

## Neonatal anthropometric indicators of infant growth and mortality in Burkina Faso

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**SHORT TITLE:** Neonatal indicators of growth and mortality

**FINANCIAL SUPPORT:** This study was supported by the Bill and Melinda Gates Foundation. The funders played no role in the design, implementation, or interpretation of data or the decision to submit for publication.

**CONFLICTS OF INTEREST:** None to report.



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DOI 10.1017/S1368980024000880

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## ABSTRACT

**Objective:** Most evidence supporting screening for undernutrition is for children aged 6-59 months. However, the highest risk of mortality and highest incidence of wasting occurs in the first 6 months of life. We evaluated relationships between neonatal anthropometric indicators, including birthweight, weight-for-age Z-score (WAZ), weight-for-length Z-score (WLZ), length-for-age Z-score (LAZ), and mid-upper arm circumference (MUAC) and mortality and growth at 6 months of age among infants in Burkina Faso.

**Design:** Data arose from a randomized controlled trial evaluating neonatal azithromycin administration for prevention of child mortality. We evaluated relationships between baseline anthropometric measures and mortality, wasting (WLZ < -2), stunting (LAZ < -2), and underweight (WAZ < -2) at 6 months of age was estimated using logistic regression models adjusted for the child's age and sex.

**Setting:** Five regions of Burkina Faso.

**Participants:** Infants aged 8 to 27 days followed until 6 months of age.

**Results:** Of 21,832 infants enrolled in the trial, 7.9% were low birthweight (<2500 g), 13.3% were wasted, 7.7% were stunted, and 7.4% were underweight at enrollment. All anthropometric deficits were associated with mortality by 6 months of age, with WAZ the strongest predictor (WAZ < -2 to  $\geq$  -3 at enrollment versus WAZ  $\geq$  -2: adjusted odds ratio, aOR, 3.91, 95% confidence interval, CI, 2.21 to 6.56). Low WAZ was also associated with wasting, stunting, and underweight at 6 months.

**Conclusions:** Interventions for identifying infants at highest risk of mortality and growth failure should consider WAZ as part of their screening protocol.

**Keywords:** Undernutrition; screening; infant mortality; underweight

## INTRODUCTION

Current World Health Organization guidelines recommend the use several indicators for identifying nutritionally at-risk in infants, including low weight-for-length Z-score (WLZ) and low weight-for-age Z-score (WAZ) in neonates.<sup>1</sup> Infants with low WLZ, or wasting (WLZ < -2), are at increased risk of morbidity and mortality compared to those with WLZ  $\geq$  -2.<sup>2</sup> Recently, evidence has suggested that WAZ and mid-upper arm circumference (MUAC) may be the best predictors of morbidity and mortality in infants under 6 months of age.<sup>3</sup> In children over 6 months of age, acute malnutrition is defined based on WLZ (or weight-for-height Z-score, WHZ) or MUAC, and guidelines for management are based on moderate (WLZ < -2 or MUAC < 12.5 cm) and severe acute malnutrition (WLZ < -3 or MUAC < 11.5 cm).<sup>4</sup> In children aged 6 to 59 months, both WAZ and MUAC are stronger predictors of mortality compared to WLZ/WHZ, and increasing attention has turned to the use of WAZ to identify nutritionally at-risk children.<sup>5,6</sup> Significantly less evidence exists to guide policy related to identification of at-risk infants under 6 months of age compared to children over 6 months of age.

Peak incidence of wasting in childhood occurs between birth and 3 months of age.<sup>7</sup> These infants struggle to catch up in growth trajectories to children who do not experience wasting, suggesting that an early wasting episode may disadvantage children for life, even if they do recover from wasting. Early identification of infants who are nutritionally at risk may allow for early intervention for these children.

The Sahelian region of West Africa is particularly vulnerable to undernutrition due to seasonal food insecurity, political instability, and climate change that can shorten growing seasons.<sup>8</sup> We used data from a randomized controlled trial of neonatal azithromycin administration for prevention of infant mortality in Burkina Faso<sup>9</sup> that included anthropometric measurements at baseline and 6 months of age to evaluate the ability of neonatal anthropometric measurements and birthweight to predict mortality and undernutrition (including wasting, stunting, and underweight) at 6 months of age.

## METHODS

**Parent study.** The *Nouveaux-nés et Azithromycine: une Innovation dans le Traitement des Enfants* (NAITRE) study was a 1:1 randomized controlled trial evaluating the efficacy of a single oral 20 mg/kg dose of azithromycin compared to placebo administered to neonates aged 8 to 27 days of age for prevention of all-cause infant mortality.<sup>9,10</sup> Infants were followed at 6 months of age to assess anthropometric outcomes and vital status.

**Study setting.** Participants were enrolled in 5 regions of Burkina Faso, a landlocked country in the West African Sahel region. Burkina Faso experiences highly seasonal rainfall, with a rainy season from approximately June through October that coincides with the high malaria transmission season. Food insecurity is typically higher during this period, as the annual harvest occurs in approximately November.<sup>11</sup>

**Participants.** Although azithromycin was hypothesized to reduce all-cause mortality in neonates based on results of trials in older infants<sup>12</sup>, some evidence from observational studies has suggested that exposure to macrolides during the neonatal period may increase risk of infantile hypertrophic pyloric stenosis, a rare but serious condition that requires surgical intervention.<sup>13</sup> As a result, while the primary aim of the parent trial was to assess efficacy of azithromycin for mortality, inclusion criteria focused on safety. Eligible participants were between 8 and 27 days of age and weighed at least 2500 g at the time of enrollment, as these subgroups of neonates were thought to have reduced risk of pyloric stenosis. Participants were enrolled in primary care facilities that were within 4 hours of a tertiary care facility that had pediatric surgical capacity. Additional inclusion criteria included ability to feed orally, planning to remain in the study area for the duration of the study, and caregiver consent.

**Anthropometric measurements.** Birthweight measurements were extracted from each child's government-issued health card. Birthweight is routinely recorded in the government health cards for all children who are delivered in facilities. Because birthweight was extracted from existing records, the measurements were not standardized or collected by trained study staff. Anthropometric measurements (height, weight, and MUAC) were measured at enrollment (age 8 to 27 days) and at 6 months of age. Weight was measured using a standard infant scale. The scale

was standardized each morning prior to measurement of any infants using a 2 kg test weight. Length was measured in triplicate using a ShorrBoard (Weight and Measure, LLC, Olney, MD) and the median was used for analysis. Mid-upper arm circumference (MUAC) was measured using a standard MUAC tape (Weight and Measure, LLC, Olney, MD). WAZ, WLZ, and LAZ were calculated based on 2006 WHO growth standards.<sup>14</sup> We defined moderate ( $WLZ < -2$  to  $\geq -3$ ) and severe ( $WLZ \leq -3$ ) wasting, moderate ( $LAZ < -3$  to  $\geq -3$ ) and severe ( $LAZ < -3$ ) stunting, and moderate ( $WAZ < -2$  to  $\geq -3$ ) and severe ( $WAZ < -3$ ) underweight at baseline to assess each measure's predictive ability for predicting mortality and moderate wasting, stunting and underweight at 6 months of age. There are no currently accepted cut-offs for MUAC for infants under 6 months of age, and previous studies have found a range of cut offs from 10.5 to 11.5 cm for identifying infants at highest risk of mortality. We therefore used cutoffs of  $\geq 11.5$  cm,  $< 11.5$  to  $\geq 10.5$  cm,  $< 10.5$  to  $\geq 9.5$  cm, and  $< 9.5$  cm. Birthweight was categorized into low birthweight ( $< 2500$  g) or normal birthweight ( $\geq 2500$  g).

**Vital status.** Vital status was measured at the 6-month follow-up visit. Children were classified as died, alive, or unknown. Vital status at 6 months of age was used as the main outcome for analysis.

**Statistical methods.** We evaluated the relationship between birthweight (pre-enrollment), WAZ, WLZ, LAZ, and MUAC (at enrollment, 8 to 27 days of age) and 6-month outcomes, including mortality, wasting, stunting, and underweight. We built a separate logistic regression model for each outcome and baseline anthropometric measurement, adjusted for age at enrollment and sex of the infant, to assess the relationship between pre-defined categories of anthropometric measures at baseline and each outcome at 6 months. To assess the discrimination of each baseline anthropometric measure to identify mortality risk, we calculated the area under the receiving operating characteristic curve. Because the study treatment (azithromycin or placebo) occurred after baseline anthropometric measurements, and because there was no effect of azithromycin versus placebo on mortality or anthropometric endpoints, analyses were not adjusted for the study treatment arm.<sup>9</sup> All analyses were conducted in R version 4.1.3 (The R Foundation for Statistical Computing, Vienna, Austria).

## RESULTS

Of 21,832 infants enrolled in the trial, 7.9% were low birthweight (weight < 2500 g) based on data extracted from their government-issued health card. Birthweight information was missing for 512 (2.4%) infants. At enrollment (8 to 27 days of age), 7.4% were underweight (WAZ < -2), 13.3% were wasted (WLZ < -2), and 7.7% were stunted (LAZ < -2; **Table 1**). Vital status information at 6 months of age was available for 20,960 children. By 6 months of age, 92 of the enrolled children had died (0.44%). At 6 months of age, 7.0% of infants were underweight, 5.8% were wasted, and 9.3% were stunted.

All baseline anthropometric measurements were associated with mortality, with children with greater anthropometric deficits for all indicators at baseline having increased risk of mortality by 6 months of age (**Table 2**). The strongest predictor of mortality in all categories was WAZ, which also had the greatest area under the ROC curve (0.68, 95% CI 0.63 to 0.74; **Table 2**; **Figure 1**). Pre-defined categories for MUAC as an indicator of undernutrition are not established for infants under 6 months of age. We found evidence of increasing risk of mortality as MUAC decreased. There was no evidence of effect modification by low birthweight, although the analysis was underpowered, especially for the low birthweight subgroup (**Supplemental Table S1**). In the overall cohort, a cutoff of 10.5 cm appeared to have the best performance for detecting children at high risk of mortality (**Figure 1**).

All anthropometric deficits at baseline were associated with anthropometric deficits at 6 months of age, including wasting, stunting, and underweight (**Table 3**). In general, children with specific anthropometric deficits at enrollment had higher risk of that deficit at 6 months of age (e.g., wasting). Low WAZ at enrollment and low birthweight were predictors of all anthropometric deficits at 6 months of age (**Table 3**). Low MUAC at enrollment was predictive of wasting and underweight at 6 months of age, but only MUAC < 9.5 cm was associated with stunting (**Table 3**).

## DISCUSSION

Consistent with previous evidence, we found that WAZ was the strongest predictor of mortality among infants under 6 months of age in Burkina Faso.<sup>3</sup> Results are consistent with a previous study in Burkina Faso, which found that MUAC and WAZ at birth better identify risk of mortality than WLZ.<sup>15</sup> WAZ is attractive as an alternative anthropometric indicator for mortality compared to WLZ, as it does not require measuring length, which can be more error-prone than measuring weight. Previous evidence has shown lower reliability of WLZ compared to WAZ or MUAC measurements.<sup>16</sup> Weight is routinely measured in primary care settings for monitoring growth in infancy using standard hanging infant scales. Using these measures to identify children at highest risk of poor outcomes and engage them in care could leverage existing health infrastructure for screening children for undernutrition. However, although WAZ is typically easier to measure than WLZ, in practice, hanging infant scales may have low precision for measuring young infants, which can introduce bias into the measurement of WAZ.

For children aged 6-59 months, MUAC is routinely used in community-based settings for mass screening of children for acute malnutrition and referral for those below set cutoffs (< 12.5 cm for moderate acute malnutrition and < 11.5 cm for severe acute malnutrition). Given the ease with which MUAC can be measured and that it does not require calibrated equipment, it may be more practical than WAZ or WLZ even if it has slightly worse performance. In 2023, the updated World Health Organization guidelines included low MUAC (< 11.0 cm) as a criterion for identifying nutritionally at-risk infants aged 6 weeks to 6 months but did not include MUAC for identification of at-risk neonates. Previous evidence has suggested a range of MUAC values between 11.5 and 10.5 cm to be optimal for identifying wasting in infants under 6 months of age.<sup>3</sup> In line with these results, the present analysis identified a cutoff of 10.5 cm in neonates aged 8-27 days, although MUAC did not perform as well as WAZ or WLZ for predicting mortality. However, the practicalities of MUAC measurement may outweigh slightly reduced performance. Further research evaluating MUAC as a criterion for identifying nutritionally at-risk neonates that includes the smallest infants is warranted.<sup>17</sup>

Although low birthweight infants had higher mortality than normal birthweight infants, birthweight did not perform as well for identifying children at risk of mortality as other neonatal

anthropometric measures.<sup>18</sup> Low birthweight can be a result of preterm birth or restricted intrauterine growth, and its etiology is diverse. The present study was unable to measure gestational age due to lack of ultrasound or last menstrual period data. As babies had to be at least 8 days of age to be eligible for the study, those who were born and died in their first week of life were not included in this cohort. Results therefore may not be generalizable to neonates in their first week of life and may underestimate the relationship between low birthweight and mortality. Low birthweight in the cohort was associated with poor growth outcomes at 6 months and was more strongly associated with stunting and underweight than with wasting, in line with previous evidence from sub-Saharan Africa.<sup>19</sup>

This analysis must be considered in the context of several limitations. Data arose from a randomized controlled trial designed to evaluate the efficacy of neonatal azithromycin for prevention of infant mortality. Inclusion criteria prioritized safety of research participants, specifically with regards to risk of infantile hypertrophic pyloric stenosis (IHPS). As some studies have suggested that smaller infants may be at increased risk of IHPS<sup>20,21</sup>, infants weighing less than 2500 g at the time of enrollment (age 8 to 27 days) were not eligible for the trial. As a result, this cohort was likely better nourished than the general population of infants in Burkina Faso, and some enrollment groups, such as low WAZ, were relatively small. However, this large cohort with enrollment from across Burkina Faso provides valuable data regarding the utility of neonatal anthropometric measurements for identifying at-risk infants. Future studies with population representative samples should be conducted to confirm these results, and results should be interpreted with the limitation that the most vulnerable neonates were not included in this study. Data were collected as part of a large randomized controlled trial, and results may not be generalizable to non-trial settings. Trials often represent best-case scenarios, as they typically have resources that are not available under real-life conditions. As previously noted, equipment used for anthropometric measurement may be poorly calibrated or have low precision for measuring small infants.<sup>16</sup> Analysis of anthropometric indicators using routinely collected programmatic data may be valuable data to understand the performance of these indicators under real-world conditions. Analyses of birthweight should be interpreted with caution. Infants who died before being screened for the trial may have been more likely to be low birthweight, thus biasing results. Birthweight measures were not standardized, as they were extracted from



government-issued health cards and not measured by trained study staff. As a result, there may be more measurement error in the birthweight measures than in anthropometric measures collected by the trial. Birthweight measurements were missing for some children, either because they were not born in a health facility and thus did not have their birthweight measured, or because their health card was missing. If these infants were more likely to be low birthweight and more likely to die or have worse growth compared to those born in a facility, there could be bias introduced via missing birthweight measurements. However, the prevalence of missing birthweight was relatively low (2.4%), and thus unlikely to introduce substantial bias.

Overall, the results of this study suggest that, in line with previous evidence, neonatal WAZ was the strongest predictor of mortality by 6 months of age. Low WAZ was also highly predictive of other anthropometric deficits at 6 months of age, including stunting and wasting. However, given the potential limitations of measuring WAZ, especially outside of trial settings, additional studies evaluating MUAC in neonates, including the smallest infants, should be considered.

#### **AUTHORSHIP**

MB, AS, EL, TML, KSO, CEO designed the study. MB, AS, AZ, GC, TO, EL, TML, CEO supervised data collection. AZ managed data collection and data cleaning. CEO analyzed data. MB and CEO wrote the paper. All authors read and approved the final manuscript.

#### **ETHICAL STANDARDS DISCLOSURE**

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving research study participants were approved by the Comité d’Ethique pour la Recherche en Santé in Ouagadougou and the Institutional Review Board at the University of California, San Francisco. Written informed consent was obtained from the caregiver of each enrolled infant.

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**Table 1.** Baseline characteristics (N=21,832) of the study sample

	<b>Characteristic</b>
Female sex, N (%)	10,844 (49.7%)
Age at enrollment, days, median (IQR)	11 (9 to 14)
Breastfeeding	
Immediate	20,661 (94.6%)
Delayed	1,140 (5.2%)
Not breastfeeding	26 (0.1%)
Missing	5 (0.02%)
Birthweight, g	
Mean (SD)	2998 (423)
Birthweight < 2500 g	1,719 (7.9%)
Missing	512 (2.4%)
WAZ at enrollment	
Mean (SD)	-0.61 (0.94)
WAZ < -2	1,617 (7.4%)
Missing	1 (0.005%)
WLZ at enrollment	
Mean (SD)	-0.64 (1.3)
WLZ < -2	2,903 (13.3%)
Missing	56 (0.3%)
LAZ at enrollment	
Mean (SD)	-0.52 (1.06)
LAZ < -2	1,673 (7.7%)
Missing	4 (0.02%)
MUAC at enrollment, cm	
Mean (SD)	10.9 (1.1)
Missing	86 (0.4%)

Abbreviations: IQR, interquartile range; SD, standard deviation; WAZ, weight-for-age Z-score; WLZ, weight-for-length Z-score; LAZ, length-for-age Z-score; MUAC, mid-upper arm circumference

**Table 2.** Associations between baseline anthropometric measures and mortality at 6 months

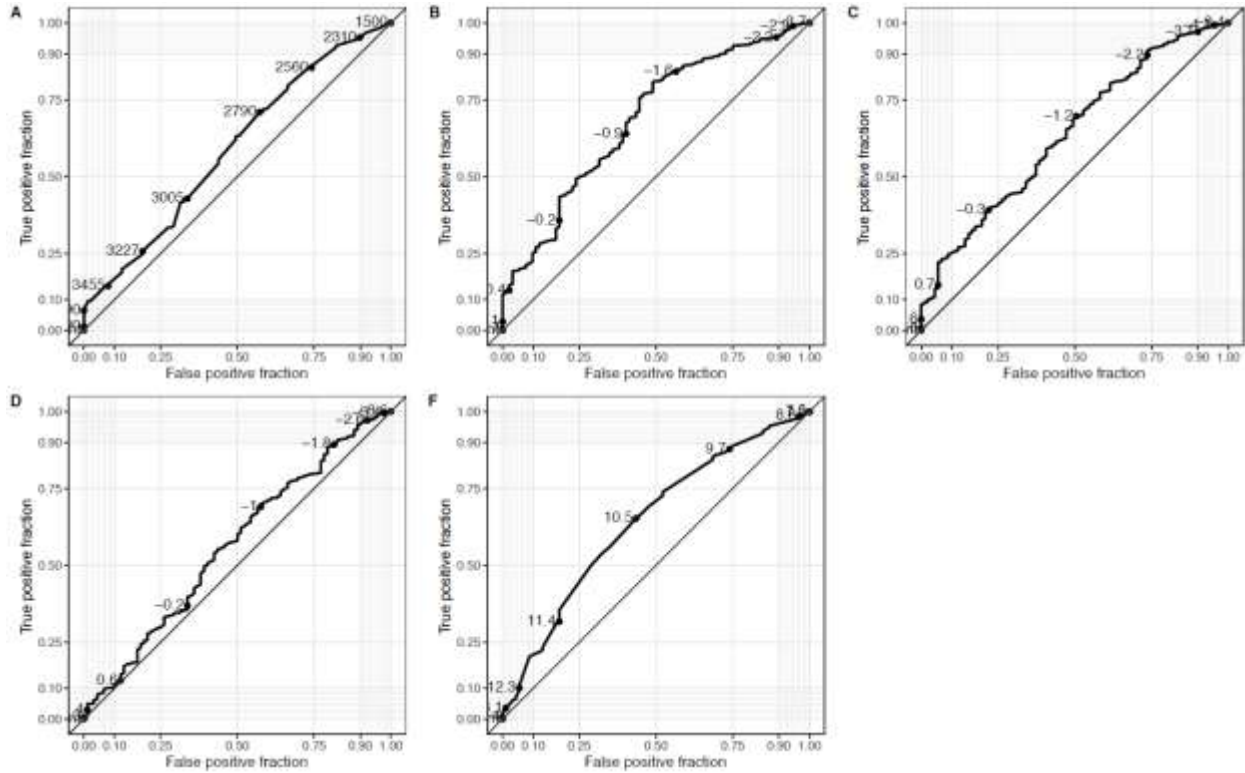
	N	Number Died (%)	Odds Ratio <sup>1</sup> (95% CI)
<b>Birthweight</b>			
≥2500 g	18,807	73 (0.37%)	1.00
<2500 g	1,654	16 (0.93%)	2.57 (1.42 to 4.36)
AUC (continuous)			0.56 (0.50 to 0.62)
<b>WAZ</b>			
≥ - 2	19,405	70 (0.35%)	1.00
< -2 and ≥ -3	1,406	18 (1.23%)	3.91 (2.21 to 6.56)
< -3	148	4 (2.55%)	11.15 (2.97 to 34.27)
AUC (continuous)			0.68 (0.63 to 0.74)
<b>WLZ</b>			
≥ - 2	18,094	65 (0.34%)	1.00
< -2 and ≥ -3	2,049	14 (0.66%)	1.92 (1.03 to 3.32)
< -3	762	12 (1.51%)	4.44 (2.28 to 7.96)
AUC (continuous)			0.64 (0.58 to 0.70)
<b>LAZ</b>			
≥ - 2	19,362	81 (0.40%)	1.00
< -2 and ≥ -3	1,344	7 (0.50%)	1.24 (0.51 to 2.54)
< -3	250	4 (1.53%)	3.82 (1.13 to 9.69)
AUC (continuous)			0.56 (0.50 to 0.62)
<b>MUAC</b>			
≥ 11.5 cm	6,419	16 (0.24%)	1.00
< 11.5 to ≥ 10.5 cm	7,177	24 (0.32%)	1.38 (0.73 to 2.64)
< 10.5 to ≥ 9.5 cm	5,790	38 (0.64%)	2.78 (1.57 to 5.16)
< 9.5 cm	1,489	14 (0.91%)	3.96 (1.90 to 8.17)
AUC (continuous)			0.61 (0.55 to 0.67)

Abbreviations: AUC, area under a receiver operating characteristic curve; WAZ, weight-for-age Z-score; WLZ, weight-for-length Z-score; LAZ, length-for-age Z-score; MUAC, mid-upper arm circumference; <sup>1</sup>Adjusted for child's age in days at enrollment and sex

**Table 3.** Associations between baseline anthropometric indicators and wasting, stunting, and underweight at 6 months of age

	<b>Wasted (WLZ &lt; -2)</b>		<b>Stunted (LAZ &lt; -2)</b>		<b>Underweight (WAZ &lt; -2)</b>	
	N (%)	OR <sup>1</sup> (95% CI)	N (%)	OR <sup>1</sup> (95% CI)	N (%)	OR <sup>1</sup> (95% CI)
<b>Birthweight</b>						
≥2500 g	959 (4.9%)	1.00	1,450 (7.4%)	1.00	1,105 (5.6%)	1.00
<2500 g	123 (7.2%)	1.49 (1.22 to 1.81)	303 (17.6%)	2.99 (2.59 to 3.45)	212 (12.3%)	2.35 (1.99 to 2.75)
AUC (continuous)		0.56 (0.54 to 0.58)		0.58 (0.57 to 0.60)		0.60 (0.58 to 0.62)
<b>WAZ</b>						
≥ -2	972 (4.8%)	1.00	1,477 (7.3%)	1.00	1,083 (5.4%)	1.00
< -2 and ≥ -3	129 (8.8%)	1.88 (1.54 to 2.29)	268 (18.4%)	2.79 (2.40 to 3.24)	231 (15.8%)	3.11 (2.65 to 3.64)
≤ -3	11 (7.0%)	1.53 (0.76 to 2.79)	43 (27.4%)	5.15 (3.43 to 7.64)	32 (20.4%)	3.93 (2.52 to 5.98)
AUC (continuous)		0.62 (0.61 to 0.64)		0.64 (0.63 to 0.66)		0.70 (0.68 to 0.71)
<b>WLZ</b>						
≥ -2	815 (4.3%)	1.00	1,544 (8.2%)	1.00	1,069 (5.7%)	1.00
< -2 and ≥ -3	218 (10.3%)	2.53 (2.16 to 2.96)	169 (8.0%)	0.99 (0.83 to 1.16)	197 (9.3%)	1.74 (1.48 to 2.04)
≤ -3	79 (10.0%)	2.56 (1.99 to 3.25)	58 (7.3%)	0.92 (0.67 to 1.20)	75 (9.5%)	1.83 (1.41 to 2.33)
AUC (continuous)		0.65 (0.63 to 0.66)		0.47 (0.46 to 0.49)		0.58 (0.56 to 0.59)
<b>LAZ</b>						
≥ -2	1,023 (5.1%)	1.00	1,410 (7.0%)	1.00	1,121 (5.6%)	1.00
< -2 and ≥ -3	79 (5.6%)	1.08 (0.85 to 1.37)	294 (20.8%)	3.70 (3.19 to 4.29)	180 (12.8%)	2.35 (1.97 to 2.79)
≤ -3	10 (3.8%)	0.71 (0.35 to 1.28)	84 (32.2%)	7.14 (5.33 to 9.52)	45 (17.2%)	3.16 (2.22 to 4.42)
AUC (continuous)		0.50 (0.48 to 0.52)		0.69 (0.67 to 0.70)		0.65 (0.63 to 0.66)
<b>MUAC</b>						
≥ 11.5 cm	229 (3.4%)	1.00	597 (8.9%)	1.00	272 (4.1%)	1.00
< 11.5 to ≥ 10.5 cm	426 (5.7%)	1.76 (1.50 to 2.08)	466 (6.2%)	0.71 (0.63 to 0.81)	461 (6.1%)	1.67 (1.43 to 1.95)
< 10.5 to ≥ 9.5 cm	346 (5.8%)	1.84 (1.55 to 2.19)	521 (8.7%)	1.09 (0.96 to 1.23)	433 (7.2%)	2.13 (1.82 to 2.50)
< 9.5 cm	107 (7.0%)	2.22 (1.75 to 2.82)	193 (12.5%)	1.65 (1.38 to 1.97)	172 (11.2%)	3.41 (2.78 to 4.18)
AUC (continuous)		0.53 (0.52 to 0.55)		0.48 (0.46 to 0.49)		0.55 (0.54 to 0.57)

Abbreviations: OR, odds ratio; AUC, area under a receiver operating characteristic curve; WAZ, weight-for-age Z-score; WLZ, weight-for-length Z-score; LAZ, length-for-age Z-score; MUAC, mid-upper arm circumference; <sup>1</sup>Adjusted for child's age in days at enrollment and sex



**Figure 1.** Receiving operator characteristic curves for neonatal anthropometric measurements predicting mortality by 6 months of age, including A) birthweight, B) weight-for-age Z-score, C) weight-for-length Z-score, D) height-for-age Z-score, and E) mid-upper arm circumference.