

WHO you calling short?

WHO growth standards vs. local references in statistical models: considerations for biological relevance

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Background

- Anthropometric measures are commonly converted to age-stratified z-scores to examine variation in growth outcomes in mixed-age and sex samples. Ideally these are calculated using established growth curves—e.g. the CDC growth references or the World Health Organization (WHO) growth standard.
- Growth trajectories of nationally representative samples have been shown to vary from those of the WHO multi-ethnic sample, even among affluent populations^{1,2}. Researchers should consider the biological implications of analyzing “representative” vs. “healthy growth” in using local growth references or the WHO standards^{3,4}.
- Blackwell et al. recently generated comparable robust growth references for Tsimane Amerindians (> 30,000 mixed-longitudinal measures)⁵
- We examined whether the use of Tsimane LMS references vs. the WHO standard may influence statistical inferences of Tsimane early child growth⁶.

Methods

- A mixed-longitudinal study was conducted in 9 Tsimane villages from July 2012 – April 2013.
- Anthropometric measures were collected at initial interview and follow-up from 152 children aged 0-35 months (281 observations total)
- Height-for-age (HAZ), weight-for-age (WAZ), and weight-for-height (WHZ) z-scores were calculated simultaneously from WHO and Tsimane growth references using the *localgrowth* package in R
- We constructed a baseline linear-mixed-effects regression model consisting of maternal height, infant age, and sex. We constructed multiple additive models of plausible growth determinants

Table 1. Visual summary of results for all WHO/Tsimane models. “+” = significant or trending positive association (p < 0.10), “-” = significant negative association, “ns” = non-significant. Red square = disagreement in significance of association in WHO/Tsimane LMS models; blue square = agreement

Independent Variable	Model	HAZ	WAZ	WHZ
Maternal height	Baseline	+ / +	+ / +	ns/ns
Male infant (vs. female reference)	Baseline	ns/ns	ns/ns	ns/ns
Infant age (months)	Baseline	- / ns	- / ns	ns/ns
Interbirth interval >= 33 vs. < 33 months (ref)	Model 2	+ / +	+ / +	ns/ns
First born vs. < 33 months (ref)	Model 2	+ / ns	ns/ns	ns/ns
Birth order vs. 7+ vs. 2-6 (ref)	Model 3	+ / +	+ / +	ns/ns
First born vs. 2-6 (ref)	Model 3	+ / ns	ns/ns	ns/ns
# siblings < 5 years old	Model 4	- / ns	- / ns	ns/ns
Remote vs. near market village (ref)	Model 5	ns/ns	ns/ns	ns/ns
Rainy vs. dry birth season (ref)	Model 6	ns/ns	ns/ns	ns/ns
Exclusive breastfeeding status (infants 0-6 months)	Model 7	ns/ns	ns/ns	ns/ns
Complementary feeding at 0-3 vs. 4-5 months (ref)	Model 8	+ / +	ns / +	ns/ns
Weaned vs. breastfeeding status (ref)	Model 9	ns / -	ns/ns	ns/ns

Results

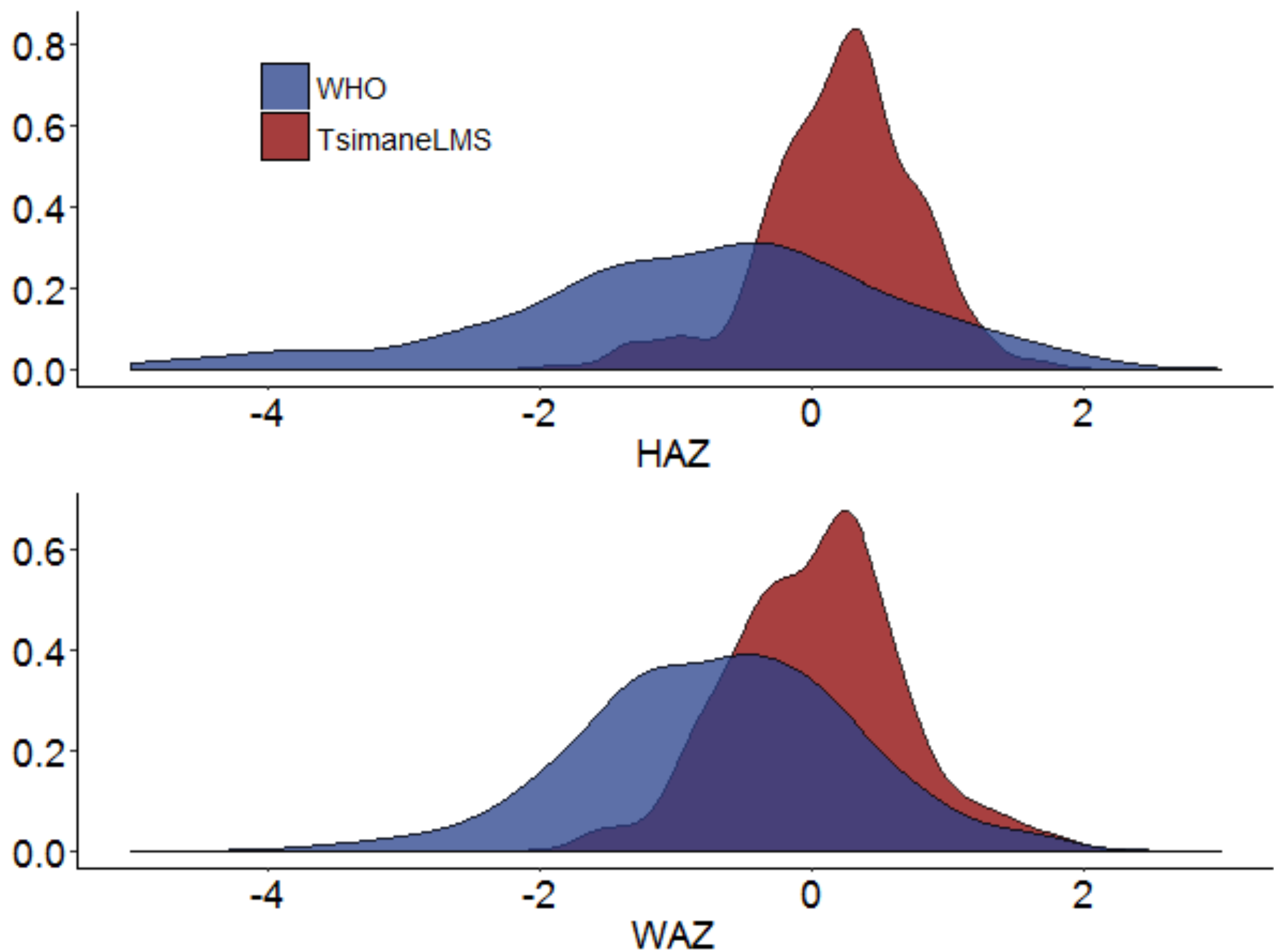


Fig. 1 (above): Density Plots of WHO and Tsimane-derived HAZ & WAZ measures (n = 156). WHO HAZ & WAZ scores are more varied and shifted left relative to Tsimane scores, with substantial negative skew in WHO in HAZ scores.

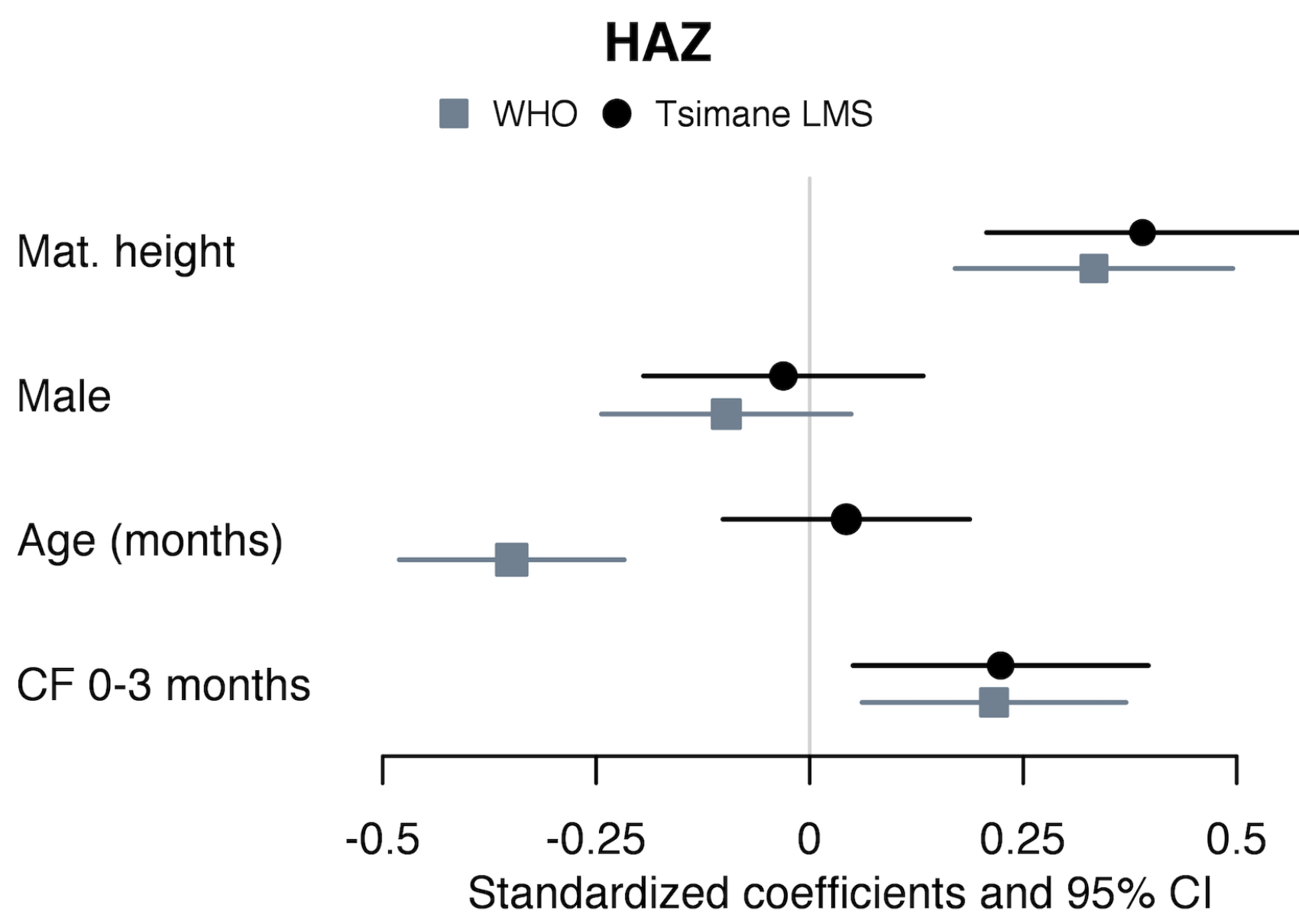


Fig. 2 (above): Standardized coefficients from Model 8. There was no difference in Tsimane vs. WHO-derived HAZ scores associated with age at complementary feeding (CF) introduction.

Discussion

- Distributions of WHO relative to Tsimane HAZ scores were negatively skewed (Fig. 1) reflecting age-related increases in prevalence of lower HAZ.
- Standardized coefficients estimated with WHO and Tsimane-derived z-scores agreed across most models. However, specific models differed in estimates of total variance explained and the significance of some coefficients (Table 1).
- Age was strongly, negatively associated with HAZ and WAZ in nearly all WHO, but not Tsimane-derived regression models (Table 1, Fig 2-4). Complementary feeding (CF) effects were similar in WHO and Tsimane-derived HAZ models, but predicted effects by age differed owing to age skew in WHO scores (Fig 2-3). Age and weaning were confounded in WHO models (Fig. 4).
- Biased estimates of WHO HAZ determinants have been noted for mixed-age samples^{7,8}. Bias may be more extreme with small samples and variables that are strongly age-patterned. Additional methodological considerations may be warranted when applying WHO standards to within-population studies, particularly for populations that systematically deviate from WHO standards owing to endemic environmental or genetic factors.

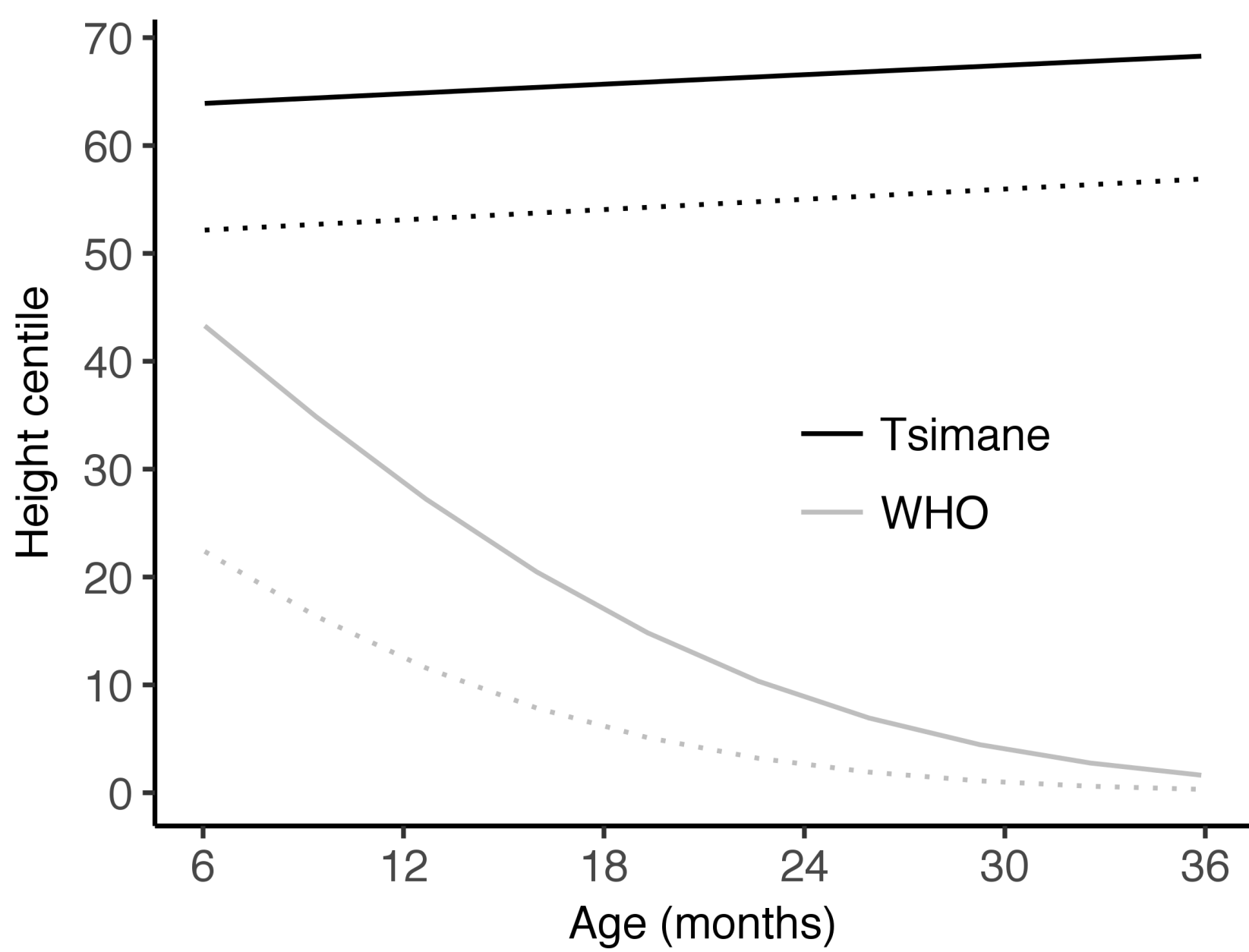


Fig. 3 (above): Predicted effects of CF on HAZ by age differ between models owing to age-related negative skew in WHO HAZ scores. Solid line = CF at 0-3 months; dotted line = CF at 4-6 months

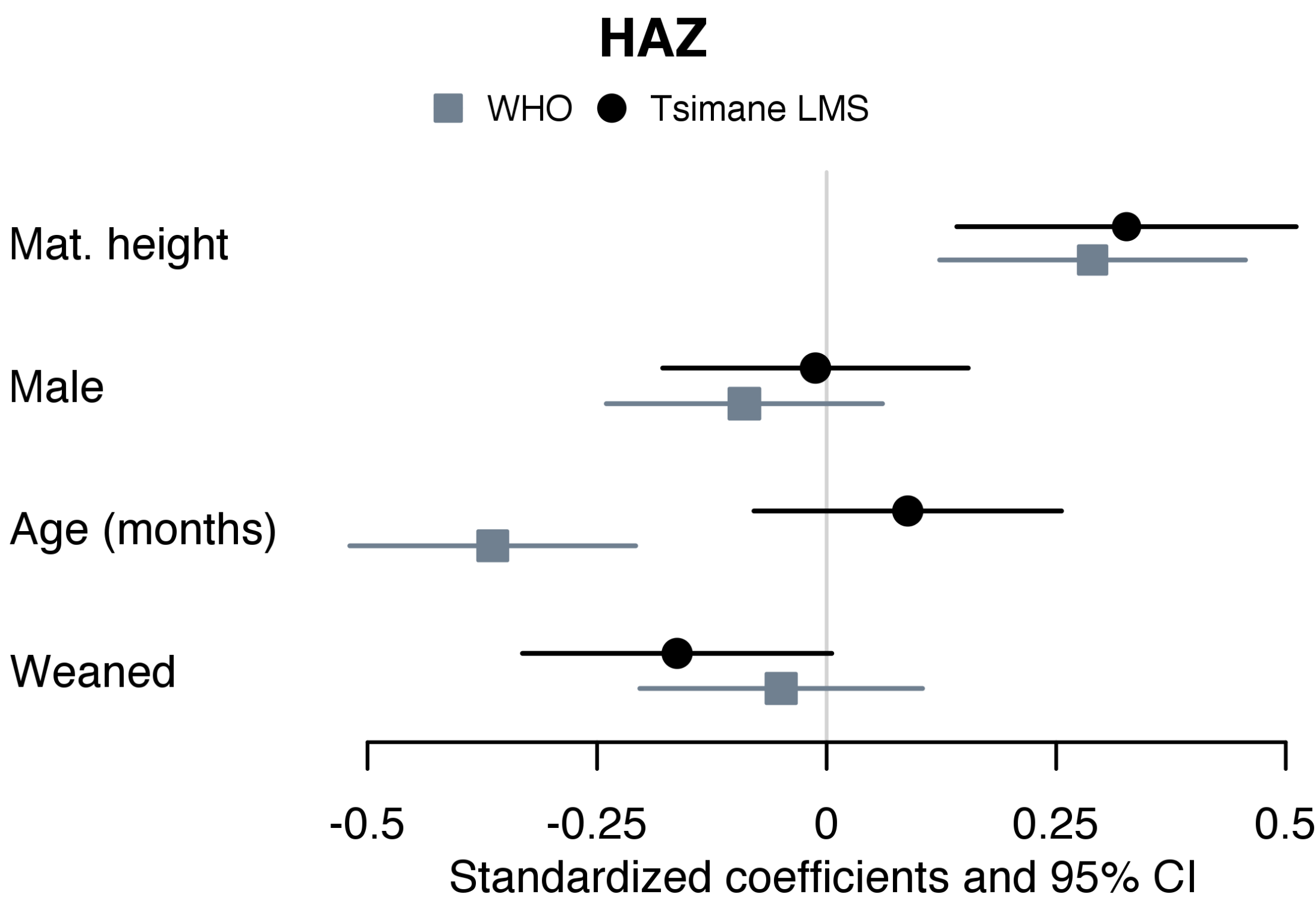


Fig. 4 (above): Standardized coefficients from Model 9. Age & weaning status are confounded in WHO-derived HAZ models.

REFERENCES: ¹Hui et al. (2008). *Arch Dis Child*. 93(7): 561-5; ²Tanaka et al. (2013). *Acta Paediatr*. 102(7): 739-43; ³Cole. (2007). *Significance*. 4: 6-10 ; ⁴Kramer et al. (2016). *PLOS ONE*. 11(3): 1-17; ⁵Blackwell et al. (2017). *Am J Phys Anthropol*. 162:441-61; ⁶Martin et al. (in press) *PLOS ONE*; ⁷Leroy et al. (2014). *J Nutr*. 144(9):1460-6. ⁸Alderman and Headley. (2018). *PLOS ONE*. 13(4):1-16.