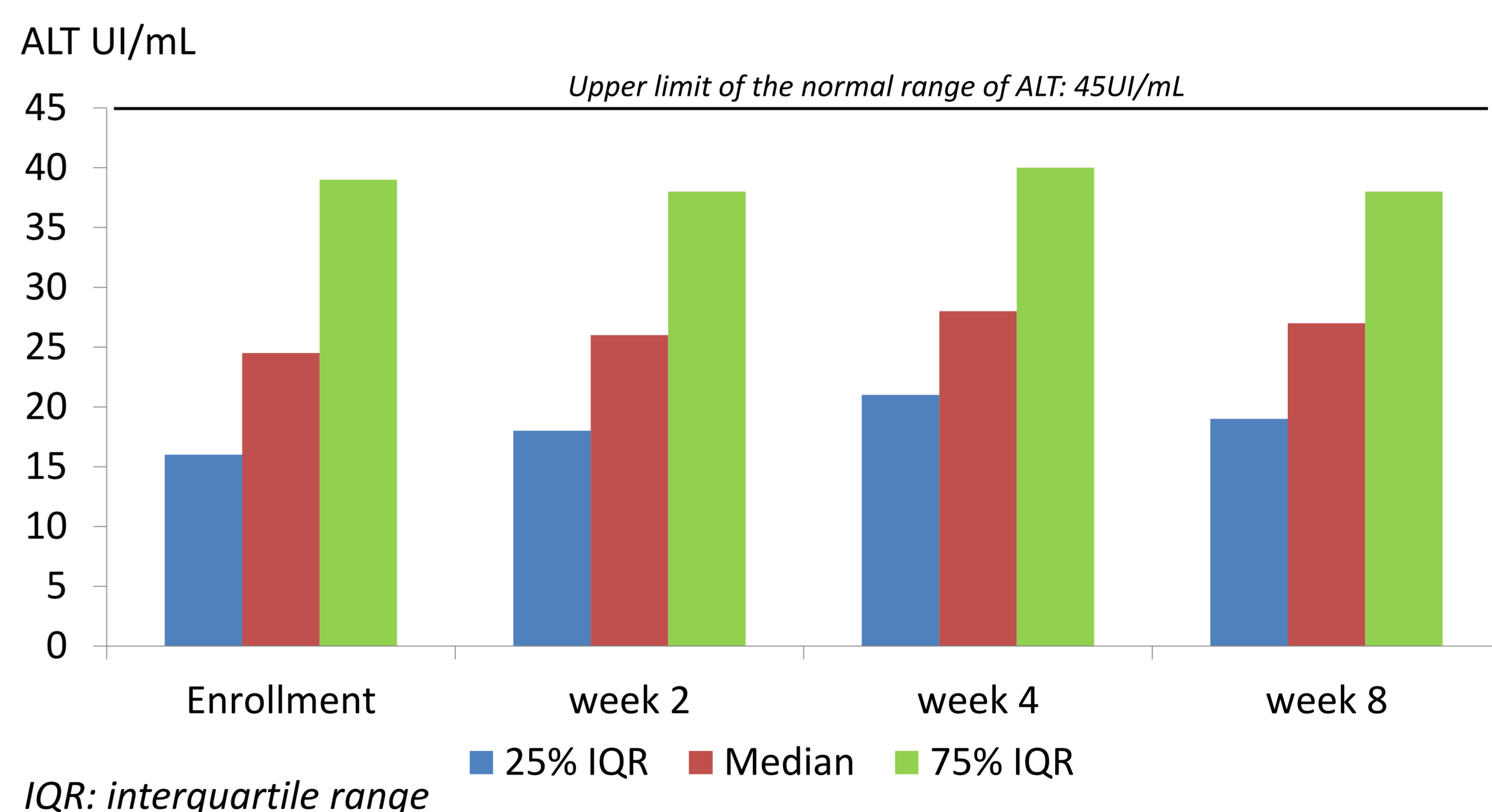
After adjusting for sex, HIV status and age, moderately to severely malnourished children had a higher risk of death: aOR 2.8 (95%CI 1.07-7.35)

Post TB treatment outcomes, N= 117

Outcomes	Sustained success	Relapse	Lost to follow up	Death
N (%)	109 (93.2)	0	6 (5.1)	2 (1.7)

Safety

Liver function test



Serious adverse events (SAE)

- 34 hospitalizations for SAE in 30 (20.8%) children
 - 16 (47.1%) acute low respiratory tract infections
 - 4 (11.8%) acute severe malnutrition
 - 3 (8.8%) malaria
 - 1 (2.9%) increase of ALT >5xULN at week 8: resolved without treatment interruption
- 28/34 SAE (82.4%) occurred in children <5 years

CONCLUSION

- Despite increased pill burden, the new TB recommended drug dosages did not result in high proportion of defaulters and treatment was well tolerated.
- More than 80% of children achieved treatment success. However, the high proportion of deaths, especially among malnourished children is a serious concern. It highlights the importance of early and better management of comorbidities in children with TB.

Acknowledgements

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