Child wasting and concurrent stunting in low- and middle-income countries

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Summary

Sustainable Development Goal 2.2.2, to end malnutrition by 2030, measures progress through elimination of child wasting, defined as weight-for-length more than 2 standard deviations below international standards. Prevailing methods to measure wasting rely on cross-sectional surveys that cannot measure onset, recovery, and persistence — key features of wasting epidemiology that could inform preventive interventions and disease burden estimates. Here, we show through an analysis of 21 longitudinal cohorts that wasting is a highly dynamic process of onset and recovery, and incidence peaks between birth and 3 months — far earlier than peak prevalence at 12-15 months. By age 24 months 29.2% of children had experienced at least one wasting episode, more than 5-fold higher than point prevalence (5.6%), demonstrating that wasting incidence is far higher than cross-sectional surveys suggest. Children wasted before 6 months were more likely to experience concurrent wasting and stunting (low height-for-age) later, increasing their risk of mortality. In diverse populations with seasonal rainfall, population average weight-for-length varied substantially (>0.5 z in some cohorts), with the lowest mean Z-scores during the rainiest months, creating potential for seasonally targeted interventions. Our results motivate a new focus on extending preventive interventions for wasting to pregnant and lactating mothers, and for preventive and therapeutic interventions to include children below age 6 months in addition to current targets of ages 6-59 months.

Introduction

Wasting is a form of undernutrition that results from a loss of muscle and fat tissue from acute malnutrition, affecting an estimated 45.4 million children under 5 years (6.7%) worldwide with over half living in South Asia.[1] Children are considered wasted if their weight-for-length z-score (WLZ) falls 2 standard deviations below the median of international standards.[2] Wasted children have weakened immune systems,[3] predisposing them to infections and more severe illness once infected.[4] Wasting in very young children increases their risk of mortality (relative risk: 2.3), with mortality risk further increasing if they are also stunted and underweight, defined as length-for-age (LAZ) below –2 and weight-for-age (WAZ) below –2 (relative risk: 12.3).[5] Longitudinal studies have shown that wasting is also associated with higher risk of stunting[6] and poor neurocognitive development at older ages.[7,8] Treatment of severely wasted children (WLZ below –3) with high calorie, ready-to-use-therapeutic foods has proven effective,[9,10] but rates of relapse and mortality remain high in this fragile subgroup.[11,12] Primary prevention of wasting would be preferable to treatment, but there are scant proven preventive interventions. Key among them, nutritional interventions have led to only small reductions in wasting, with breastfeeding support from birth not reducing wasting and small-quantity lipid-based nutrient supplementation between ages 6-24 months leading to a 14% relative reduction in wasting.[13–15]

Wasting is thought to occur primarily from ages 6-24 months during the critical period for adequate, appropriate and safe complementary feeding,[16,17] but a more complete understanding of the epidemiology of wasting and how it varies by age is key to develop and target preventive interventions.[16,18,19] Unlike the cumulative process of linear growth faltering and stunting,[20] wasting varies considerably over time, both within-individuals and within-populations.[21,22] The dynamic nature of wasting means that the number of distinct episodes a child experiences may be poorly captured in cross-sectional, survey-based estimates.[23] Furthermore, seasonal patterns of wasting onset in relation to changes in food insecurity or disease can only be measured accurately with longitudinal data.[19,24,25] A synthesis of longitudinal cohort data across diverse populations provides a unique opportunity to study the timing, dynamics, and burden of wasting in infants and young children — key knowledge gaps to inform future prevention efforts.

Pooled longitudinal analyses

Here, we report a pooled analysis of 21 longitudinal cohorts from 10 low- and middle-income countries (LMICs) in South Asia, Sub-Saharan Africa, and Latin America, that measured length and weight monthly among children 0-24 months of age. Our primary objectives were to produce the first large-scale estimates of wasting incidence and recovery and to quantify the temporal and regional variation. We also assessed the concurrence of wasting and stunting and compared estimates of wasting prevalence and incidence. We analyzed data from the Bill & Melinda Gates Foundation's Knowledge Integration (*ki*) database, which has aggregated studies on child growth and development.[26] Inclusion criteria were defined to select cohorts representative of general populations in LMICs with sufficiently frequent measurements to investigate the acute, dynamic nature of wasting: 1) conducted in low- or middle-income countries; 2) enrolled children between birth and age 24 months and measured their length and weight repeatedly over time; 3) did not restrict enrollment to acutely ill children; 4) had median birth year of 1990 or later 5) measured anthropometry at least monthly (Extended Data Fig 1). Twenty-one cohorts met the inclusion criteria, encompassing 11,448 children and 198,154 total anthropometry measurements from birth to age 24 months (Fig 1).

We calculated WLZ and LAZ-scores using WHO 2006 growth standards.[27] We dropped 385 biologically implausible measurements (0.2%) of WLZ (> 5 or < –5 Z-score) and 212 (0.1%) of LAZ (> 6 or < –6 Z-score), following WHO recommendations.[28] Most included cohorts did not measure children past 24 months, so analyses focused on birth to 24 months. Cohorts ranged in size from 160 children in the TDC cohort to 2,931 children from the MRC Keneba cohort (Fig 1). Unless otherwise indicated, we conducted individual-level analyses within cohorts and then pooled cohort-specific estimates using random effects models fit with restricted maximum likelihood estimation, a conservative approach when cohort-specific estimates are heterogeneous. Cohorts were distributed throughout South Asia, Africa, and Latin America, but did not cover entire regions (Extended Data Fig 2). Most cohorts measured children every month through age 24 months, but there was some attrition as children aged and there were four cohorts with few measurements beyond 15 months (Extended Data Fig 3). Pooled estimates at older ages could be slightly biased if cohorts or children who were not measured were systematically different from those that were included — for example, if children who were lost were more likely to be wasted, we might have under-estimated wasting at older ages.

We assessed *ki* cohort representativeness by comparing Z-score measurements to population-based samples in Demographic and Health Surveys (DHS). Mean z-scores in *ki* cohorts were generally representative based on country-level DHS estimates, with lower WLZ (overall and by age) in Guatemala, Pakistan, and South Africa and higher WLZ in Brazil and Guatemala (Extended Data Fig 4). LAZ was generally lower in *ki* cohorts, so estimates of concurrent wasting and stunting may be higher than estimates from population-based samples, and rates of wasting recovery in early life may be higher compared with the general population.

Age-specific patterns of wasting

Across all cohorts, mean WLZ was near –0.5 at birth and then increased over the first 6 months before decreasing until 12 months (Fig 2a). Age-specific patterns in WLZ were similar across geographic regions, but levels varied substantially by region. WLZ was markedly lower among South Asian cohorts, reflecting a much higher burden of malnutrition (Fig 2a). Children were wasted for 16,139 (8.6%) measurements, and severely wasted for 3,391 (1.8%) measurements. Wasting prevalence was highest at birth (11.9%; 95% CI: 7.0, 19.5) in contrast with prior studies that showed peak wasting prevalence between 6-24 months old (Fig 2b).[6,29–31] Across regions, wasting prevalence decreased from birth to three months and then increased until 12 months old, but was far higher in South Asian cohorts. In South Asian cohorts, where low birthweight is common,[32] at-birth wasting prevalence was 18.9% (95% CI: 15.0, 23.7), implicating causes of poor fetal growth like maternal malnutrition, maternal morbidities, and maternal small stature as key regional drivers of wasting.[33,34] Severe wasting followed a similar pattern but was much rarer (Extended Data Fig 5).

Wasting onset was highest during the first 3 months largely due to its high occurrence at birth (Fig 2c). Overall, 12.9% (95% CI: 7.6, 20.1) of all children experienced wasting by age 3 months, which accounted for almost half (47.8%) of children who ever experienced wasting in their first two years of life. A focus on wasting prevalence alone masked how common it was for children to experience wasting in their first 24 months. After birth, up to 6.5% (95% CI: 4.9, 8.6) of children were wasted at a specific visit, but 29.2% (95% CI: 17.5, 44.7) of children experienced at least one wasting episode by age 24 months, and in South Asian cohorts the cumulative incidence by age 24 months was 52.2% (95% CI: 43.5, 60.7, Figs 2b, c).

WHO Child Growth Standards overestimate wasting at birth among children born preterm,[35] though adjustment for gestational age among four cohorts with available data only reduced at-birth stunting prevalence by 0.8% and increased underweight prevalence by 0.7% (Extended data Fig 6). Even if preterm birth were to account for some of at-birth wasting, the small birth size, irrespective of cause, documented in this analysis raises concern because of its consequences for child growth faltering and mortality during the first 24 months.[34]

Seasonality of wasting

We joined monthly rainfall totals to cohorts by location and year, and for each cohort we estimated a seasonality index based on rainfall (details in Methods). We examined average WLZ over the calendar year and examined seasonal changes with respect to rainfall, under the hypothesis that seasonal changes in food availability and infection tied to rainfall could cause seasonal wasting.[36] Mean WLZ varied dramatically by calendar date in almost all cohorts, with a consistent minimum mean WLZ coinciding with peak rainfall (Fig 3a). Mean WLZ was -0.16 (95% CI: -0.19, -0.14) lower during the three-month period of peak rainfall, compared to the mean WLZ in the opposite three-month period of the year, when pooled across cohorts (Fig. 3b). Mean seasonal decline in WLZ was -0.27 (95% CI: -0.31, -0.24) in cohorts with a seasonality index > 0.9, but some cohorts evidenced seasonal WLZ declines of more than –0.5 (Fig. 3b).

South Asian cohorts had temporally synchronous rainfall, so we estimated WLZ at birth by calendar month, pooled across the 11 South Asian cohorts. Mean WLZ at birth varied by up to 0.72 Z (95% CI: 0.43, 1.02) depending on the month the child was born (range: -0.5 Z to -1.3 Z; Fig 3c), which suggests that seasonally-influenced maternal nutrition,[37] likely mediated through intrauterine growth restriction or preterm birth,[38] was a major determinant of child WLZ at birth. Birth month also influenced the effect of season on WLZ trajectories that persisted through a child's second year of life (Extended Data Fig 7).

Wasting incidence and recovery

There was high variability in WLZ across longitudinal measurements, with an average within-child standard deviation of WLZ measurements of 0.76, compared to 0.64 for LAZ and 0.52 for WAZ. We thus defined unique wasting episodes by imposing a 60-day recovery period, covering two consequent monthly measurements when a child's WLZ measurements needed to remain above –2 to be considered recovered and at risk for a future episode (Fig 4a). Children who were born wasted were considered to have an incident episode of wasting at birth. The mean number of wasting episodes experienced and wasting incidence at all ages was higher in South Asia, with highest incidence in the first 3 months with- or without- including episodes at birth (Fig 4b).

Ultimately, most children recovered from moderate or severe wasting episodes, reinforcing its status as an acute condition. Children met our definition of "recovered" in 91.5% of episodes of moderate and 82.5% of episodes of severe wasting. Loss-to-followup may have affected recovery estimates, recovery can only occur in children surviving the episode, and we did not have data on wasting treatment, so recovery may be higher in these highly monitored cohorts than in the general population due to treatment referrals. Pooling across cohorts, children recovered from 39.0% (95% CI: 34.0, 44.3) of wasting episodes within 30 days, 64.7% (95% CI: 59.3, 69.4)) within 60 days, and 71.1% (95% CI: 66.1, 75.6) within 90 days. Median episode length was 42 (95% CI: 39, 44) days. We examined the distribution of WLZ in the three-month period after a child was considered recovered from wasting, stratified by the age at which the episode occurred. We found that children recovered to a higher WLZ from at-birth wasting or wasting episodes in the 0-6 month age window compared with episodes that occurred at older ages (Fig 4c). Regression to the mean (RTM) could explain some wasting recovery, especially the rapid WLZ gain among children born wasted (Figure 4e), but there was catch-up growth beyond the calculated RTM effect (Extended Data Fig 8).[39] Additionally, we required a 60-day recovery period to better capture true recovery, and mean WLZ of recovered children did not regress to cohort means (Figure 4e), especially among older children (Figure 4c). Consistent with larger WLZ increases during recovery from wasting at younger ages, a larger proportion of children recovered within 30, 60, and 90 days if the wasting episode occurred before age 6 months (Fig 4d). South Asian cohorts had lower rates of recovery in the 6-18 month age period compared with other regions (Fig 4d). On average, however, the WLZ of children born wasted did not catch up to the WLZ of children not born wasted, and children who were born wasted but recovered had a higher cumulative incidence of wasting after 6 months of age (38.1% cumulative incidence in children born wasted [95% CI: 28.2, 49.2] vs. 24.2% cumulative incidence in children not born wasted [95% CI: 17.6, 32.4], Fig 4e-f).

Persistent and concurrent growth faltering

We examined more severe forms of growth faltering, including persistent wasting and concurrent wasting and stunting, because these conditions are associated with higher mortality risk.[5] We first identified a subset of children who experienced persistent wasting during their first 24 months.

We used a pragmatic definition[40] that classified children as persistently wasted if ≥ 50% of their WLZ measurements from birth to 24 months fell below –2, capturing both frequent short wasting episodes or less frequent, longer episodes. Among 10,374 children with at least four measurements, 3.4% (95% CI: 2.0, 5.6) were persistently wasted. Persistent wasting over the first 24 months of life was highest in South Asia (7.2%, 95% CI: 5.1, 10.4, Extended Data Fig 5a). Among children wasted at birth, 10.9% were persistently wasted after 6 months (95% CI: 8.7, 13.5) in contrast to 6.3% of children not born wasted who were persistently wasted after 6 months (95% CI: 4.3, 9.0).

Next, we examined the cumulative incidence of concurrent wasting and stunting and the timing of their overlap. Overall, 10.6% of children experienced concurrent wasting and stunting before 2 years of age (Extended data figure 5d), and a further 1.5% experienced concurrent severe wasting and stunting — far higher than point prevalence estimates in the present study (4.1% at 24 months, 95% CI: 2.6, 6.4; Fig 5a) or the 4.3% prevalence estimated in children under 5 in LMIC from cross-sectional surveys.[41,42] Concurrent wasting and stunting was most common in South Asia, with highest prevalence at age 21 months (Fig 5a), driven primarily by increases in stunting prevalence as children aged.[20] Children wasted and stunting are also underweight, as their maximum possible weight-for-age z-score is below -2.35.[43] Almost half of children who had prevalent growth faltering met two or more of these three growth faltering conditions, with 17-22% of all children experiencing multiple conditions after age 12 months (Fig 5b). Longitudinal analyses showed early growth faltering predisposed children to experience concurrent growth faltering at older ages: children who were wasted by age 6 months were 1.8 (95% CI: 1.6, 2.1) times and children stunted before 6 months were 2.9 (95% CI: 2.5, 3.4) times more likely to experience concurrent wasting and stunting between ages 18-24 months. A companion article reports an in depth investigation of key determinants of persistent wasting and concurrent wasting and stunting, along with their consequences for severe growth faltering and mortality.[34]

Discussion

Nearly all large-scale studies of child wasting including DHS report point prevalence of wasting, which has enabled broad comparisons between populations but failed to capture the number of episodes of wasting during the course of childhood.[44,45] By combining information across several longitudinal cohorts, this study demonstrated that children experience far higher cumulative incidence of wasting between birth and 24 months (29.2%) than previously known. Children in all included cohorts experienced higher incidence compared with prevalence due to the episodic nature of acute malnutrition, but the pattern was most stark in South Asian cohorts where, from birth to 24 months and pooled across cohorts, 29.2% of children experienced at least one wasting episode, 3.4% were persistently wasted, and 10.6% had experienced concurrent wasting and stunting. This evidence shows that the cumulative, child-level burden of wasting is higher than cross-sectional prevalence measures would suggest, and assessments of wasting and stunting in isolation fail to account for their joint burden, which can be substantial. This is of particular relevance in South Asia where the largest number of stunted and wasted children live, and while stunting prevalence is decreasing, wasting prevalence is not.[1,46]

Our results show consistent patterns in the timing of wasting onset by season and by age, with important implications for preventive interventions. WLZ varied dramatically by season in most cohorts, and in South Asia WLZ varied by up to 0.7 z-scores at-birth with consequences that persisted throughout the first 24 months (Fig 3c, Extended Data Figure 7). The present study has not elucidated the mechanism that links seasonal rainfall with wasting, indeed mechanisms could differ by geographic and cultural context. Nevertheless, the high degree of consistency of the rainfall-wasting association provides strong support for the development of seasonally targeted interventions to prevent wasting in food-insecure populations, akin to seasonal malaria chemoprevention programs in the Sahel.[47] Wasting incidence was highest from birth to 3 months, and among children who experienced any wasting during their first 24 months, 48% experienced their first episode by 3 months. Children born wasted were far more likely to experience more severe forms of growth faltering at older ages including persistent wasting from 6-24 months and concurrent wasting and stunting at 18 months. Wasting treatment programs have traditionally focused on children from 6-59 months.

Sustainable Development Goal 2.2.2 calls to eliminate malnutrition by 2030, with the elimination of child wasting as its primary indicator.[48] To help achieve this goal, preventive interventions could complement a historic focus on treatment for acutely malnourished children. Our results should motivate preventive and therapeutic programs to consider extending efforts to maternal support and education during pregnancy, and community-based breastfeeding support through infancy.[49,50] If preventive or therapeutic interventions focus on ages earlier than 6 months, then they must integrate carefully with current recommendations for exclusive breastfeeding.

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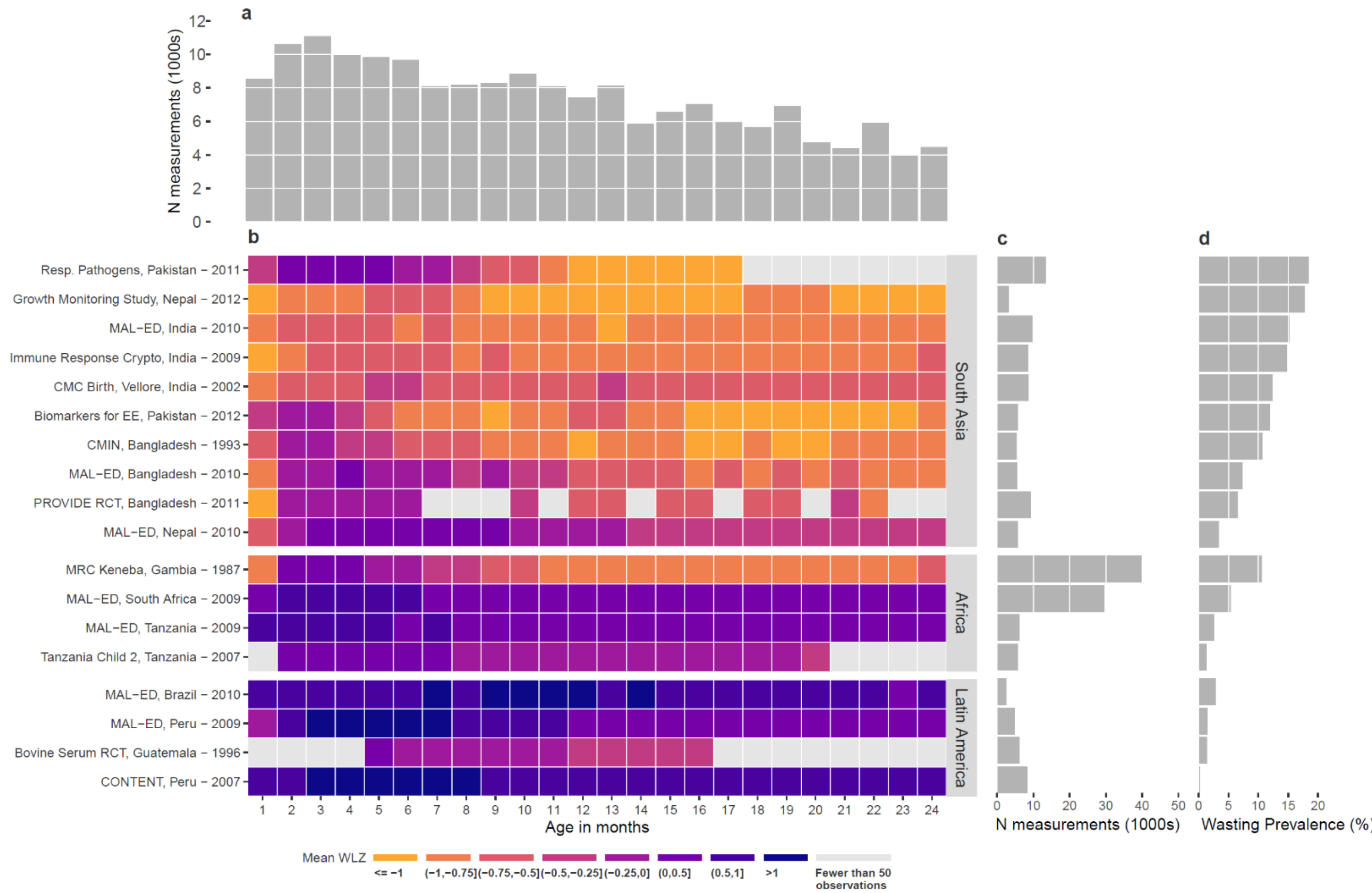


Figure 1 | Summaries of included cohorts.

(**a**) Number of observations (1000s) across cohorts by age in months. (**b**) Mean weight-for-length Z-scores (WLZ) by age in months for each included cohort. Cohorts are sorted by geographic region and overall mean weight-for-length Z-score. The country of each cohort and the start year is printed by each cohort name. (**c**) The number of observations included in each cohort. (**d**) Overall wasting prevalence by cohort, defined as proportion of measurements with WLZ < –2.

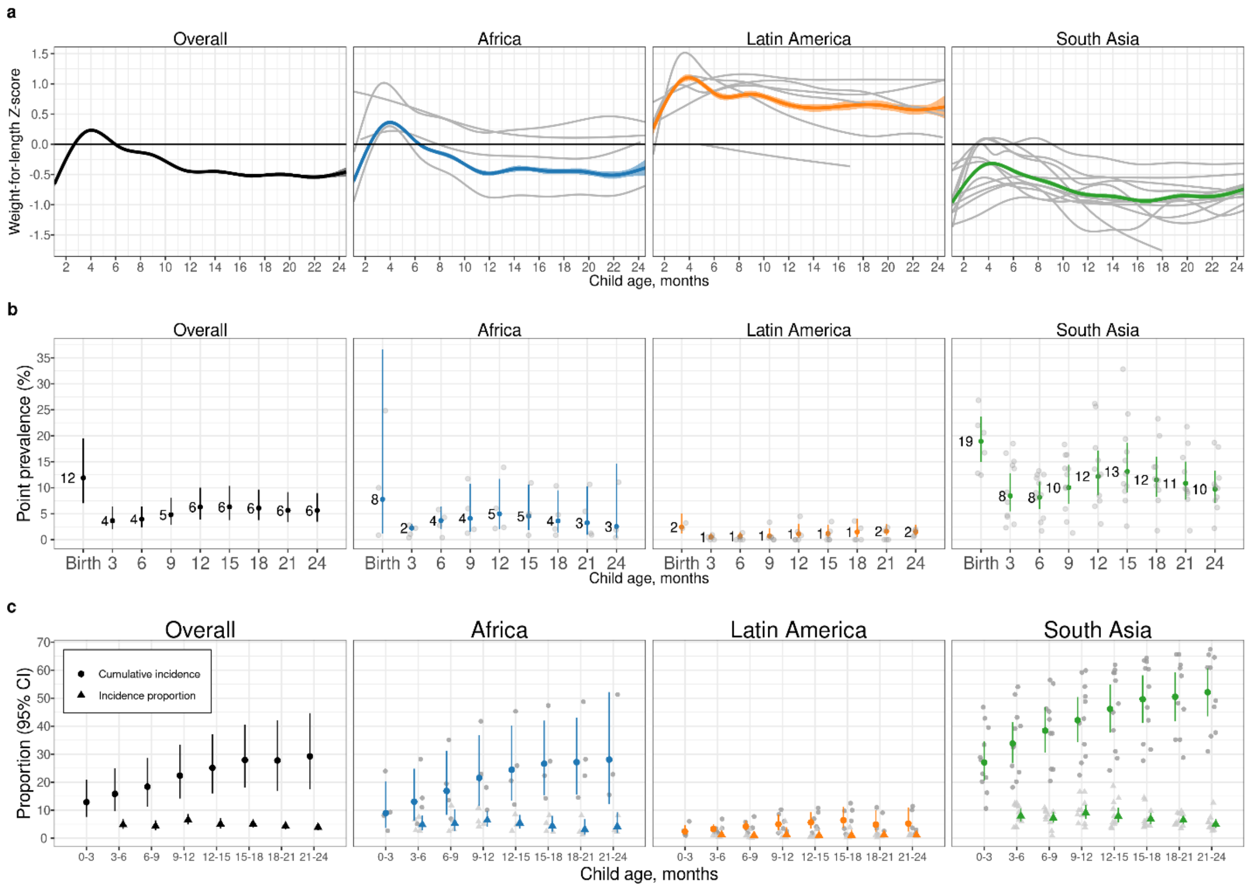


Figure 2 | WLZ, prevalence and incidence of wasting by age and region.

(**a**) Mean weight-for-length Z-score (WLZ) by age in 21 longitudinal cohorts, overall (N=21 studies; N=4,165-10,886 observations per month) and stratified by region (Africa: N=4 studies, N=1,067-5,428 observations; Latin America: N=6 studies, N= 569-1718 observations, South Asia 11 studies, N=2,382-4,286 observations).

(**b**) Age-specific wasting prevalence, defined as WLZ < –2, overall (N=3,985-9,906children) and stratified by region (Africa: 1,701-5,017 children, Latin America: N= 290-1397 children, South Asia: N=1,994-3,751 children).

(**c**) Age-specific wasting incidence overall (N=6,199 -10,377 children) and stratified by region (Africa: N=2,249-5,259 children, Latin America: N=763-1,437 children, South Asia: N=3,076-3,966 children). Cumulative incidence measures the proportion of children who have ever experienced wasting since birth, while the new incident cases represent the proportion of children at risk who had an episode of wasting begin during the age period.

Error bars in panels **b** and **c** are 95% confidence intervals for pooled estimates. In each panel, grey curves or points show cohort-specific estimates.

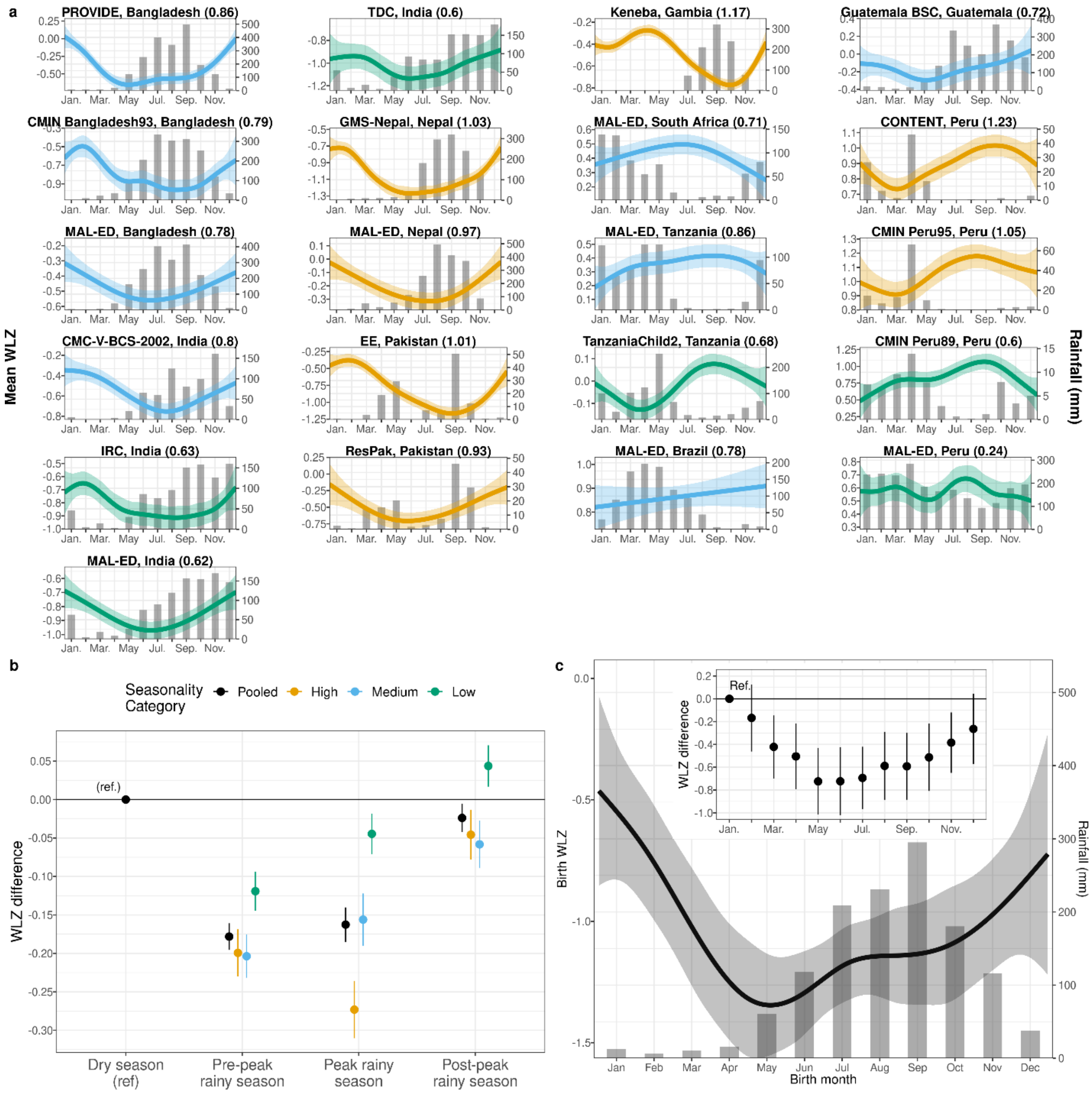
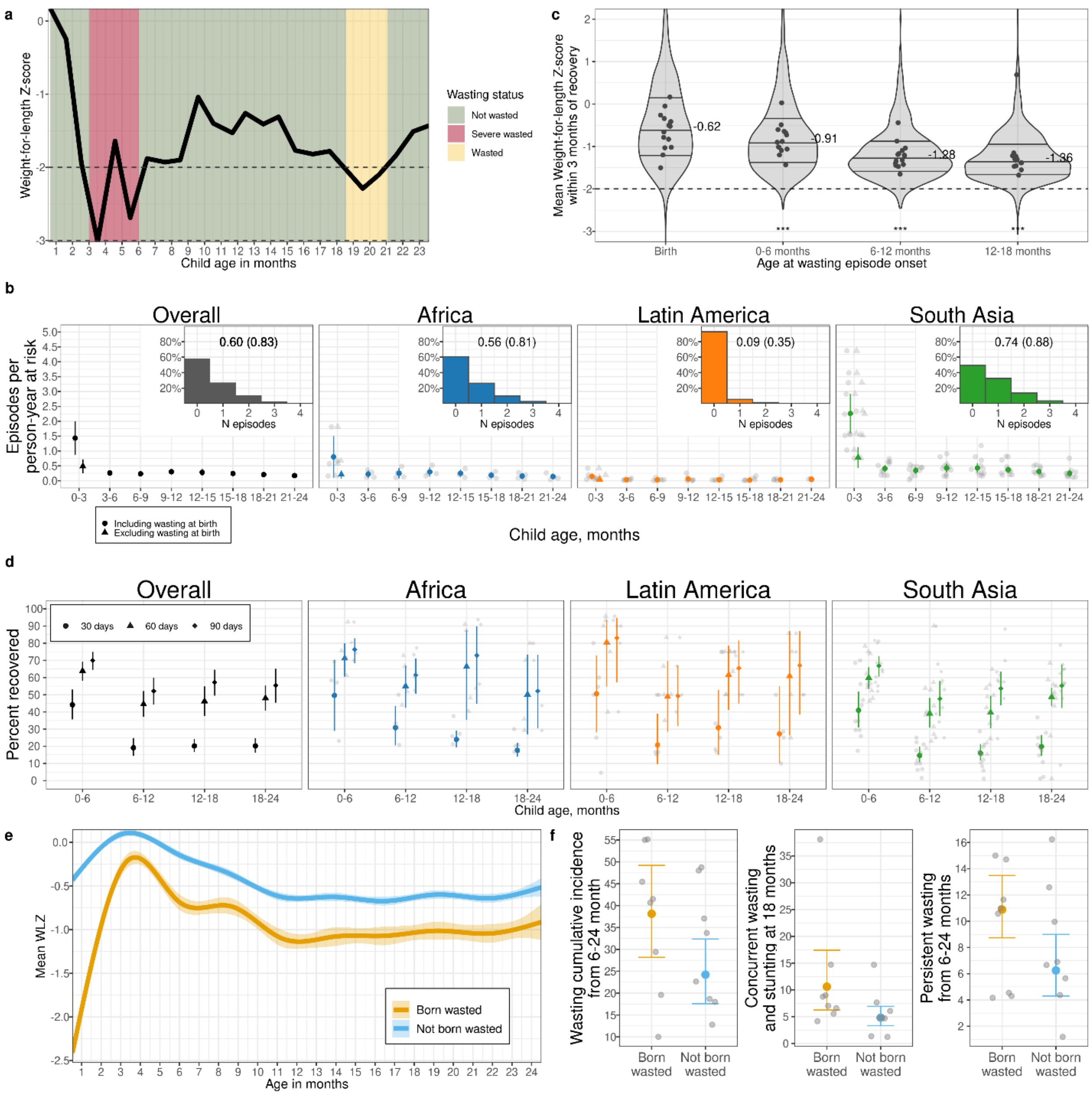


Figure 3 | Mean weight-for-length Z-scores by age and season.

(a) Cubic splines of mean WLZ over day of the year, superimposed over histograms of monthly mean rainfall over study periods, with the seasonality index printed in parentheses beside the cohort name. Panels are sorted by country and splines colored by high (≥ 0.9), medium (< 0.9 and ≥ 0.7), and low seasonality categories (< 0.7). Sample sizes range from 160 children (2,545 measurements) in TDC to 2,545 (40,115 measurements) in the Keneba cohort. **(b)** Mean differences in child WLZ between quarters of the year defined around the adjacent 3-month periods with the highest mean rainfall, pooled across cohorts in panel **a,** overall (N= 21 cohorts, 2,545-40,115 observations) and by seasonality index (high: N=7 cohorts, 3,164-40,115 observations, medium: N=8 cohorts, 2,545-9,202 observations, low: N=6 cohorts, 2,741-29,518observations).

(c) Cubic spline of mean WLZ at birth across birth months among 1,821 children with WLZ measured at birth in ten South Asian cohorts, with mean differences in birth WLZ by month of birth in the inset plot.



(**a**) Example child WLZ trajectory and wasting episode classifications. The age of wasting onset was assumed to occur halfway between a measurement of WLZ < –2 and the previous measurement of WLZ ≥ –2. Recovery from an episode of wasting or severe wasting occurred when a child had measurements of WLZ ≥ –2 for at least 60 days, with the age of recovery assumed to be halfway between the last measurement of WLZ < –2 and the first measurement of WLZ ≥ –2.

(**b**) Wasting incidence rate per 1,000 days at risk, stratified by age and region (Overall: N= 510,070-822,802 person-days per estimate, Africa: N=245,046-407,940 person-days, Latin America: N= 65,058-142,318 person-days, South Asia: N=182,694-315,057 person-days). Insets are histograms of the number of wasting episodes per child by region, with the distribution mean (SD) printed within the plot.

(**c**) The distribution of children's mean WLZ in the three months following recovery from wasting, with inter-quartile range marked. The median WLZ is annotated, and gray points mark cohort-specific medians. Children wasted before age 6 months experienced larger improvements in WLZ compared with children wasted at older ages (p<0.001). The analysis uses 3,686 observations of 2,301 children who recovered from wasting episodes, with 1,264 observations at birth, 628 observations from 0-6 months, 824 observations from 6-12 months, and 970 observations from 12-18 months.

(**d**) Percentage of children who recovered from wasting within 30, 60, and 90 days of episode onset (N=21 cohorts, 5,549 wasting episodes).

(**e**) Mean WLZ by age, stratified by wasting status at birth (which includes the first measure of a child within 7 days of birth), shows that children born wasted (N= 814 children, 14,351 observations) did not catch up to children not born wasted (N= 3,355 children, 62,568 observations).

(**f**) Higher measures of wasting after 6 months of age among children born wasted (N=814) compared to those who were not (N=3,355). In panels b, d, and f, vertical lines mark 95% confidence intervals for pooled means of study specific estimates (light points).

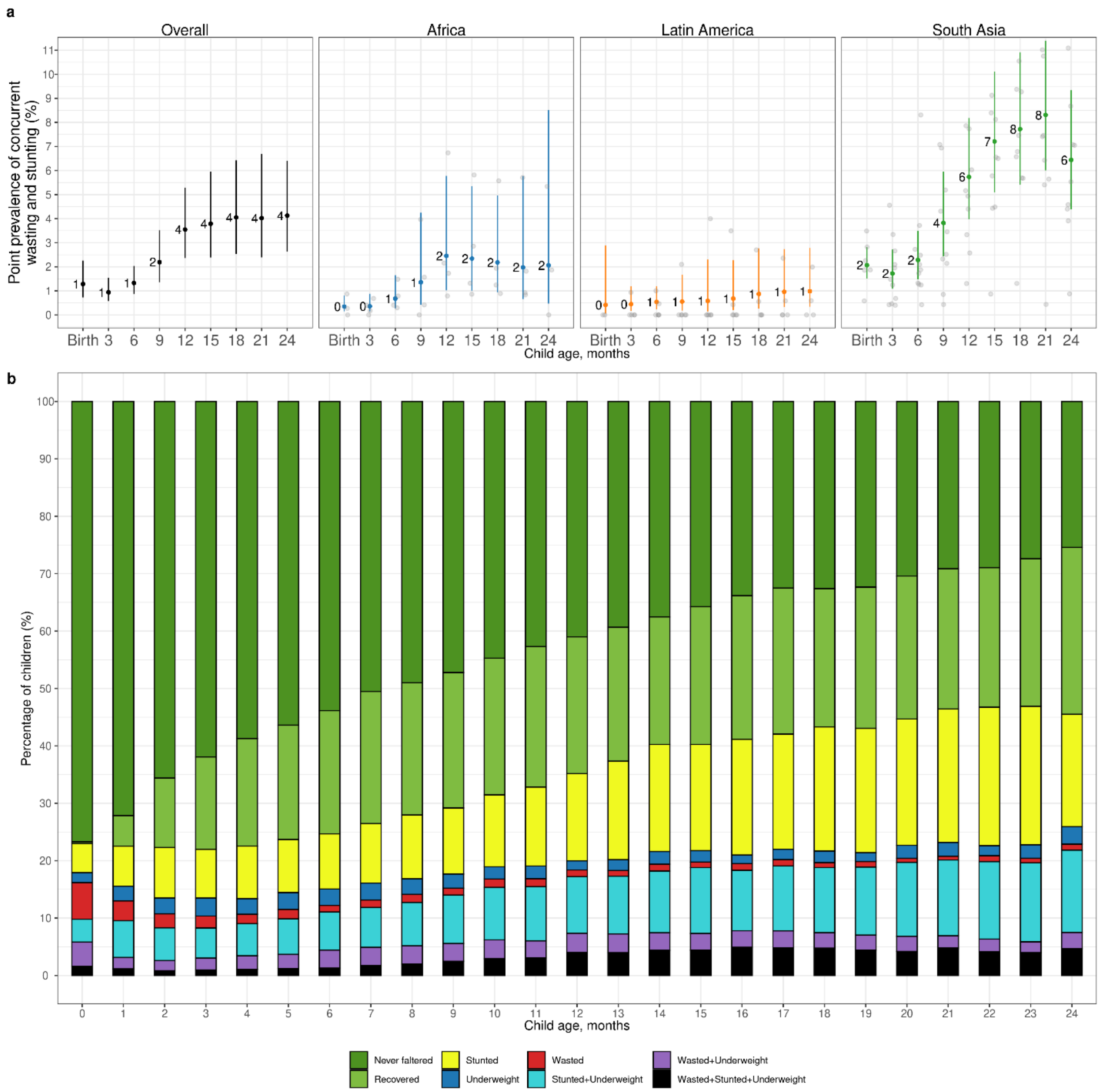


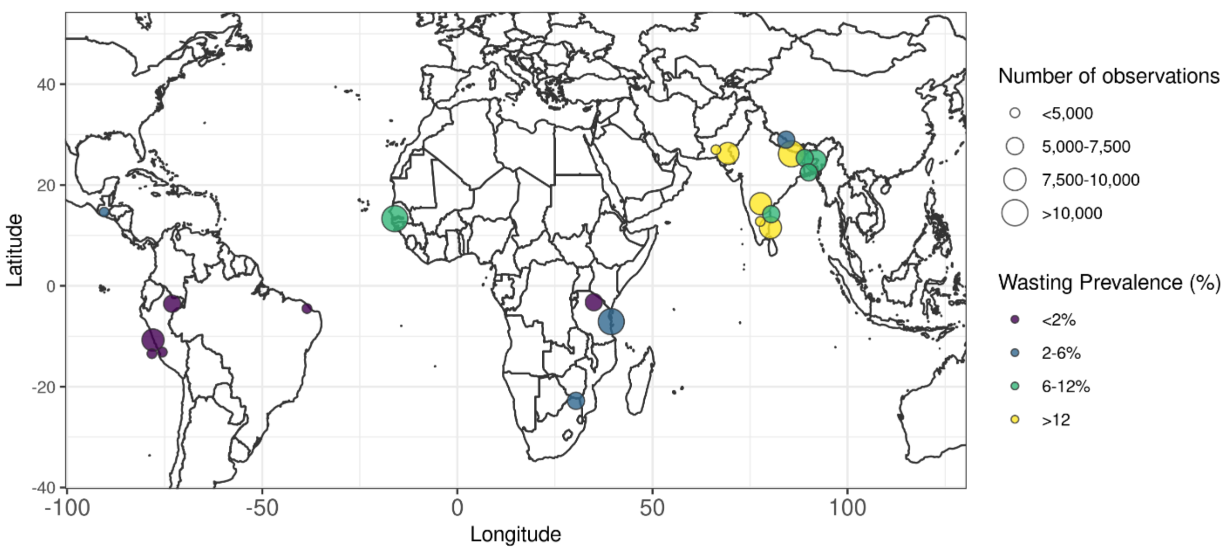
Figure 5| Co-occurrence of wasting, stunting, and underweight.

(**a**) Age-specific prevalence of co-occurrent wasting and stunting overall (N=3,984 to 9,899 children) and stratified by region (Africa: N=1,799-5,014, Latin America: N=290-1,397 children, South Asia: N=1,994-3,747 children). Vertical lines mark 95% confidence intervals for pooled means across study-specific estimates (gray points).

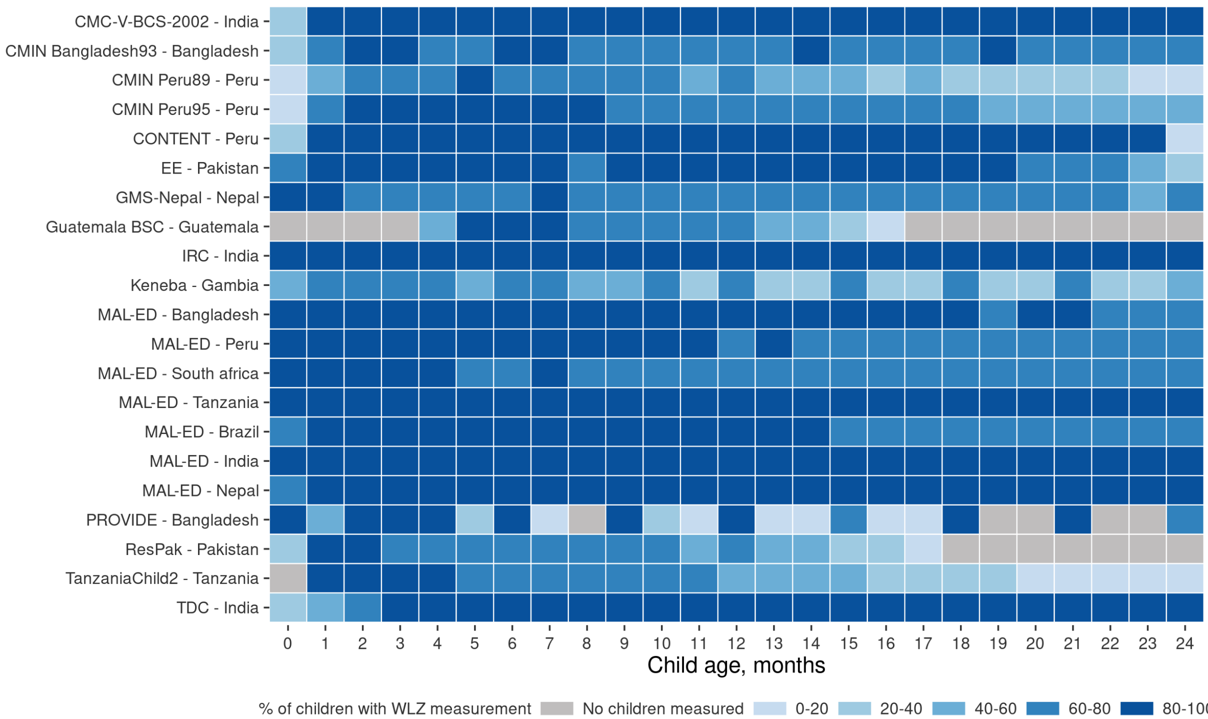
(**b**) Percentage of children classified by different measures of growth faltering, alone or combined. Children classified as “never faltered” had not previously been wasted, stunted, or underweight. Children in the “recovered” category were not wasted, stunted, or underweight but had experienced at least one of these conditions previously. All children who were wasted and stunted were also underweight. Proportions in each category were calculated within cohorts, pooled using random effects, and scaled so percentages added to 100%. The number of children contributing to each age ranges from 3,920 to 9,077 children, with 11,409 total children.


Longitudinal cohorts (n=98)
Includes anthropometry data (n=98)
Located in low- or middle income countries (n=74)
Enrollment not restricted to acutely ill children (n=76)
Children born after 1990 (n=82)
Enrolled children between ages 0-2 (n=78)
Quarterly growth measurements (n=35)
Monthly growth measurements (n=20)
Total Observations (x 10,000)
20
15
10
5
0
Sample size
INTERBIO-21-South Africa
INTERBIO-21-Kenya
INTERGROWTH-21-Kenya
GEMS-1A-Kenya
GEMS-1A-Mozambique
iLiNS-DYAD-M-Malawi
COHORTS-South Africa
GEMS-1-Mozambique
GEMS-1A-Gambia
GEMS-1A-Mali
GEMS-1-Gambia
GEMS-1-Kenya
GEMS-1-Mali
WASH-Kenya-Kenya
CMIN-Guinea-Bissau
iLiNS-DOSE-Malawi
Zinc RCT-Burkina Faso
Lungwena Child Nutr RCT-Malawi
MRC Keneba-Gambia
iLiNS-Zinc RCT-Burkina Faso
ZVITAMBO RCT-Zimbabwe
MAL-ED-Tanzania
MAL-ED-South Africa
Tanzania Child 2-Tanzania
Africa
INTERBIO-21-Pakistan
INTERBIO-21-Thailand
INTERGROWTH-21-China
INTERGROWTH-21-India
INTERGROWTH-21-Oman
GUSTO-Singapore
Bangladesh Diarrhea-Bangladesh
Grip-Pakistan
ZincInf-India
GEMS-1A-India
GEMS-1A-Pakistan
GEMS-1A-Bangladesh
ZincSGA-India
GEMS-1-Pakistan
GEMS-1-India
GEMS-1-Bangladesh
WASH-Bangladesh-Bangladesh
Transmission Dyn. Crypto-India
Vitamin-B12-India
Aga Khan Nutr RCT-Pakistan
Zn Supp RCT-India
LBW-India
DIVIDS-India
PROVIDE RCT-India
Cebu Cohort-Philippines
BIGCS Ultrasound-China
VITAMIN-A-India
New Delhi Birth Cohort-India
JiVitA-3-Bangladesh
CMIN-Bangladesh
Food Suppl RCT-India
NIH Birth Cohort-Bangladesh
NIH Crypto-Bangladesh
Optimal Infant Feeding-India
JiVitA-4-Bangladesh
MAL-ED-Nepal
MAL-ED-India
MAL-ED-Bangladesh
Resp. Pathogens-Pakistan
CMC Birth, Vellore-India
Biomarkers for EE-Pakistan
Immune Response Crypto-India
Growth Monitoring Study-Nepal
PROVIDE RCT-Bangladesh
Asia
INTERBIO-21-Brazil
Infant growth in Huascar-Peru
Peru Zn-Peru
Peru PersistDiarrhea-Peru
COHORTS-Brazil
CMIN-Brazil
Ecuador Egg-Ecuador
Ecuador Zn-Ecuador
INCAP Nutr Supp RCT-Guatemala
CMIN-Peru
CONTENT-Peru
MAL-ED-Brazil
MAL-ED-Peru
Bovine Serum RCT-Guatemala
Latin America
UMN-MOD-United States
UMN-Amplatz-United States
UMN-MINNoWS-United States
UMN-NORM-United States
Detroit Longitudinal-United States
INTERGROWTH-21-Italy
INTERBIO-21-United Kingdom
INTERGROWTH-21-United Kingdom
Fels-United States
POPS-Netherlands
HealthyStart-United States
SMOCC-Netherlands
BAMBAM-United States
PROBIT RCT-Belarus
North America & Europe
Inclusion Reason
0
40
80
120
Total Observations (x1000)

Extended Data Figure 1| *ki* cohort selection. Analyses focused on longitudinal cohorts to enable the estimation of prospective incidence rates and growth velocity. On July 15, 2018, there were 86 longitudinal studies on GHAP. From this set, we applied five inclusion criteria to select cohorts for analysis. Our rationale for each criterion follows. (1) *Studies were conducted in lower income or middle-income countries*. Our target of inference for analyses was children in LMICs, which remains a key target population for preventive interventions. (2) *Studies measured length and weight between birth and age 24 months*. We were principally interested in growth faltering during the first two years of life including at birth, thought to be the key window for linear growth faltering [7]. (3) *Studies did not restrict enrollment to acutely ill children*. Our focus on descriptive analyses led us to target, to the extent possible, the general population. We thus excluded some studies that exclusively enrolled acutely ill children, such as children who presented to hospital with acute diarrhea or who were severely malnourished. (4) *Studies enrolled at least 200 children*. Age-stratified incident episodes of stunting and wasting were sufficiently rare that we wanted to ensure each cohort would have enough information to estimate rates before contributing to pooled estimates. (5) *Studies collected anthropometry measurements at least every 3 months*. We limited studies to those with higher temporal resolution to ensure that we adequately captured incident episodes and recovery. We further restricted analyses of wasting incidence and recovery to cohorts with monthly measurements because of high temporal variation in WHZ within individuals.

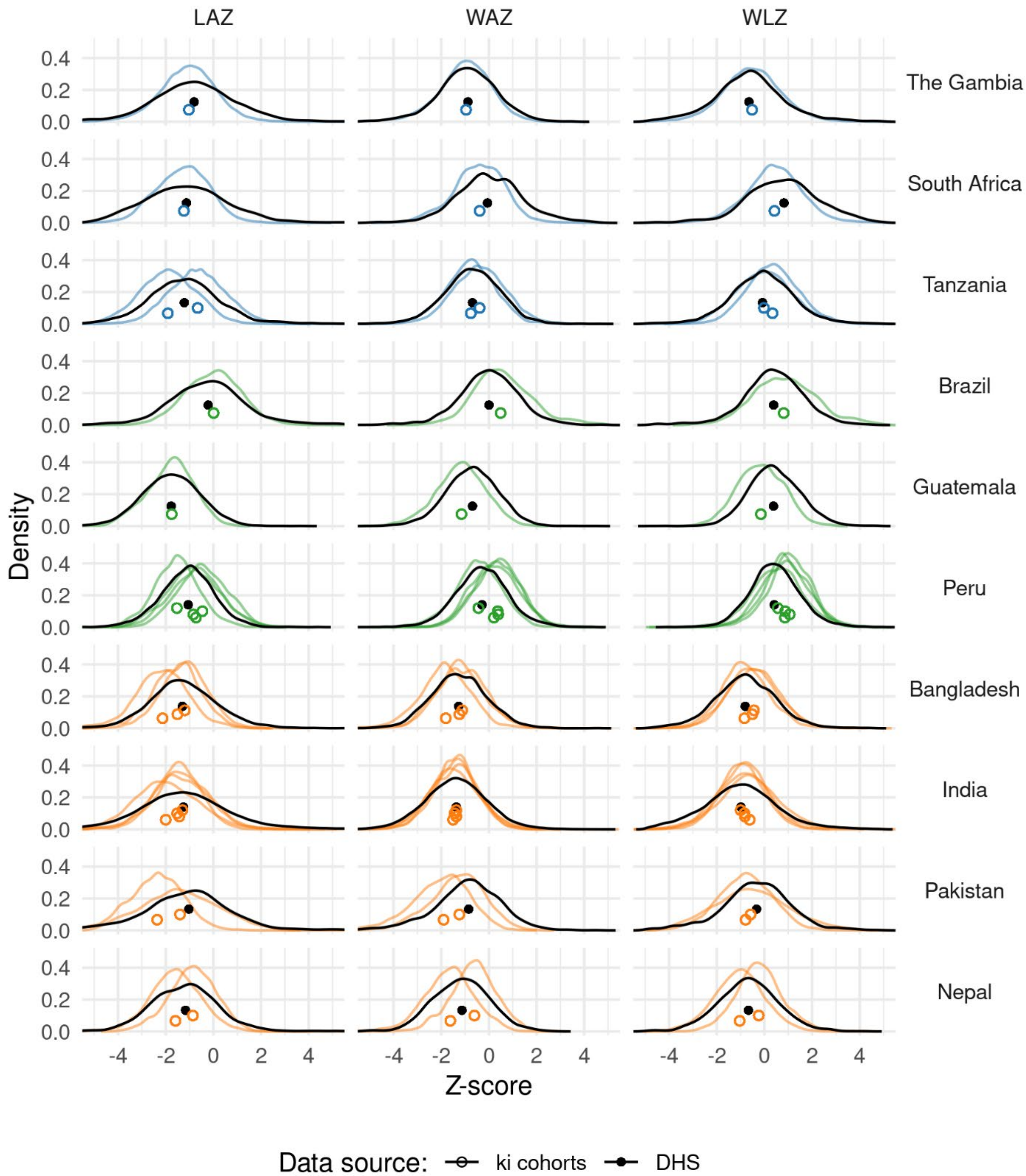


Extended Data Figure 2 | Geographic location of *ki* cohorts. Locations are approximate and jittered slightly for display.

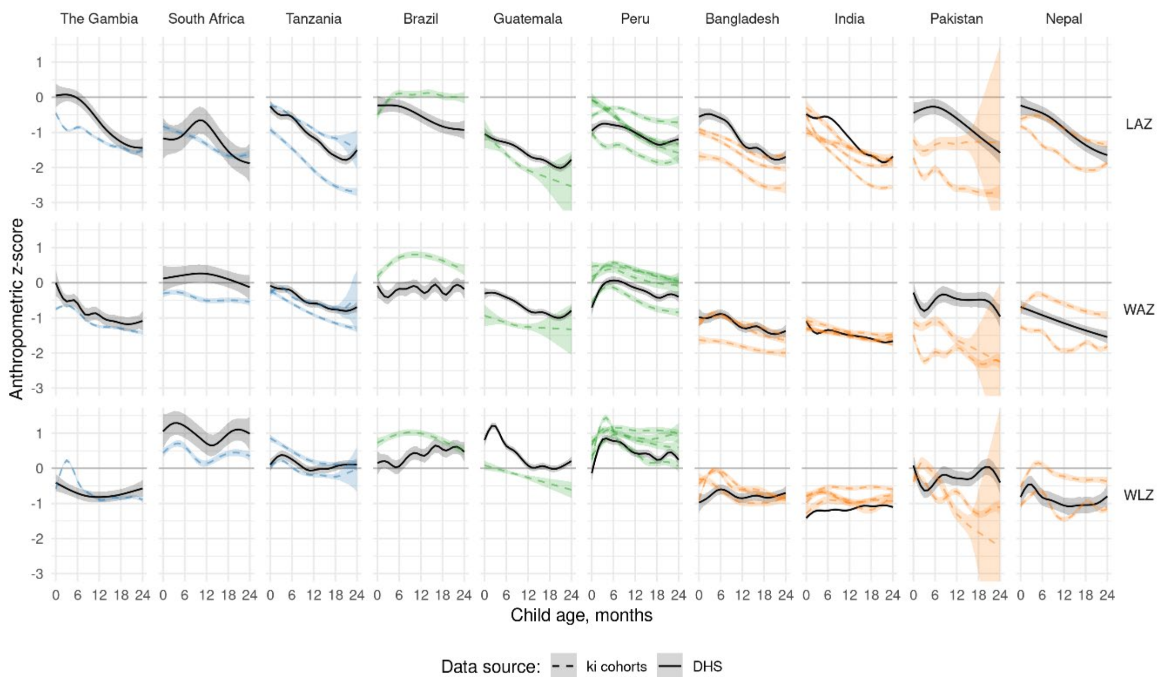


Extended Data Figure 3 | Percentage of enrolled children measured in each ki cohort with monthly measurements.

a


LAZ
WAZ
WLZ
The Gambia
South Africa
Tanzania
Brazil
Guatemala
Peru
Bangladesh
India
Pakistan
Nepal
Density
Z-score
0.0
0.2
0.4
-4
-2
0
2
4
Data source: ki cohorts DHS

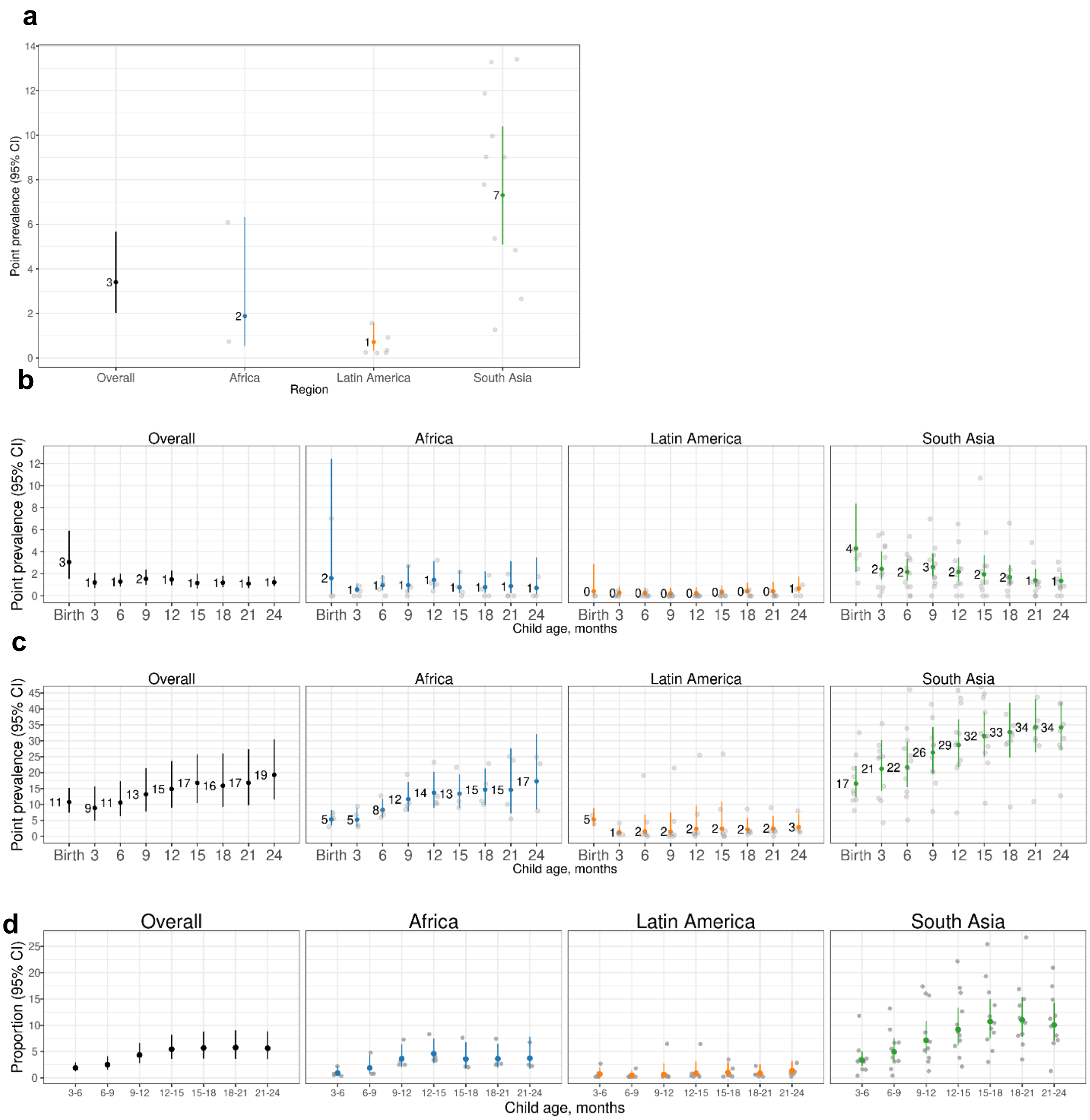
b



Extended Data Figure 4 | Comparison of cohort anthropometry to population-based samples

(**a**) Kernel density distributions of length-for-age (LAZ), weight-for-age (WAZ), and weight-for-length Z-scores (WLZ) from measurements among children under 24 months old in 21 *ki* longitudinal cohorts (colored line) and among children measured in the most recent population-based, Demographic and Health Survey for each country (black). Sub-Saharan African countries are colored blue, Latin American countries are colored green, and south Asian countries are colored orange. Median Z-scores are denoted with points under the density curves, with open circles for *ki* cohorts and solid points for Demographic and Health Surveys.

(**b**) Mean LAZ, WAZ, and WLZ by age and country among 21 *ki* longitudinal cohorts (dashed lines) and in Demographic and Health Surveys (solid). Means estimated with cubic splines and shaded regions show approximate, simultaneous 95% confidence intervals.



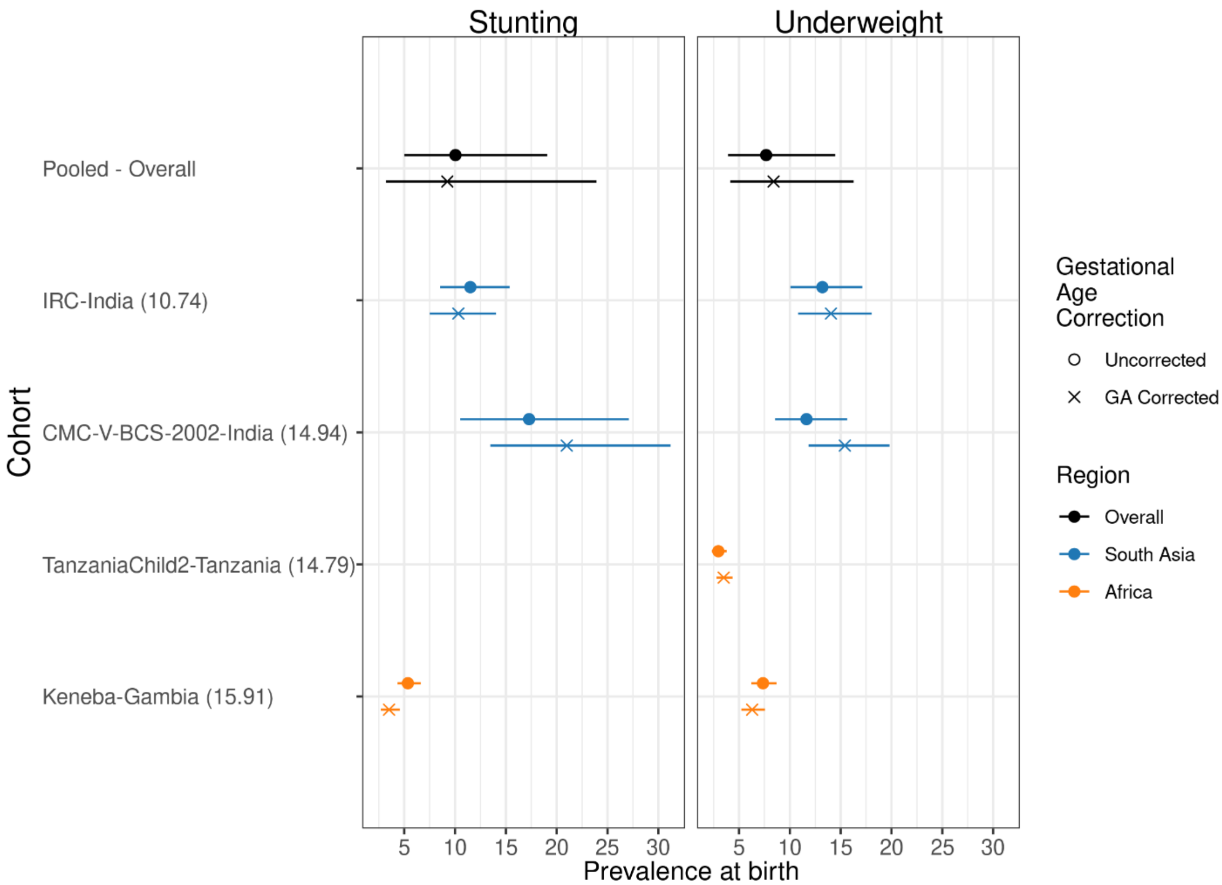
Extended Data Figure 5 | Prevalence of persistent wasting, severe wasting, and underweight by region.

(**a**) Proportion of children persistently wasted (≥50% of measurements from birth to 24 months of age, overall and stratified by region.

(**b**) Prevalence of severe wasting (WLZ < –3) by age and region.

(**c**) Prevalence of underweight (weight-for-age Z-score < –2) by age and region.

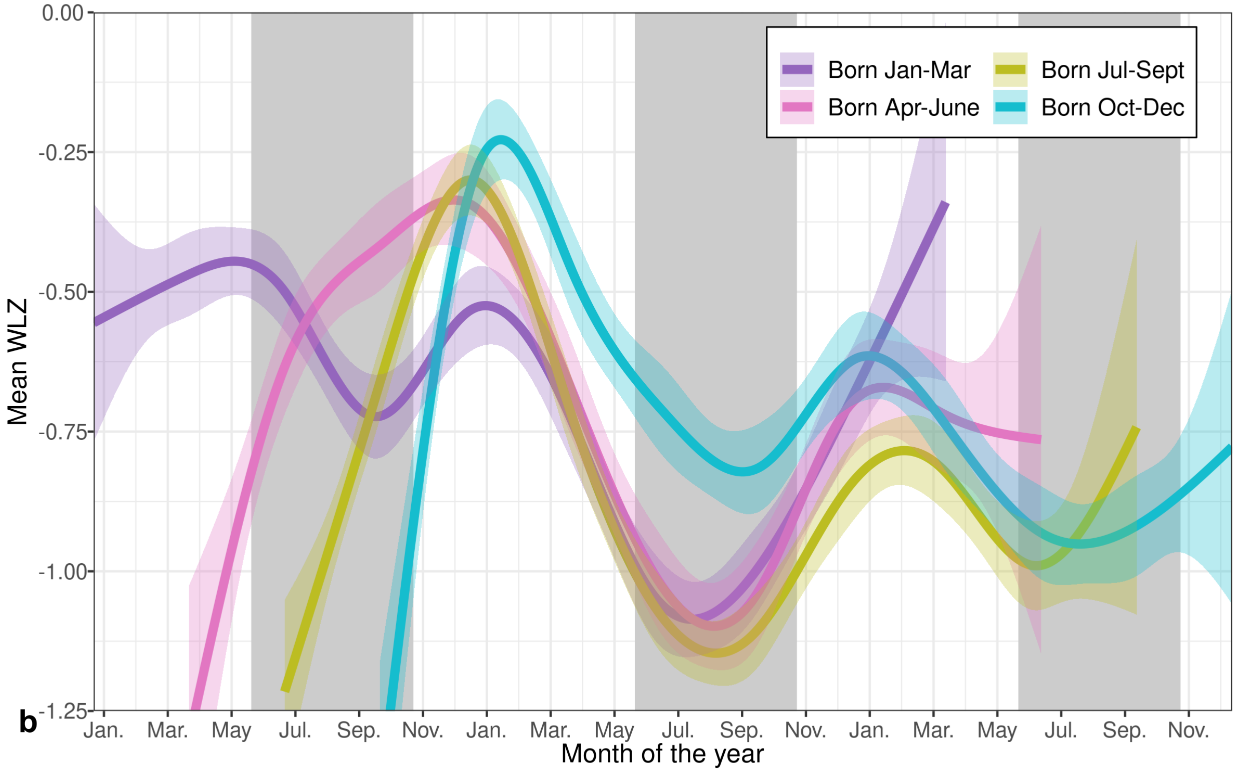
(**d**) Incidence proportion of concurrent wasting and stunting by age and region. Across all ages before 24 months, 10.6% of children experienced at least one concurrently wasted and stunted measurement.



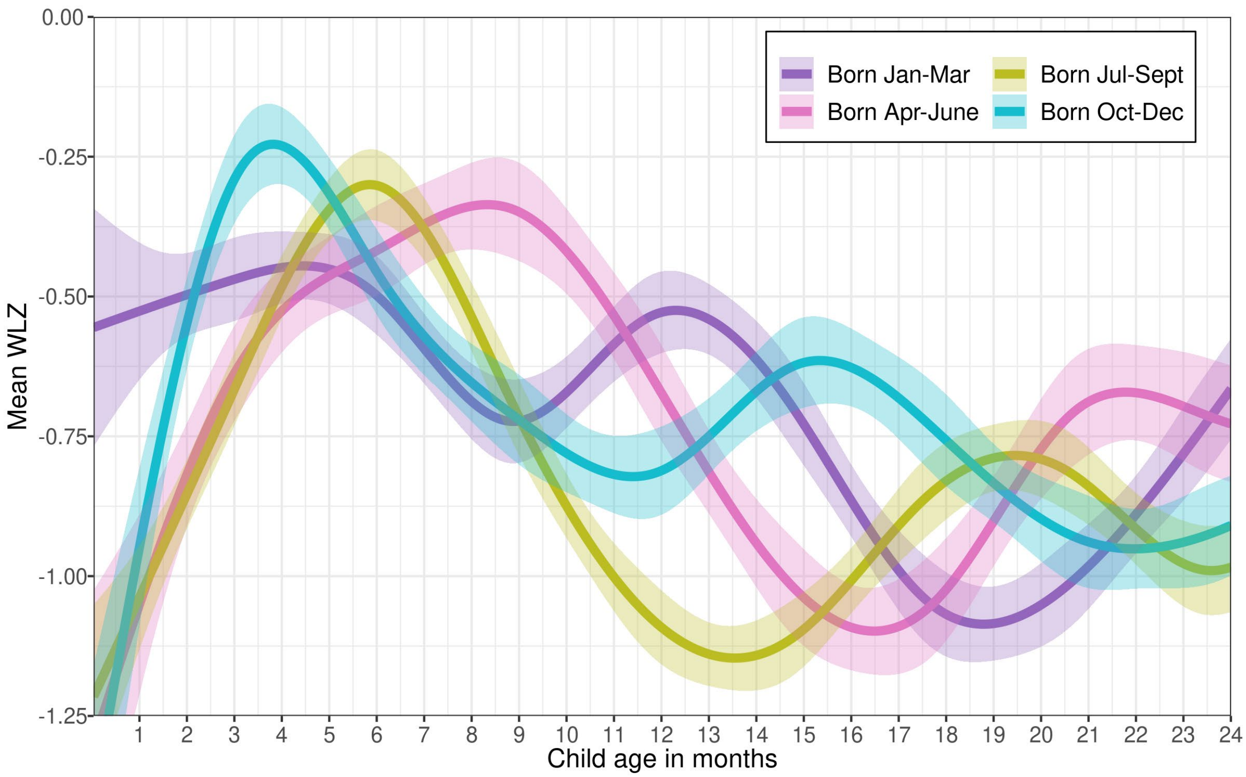
Extended Data Figure 6 | Comparison of underweight and stunting prevalence at birth with and without gestational age correction

This figure includes the results from correcting at-birth Z-scores in the *ki* cohorts that measured gestational age (GA). The corrections are using the Intergrowth standards and are implemented using the R *growthstandards* package (https://ki-tools.github.io/growthstandards/). Overall, the prevalence at birth decreased slightly after correcting for gestational age, but the cohort-specific results are inconsistent. Observations with GA outside of the Intergrowth standards range (<168 or > 300 days) were dropped for both the corrected and uncorrected data. Prevalence increased after GA correction in some cohorts due to high rates of late-term births based on reported GA. There were no length measurements at birth in the Tanzania Child 2 cohort, so they do not have stunting estimates. There were 4,449 measurements used in the underweight analysis and 1,931 measurements used in the stunting analysis. Gestational age was estimates based on mother's recall of the last menstrual period in the IRC, CMC-V-BCS-2002, and Tanzania Child cohorts, and was based on the Dubowitz method (newborn exam) in the MRC Keneba cohort.

a


Born Jan-Mar
Born Apr-June
Born Jul-Sept
Born Oct-Dec
Mean WLZ
0.00
-0.25
-0.50
-0.75
-1.00
-1.25
Jan.
Mar.
May
Jul.
Sep.
Nov.
Month of the year

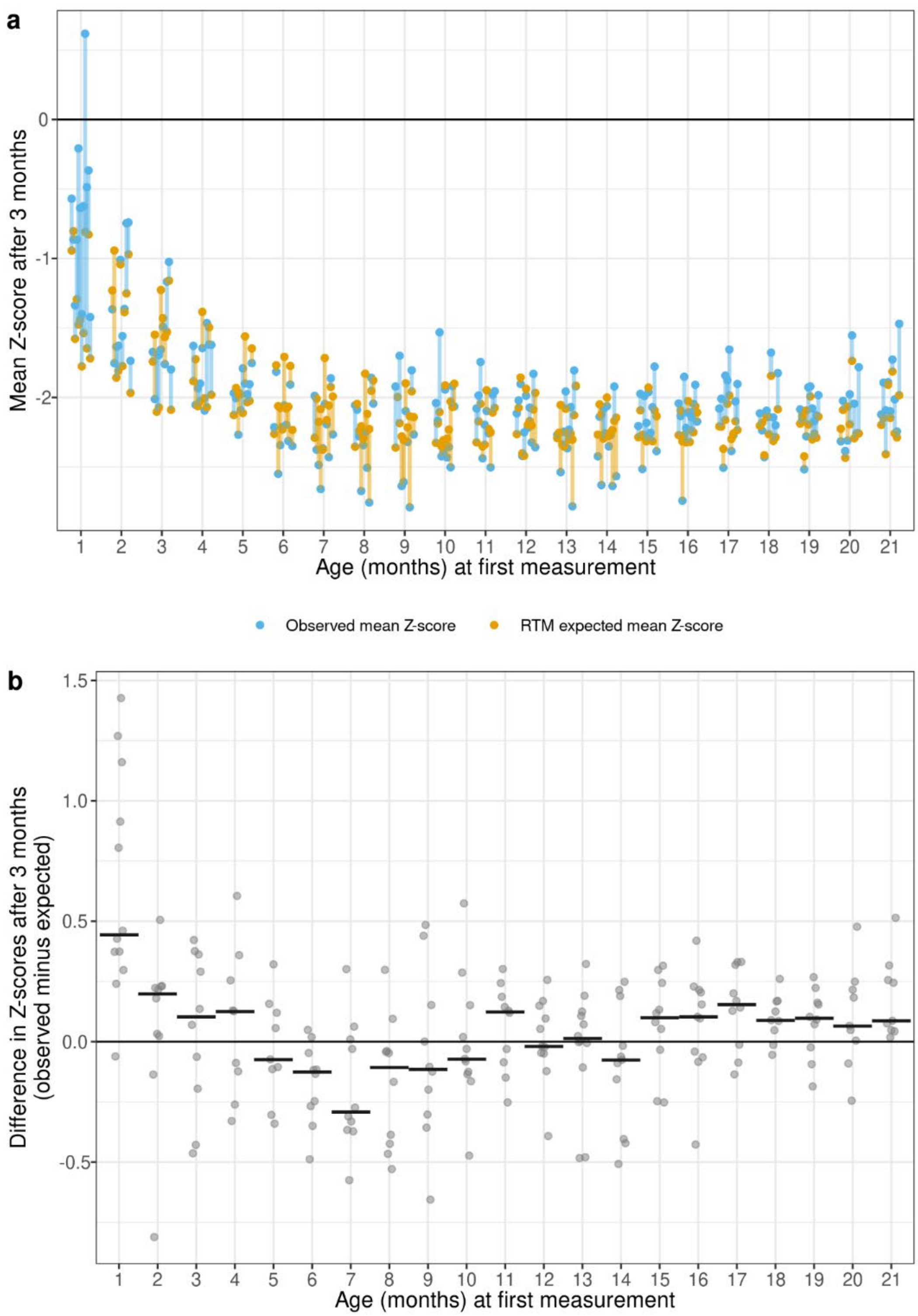
b


Born Jan-Mar
Born Apr-June
Born Jul-Sept
Born Oct-Dec
Mean WLZ
0.00
-0.25
-0.50
-0.75
-1.00
-1.25
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24
Child age in months

Extended Data Figure 7 | Month of birth affects seasonal patterns in WLZ

(**a**) Mean WLZ by calendar month among South Asian cohorts, with children stratified by birth month. The X-axis begins at January 1st of the year of the first January birthday in each cohort. Grey backgrounds indicate the approximate timing of seasonal monsoons in South Asia (June-September) Shaded regions around spline fits indicate 95% simultaneous confidence intervals. Eleven cohorts, 4,040 children, and 78,573 measurements were used to estimate the splines. South Asian children born in July-September had the lowest mean WLZ overall and children born April-September had larger seasonal declines in WLZ during their second year of life than children born October-March.

(**b**) Mean WLZ from birth to age 24 months among children from South Asian cohorts stratified by birth month. Shaded regions around spline fits indicate 95% simultaneous confidence intervals. Data used is the same as in panel (a).



Extended Data Figure 8 | Regression to the mean effects in wasted children

(a) Expected mean Z-scores based on the regression to the mean effect (orange) and observed mean Z-scores (blue) 3 months after wasted children are measured. The lines connecting cohort-specific observed and expected WLZ at each age are colored orange if the expected estimate under RTM was higher than the observed mean (indicating lower than expected change in WLZ under RTM alone), and blue if the observed mean was higher than the expected estimate under RTM (indicating higher than expected change in WLZ under RTM alone). For examples, most cohorts experienced larger increases in WLZ than expected in the three-month period beginning in their first month of life (blue lines) and most cohorts experienced smaller increases in WLZ than expected in the three month periods beginning at ages 6-9 months (orange lines).

(b) Difference between observed means and expected means under a pure RTM effect by cohort, with the median differences by age indicated with horizontal lines.

Details on estimation of the RTM effects are in the methods

656 **Extended Data Table 1| Summary of *ki* cohorts**

Region, Study ID	Country	Study Years	Design	Children Enrolled*	Anthropometry measurement ages (months)	Total WLZ measurements*	Primary References
South Asia							
Biomarkers for EE	Pakistan	2013-2015	Prospective cohort	380	Birth, 1, 2, ..., 18	8428	Iqbal et al 2018 Nature Scientific Reports[1]
Resp. Pathogens	Pakistan	2011 - 2014	Prospective cohort	284	Birth, 1, 2, ..., 17	3164	Ali et al 2016 Journal of Medical Virology[2]
Growth Monitoring Study	Nepal	2012 - Ongoing	Prospective cohort	686	Birth, 1, 2, …, 24	13340	Not yet published
MAL-ED	Nepal	2010 - 2014	Prospective cohort	240	Birth, 1, 2, …, 24	5695	Shrestha et al 2014 Clin Infect Dis[3]
CMIN93	Bangladesh	1993 - 1996	Prospective Cohort	272	Birth, 3, 6, ..., 24	5372	Pathela et al. 2006 Acta Paediatrica
TDC	India	2008-2011	Quasi-experimental	160	Birth, 1, 2, ..., 24	3591	Sarkar et al. 2013 BMC Public Health
CMC Birth Cohort, Vellore	India	2002 - 2006	Prospective cohort	373	Birth, 0.5, 1, 1.5, ..., 24	8697	Gladstone et al. 2011 NEJM[4]
MAL-ED	India	2010 - 2012	Prospective cohort	251	Birth, 1, 2, ..., 24	5697	John et al 2014 Clin Infect Dis[5]
Vellore Crypto Study	India	2008 - 2011	Prospective cohort	410	Birth, 1, 2, ..., 24	9729	Kattula et al. 2014 BMJ Open[6]
MAL-ED	Bangladesh	2010 -2014	Prospective cohort	263	Birth, 1, 2, ..., 24	5592	Ahmed et al 2014 Clin Infect Dis[7]
PROVIDE RCT	Bangladesh	2011 -2014	Individual RCT	700	Birth, 6, 10, 12, 14. 17, 18, 24, 39, 40, 52, 53 (weeks)	9202	Kirkpatrick et al 2015 Am J Trop Med Hyg[8]
Africa							
MAL-ED	Tanzania	2009 - 2014	Prospective cohort	261	Birth, 1, 2, ..., 24	5698	Mduma et al 2014 Clin Infect Dis[9]
Tanzania Child 2	Tanzania	2007 - 2011	Individual RCT	2396	1, 2, ..., 20	29518	Locks et al Am J Clin Nutr 2016[10]
MAL-ED	South Africa	2009 - 2014	Prospective cohort	312	Birth, 1, 2, ..., 24	6151	Bessong et al 2014 Clin Infect Dis[11]
MRC Keneba	Gambia	1987 - 1997	Cohort	2920	Birth, 1, 2, ..., 24	40117	Schoenbuchner et al. 2019, AJCN[12]
Latin America							
CMIN Peru95	Peru	1995 - 1998	Prospective Cohort	224	Birth, 1, 2, ..., 24	3978	Checkley et al. 2003 Am J Epidemiol.
CMIN Peru89	Peru	1989 - 1991	Prospective Cohort	210	Birth, 1, 2, ..., 24	2741	Checkley et al. 1998 Am J Epidemiol.
MAL-ED	Peru	2009 - 2014	Prospective cohort	302	Birth, 1, 2, ..., 24	6127	Yori et al 2014 Clin Infect Dis[13]
CONTENT	Peru	2007 - 2011	Prospective cohort	215	Birth, 1, 2, ..., 24	8339	Jaganath et al 2014 Helicobacter[14]

Bovine Serum RCT	Guatemala	1997 - 1998	Individual RCT	315	Baseline, 1, 2, ...,8	2545	Begin et al. 2008, EJCN[15]
MAL-ED	Brazil	2010 - 2014	Prospective cohort	233	Birth, 1, 2, ..., 24	4838	Lima et al 2014 Clin Infect Dis[16]
*Children enrolled is for children with measurements under 2 years of age. Total measurements are number of measurements of anthropometry on children under 2 years of age.							

Extended Data Table 2| Summary of baseline characteristics in *ki* cohorts

	CMC-V-BCS-2002, India	CMIN Bangladesh93	CMIN Peru89	CMIN Peru95	CONTENT, Peru	EE, Pakistan	GMS-Nepal	Guatemala BSC	IRC, India	Keneba, The Gambia
	(N=373)	(N=280)	(N=210)	(N=224)	(N=215)	(N=380)	(N=698)	(N=315)	(N=410)	(N=2954)
Sex										
Female	187 (50.1%)	122 (43.6%)	100 (47.6%)	96 (42.9%)	109 (50.7%)	185 (48.7%)	328 (47.0%)	162 (51.4%)	185 (45.1%)	1426 (48.3%)
Male	186 (49.9%)	158 (56.4%)	110 (52.4%)	128 (57.1%)	106 (49.3%)	195 (51.3%)	370 (53.0%)	153 (48.6%)	225 (54.9%)	1528 (51.7%)
Birthweight										
Mean (SD)	2910 (434)	2560 (967)	3550 (492)	3690 (367)	3070 (323)	2640 (506)	2660 (423)		2890 (448)	2970 (421)
Maternal age										
Mean (SD)	24.1 (4.11)					30.0 (3.99)	24.0 (5.09)	25.2 (6.21)	23.7 (3.68)	27.4 (7.16)
Maternal weight										
Mean (SD)										
Maternal education (years)										
Mean (SD)	5.43 (4.10)					0.873 (2.51)	2.48 (4.01)	4.07 (2.95)	5.06 (4.61)	
Number of rooms										
4+	14 (3.75%)				78 (36.3%)		323 (46.3%)		17 (4.17%)	
1	202 (54.2%)				44 (20.5%)		49 (7.02%)		185 (45.3%)	
2	106 (28.4%)				54 (25.1%)		145 (20.8%)		170 (41.7%)	
3	51 (13.7%)				39 (18.1%)		181 (25.9%)		36 (8.82%)	
Number of children <5yrs										
1									89 (21.7%)	

	CMC-V-BCS-2002, India	CMIN Bangladesh93	CMIN Peru89	CMIN Peru95	CONTENT, Peru	EE, Pakistan	GMS-Nepal	Guatemala BSC	IRC, India	Keneba, The Gambia
2+									321 (78.3%)	
Improved sanitation										
1					201 (93.5%)					
0					14 (6.51%)					
Food security level										
Food Secure							479 (71.1%)			
Mildly Food Insecure							106 (15.7%)			
Food Insecure							89 (13.2%)			

	MAL-ED, Bangladesh	MAL-ED, Brazil	MAL-ED, India	MAL-ED, Nepal	MAL-ED, Peru	MAL-ED, South Africa	MAL-ED, Tanzania	PROVIDE, Bangladesh	ResPak, Pakistan	Tanzania Child2	TDC, India
	(N=265)	(N=233)	(N=251)	(N=240)	(N=303)	(N=314)	(N=262)	(N=700)	(N=284)	(N=2400)	(N=160)
Sex											
Female	136 (51.3%)	113 (48.5%)	138 (55.0%)	110 (45.8%)	143 (47.2%)	159 (50.6%)	133 (50.8%)	332 (47.4%)	136 (47.9%)	1184 (49.3%)	75 (46.9%)
Male	129 (48.7%)	120 (51.5%)	113 (45.0%)	130 (54.2%)	160 (52.8%)	155 (49.4%)	129 (49.2%)	368 (52.6%)	148 (52.1%)	1216 (50.7%)	85 (53.1%)
Birthweight											
Mean (SD)	2800 (412)	3340 (483)	2890 (442)	2980 (390)	3130 (430)	3130 (464)	3180 (452)	2780 (371)	2930 (525)	3230 (474)	2910 (450)
Maternal age											
Mean (SD)	24.8 (4.99)	24.8 (5.53)	23.9 (4.10)	26.4 (3.76)	24.2 (6.06)	26.4 (6.86)	28.4 (6.67)	24.7 (4.65)		26.4 (5.04)	
Maternal weight											
Mean (SD)	49.6 (8.54)	61.9 (11.8)	50.4 (9.37)	56.3 (8.27)	55.5 (8.95)	67.5 (14.9)	55.7 (9.11)	49.3 (9.41)		62.2 (11.7)	
Maternal education (years)											
Mean (SD)	5.63 (2.58)	9.18 (2.81)	7.88 (3.17)	8.77 (3.44)	7.81 (2.79)	10.3 (1.94)	6.17 (1.79)	4.33 (3.62)		7.90 (2.27)	
Number of rooms											
4+	12 (4.96%)	127 (60.5%)	25 (10.6%)	131 (55.5%)	139 (51.1%)	196 (76.3%)	108 (43.2%)	23 (3.29%)			5 (3.13%)
1	152 (62.8%)	4 (1.90%)	84 (35.7%)	52 (22.0%)	19 (6.99%)	14 (5.45%)	13 (5.20%)	507 (72.4%)			91 (56.9%)
2	50 (20.7%)	20 (9.52%)	78 (33.2%)	31 (13.1%)	52 (19.1%)	22 (8.56%)	63 (25.2%)	108 (15.4%)			49 (30.6%)
3	28 (11.6%)	59 (28.1%)	48 (20.4%)	22 (9.32%)	62 (22.8%)	25 (9.73%)	66 (26.4%)	62 (8.86%)			15 (9.38%)
Number of children <5yrs											
1								512 (73.1%)		1640 (68.6%)	

	MAL-ED, Bangladesh	MAL-ED, Brazil	MAL-ED, India	MAL-ED, Nepal	MAL-ED, Peru	MAL-ED, South Africa	MAL-ED, Tanzania	PROVIDE, Bangladesh	ResPak, Pakistan	Tanzania Child2	TDC, India
2+								188 (26.9%)		749 (31.4%)	
Improved sanitation											
1	204 (84.3%)	206 (98.1%)	108 (46.4%)	235 (99.6%)	65 (24.7%)	4 (1.60%)		58 (96.7%)			
0	38 (15.7%)	4 (1.90%)	125 (53.6%)	1 (0.424%)	198 (75.3%)	246 (98.4%)		2 (3.33%)			
Food security level											
Food Secure	161 (83.0%)	3 (2.33%)	190 (89.6%)	94 (73.4%)	27 (23.9%)	132 (56.7%)					
Mildly Food Insecure	4 (2.06%)	11 (8.53%)	5 (2.36%)	15 (11.7%)	29 (25.7%)	19 (8.15%)					
Food Insecure	29 (14.9%)	115 (89.1%)	17 (8.02%)	19 (14.8%)	57 (50.4%)	82 (35.2%)					

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Materials and Methods

Study designs and inclusion criteria

We included all longitudinal observational studies and randomized trials available through the *ki* project on April 2018 that met five inclusion criteria (Extended Data Figure 1): 1) conducted in low- or middle-income countries; 2) enrolled children between birth and age 24 months and measured their length and weight repeatedly over time; 3) did not restrict enrollment to acutely ill children; 4) enrolled at least 200 children; 5) collected anthropometry measurements at least monthly. The frequency of measurements was assessed by calculating the median days between measurements. Our pre-specified analysis protocol stipulated that if randomized trials found effects of interventions on growth, the analysis would only include the control arm only; yet, all intervention trials that met the inclusion criteria had null effects on growth, so all arms were included. We included all children under 24 months of age, assuming months were 30.4167 days. We excluded extreme measurements of WLZ > 5 or < –5 and of WAZ < -6 or > 5, consistent with 2006 WHO Growth Standards recommendations.[1] We checked for cohort-wide anthropometry measurement quality by plotting Z-score densities and calculating the proportion of length measurements where length decreased beyond the expected technical error of measurement compared to the last measurement on a child. One cohort, MAL-ED Pakistan, was excluded because measurements exhibited a multimodal WLZ distribution with scores binned at –2, –1.5, and –1 instead of continuously distributed.

Outcome definitions

We used the following outcome measures in the analysis:

<u>Weight-for-Length Z-scores</u> were calculated using the 2006 WHO growth standards,[2] and mean WLZ was calculated within strata of interest. We used the medians of triplicate measurements of lengths and weights of children from pre-2006 cohorts to re-calculate Z scores to the 2006 standard.

<u>Prevalent wasting</u> was defined as the proportion of measurements within a specific stratum (e.g., age) below the 2006 WHO standard –2 WLZ, and analogously below the 2006 WHO standard –3 WLZ for severe wasting. For each age, we included children with WLZ measurements within one month before and after that age in the point prevalence estimate (e.g., for point prevalence at 6 months, we include children aged 5-7 months). WLZ is not calculable for children with lengths <45cm (10.2% of children at birth), so using WLZ underestimates wasting at birth.

<u>Incident wasting episodes</u> were defined as a change in WLZ from above –2 Z in the prior measurement to below –2 Z in the current measurement. Similarly, we defined severe wasting episodes using –3 Z cutoff. We assumed a 60-day washout period between episodes of wasting before a new episode of wasting could occur (Fig 4a). Children were considered at risk for wasting at birth, so children born wasted were considered to have an incident episode of wasting at birth. Children were also assumed to be at risk of wasting at the first measurement in studies that enrolled children after birth, so children wasted at the first measurement in a non-birth cohort were assumed to have incident wasting occurring at the age halfway between birth and the first measurement.

Incidence proportion of wasting was calculated during a defined age range (e.g. 6-12 months) as the proportion of children not wasted at the start of the period who became wasted during the age period (the proportion of children who had the onset of new episodes during the period). This differs from period prevalence, which would include any children who had any measurement of WLZ < -2 during the period (including children who began the period wasted). Period prevalence would thus additionally include in the numerator and denominator children who were wasted at the start of the period, whereas incidence proportion excludes them.

Recovery from wasting was defined as a WLZ change from below to above –2 Z among children who are currently wasted or severely wasted. We required a child to maintain WLZ above –2 for 60 days to be considered "recovered". Children were only considered "at risk" for recovery if their prior measurement was below –2 WLZ. We measured the proportion of children who recover from moderate wasting (WLZ < –2) within 30, 60, and 90 days of the onset of the episode. We assumed recovery from wasting was spontaneous because we did not have consistent information on referral guidelines across cohorts in the analysis, but some children with moderate wasting may have been referred to clinical facilities for outpatient treatment. Wasting recovery may thus be higher in these highly monitored cohorts than in the general population due to treatment referrals.

Wasting duration was estimated by counting the days between the onset of wasting and recovery within an individual child. We assumed that the episode started or ended at the midpoint between measurements. For example, if a child was not wasted at age 40 days, wasted at age 70 days, and not wasted at age 100 days, the duration of the wasting episode was: (70-40)/2 + (100-70)/2 = 30 days. We calculated the median duration of wasting episodes among cohorts where children recovered during the study period from >50% of observed wasting episodes, as the duration of episodes that extended beyond study period is unknown. Therefore, the median duration could only be calculated when less than half of episodes were censored. Confidence intervals were calculated using the quantile method.

Incidence rate of wasting was calculated during defined age ranges as the number of incident episodes of wasting per 1,000 child-days at risk during the age range. Children were considered "at risk" for incident wasting episodes if they were not currently wasted and were classified as recovered from any prior wasting episode (beyond the 60-day washout period). Therefore, wasted children, or children within the washout period, did not contribute to the person-time at risk for wasting used to calculate wasting incidence. To calculate person-time at risk of wasting, we assumed that the onset of a wasting episode occurred when the child's age was at the midpoint between the measurement of WLZ ≥ –2 and the measurement of WLZ < –2, and conversely the time of recovery occurred when the child's age was at the midpoint between the last measurement of WLZ < –2 and the first measurement of WLZ ≥ –2 within the 60-day washout period (Fig 4a).

Persistent wasting was defined as a >50% longitudinal prevalence of below –3 WLZ (wasting), and analogously >50% longitudinal prevalence of below –3 WLZ for persistent severe wasting.[3]

Concurrent prevalence of wasting and stunting was defined as the proportion of measurements at a specific age when a child was both wasted and stunted at the same measurement. For each age, we included children with WLZ and LAZ measurements within one month before and after that age in the point prevalence estimate (e.g., for point prevalence at 6 months, we include children aged 5-7 months).

Prevalent underweight was defined as the proportion of measurements at a specific age below the 2006 WHO standard –2 WAZ. For each age, we included children with WAZ measurements within one month before and after that age in the point prevalence estimate (e.g., for point prevalence at 6 months, we include children aged 5-7 months).

Subgroups of interest

We stratified the above outcomes of interest within the following subgroups: Child age, grouped into one, three, or six month intervals, (depending on the outcome); the region of the world (Asia, sub-Saharan Africa, Latin America); the month of the year, and the combinations of the above categories.

Statistical analysis

All analyses were conducted in R version 4.0.5. Supplementary pooled, regional, and cohort-specific results, and sensitivity analyses are available in online supplements at (https://child-growth.github.io/wasting).

Fixed and random effects models

We conducted a 2-stage individual participant meta-analysis, estimating wasting outcomes within specific cohorts and pooling estimates within each age strata using random effects models. For example, we estimated each age-specific mean using a two-step process. We first estimated the mean in each cohort, and then pooled age-specific means across cohorts allowing for a cohort-level random effect. We estimated overall pooled effects, and pooled estimates specific to South Asian, African, or Latin American cohorts, depending on the analysis. We repeated the pooling of all statistics presented in the figures using fixed effects models as a sensitivity analysis (https://child-growth.github.io/wasting/fixed-effects.html). The pooling methods are described in greater detail in Benjamin-Chung (2020).[4] All pooling was completed using the rma() function from the "metafor" package in the R language (version 3.4.0).[5]

Fitted spline curves

Fitted smoothers used in manuscript figures were fit using cubic splines and generalized cross-validation.[6] We estimated approximate 95% simultaneous confidence intervals around the cubic splines using a parametric bootstrap that resampled from the posterior the generalized additive model parameter variance-covariance matrix.[7]

Seasonality analysis

We compared mean WLZ over day of the year, over child birth day, and over seasons defined by rainfall. We estimated mean WLZ by cohort over day of the year and child birth day using cubic splines (Fig. 3a, c).[8] Splines of WLZ over day of the year were plotted over monthly mean rainfall averaged over the years a study measured child anthropometry below ages 24 months (Fig. 3a). We pulled monthly precipitation values from Terrraclimate, a dataset that combines readings from WorldClim data, CRU Ts4.0, and the Japanese 55-year Reanalysis Project.[9] For each study region, we averaged all readings within a 50 km radius from the study coordinates. If GPS locations were not in the data for a cohort, we used the approximate location of the cohort based on the published descriptions of the cohort. Monthly measurements were matched to study data based on the calendar month and year in which measurements were taken.

The season of peak rainfall was defined as the three-month period with the highest mean rainfall. Mean differences in WLZ between three-month quarters was estimated using linear regression models. We compared the consecutive three months of the maximum average rainfall over the study period, as well as the three months prior and the three months after the maximum-rainfall period, to a reference level of the three months opposite the calendar year of the maximum-rainfall period. We used all WLZ measurements of children under two years of age (e.g., if June-August was the period of maximum rainfall, the reference level is child mean WLZ during January-March).

Estimates were unadjusted for other covariates because we assumed that seasonal effects on WLZ were exogenous and could not be confounded. Mean differences in WLZ were pooled across cohorts using random-effects models, with cohorts grouped by the Walsh and Lawler seasonality index.[10] Cohorts from years with a seasonal index ≥ 0.9 were classified as occurring in locations with high seasonality, cohorts with a seasonal index < 0.9 and ≥ 0.7 were classified as occurring in locations with medium seasonality, and cohorts with a seasonal index < 0.7 were classified as occurring in locations with low seasonality.

$$Seasonal\ Index = \frac{1}{R}\sum_{n=1}^{n=12} |X_n - \frac{R}{12}|$$

Where R = total annual precipitation and X_n = monthly precipitation.

Estimation of mean LAZ, WAZ, and WLZ by age in Demographic and Health Surveys and *ki* cohorts

We downloaded standard DHS individual recode files for each country from the DHS program website (https://dhsprogram.com/). We used the most recent standard DHS datasets for the individual women's, household, and length and weight datasets from each country, and we estimated age-stratified mean LAZ, WAZ, and WLZ from ages 0 to 24 months within each DHS survey, accounting for the complex survey design and sampling weights. See Benjamin-Chung et. al (2020) for additional details on the DHS data cleaning and analysis.[4] We compared DHS estimates with mean LAZ, WAZ, and WLZ by age in the *ki* study cohorts with penalized cubic-splines with bandwidths chosen using generalized cross-validation.[8] We did not seasonally adjust DHS measurements.

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Sensitivity analyses

We estimated incidence rates and of wasting after excluding children born or enrolled wasted (Fig. 4b). The rationale for this sensitivity analysis is that incident cases at birth imply a different type of intervention (i.e., prenatal) compared with postnatal onset of wasting. We estimated the overall and region stratified prevalence of persistent wasting and of underweight and severe wasting by age (Extended data fig. 5). Within cohorts that measured child gestational age at birth, we estimated the prevalence of stunting and underweight at birth both uncorrected and corrected for gestational age at birth using the Intergrowth standards (Extended data figure 6).[11] We also assessed how much change in Z-scores after children became wasted could be explained by regression to the mean (RTM) and how much is catch-up growth beyond that expected by RTM.[12] We calculated the cohort-specific RTM effect and plotted the mean Z-scores expected from RTM 3 months later among children who were wasted at each age in months from birth to 21 months. We used the cohort means as the population mean Z-scores, and compared the expected mean WLZ with the observed mean WLZ (Extended Data Fig. 8).[13,14] We also compared wasting prevalence defined using middle-upper-arm circumference (MUAC), an alternative measurement for classifying wasting, with wasting prevalence estimated using WLZ within the cohort that measured MUAC (https://child-growth.github.io/wasting/muac.html). We also re-estimate primary results dropping observations of children at birth within the MRC Keneba cohort, which used a different team to measure child anthropometry at birth from the trained anthropometrists used in follow-up measurements (https://child-growth.github.io/wasting/no-kenaba.html). We also examined the effect of shorter (30 day) and longer (90) day washout period when determining if a child was again at risk when estimating wasting incidence and wasting recovery rates (https://child-growth.github.io/wasting/ir_sensitivity.html). Lastly, we compared estimates pooled using random effects models, which are more conservative in the presence of study heterogeneity, with estimates pooled using fixed effects (inverse variance weighted) models (https://child-growth.github.io/wasting/fixed-effects.html).

Data and code availability

The data that support the findings of this study are available from the Bill and Melinda Gates Foundation Knowledge Integration project upon reasonable request. Replication scripts for this analysis are available here: https://github.com/child-growth/ki-longitudinal-growth.

Methods References

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Competing interest declaration

Thea Norman is an employee of the Bill & Melinda Gates Foundation (BMGF). Kenneth H Brown and Parul Christian are former employees of BMGF. Jeremy Coyle, Vishak Subramoney, Ryan Hafen, and Jonas Häggström work as research contractors funded by the BMGF.

Additional information

Supplementary Information is available for this paper at https://child-growth.github.io/wasting.

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