medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. It is made available under a CC-BY 4.0 International license .

Early childhood linear growth faltering in low- and middle-income countries

Jade Benjamin-Chung,[1,2]* Andrew Mertens,[2] John M Colford Jr,[2] Alan E Hubbard,[2] Mark J van der Laan,[2] Jeremy Coyle[2], Oleg Sofrygin,[2] Wilson Cai,[2] Anna Nguyen,[1,2] Nolan N Pokpongkiat,[2] Stephanie Djajadi,[2] Anmol Seth,[2] Wendy Jilek,[2] Esther Jung,[2] Esther O Chung,[2] Sonali Rosete,[2] Nima Hejazi,[2] Ivana Malenica,[2] Haodong Li,[2] Ryan Hafen,[3] Vishak Subramoney,[4] Jonas Häggström,[5] Thea Norman,[6] Kenneth H. Brown,[7] Parul Christian,[8] Benjamin F. Arnold,[9]* and members of the *ki* Child Growth Consortium[‡]

[1] Department of Epidemiology & Population Health, Stanford University, Stanford University, 259 Campus Drive, HRP Redwood Building T152A, Stanford, CA 94305
[2] Division of Epidemiology & Biostatistics, University of California, Berkeley, 2121 Berkeley Way Rm 5302 Berkeley, CA 94720-7360
[3] Hafen Consulting, LLC, West Richland WA, 99353
[4] DVPL Tech
[5] Cytel Inc, 1050 Winter St Suite 2700 Waltham, MA 02451, USA
[6] Quantitative Sciences, Bill & Melinda Gates Foundation, 500 5th Ave N, Seattle, WA 98109
[7] Department of Nutrition, University of California, Davis, 3135 Meyer Hall, Davis, CA 95616-5270
[8] Center for Human Nutrition, Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD 21205.
[9] Francis I. Proctor Foundation and Department of Ophthalmology, University of California, San Francisco, 490 Illinois St, San Francisco, CA 94158

* Corresponding authors:

Jade Benjamin-Chung, PhD, jadebc@stanford.edu, Assistant Professor, Department of Epidemiology & Population Health, Stanford University, 259 Campus Drive, HRP Redwood Building T152A, Stanford, CA 94305

Benjamin F. Arnold, PhD, ben.arnold@ucsf.edu, Associate Professor, Francis I. Proctor Foundation, University of California, San Francisco, 490 Illinois St, San Francisco, CA 94158

Summary

Globally 149 million children under five are estimated to be stunted (length more than 2 standard deviations below international growth standards). Stunting, a form of linear growth faltering, increases risk of illness, impaired cognitive development, and mortality. Global stunting estimates rely on cross-sectional surveys, which cannot provide direct information about the timing of onset or persistence of growth faltering— a key consideration for defining critical windows to deliver preventive interventions. We performed the largest pooled analysis of longitudinal studies in low- and middle-income countries to date (n=32 cohorts, 52,640 children, ages 0-24 months), allowing us to identify the typical age of linear growth faltering onset and to investigate recurrent faltering in early life. The highest incidence of stunting onset occurred from birth to age 3 months. From 0 to 15 months, less than 5% of children per month reversed their stunting status, and among those who did, stunting relapse was common. Early timing and low reversal rates emphasize the importance of preventive intervention delivery within the prenatal and early postnatal phases coupled with continued delivery of postnatal interventions through the first 1000 days of life.

NOTE: This preprint reports new research that has not been certified by peer review and should not be used to guide clinical practice.

medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint
(which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity.
It is made available under a CC-BY 4.0 International license .

‡ Members of the *ki* Child Growth Consortium

1. Souheila Abbeddou, Food Safety and Nutrition Unit, Department of Public Health and Primary Care, Ghent University, Belgium
2. Linda S. Adair, Department of Nutrition, University of North Carolina at Chapel Hill, USA
3. Tahmeed Ahmed, International Centre for Diarrhoeal Disease Research, Bangladesh
4. Asad Ali, Aga Khan University
5. Hasmot Ali, JiVitA Project, Bangladesh, Johns Hopkins
6. Per Ashorn, Center for Child Health Research, Tampere University and Tampere University Hospital, Finland
7. Rajiv Bahl, World Health Organization, Switzerland
8. Mauricio L. Barreto, Center of Data and Knowledge Integration for Health, Fundação Oswaldo Cruz, Salvador, Brazil.
10. France Begín, UNICEF, USA
11. Pascal Obong Bessong, HIV/AIDS & Global Health Research Programme, University of Venda, South Africa
12. Maharaj Kishan Bhan, Indian Institute of Technology, New Delhi, India
13. Nita Bhandari, Centre for Health Research and Development, Society for Applied Studies, New Delhi, India
14. Santosh K. Bhargava, Senior Consultant Pediatrics, Sunder Lal Jain Hospital, Ashok Vihar, India
15. Zulfiqar A. Bhutta, Institute for Global Health & Development & Center of Excellence in Women and Child Health, The Aga Khan University South-Central Asia, East Africa & United Kingdom
17. Robert E. Black, Johns Hopkins University
18. Ladaporn Bodhidatta, Armed Forces Research Institute of Medical Sciences, Bangkok, Thailand
19. Delia Carba, USC Office of Population Studies Foundation, Inc., University of San Carlos, Cebu, Philippines
20. Ines Gonzales Casanova, Rollins School of Public Health, Emory University, USA
21. William Checkley, Johns Hopkins University, USA
22. Jean E. Crabtree, Leeds Institute for Medical Research, St. James's University Hospital, University of Leeds, United Kingdom
23. Kathryn G. Dewey, Institute for Global Nutrition, Department of Nutrition, University of California, USA
24. Christopher P. Duggan, Center for Nutrition, Boston Children's Hospital, USA
25. Caroline H.D. Fall, Emeritus Professor of International Paediatric Epidemiology, MRC Lifecourse Epidemiology Centre, University of Southampton, UK
26. Abu Syed Golam Faruque, International Centre for Diarrhoeal Disease Research, Bangladesh
27. Wafaie W. Fawzi, Department of Global Health and Population, Harvard TH Chan School of Public Health, USA
28. José Quirino da Silva Filho, Federal University of Ceará, Brazil
29. Robert H. Gilman, Johns Hopkins University Bloomberg School of Public Health, USA
30. Richard Guerrant, University of Virginia, USA
31. Rashidul Haque, International Centre for Diarrhoeal Disease Research, Bangladesh
32. Sonja Y. Hess, Dept of Nutrition and Institute for Global Nutrition, University of California Davis, USA
33. Eric R. Houpt, University of Virginia, USA
34. Jean H. Humphrey, Johns Hopkins Bloomberg School of Public Health, USA
35. Najeeha Talat Iqbal, Department of Pediatrics and Child Health, Aga Khan University, Pakistan

medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint
(which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity.
It is made available under a CC-BY 4.0 International license .

36. Elizabeth Yakes Jimenez, Departments of Pediatrics and Internal Medicine, University of New Mexico Health Sciences Center, USA
37. Jacob John, Christian Medical College, Vellore, Tamil Nadu, India
38. Sushil Matthew John, Low Cost Effective Care Unit, Christian Medical College, Vellore, Tamil Nadu, India
39. Gagandeep Kang, Translational Health Science and Technology Institute, Faridabad, Haryana, India
40. Margaret Kosek, University of Virginia, USA
41. Michael S. Kramer, McGill University and McGill University Health Centre, Canada
42. Alain Labrique, Center of Human Nutrition, Department of International Health, Johns Hopkins Bloomberg School of Public Health, USA
43. Nanette R. Lee, USC-Office of Population Studies Foundation Inc., University of San Carlos, Cebu, Philippines
44. Aldo Ângelo Moreira Lima, Federal University of Ceará, Brazil
45. Mustafa Mahfuz, International Centre for Diarrhoeal Disease Research, Bangladesh
46. Tjale Cloupas Mahopo, Department of Nutrition, School of Health Sciences, University of Venda, South Africa
47. Kenneth Maleta, Department of Public Health, School of Public Health and Family Medicine, College of Medicine, University of Malawi, Malawi
48. Dharma S. Manandhar, Mother and Infant Research Activities, Nepal
49. Karim P. Manji, Department of Pediatrics and Child Health, Muhimbili University School of Health and Allied Sciences, Dar es Salaam, Tanzania
50. Reynaldo Martorell, Rollins School of Public Health, Emory University, USA
51. Sarmila Mazumder, Centre for Health Research and Development, Society for Applied Studies, New Delhi, India
52. Estomih Mduma, Haydom Lutheran Hospital, Haydom, Tanzania
53. Venkata Raghava Mohan, Professor, Community Medicine, Christian Medical College, Vellore Tamil Nadu, India
54. Sophie E. Moore, Department of Women and Children's Health, Kings College London, London, UK & MRC Unit The Gambia at London School of Hygiene and Tropical Medicine, United Kingdom
55. Ishita Mostafa, International Centre for Diarrhoeal Disease Research, Bangladesh
56. Robert Ntozini, Zvitambo Institute for Maternal and Child Health Research, Zimbabwe
57. Mzwakhe Emanuel Nyathi, Department of Animal Sciences, School of Agriculture, University of Venda, South Africa
58. Maribel Paredes Olortegui, AB PRISMA, Peru
59. William A. Petri, University of Virginia, USA
60. Prasanna Samuel Premkumar, Christian Medical College, Vellore, Tamil Nadu, India
61. Andrew M. Prentice, MRC Unit The Gambia at London School of Hygiene and Tropical Medicine, Banjul, The Gambia
62. Najeeb Rahman, Aga Khan University, Pakistan
63. Harshpal Singh Sachdev, Senior Consultant Pediatrics and Clinical Epidemiology, Sitaram Bhartia Institute of Science and Research, B-16 Qutab Institutional Area, New Delhi, India
64. Kamran Sadiq, Aga Khan University, Pakistan
65. Rajiv Sarkar, Christian Medical College, Vellore, Tamil Nadu, India
66. Naomi M. Saville, Institute for Global Health, University College London, United Kingdom
67. Saijuddin Shaikh, Johns Hopkins and JiVitA Project, Bangladesh
68. Bhim P. Shrestha, Health Research and Development Forum, Kathmandu, Nepal

medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint
(which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity.
It is made available under a CC-BY 4.0 International license .

69. Sanjaya Kumar Shrestha, MD, Walter Reed/AFRIMS Research Unit, Kathmandu, Nepal, Centre for International Health, University of Bergen, Norway
70. Alberto Melo Soares, Federal University of Ceará, Brazil
71. Bakary Sonko, MRC Unit The Gambia at London School of Hygiene and Tropical Medicine, Banjul, The Gambia
72. Aryeh D. Stein, Hubert Department of Global Health, Rollins School of Public Health, Emory University, USA
73. Erling Svensen, Haukeland University Hospital, Norway
74. Sana Syed, Department of Pediatrics, Division of Gastroenterology, Hepatology & Nutrition University of Virginia School of Medicine, and Aga Khan University, Pakistan
75. Fayaz Umrani, Aga Khan University, Pakistan
76. Honorine D. Ward, Tufts Medical Center, Tufts University School of Medicine, USA
77. Keith P. West Jr., Center for Human Nutrition, Department of International Health, Johns Hopkins Bloomberg School of Public Health, USA
78. Lee Shu Fune Wu, Center for Human Nutrition, Department of International Health, Johns Hopkins Bloomberg School of Public Health, USA
79. Seungmi Yang, McGill University, Canada
80. Pablo Penataro Yori, University of Virginia, USA

medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. It is made available under a CC-BY 4.0 International license .

Introduction

In 2018, 149 million children under 5 years (22% globally) were stunted (length-for-age Z-score >2 standard deviations below the median of the growth standard for age and sex), with the largest burden in South Asia and Africa.[1,2] Early-life stunting is associated with increased risk of mortality,[3] diarrhea, pneumonia, and measles in childhood[4,5] and impaired cognition and productivity in adulthood.[6–8] Global income would increase by an estimated $176.8 billion per year if linear growth faltering could be eliminated.[9] The WHO 2025 Global Nutrition Targets[10] and Sustainable Development Goal 2.2.1 propose to reduce stunting prevalence among children under 5 years from 2012 levels by 40% by 2025.[11]

In low-resource settings, the first 1000 days of life – including the prenatal period – is considered the critical window in which to intervene to prevent stunting.[12] Intrauterine growth restriction and preterm birth are strongly associated with stunting at 24 months of age.[13] Most linear growth faltering occurs by age 2 years, and 70% of absolute length deficits by age 5 years occur before age 2 years.[6] Children who experience linear growth faltering prior to prior to age 2 years can experience catch-up growth at older ages, particularly with improvements to their nutrition, health, and environment.[14–18] However, the extent of catch-up growth is associated with the timing and extent of early life linear growth faltering.[19]

Granular information about the age of linear growth faltering onset and its persistence in early life will best inform when and how to intervene with preventive measures. Yet, most studies of the global epidemiology of stunting have used nationally representative, cross-sectional surveys – predominantly Demographic Health Surveys (DHS) – to estimate age-specific stunting prevalence.[15,20–22] Analyses of cross-sectional studies cannot identify longitudinal patterns of linear growth faltering or reversal. Further, they may be subject to survivor bias and fail to include those children most vulnerable to undernutrition. Few studies have estimated age-specific incidence within the first two years of life.[23–27]

We estimated linear growth faltering incidence and reversal and linear growth velocity in 32 longitudinal cohorts in LMICs with multiple, frequent measurements. The analysis provides new insights into the timing of onset and duration of linear growth faltering, with important implications for interventions. We found that linear growth faltering occurs very early in the prenatal and postnatal phase – before age 6 months, when most postnatal linear growth interventions begin. Our findings confirm the importance of the first 1,000 days as a critical window to intervene to prevent linear growth faltering but motivate a renewed focus on prenatal and early postnatal interventions.

Pooled longitudinal analyses

Here, we report a pooled analysis of 32 longitudinal cohorts from 14 LMICs in South Asia, Sub-Saharan Africa, and Latin America followed between 1987 and 2017. Our objective was to estimate age-specific incidence and reversal of stunting and linear growth velocity from 0 to 24 months. Companion articles report results for child wasting (weight-for-length Z-score < 2 standard deviations below the reference median)[28] and household, maternal, and child-level risk factors associated with linear growth faltering.[29] These data were aggregated by the Bill & Melinda Gates Foundation Knowledge Integration (*ki*) initiative and comprise approximately 100 longitudinal studies on child birth, growth and development.[30] We included cohorts from the database that met five inclusion criteria: 1) conducted in LMICs; 2) had a median year of birth in 1990 or later; 3) enrolled children between birth and age 24 months and measured their length and weight repeatedly over time; 4) did not restrict enrollment to acutely ill children; and 5) collected anthropometry measurements at least every 3 months (Extended Data Fig 1). These criteria ensured we could rigorously evaluate the timing and onset of stunting among children who were broadly representative of general populations in LMICs. Thirty-two cohorts met

medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. It is made available under a CC-BY 4.0 International license .

inclusion criteria, including 52,640 children and 412,458 total measurements from 1987 to 2017 (Fig 1, Extended Data Tables 1-2). Cohorts were located in South Asia (N=17 cohorts in 4 countries), Africa (N=7 in 6 countries), Latin America (N=7 in 3 countries), and Eastern Europe (N=1) (Extended Data Fig 2). 21 cohorts measured children at least monthly, and 11 measured children every 3 months. Cohort sample sizes varied from 119 to 14,074 children. In most cohorts, over 80% of enrolled children had LAZ measurements at each age of measurement (Extended Data Figs 3-4).

We calculated length-for-age Z-scores (LAZ) using WHO 2006 growth standards.[31] We dropped 859 of 413,317measurements (0.2%) because LAZ was unrealistic (> 6 or < –6 Z), and we defined stunting as LAZ < –2 and severe stunting as LAZ < –3.[31] Unless otherwise indicated, estimates that pool across cohorts used random effects models fit with restricted maximum likelihood estimation.[32,33] Within each cohort the monthly mean LAZ ranged from –3.06 to +1.31, and the monthly proportion stunted ranged from 0% to 91% (Fig 1).

To assess *ki* cohort representativeness, we compared LAZ from cohorts with LAZ for children 0-24 months of age in contemporary population-based, cross-sectional DHS data in the same countries. *ki* cohorts and DHS Z-score distributions were similar (Fig 2a). Mean LAZ by age was generally lower in *ki* cohorts than in DHS surveys, especially in South Asia, but was slightly higher at certain ages in two Peruvian cohorts (Fig 2b).

Linear growth faltering as a whole population condition

In approximately half of cohorts, the 95th percentile of the LAZ distribution dropped below 0 by age 15 months (Extended Data Fig 5). This pattern is consistent with the characterization of linear growth faltering as a "whole population" condition.[21] In most cohorts, as children aged, LAZ distributions shifted downwards (Extended Data Fig 6), and standard deviations and skewness were similar across ages (Extended Data Fig 7).

Onset of stunting in early life

To measure the timing of stunting onset, we classified a child as a new incident case in three-month age periods if their LAZ dropped below –2 for the first time in that age period. The percentage of children that were stunted at birth ranged from 0.3% to 42% in each cohort and was 13% overall (Fig 3a). The percentage that experienced incident stunting onset between birth and 3 months ranged from 6% to 47% in each cohort and was 16% overall. Children stunted between birth and 3 months accounted for 23% of all children who experienced stunting by age 24 months (69% of children). Very early life stunting onset was most common in South Asia. Trends were similar for severe stunting (https://child-growth.github.io/stunting/severe-stunting.html).

In an exploratory analysis, we stratified age-specific mean LAZ by age of stunting onset among children in monthly measured cohorts and observed three subgroups whose mean LAZ followed statistically different trajectories (Fig 3b). 21% of all children were born with mean LAZ < –1, and their mean LAZ stabilized around –2 from age 1 month onward, with differences at birth in this group narrowing over time, likely via regression to the mean. 14% of children were born with mean LAZ between –1 and 0 at birth, and in these children, mean LAZ approached –2 at subsequent ages. The remaining 65% never met the criteria for stunting; yet, among these children, mean LAZ was between –0.5 and 0 at birth, and it declined steadily, reaching close to –1 by age 15 months. A companion article reports characteristics that increase risk of earlier versus later growth faltering.[30]

medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. It is made available under a CC-BY 4.0 International license .

Stunting reversal and relapse

We hypothesized that 1) lower than average linear growth (LAZ <0) would persist among children who experienced stunting reversal (i.e., LAZ increased from below –2 to above –2), and 2) children who experienced stunting reversal would experience stunting relapse at later ages. To test these hypotheses, we classified a child's change in stunting status from birth to 15 months among monthly-measured cohorts (measurement frequency beyond 15 months was less consistent). The proportion previously stunted who were either reversed or no longer stunted at 15 months was 16% (Fig 4a). New incidence of stunting was highest at birth and declined steadily to 3.3% per month by age 4 months (Fig 4b). Incidence rates of new and relapse stunting exceeded rates of reversal at all ages (Fig 4b). The proportion with stunting relapse following reversal ranged from 2-3.5% from ages 6 to 15 months. Within each cohort, 0.5% to 10% of children experienced stunting reversal each month, and 0.1% to 11% of experienced stunting relapse each month (Fig 4b).

Among children who experienced stunting reversal, we summarized the LAZ distribution at older ages. We then estimated the mean difference in LAZ measured at older ages compared to when stunting was reversed. At the time of stunting reversal, the LAZ distribution mode was close to the –2 cutoff (Fig 4c, Extended Data Fig 8). As children aged, LAZ distributions gradually shifted downwards, illustrating that linear growth deficits continued to accumulate. Among children who experienced stunting reversal before 6 months, mean difference in LAZ 9 months later was -0.69 (95% CI -0.84, -0.55; cohort-specific range: -1.04, -0.22) (Fig 4d). Children who were older at the time of reversal experienced larger decline in subsequent LAZ compared to younger children (Fig 4d). Overall, improvements in LAZ following stunting reversal were neither sustained nor large enough to erase linear growth deficits and did not resemble a biological recovery process for most children.

Growth velocity by age and sex

We defined linear growth velocity as the change in length between two time points divided by the number of months between the time points (cm/month). We also estimated within-child rates of LAZ change per month, which compares changes in a child's length relative to the WHO standard over time. After 6 months, changes in length and LAZ within-child were minimal. From 0-3 months, cohort-specific length velocity ranged from below the 1st percentile of the WHO standard to above the 50th for boys and above the 75th percentile for girls (Fig 5a). At subsequent ages, length velocity in each cohort was mostly between the 15th and 50th percentiles of the WHO standard, except in one cohort in Belarus, which had higher length velocity. Larger deficits at the youngest ages were consistent with highest incidence of stunting from birth to age 3 months (Fig 3a). The difference in LAZ within child per month was largest from 0-3 months; after age 3 months, the mean change in LAZ within child was <0.3 between different age intervals (Fig 5b). Generally, velocity within age was higher in Latin America than in South Asia and Africa (Extended Data Fig 8).

Discussion

This large-scale analysis of 32 longitudinal cohorts from LMICs revealed new insights into the timing, persistence, and recurrence of linear growth faltering from birth to age 2 years. Prior cross-sectional studies found that stunting prevalence increased gradually with age.[15,20–22] In contrast, we found that overall, 13% of children were born stunted, 25% of children experienced stunting onset between birth and 6 months, and 31% experienced onset from 6 to 24 months (Fig 3, Fig 4b). Most children who

medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. It is made available under a CC-BY 4.0 International license .

experienced stunting reversal continued to experience linear growth deficits, and over 20% were stunted again at later measurements (Fig 4). Even among children who were never met criteria for stunting before age 2 years, mean LAZ steadily declined with age (Fig 3b). Our findings reinforce that linear growth faltering among children in LMICs is a whole-population phenomenon, with both stunted and not stunted children experiencing suboptimal growth trajectories in early life.[21]

Our findings that 13% of children were stunted at birth and that the birth prevalence was 20% in South Asia underscores the importance of pre-pregnancy and prenatal interventions to reduce stunting, especially in South Asia where at-birth stunting was 24%. These interventions include maternal micronutrient and macronutrient supplementation,[34,35] increasing women's autonomy and education,[36] reducing adolescent pregnancies in LMICs by delaying the age of marriage and first pregnancy,[37] and promoting family planning.[38] Interventions to prevent prenatal infections, such as intermittent preventive treatment for malaria, may also increase fetal linear growth in regions where such infections co-occur with linear growth faltering.[39]

In this study, 25% of children became stunted between birth and age 6 months, yet few child nutrition interventions are recommended by the World Health Organization in this age range. In the neonatal period, those interventions include delayed cord clamping, neonatal vitamin K administration, and kangaroo mother care.[40] Beyond the neonatal period, the sole recommended intervention is exclusive breastfeeding,[40] which significantly reduces the risk of mortality and morbidity but has not been found to reduce infant stunting.[4,41–44] Additional research is needed to identify interventions that prevent linear growth faltering between birth and 6 months, including nutritional support of the lactating parent and the vulnerable infant.[45] Interventions may need to focus on upstream risk factors, such as maternal pre-conception and prenatal health and nutrition, and microbiota.

We found that 31% of children became stunted during complementary feeding (age 6-24 months). Meta-analyses evaluating the effectiveness of interventions during this phase on linear growth have reported modest impacts of lipid-based nutrient supplements,[46] modest or no impact of micronutrient supplementation,[47] and no impact of water and sanitation improvements, deworming, or maternal education.[47] The dearth of effective postnatal interventions to improve linear growth motivates renewed efforts to identify alternative, possibly multisectoral interventions, and to improve intervention targeting and implementation.[48,49]

There were several limitations to the analyses. First, length estimates may be subject to measurement error; stunting reversal and relapse analyses that rely on thresholds are more sensitive to such errors. However, detailed assessments of measurement quality indicated that measurement quality was high across cohorts (https://child-growth.github.io/stunting/QA.html). Second, estimates of LAZ at birth using the WHO Child Growth Standards overestimate stunting in preterm infants. Accurate estimates of gestational age were not available in included cohorts; seven cohorts measured gestational age by recall of last menstrual period or newborn examination, and one cohort measured gestational age by ultrasound. In a sensitivity analysis adjusting for gestational age pooling across cohorts that measured it, stunting prevalence at birth was 1% lower (Extended Data Fig 9). Third, included cohorts were not inclusive of all countries in the regions presented here, and linear growth faltering was more common in included African and South Asian cohorts than in corresponding contemporary representative surveys. The consistency between attained linear growth patterns in this and nationally representative DHS surveys (Fig 2) suggests that overall, our results have reasonably good external validity. For growth velocity, the cohorts represented populations close to the 25th percentile of international standards (Figure 5a). Fourth, the included cohorts measured child length every 1-3

medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint
(which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity.
It is made available under a CC-BY 4.0 International license .

months, and ages of measurement varied, so different numbers of children and cohorts contributed to each estimate. However, when we repeated analyses in cohorts with monthly measurements from birth to 24 months (n=18 cohorts in 10 countries, 10,830 children), results were similar (https://child-growth.github.io/stunting/monthly.html). Finally, our inferences are limited to the first two years of life since very few included studies measured children at older ages. Other studies, however, have found that stunting status in early life is associated with health outcomes later in life, and the timing and extent of early life linear growth faltering is associated with the magnitude of later catch up growth.[6–8,16,17,19]

Conclusion

Current WHO 2025 Global Nutrition Targets and Sustainable Development Goal 2.2.1 aim to reduce stunting prevalence among children under 5 years by 2025. Our findings suggest that defining stunting targets at earlier ages (e.g., stunting by 3 or 6 months) would help focus attention on the period when interventions may be most impactful. In addition, our results motivate renewed efforts to identify effective prenatal and early postnatal interventions and improve delivery of early life interventions to prevent linear growth faltering among children in LMICs.

medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint
(which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity.
It is made available under a CC-BY 4.0 International license .

References

1. *WHO | Joint child malnutrition estimates - Levels and trends (2019 edition)*. http://www.who.int/nutgrowthdb/estimates2018/en/ (2019).
2. Kinyoki, D. K. *et al.* Mapping child growth failure across low- and middle-income countries. *Nature* **577**, 231–234 (2020).
3. McDonald, C. M. *et al.* The effect of multiple anthropometric deficits on child mortality: meta-analysis of individual data in 10 prospective studies from developing countries. *Am. J. Clin. Nutr.* **97**, 896–901 (2013).
4. Black, R. E. *et al.* Maternal and child undernutrition and overweight in low-income and middle-income countries. *The Lancet* **382**, 427–451 (2013).
5. Olofin, I. *et al.* Associations of Suboptimal Growth with All-Cause and Cause-Specific Mortality in Children under Five Years: A Pooled Analysis of Ten Prospective Studies. *PLoS ONE* **8**, (2013).
6. de Onis, M. & Branca, F. Childhood stunting: a global perspective. *Matern. Child. Nutr.* **12**, 12–26 (2016).
7. Prendergast, A. J. & Humphrey, J. H. The stunting syndrome in developing countries. *Paediatr. Int. Child Health* **34**, 250–265 (2014).
8. Adair, L. S. *et al.* Associations of linear growth and relative weight gain during early life with adult health and human capital in countries of low and middle income: findings from five birth cohort studies. *Lancet* **382**, 525–534 (2013).
9. Fink, G. *et al.* Schooling and wage income losses due to early-childhood growth faltering in developing countries: national, regional, and global estimates. *Am. J. Clin. Nutr.* **104**, 104–112 (2016).
10. World Health Organization. Global Targets 2025. *WHO* http://www.who.int/nutrition/global-target-2025/en/.

medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. It is made available under a CC-BY 4.0 International license .

11. United Nations. Goal 2. Sustainable Development Knowledge Platform. https://sustainabledevelopment.un.org/sdg2.
12. Martorell, R. Improved nutrition in the first 1000 days and adult human capital and health. *Am. J. Hum. Biol.* **29**, e22952 (2017).
13. Christian, P. *et al.* Risk of childhood undernutrition related to small-for-gestational age and preterm birth in low- and middle-income countries. *Int J Epidemiol* **42**, 1340–1355 (2013).
14. Dewey, K. G. & Begum, K. Long-term consequences of stunting in early life. *Matern. Child. Nutr.* **7**, 5–18 (2011).
15. Leroy, J. L., Ruel, M., Habicht, J.-P. & Frongillo, E. A. Using height-for-age differences (HAD) instead of height-for-age z-scores (HAZ) for the meaningful measurement of population-level catch-up in linear growth in children less than 5 years of age. *BMC Pediatr.* **15**, 145 (2015).
16. Aizawa, T. Trajectory of inequality of opportunity in child height growth: Evidence from the Young Lives study. *Demogr. Res.* **42**, 165–202 (2020).
17. Georgiadis, A. *et al.* Growth recovery and faltering through early adolescence in low- and middle-income countries: Determinants and implications for cognitive development. *Soc. Sci. Med.* **179**, 81–90 (2017).
18. Prentice, A. M. *et al.* Critical windows for nutritional interventions against stunting123. *Am. J. Clin. Nutr.* **97**, 911–918 (2013).
19. Gausman, J., Kim, R. & Subramanian, S. V. Stunting trajectories from post-infancy to adolescence in Ethiopia, India, Peru, and Vietnam. *Matern. Child. Nutr.* **15**, (2019).
20. Victora, C. G., Onis, M. de, Hallal, P. C., Blössner, M. & Shrimpton, R. Worldwide Timing of Growth Faltering: Revisiting Implications for Interventions. *Pediatrics* **125**, e473–e480 (2010).

medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint
(which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity.
It is made available under a CC-BY 4.0 International license .

21. Roth, D. E. *et al.* Early childhood linear growth faltering in low-income and middle-income countries as a whole-population condition: analysis of 179 Demographic and Health Surveys from 64 countries (1993–2015). *Lancet Glob. Health* **5**, e1249–e1257 (2017).
22. Leroy, J. L., Ruel, M., Habicht, J.-P. & Frongillo, E. A. Linear growth deficit continues to accumulate beyond the first 1000 days in low- and middle-income countries: global evidence from 51 national surveys. *J. Nutr.* **144**, 1460–1466 (2014).
23. Kumar, R., Deshmukh, P. R. & Garg, B. S. Incidence and Correlates of "Growth Faltering" Among 0–6 y Children: A Panel Study from Rural Wardha. *Indian J. Pediatr.* **79**, 333–341 (2012).
24. Lundeen, E. A. *et al.* Growth faltering and recovery in children aged 1–8 years in four low- and middle-income countries: Young Lives. *Public Health Nutr.* **17**, 2131–2137 (2014).
25. Mangani, C. *et al.* Effect of complementary feeding with lipid-based nutrient supplements and corn–soy blend on the incidence of stunting and linear growth among 6- to 18-month-old infants and children in rural Malawi. *Matern. Child. Nutr.* **11**, 132–143 (2015).
26. Maleta, K., Virtanen, S. M., Espo, M., Kulmala, T. & Ashorn, P. Childhood malnutrition and its predictors in rural Malawi. *Paediatr. Perinat. Epidemiol.* **17**, 384–390 (2003).
27. Mongkolchati, A., Thinkhamrop, B., Mo-Suwan, L., Chittchang, U. & Choprapawon, C. Prevalence and incidence of child stunting from birth to two years of life in Thai children: based on the Prospective Cohort Study of Thai Children (PCTC). *J. Med. Assoc. Thail. Chotmaihet Thangphaet* **93**, 1368–1378 (2010).
28. Mertens, A. *et al.* (submitted). Child wasting and concurrent stunting in low- and middle-income countries. (2020).
29. Mertens, A. *et al.* (submitted). Causes and consequences of child growth faltering in low- and middle-income countries. (2020).

medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint
(which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity.
It is made available under a CC-BY 4.0 International license .

30. Peppard, T. *et al.* (submitted). Combined longitudinal growth cohorts from infants born in South Asia, Sub-Saharan Africa and Latin America. (2020).
31. WHO Multicentre Growth Reference Study Group. WHO child growth standards: length/height-for-age, weight-for-age, weight-for-length, weight-for-height and body mass index-for-age: Methods and development. *Geneva World Health Organ.* 312 pages (2006).
32. Viechtbauer, W. Bias and Efficiency of Meta-Analytic Variance Estimators in the Random-Effects Model. *J. Educ. Behav. Stat.* **30**, 261–293 (2005).
33. Raudenbush, S. W. Analyzing Effect Sizes: Random-Effects Models. in *The Handbook of Research Synthesis and Meta-Analysis* 295–315 (Russell Sage Foundation, 2009).
34. Das, J. K. *et al.* Lipid-based nutrient supplements for maternal, birth, and infant developmental outcomes. *Cochrane Database Syst. Rev.* **8**, CD012610 (2018).
35. Lassi, Z. S., Das, J. K., Zahid, G., Imdad, A. & Bhutta, Z. A. Impact of education and provision of complementary feeding on growth and morbidity in children less than 2 years of age in developing countries: a systematic review. *BMC Public Health* **13**, S13 (2013).
36. Carlson, G. J., Kordas, K. & Murray-Kolb, L. E. Associations between women's autonomy and child nutritional status: a review of the literature. *Matern. Child. Nutr.* **11**, 452–482 (2015).
37. Svanemyr, J., Chandra-Mouli, V., Raj, A., Travers, E. & Sundaram, L. Research priorities on ending child marriage and supporting married girls. *Reprod. Health* **12**, 80 (2015).
38. Dhingra, S. & Pingali, P. L. Effects of short birth spacing on birth-order differences in child stunting: Evidence from India. *Proc. Natl. Acad. Sci.* **118**, (2021).
39. Luntamo, M., Kulmala, T., Cheung, Y. B., Maleta, K. & Ashorn, P. The effect of antenatal monthly sulphadoxine–pyrimethamine, alone or with azithromycin, on foetal and neonatal growth faltering in Malawi: a randomised controlled trial. *Trop. Med. Int. Health* **18**, 386–397 (2013).

medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint
(which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity.
It is made available under a CC-BY 4.0 International license .

40. World Health Organization. *Reducing Stunting in Children: Equity Considerations for Achieving the Global Nutrition Targets 2025*. Licence: CC BY-NC-SA 3.0 IGO (2018).

41. Victora, C. G. *et al.* Breastfeeding in the 21st century: epidemiology, mechanisms, and lifelong effect. *The Lancet* **387**, 475–490 (2016).

42. Bhutta, Z. A. *et al.* What works? Interventions for maternal and child undernutrition and survival. *The Lancet* **371**, 417–440 (2008).

43. Giugliani, E. R. J., Horta, B. L., Mola, C. L. de, Lisboa, B. O. & Victora, C. G. Effect of breastfeeding promotion interventions on child growth: a systematic review and meta-analysis. *Acta Paediatr.* **104**, 20–29 (2015).

44. Eriksen, K. G. *et al.* Following the World Health Organization's Recommendation of Exclusive Breastfeeding to 6 Months of Age Does Not Impact the Growth of Rural Gambian Infants. *J. Nutr.* **147**, 248–255 (2017).

45. Christian, P. *et al.* The need to study human milk as a biological system. *Am. J. Clin. Nutr.* **113**, 1063–1072 (2021).

46. Dewey, K. G. *et al.* Characteristics that modify the effect of small-quantity lipid-based nutrient supplementation on child growth: an individual participant data meta-analysis of randomized controlled trials. *Am. J. Clin. Nutr.* nqab278 (2021) doi:10.1093/ajcn/nqab278.

47. Park, J. J. H. *et al.* Association of Early Interventions With Birth Outcomes and Child Linear Growth in Low-Income and Middle-Income Countries: Bayesian Network Meta-analyses of Randomized Clinical Trials. *JAMA Netw. Open* **2**, e197871–e197871 (2019).

48. Casanovas, M. del C. *et al.* Multi-sectoral interventions for healthy growth - Carmen Casanovas - 2013 - Maternal & Child Nutrition - Wiley Online Library. *Matern. Child. Nutr.* **9**, 46–57 (2013).

medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint
(which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity.
It is made available under a CC-BY 4.0 International license .

485 49. Ruel, M., Alderman, H. & Maternal and Child Nutrition Study Group. Nutrition-sensitive
486 interventions and programmes: how can they help to accelerate progress in improving maternal and
487 child nutrition? *Lancet* **382**, 536–51 (2013).
488 50. Perumal, N. *et al.* Effect of correcting for gestational age at birth on population prevalence of early
489 childhood undernutrition. *Emerg. Themes Epidemiol.* **15**, 3 (2018).
490

medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. It is made available under a CC-BY 4.0 International license .

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 5 inclusion criteria (Extended Data Fig 1).

(1) *Studies that were conducted in low- or middle-income countries*. Children in these countries have the largest burden linear growth faltering and are the key target population for preventive interventions.
(2) *Studies that had a median year of birth in 1990 or later.* This restriction resulted in a set of studies spanning the period from 1987 to 2017 and excluded older studies that are less applicable to current policy dialogues.
(3) *Studies that enrolled children between birth and age 24 months and measured their length and weight repeatedly over time*. We were principally interested in growth faltering during the first 1,000 days (including gestation), thought to be the key window for linear growth faltering.
(4) *Studies that 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.
(5) *Studies that collected anthropometry measurements at least every 3 months* to ensure that we adequately captured incident episodes and recovery.

Thirty-two longitudinal cohorts in 14 countries followed between 1987 and 2017 met inclusion criteria. There was no evidence of secular trends in LAZ (https://child-growth.github.io/stunting/secular-trends.html). We calculated cohort measurement frequency as the median days between measurements. If randomized trials found effects on growth within the intervention arms, the analyses were limited to the control arm. We included all measurements under 24 months of age, assuming months were 30.4167 days. We excluded extreme measurements of LAZ > 6 or < –6 following WHO growth standard recommendations.[1] In many studies, investigators measured length shortly after birth because deliveries were at home, but the majority of measurements were within the first 7 days of life (https://child-growth.github.io/stunting/age-meas.html); for this reason, we grouped measurements in the first 7 days as birth measurements. Gestational age was measured in only eight cohorts (7 cohorts measured it by recall of last menstrual period or newborn examination; 1 measured it by ultrasound); thus, we did not attempt to exclude preterm infants from the analyses.

Quality assurance

The *ki* data team assessed the quality of individual cohort datasets by checking the range of each variable for outliers and values that are not consistent with expectation. Z-scores were calculated using the median of replicate measurements and the 2006 WHO Child Growth Standards.[1] In a small number of cases a child had two anthropometry records at the same age, in which case we used the mean of the records. Analysts reviewed bivariate scatter plots to check for expected correlations (e.g., length by height, length/height/weight by age, length/height/weight by corresponding Z-score). Once the individual cohort data was mapped to a single harmonized dataset, analysts conducted an internal peer review of published articles for completeness and accuracy. Analysts contacted contributing investigators to seek clarification about potentially erroneous values in the data and revised the data as needed.

medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. It is made available under a CC-BY 4.0 International license .

Outcome definitions

We used the following summary measures in the analysis:

Incident stunting episodes were defined as a change in LAZ from above –2 Z in the prior measurement to below –2 Z in the current measurement. Similarly, we defined severe stunting episodes using the –3 Z cutoff. Children were considered at risk of stunting at birth, so children born stunted were considered to have an incident episode of stunting at birth. Children were also assumed to be at risk of stunting at the first measurement in non-birth cohorts and trials. Children whose first measurement occurred after birth were assumed to have experienced stunting onset at the age halfway between birth and the first measurement. The vast majority of children were less than 5 days of age at their first measurement life (https://child-growth.github.io/stunting/age-meas.html).

Incidence proportion We calculated the incidence proportion of stunting during a defined age range (e.g. 3-6 months) as the proportion of children at risk of becoming stunted who became stunted during the age range (the onset of new episodes).

Changes in stunting status were classified using the following categories: "Never stunted": children with LAZ ≥–2 at previous ages and the current age. "No longer stunted": children who previously reversed their stunting status with LAZ ≥–2 at the current age. "Stunting reversal": children with LAZ <–2 at the previous age and LAZ ≥ –2 at the current age. "Newly stunted": children whose LAZ was previously always ≥–2 and with LAZ <–2 at the current age. "Stunting relapse": children who were previously stunted with LAZ ≥–2 at the previous age and LAZ <–2 at the current age. "Still stunted": children whose LAZ was <–2 at the previous and current age.

Growth velocity was calculated as the change in length in centimeters between two time points divided by the number of months between the time points. We compared the change in length in centimeters per month measures to the WHO Child Growth Standards for linear growth velocity.[2] We also estimated within-child rates of change in LAZ per month.

Measurement frequency

Analyses of incidence and growth velocity (Figs 3 and 5) included cohorts with at least quarterly measurements in order to include as many cohorts as possible. Analyses of stunting reversal (Fig 4) were restricted to cohorts with at least monthly measurements to allow evaluation of changes in stunting status with higher resolution.

Subgroups of interest

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

Statistical analysis

All analyses were conducted in R version 3.4.2.[3]

Estimation of mean LAZ 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 height and weight datasets from each country. We obtained variables for

medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. It is made available under a CC-BY 4.0 International license .

country code, sample weight, cluster number, primary sampling unit, and design stratification from the women's individual survey recode files. From the height and weight dataset, we used standard recode variables corresponding to the 2006 WHO growth standards for height-for-age.

After excluding missing observations, restricting to measurements of children 0-24 months of age, and restricting to z-scores within WHO-defined plausible values, surveys collected from 1996 to 2018 in countries that overlapped with *ki* cohorts with the exception of Guinea-Bissau because the DHS survey was not conducted there during the study period (Extended Data Table 3).

We classified countries into regions (South Asia, Latin America, and Africa) using the World Health Organization regional designations with the exception of the classification for Pakistan, which we included in South Asia to be consistent with prior linear growth studies using DHS.[4] One included cohort was from Belarus, and we chose to exclude it from region-stratified analyses as it was the only European study.

We estimated age-stratified mean from ages 0 to 24 months within each DHS survey, accounting for the complex survey design and sampling weights. We then pooled estimates of mean LAZ for each age in months across countries using a fixed effects estimator (details below). We computed two sets of pooled results: 1) DHS measuring children 0-24 months in countries that overlapped with *ki* study countries and 2) all DHS countries measuring children 0-24 months in each geographic region (as in Fig 2) and (https://child-growth.github.io/stunting/DHS.html). We compared DHS estimates with mean LAZ by age in the ki study cohorts, which we estimated using penalized cubic-splines with bandwidth chosen using generalized cross-validation.[5] We used splines to estimate age-dependent mean LAZ in the *ki* study cohorts to smooth any age-dependent variation in the mean caused by less frequently measured cohorts.

Distribution models

To investigate how the mean, standard deviation, and skewness of LAZ distributions varied by age, we fit linear models with skew-elliptical error terms using maximum likelihood estimation. We fit models separately by cohort.

Fixed and random effects models

Several analyses pooled results across study cohorts. We estimated each age-specific mean using a separate estimation and pooling step. We first estimated the mean in each cohort, and then pooled age-specific means across cohorts, while allowing for a cohort-level random effect. This approach enabled us to include the most information possible for each age-specific mean, while accommodating slightly different measurement schedules across the cohorts. Each cohort's data only contributed to LAZ or stunting incidence estimates at the ages for which it contributed data.

The primary method of pooling was using random effects models. This modeling approach assumes that studies are randomly drawn from a hypothetical population of longitudinal studies that could have been conducted on children's linear growth in the past or future. We also fit fixed effects models as a sensitivity analysis (https://child-growth.github.io/stunting/fixed-effects.html); inferences about estimates from fixed effects models are restricted to only the included studies.[6]

medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. It is made available under a CC-BY 4.0 International license .

Random effects models assume that the true population outcomes θ are normally distributed with mean μ and variance τ^2 (i.e., that $\theta \sim \mathrm{N}(\mu, \tau^2)$). To estimate outcomes in this study, the random effects model is defined as follows for each study in the set of $i = 1, \ldots, k$ studies:

$$y_i = \mu + u_i + e_i \quad (1)$$

where y_i is the observed outcome in study i, u_i is the random effect for study i, and e_i is the estimated outcome for study i, and e_i is the sampling error within study i. The model assumes that $u_i \sim \mathrm{N}(0, \tau^2)$ and $e_i \sim \mathrm{N}(0, v_i)$, where v_i is the study-specific sampling variance. We fit random effects models using the restricted maximum likelihood estimator.[7,8] If a model failed to converge, models were fit using a maximum likelihood estimator instead. The estimate of μ is the estimated mean outcome in the hypothetical population of studies (i.e., the estimated outcome pooling across study cohorts).

We also fit inverse variance weighted fixed effects models defined as follows:

$$\overline{\theta}_w = \sum_{i=1}^{k} w_i \theta_i \Big/ \sum_{i=1}^{k} w_i \quad (2)$$

where $\overline{\theta}_w$ is the weighted mean outcome in the set of *k* included studies, and w_i is a study-specific weight, defined as the inverse of the study-specific sampling variance v_i. $\overline{\theta}_w$ is the estimated mean outcome in the specific studies included in this analysis.

For both types of outcomes, we pooled binary outcomes on the logit scale and then back-transformed estimates after pooling to constrain confidence intervals between 0 and 1. While the probit transformation more closely resembles common distributions for physiologic variables, in practice the logit transformation produces nearly identical estimates and is more convenient for estimation. For cohort-stratified analyses, which did not pool across studies, we estimated 95% confidence intervals using the normal approximation (https://child-growth.github.io/stunting/cohort.html).

Estimation of incidence

We estimated incidence as defined above in 3-month age intervals within specific cohorts and pooled within region and across all studies (Fig 3). Pooled analyses used random effects models for the primary analysis and fixed effects models for sensitivity analyses as described above.

Estimation of changes in stunting status

To assess fluctuations in stunting status over time, we conducted an analysis among cohorts with at least monthly measurements from birth through age 15 months to provide sufficient granularity to capture changes in stunting status. We estimated the proportion of children in each stunting category defined above under "Changes in stunting status" at each month from birth to 15 months. To ensure that percentages summed to 100%, we present results that were not pooled using random effects. Analyses using random effects produced similar results (https://child-growth.github.io/stunting/fixed-effects.html#changes-in-stunting-status-by-age).

To examine the distribution of LAZ among children with stunting reversal, we created subgroups of children who experienced stunting reversal at ages 3, 6, 9, and 12 months and then summarized the distribution of the children's LAZ at ages 6, 9, 12, and 15 months. Within each age interval, we estimated the mean difference in LAZ at older ages compared to the age of stunting reversal and estimated 95%

medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. It is made available under a CC-BY 4.0 International license .

188 confidence intervals for the mean difference. Pooled analyses used random effects models for the
189 primary analysis and fixed effects models for sensitivity analyses as described above.
190
191 Linear growth velocity
192 We estimated linear growth velocity within 3-month age intervals stratified by sex, pooling across
193 study cohorts (Fig 5) as well as stratified by geographic region (Extended Data Fig 9) and study cohort
194 (https://child-growth.github.io/stunting/cohort.html#length-velocity-by-age-and-sex). Analyses included
195 cohorts that measured children at least quarterly. We included measurements within a two-week
196 window around each age in months to account for variation in the age of each length measurement.
197 Pooled analyses used random effects models for the primary analysis and fixed effects models for
198 sensitivity analyses as described above (https://child-growth.github.io/stunting/fixed-
199 effects.html#linear-growth-velocity-1).
200
201 **Sensitivity Analyses**
202 We conducted three sensitivity analyses. First, to assess whether inclusion of PROBIT, the single
203 European cohort, influenced our overall pooled inference, we repeated analyses excluding the PROBIT
204 cohort. Results were very similar with and without the PROBIT cohort (https://child-
205 growth.github.io/stunting/exclude-PROBIT.html). Second to explore the influence of differing numbers
206 of cohorts contributing data at different ages, we conducted a sensitivity analysis in which we subset
207 data to cohorts that measured anthropometry monthly from birth to 24 months (n=21 cohorts in 10
208 countries, 11,424 children (https://child-growth.github.io/stunting/monthly.html). Third, we compared
209 estimates pooled using random effects models presented in the main text with estimates pooled using
210 fixed effects inverse variance weighted models. The random effects approach was more conservative in
211 the presence of study heterogeneity (https://child-growth.github.io/stunting/fixed-effects.html).
212
213 **Data and code availability:** The data that support the findings of this study are available from the Bill
214 and Melinda Gates Foundation Knowledge Integration project upon reasonable request. Replication
215 scripts for this analysis are available here: https://github.com/child-growth/ki-longitudinal-growth.
216
217 ## Methods References
218 1. WHO Multicentre Growth Reference Study Group. WHO child growth standards: length/height-for-
219 age, weight-for-age, weight-for-length, weight-for-height and body mass index-for-age: Methods and
220 development. *Geneva World Health Organ.* 312 pages (2006).
221 2. WHO. *WHO Child Growth Standards: Growth Velocity Based on Weight, Length and Head*
222 *Circumference: Methods and Development.* (2009).
223 3. R Core Team. *R: A language and environment for statistical computing*. https://www.R-project.org/
224 (2019).
225 4. Victora, C. G., de Onis, M., Hallal, P. C., Blössner, M. & Shrimpton, R. Worldwide timing of growth
226 faltering: revisiting implications for interventions. *Pediatrics* **125**, e473-480 (2010).

medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint
(which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity.
It is made available under a CC-BY 4.0 International license .

5. Wood, S. N., Pya, N. & Säfken, B. Smoothing Parameter and Model Selection for General Smooth Models. *J. Am. Stat. Assoc.* **111**, 1548–1563 (2016).

6. Hedges, L. V. & Vevea, J. L. Fixed- and random-effects models in meta-analysis. *Psychol. Methods* **3**, 486–504 (1998).

7. Viechtbauer, W. Bias and Efficiency of Meta-Analytic Variance Estimators in the Random-Effects Model. *J. Educ. Behav. Stat.* **30**, 261–293 (2005).

8. Raudenbush, S. W. Analyzing Effect Sizes: Random-Effects Models. in *The Handbook of Research Synthesis and Meta-Analysis* 295–315 (Russell Sage Foundation, 2009).

medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint
(which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity.
It is made available under a CC-BY 4.0 International license .

Acknowledgments

This research was financially supported by a global development grant (OPP1165144) from the Bill & Melinda Gates Foundation to the University of California, Berkeley, CA, USA. We would also like to thank the following collaborators on the included cohorts and trials for their contributions to study planning, data collection, and analysis: Muhammad Sharif, Sajjad Kerio, Ms. Urosa, Ms. Alveen, Shahneel Hussain, Vikas Paudel (Mother and Infant Research Activities), Anthony Costello (University College London), Benjamin Torun, Lindsey M Locks, Christine M McDonald, Roland Kupka, Ronald J Bosch, Rodrick Kisenge, Said Aboud, Molin Wang, Azaduzzaman, Abu Ahmed Shamim, Rezaul Haque, Rolf Klemm, Sucheta Mehra, Maithilee Mitra, Kerry Schulze, Sunita Taneja, Brinda Nayyar, Vandana Suri, Poonam Khokhar, Brinda Nayyar, Poonam Khokhar, Jon E Rohde, Tivendra Kumar, Jose Martines, Maharaj K Bhan, and all other members of the study staffs and field teams. We would also like to thank all study participants and their families for their important contributions.

Author contributions

Conceptualization: J.B., A.M., J.M.C., K.H.B., P.C., B.F.A
Funding Acquisition: J.M.C., A.E.H., M.J.V., B.F.A.
Data curation: J.B., A.M., J.C., O.S., W.C., A.N., N.N.P., W.J., E.J., E.O.C., S.D., N.H., I.M., H.L., R.H., V.S., J.H., T.N.
Formal analyses: J.B., A.M., J.C., O.S., W.C., A.N., N.N.P., W.J., E.J., E.O.C., S.D., N.H., I.M., H.L., V.S., B.F.A
Methodology: J.B., A.M., J.M.C, J.C., O.S., N.H., I.M., A.E.H., M.J.V.,K.H.B., P.C., B.F.A.
Visualization: J.B., A.M., A.N., N.N.P., S.D., A.S., J.C., R.H., E.J., K.H.B., P.C., B.F.A.
Writing – Original Draft Preparation: J.B., A.M., B.F.A.
Writing – Review & Editing: J.B., A.M., J.M.C., K.H.B., P.C., B.F.A., *ki* Child Growth Consortium members

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 here: https://child-growth.github.io/stunting/

Correspondence and requests for materials should be addressed to Jade Benjamin-Chung (jadebc@berkeley.edu) and Benjamin F. Arnold (ben.arnold@ucsf.edu).

medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint
(which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity.
It is made available under a CC-BY 4.0 International license .

Early childhood linear growth faltering in low- and middle-income countries

Manuscript figures

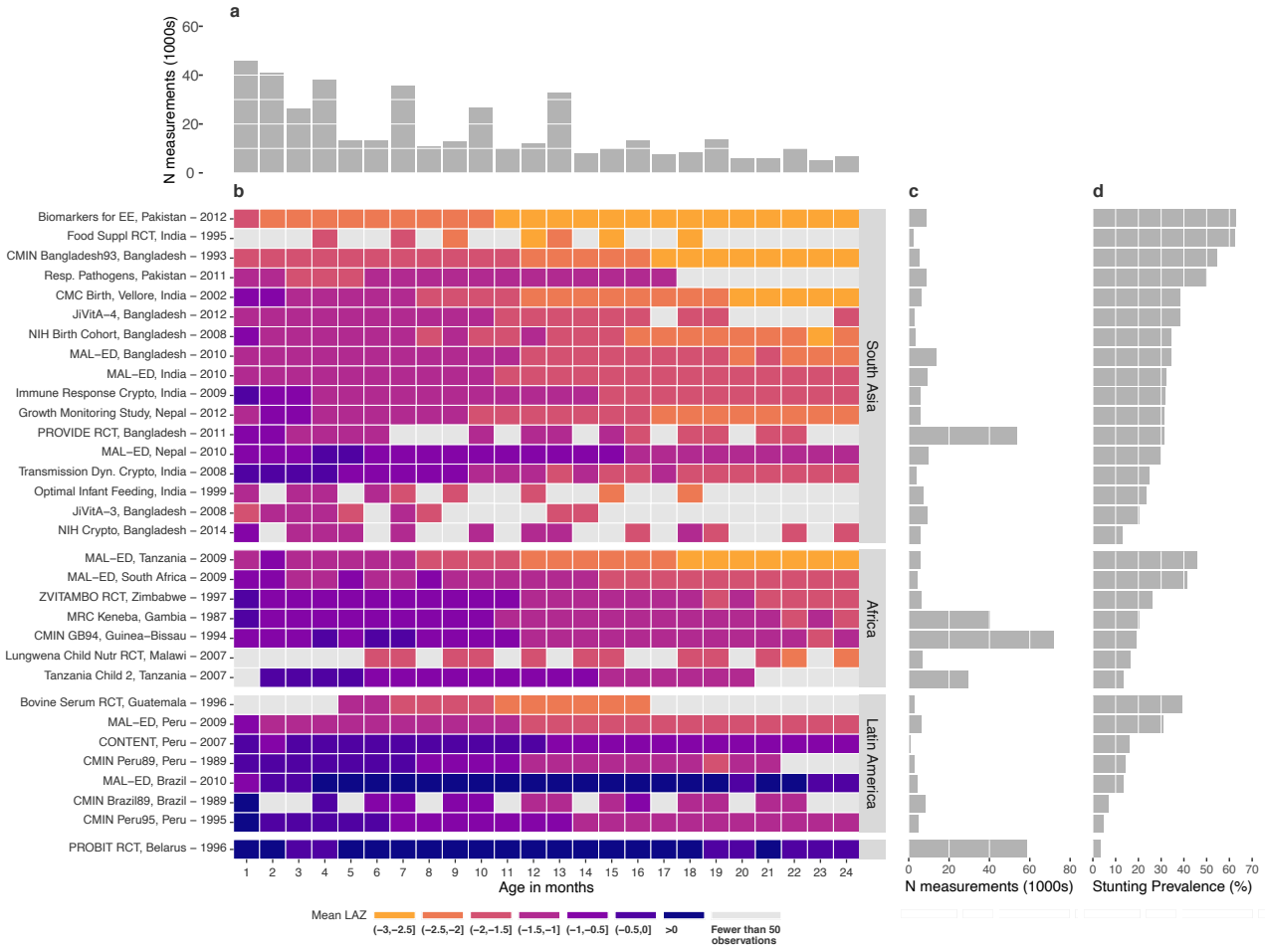


Figure 1 | Summaries of included *ki* cohorts. (**a**) Number of observations (1000s) by age in months. (**b**) Mean length-for-age Z-scores by age in months for each cohort. Cohorts are sorted by geographic region and mean length-for-age Z-score. (**c**) Number of observations contributed by each cohort. (**d**) Overall stunting prevalence in each cohort, defined as proportion of measurements with length-for-age z-score < –2.

medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint
(which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity.
It is made available under a CC-BY 4.0 International license .

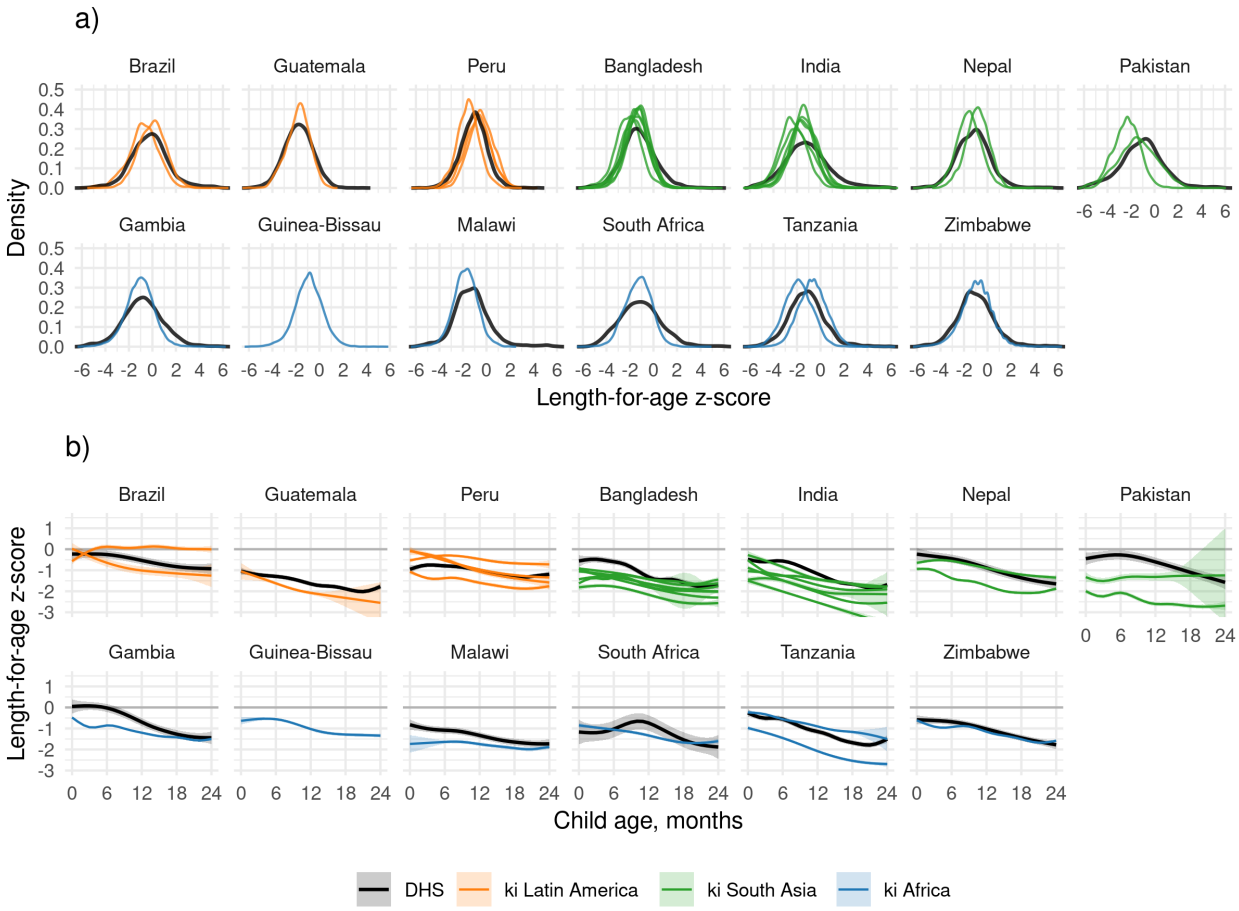


Figure 2 | Length-for-age Z-scores by age and region. (**a**) Kernel density distributions of LAZ in DHS in countries that overlap with *ki* cohorts (black lines) and in each *ki* cohort (colored lines). (**b**) Mean length-for-age z-scores (LAZ) by age for Demographic and Health Surveys (DHS) countries overlapping with *ki* cohorts (black lines) and pooled across *ki* longitudinal cohorts with at least quarterly measurement (colored lines) estimated with cubic splines. Shaded bands are approximate 95% simultaneous confidence intervals. The DHS survey was not conducted in Guinea-Bissau during the study period.

medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint
(which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity.
It is made available under a CC-BY 4.0 International license .

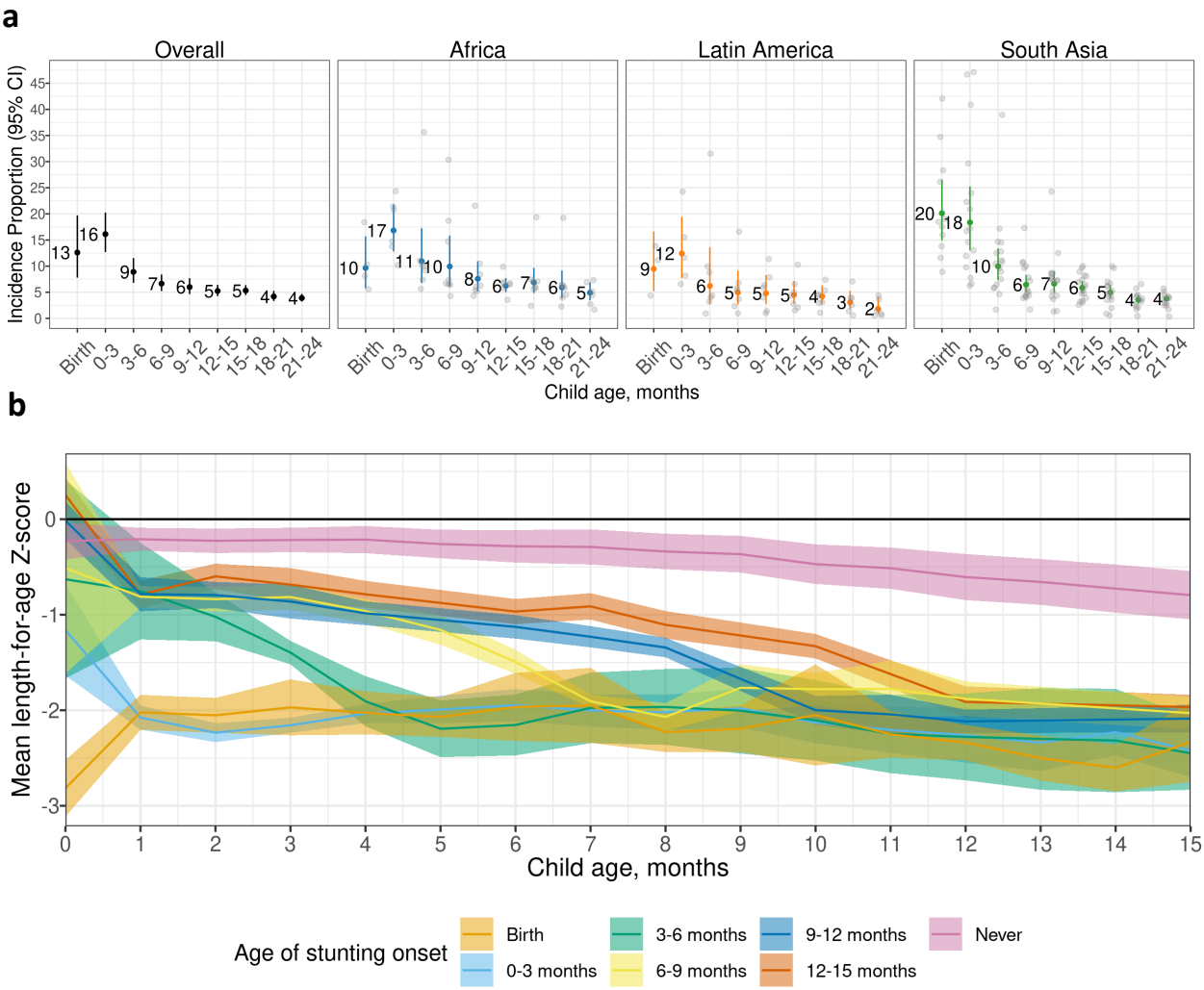


Figure 3 | Incidence of stunting and mean LAZ by age. (**a**) Proportion of children experiencing incident stunting onset overall (N=19-32 studies; N= 11,929-42,902 children) and stratified by region (Africa: N=4-8 studies, N = 5,529-15,837 children; Latin America: N=3-7 studies, N=413-1,528 children; South Asia 11-17studies, N=4,514-17,802 children). "0-3" includes age 2 days up to 3 months. Analyses include cohorts with at least quarterly measurements; vertical bars indicate 95% confidence intervals. Gray points indicate cohort-specific estimates. (**b**) Mean length-for-age Z-score (LAZ) stratified by age of incident stunting from birth to age 15 months (N=21 cohorts that measured children at least monthly between birth and age 15 months, N=11,243 children). "Never" includes children who did not become stunted by age 15 months. Shaded ribbons indicate 95% confidence intervals. Pooled results were derived from random effects models with restricted maximum likelihood estimation.

medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint
(which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity.
It is made available under a CC-BY 4.0 International license .

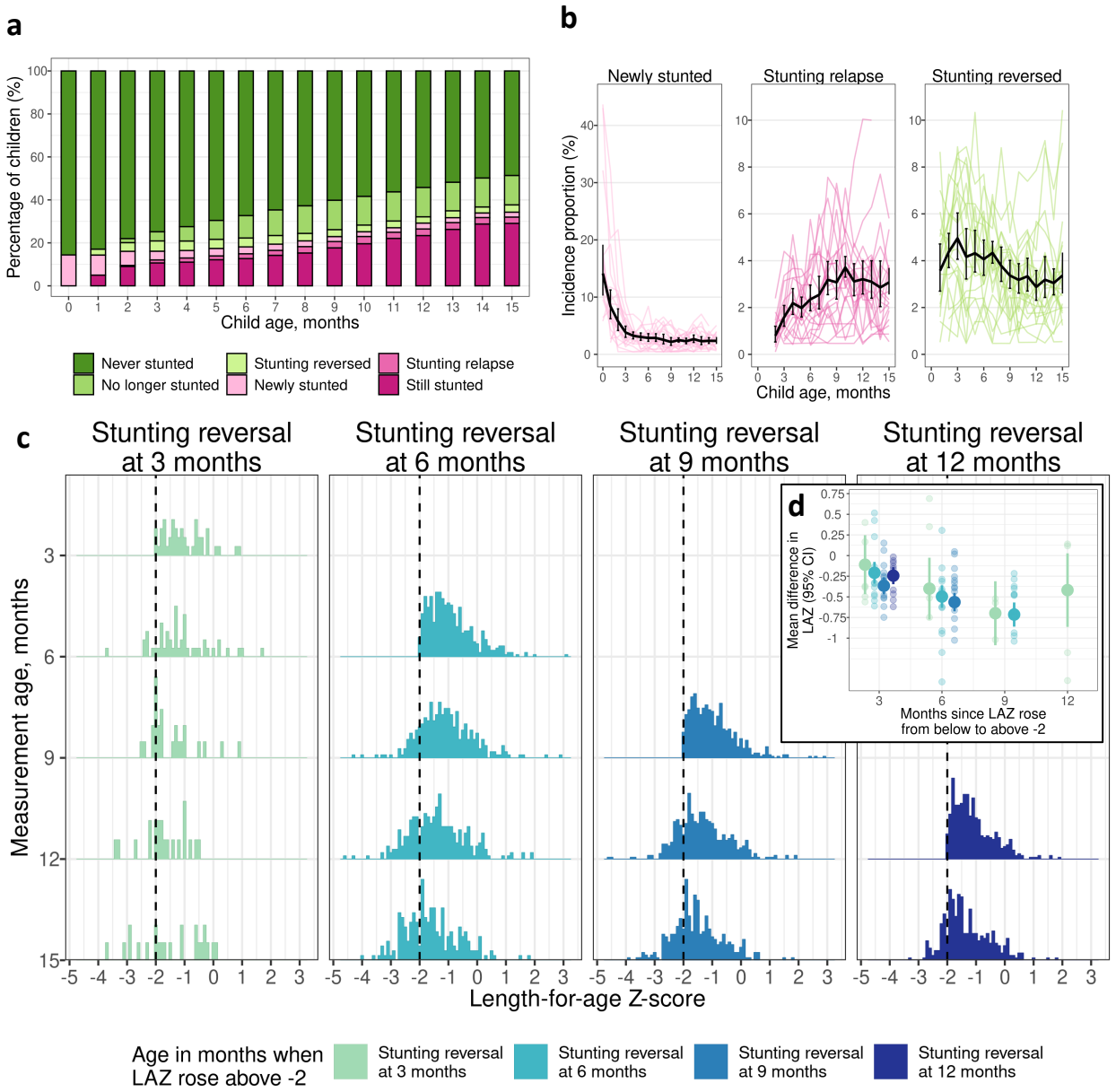


Figure 4| Stunting reversal and relapse. (**a**) Percentage of children with stunting reversal and relapse by age. (**b**) Incidence proportion of new stunting, stunting relapse, and stunting reversal by age. The black line presents estimates pooled using random effects with restricted maximum likelihood estimation. Colored lines indicate cohort-specific estimates. (**c**) Distribution of LAZ at subsequent measurements among children who experienced stunting reversal. (**d**) Mean difference in LAZ following stunting reversal at each subsequent age of measurement compared to the age of reversal. Panels a, c, d include data from 21 cohorts in 10 countries with at least monthly measurement (N =11,424). All panels contain data up to age 15 months because in most cohorts, measurements were less frequent above 15 months.

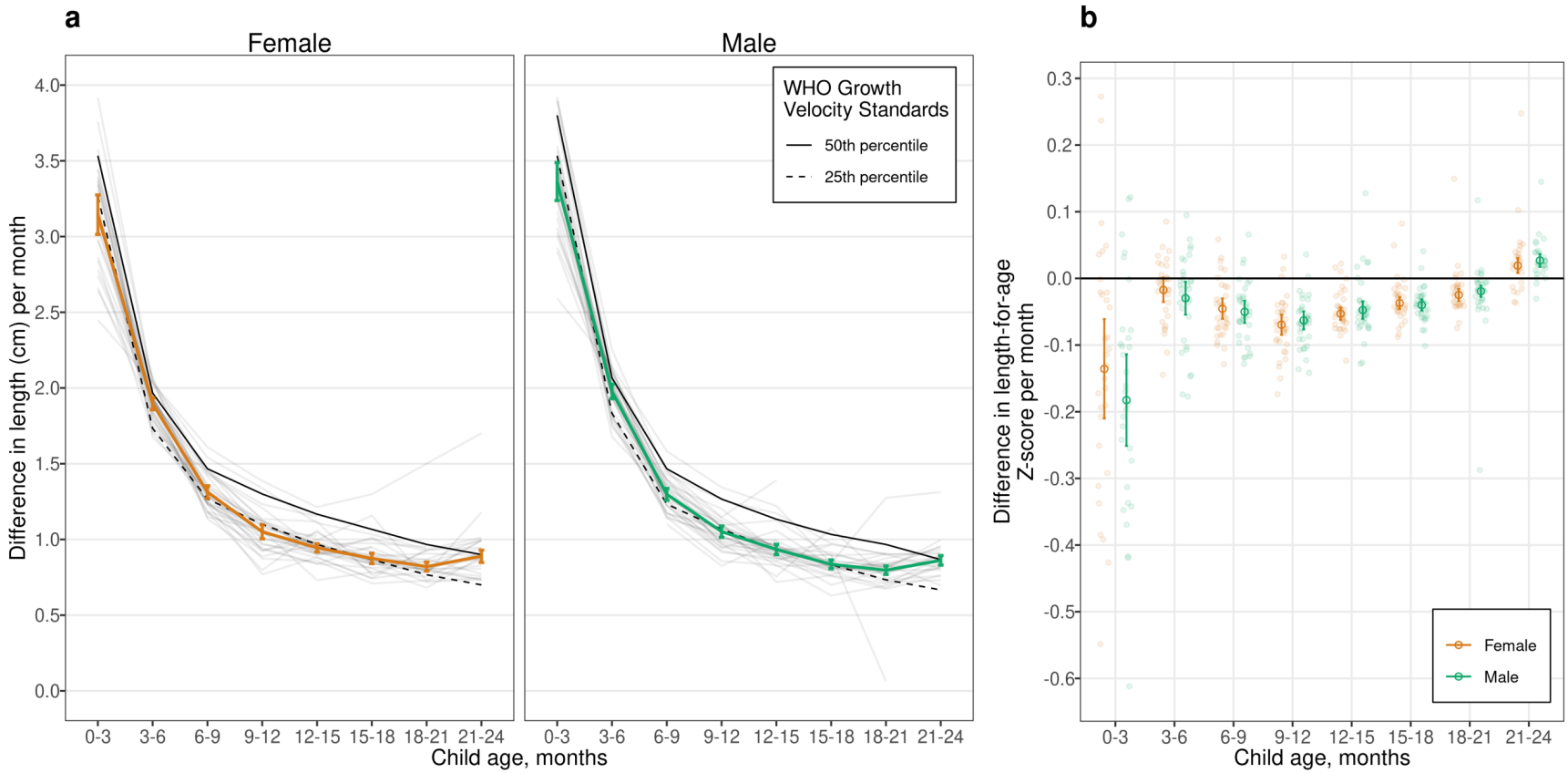
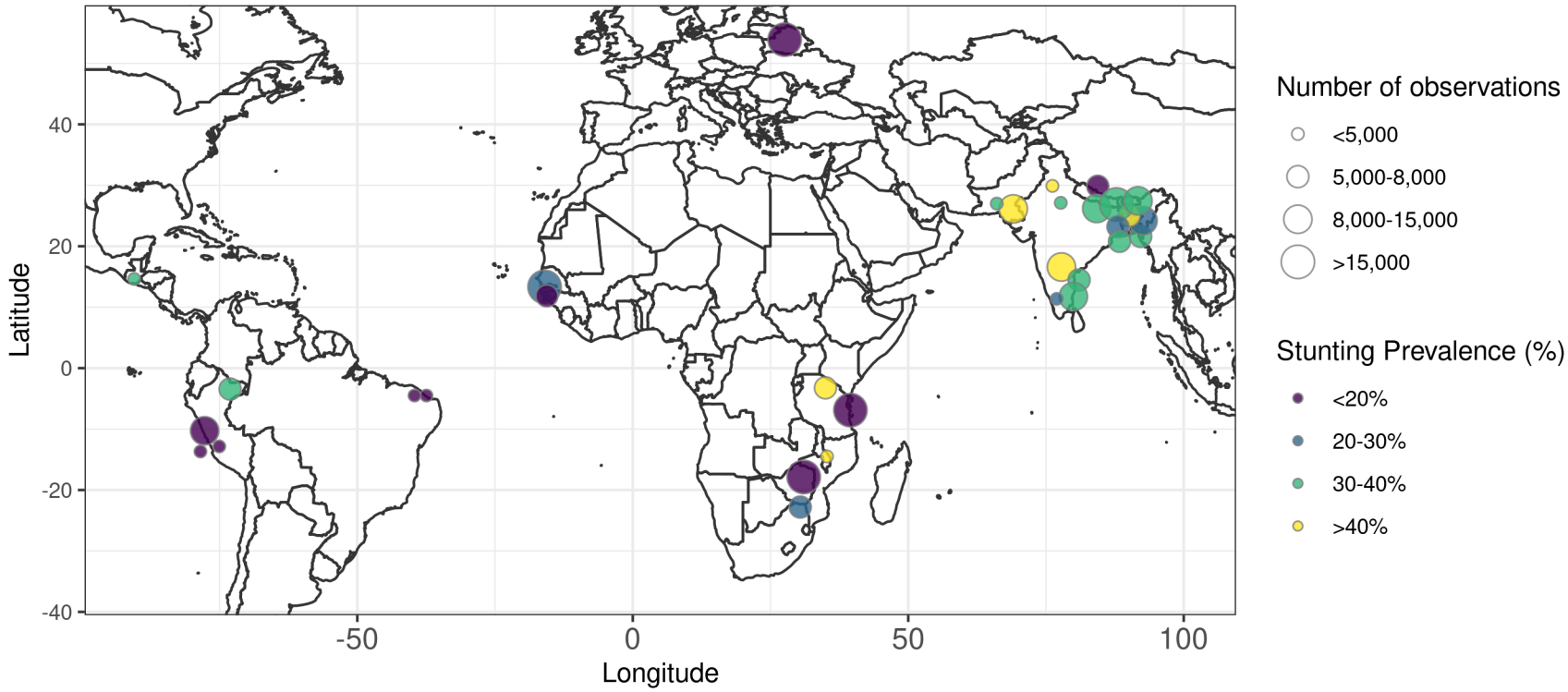


Figure 5| Linear growth velocity by age and sex. (**a**) Within-child difference in length in centimeters per month stratified by age among male (green line) and female (orange line) children; 25th percentile of the WHO Growth Velocity Standards (dashed black lines); and the 50th percentile (solid black line). Light gray lines indicate cohort-specific linear growth velocity curves. (**b**) Within-child difference in length-for-age Z-score per month by age and sex. Smaller partially transparent points indicate cohort-specific estimates. Both panels include 32 *ki* cohorts in 14 countries that measured children at least quarterly (n = 52,640 children) pooled using random effects models fit with restricted maximum likelihood estimation. Vertical bars indicate 95% confidence intervals.

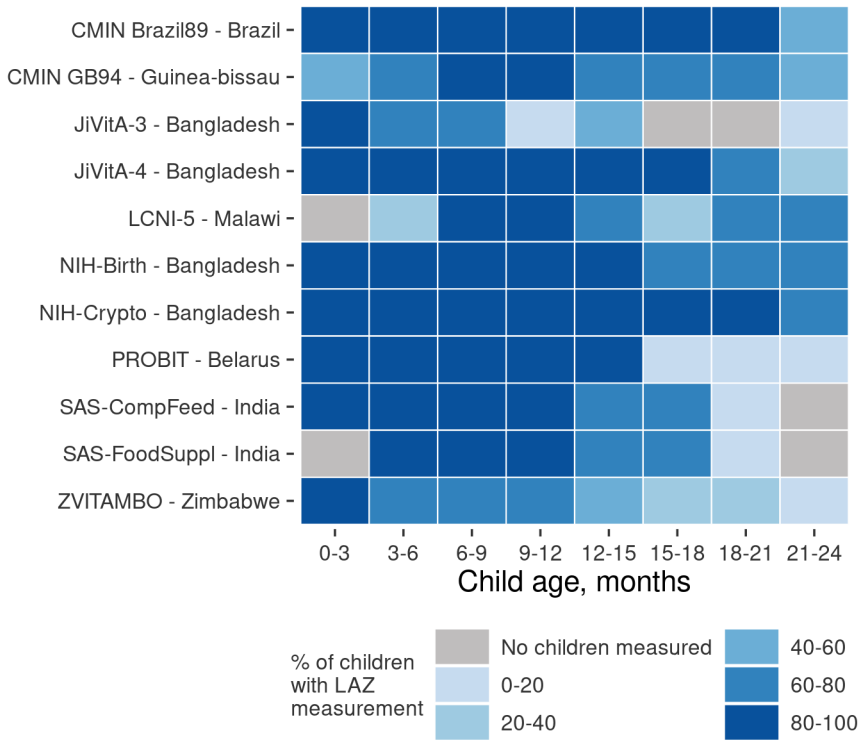
medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint
(which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity.
It is made available under a CC-BY 4.0 International license .

medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint
(which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity.
It is made available under a CC-BY 4.0 International license .

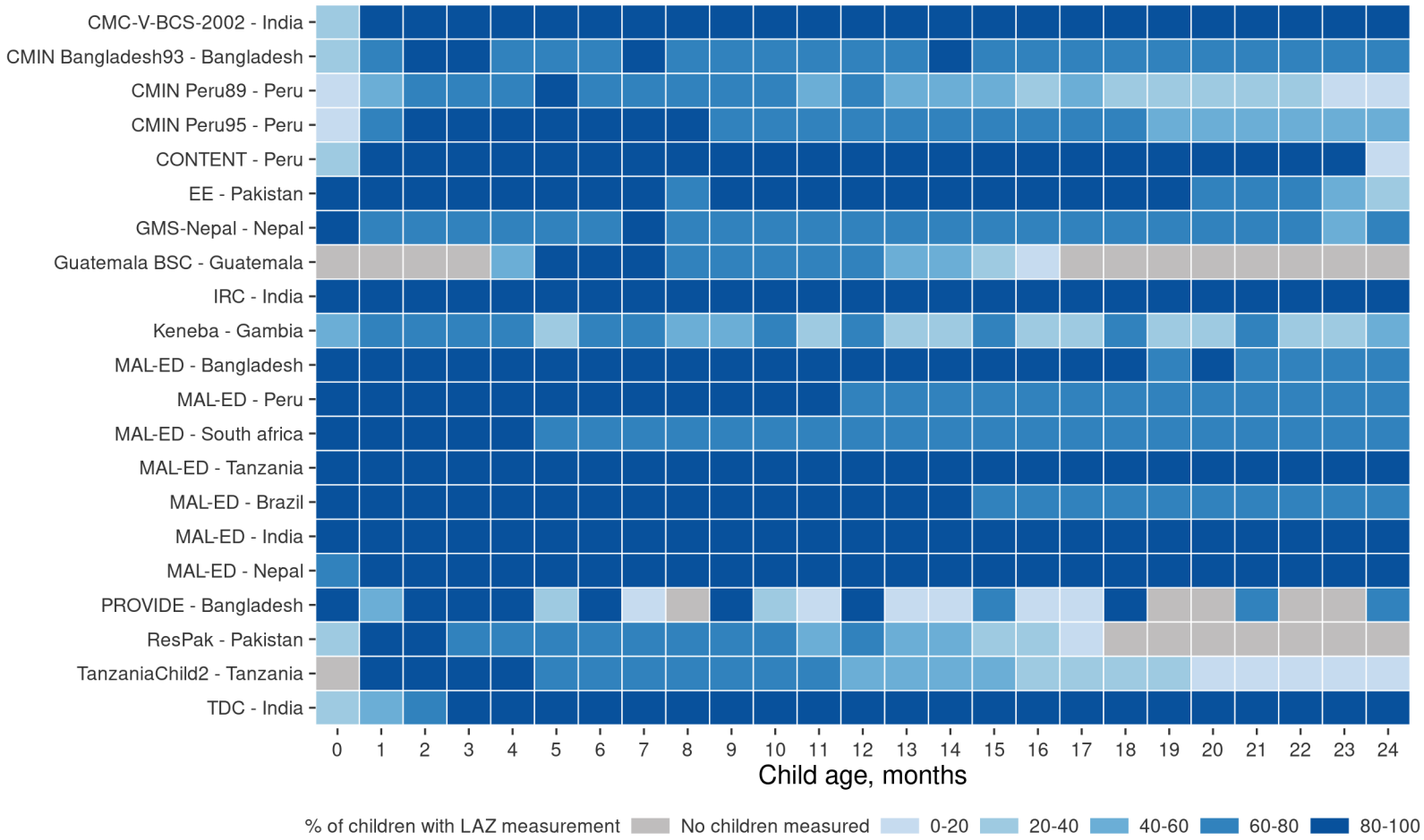
Extended Data Figure 1| *ki* cohort selection. Analyses focused on longitudinal cohorts to enable the estimation of prospective incidence rates and growth velocity. In April 2018, there were 86 longitudinal studies on GHAP. From this set, we applied five inclusion criteria to select cohorts for analysis. Our rationale for each criterion follows. (1) Studies were conducted in lower income or middle-income countries. (2) Studies had a median year of birth in 1990 or later. (3) Studies measured length and weight between birth and age 24 months. (4) Studies did not restrict enrollment to acutely ill children. (5) Studies collected anthropometry measurements at least every 3 months. Each colored cell indicates a criterion that was met. For studies that met all inclusion criteria, all cells in their row are colored. The bars at the top of the plot show the number of observations in each study that met each inclusion criterion by region.



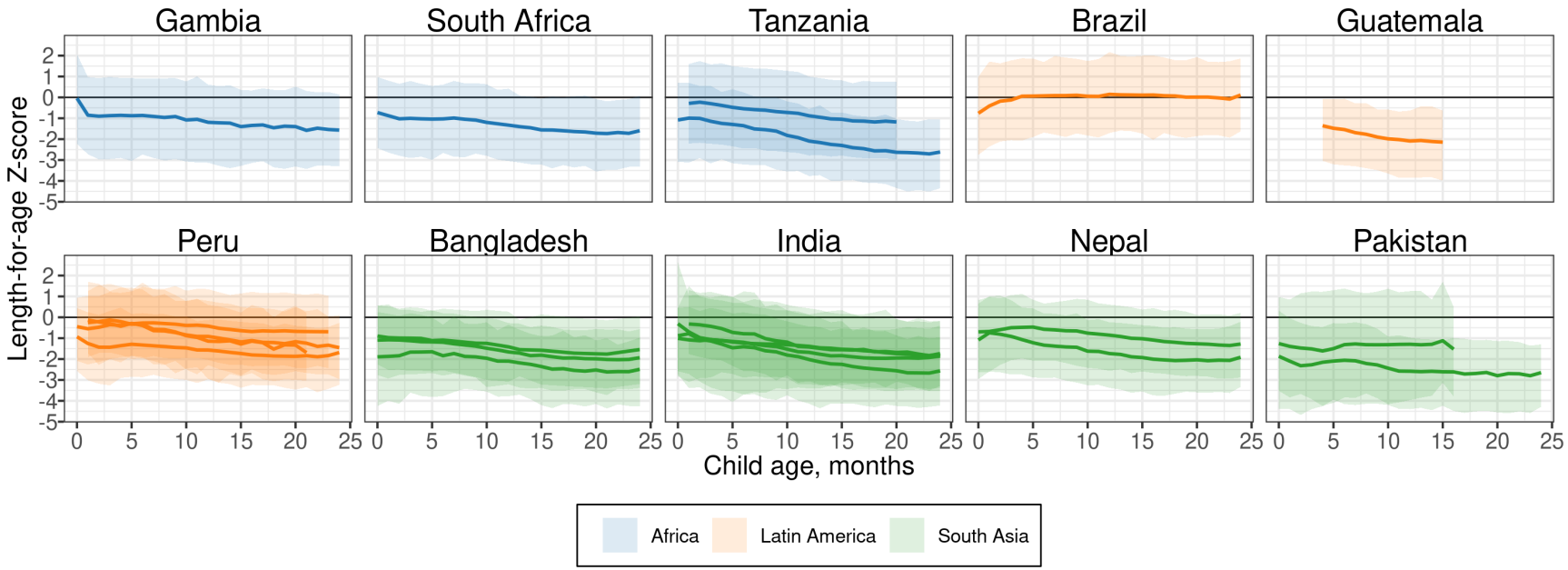
Extended Data Figure 2 | Stunting prevalence by geographic location of *ki* cohorts. Locations are approximate, represented as nation-level centroids and jittered slightly for display. The size of each centroid indicates the number of observations contributing to each estimate. The color of each centroid indicates the level of stunting prevalence.



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

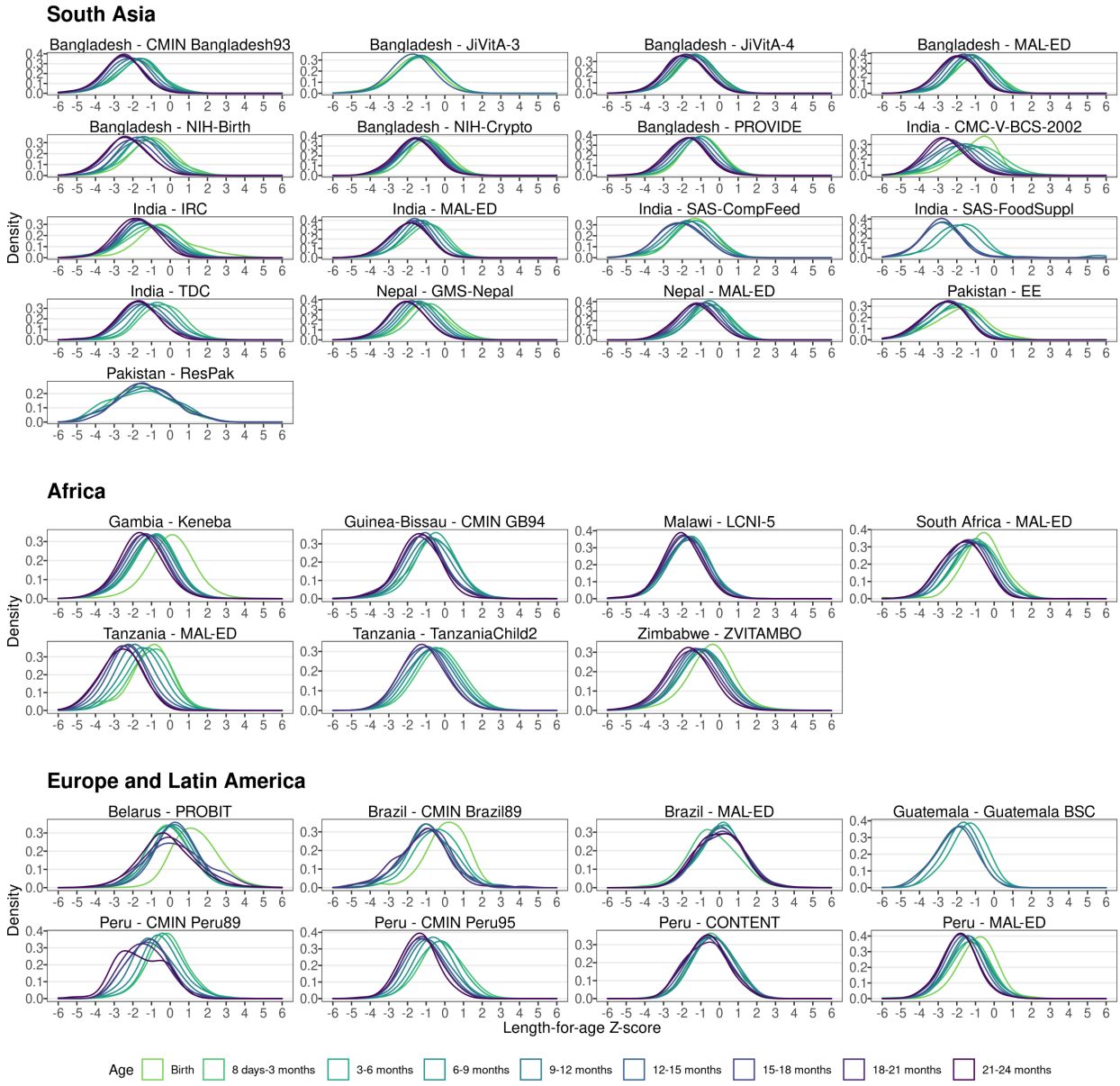


Extended Data Figure 4 | Percentage of enrolled children measured in each *ki* cohort with monthly measurements.



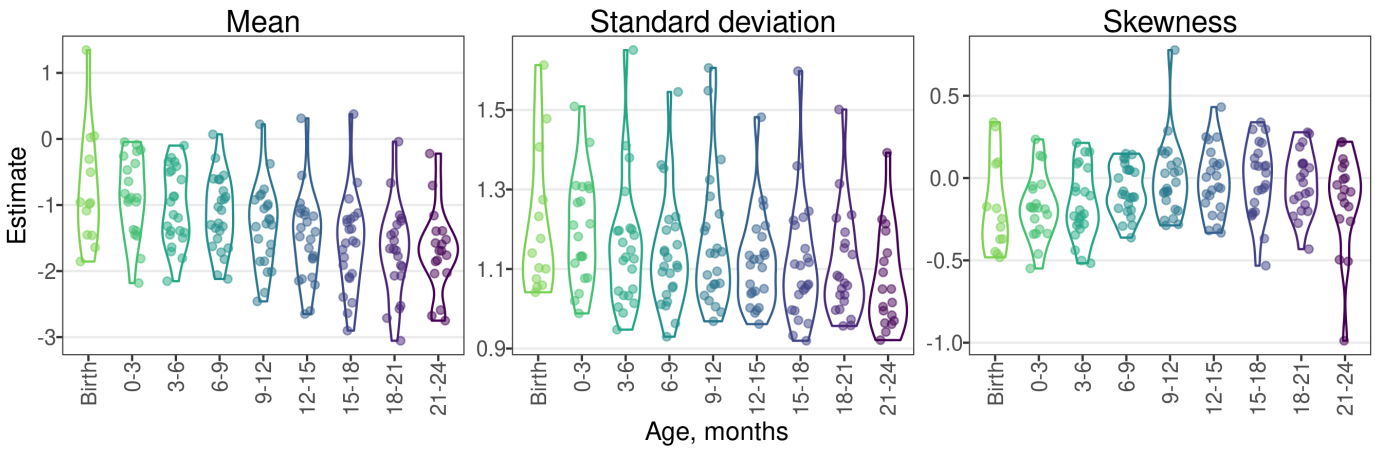
Extended Data Figure 5 | Mean, 5th and 95th percentile of length-for-age Z-score by age in *ki* longitudinal cohorts estimated with cubic splines in cohorts with at least monthly measurement. The shaded bands span the 5th to the 95th percentile of length-for-age Z-score in each cohort. The solid line indicates the mean in each cohort at each age (N=21 cohorts that measured children at least monthly, N=11,424 children).

medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint
(which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity.
It is made available under a CC-BY 4.0 International license .



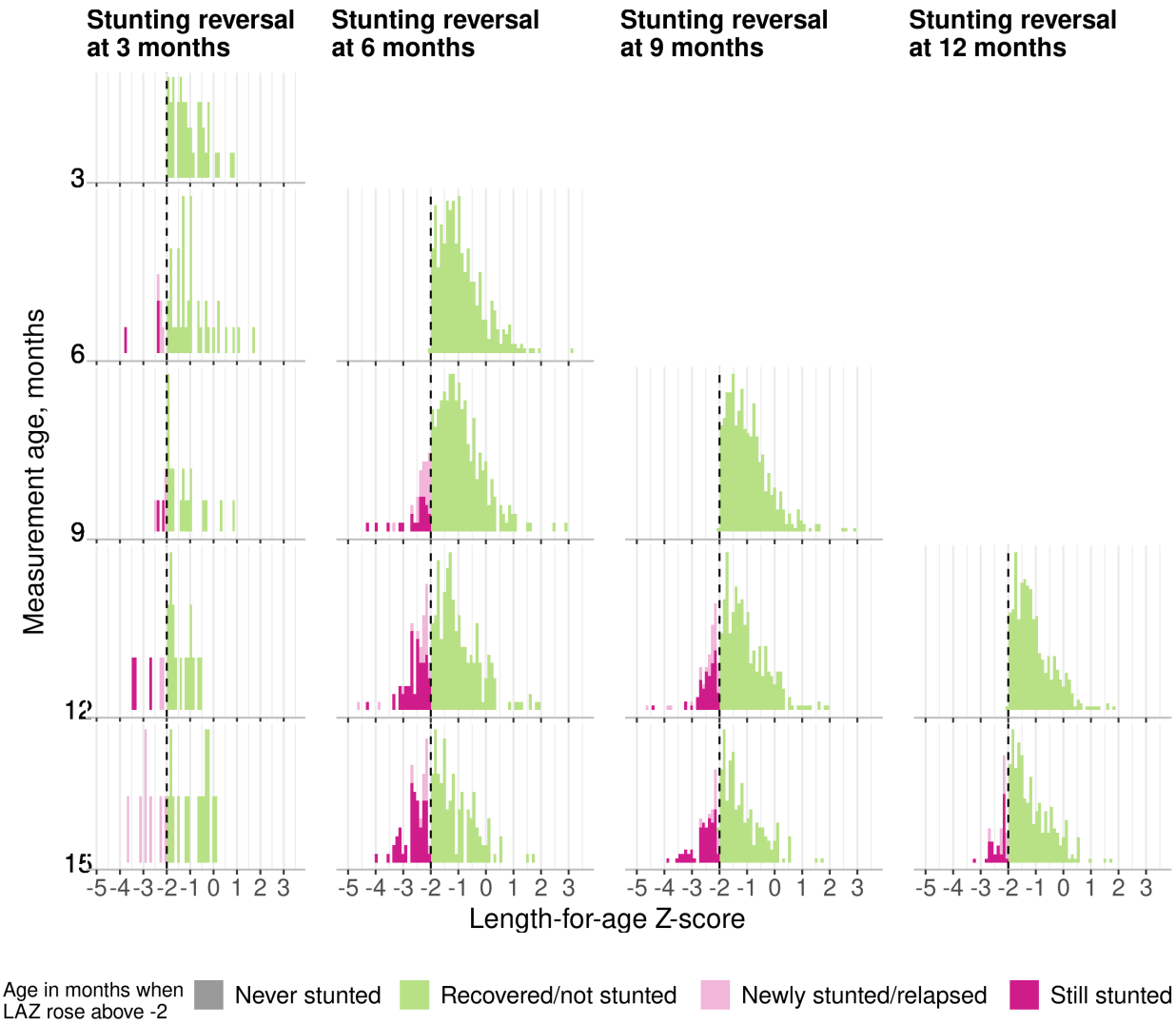
Extended Data Figure 6 | Kernel density of length-for-age Z-score by age and cohort. In South Asia, includes data from 17 cohorts, 21,223 children, and 159,884 measurements. In Africa, includes 7 cohorts, 21,671 children, and 164,431 measurements. In Europe and Latin America, includes 8 cohorts, 9,746 children, and 88,143 measurements.

medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint
(which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity.
It is made available under a CC-BY 4.0 International license .



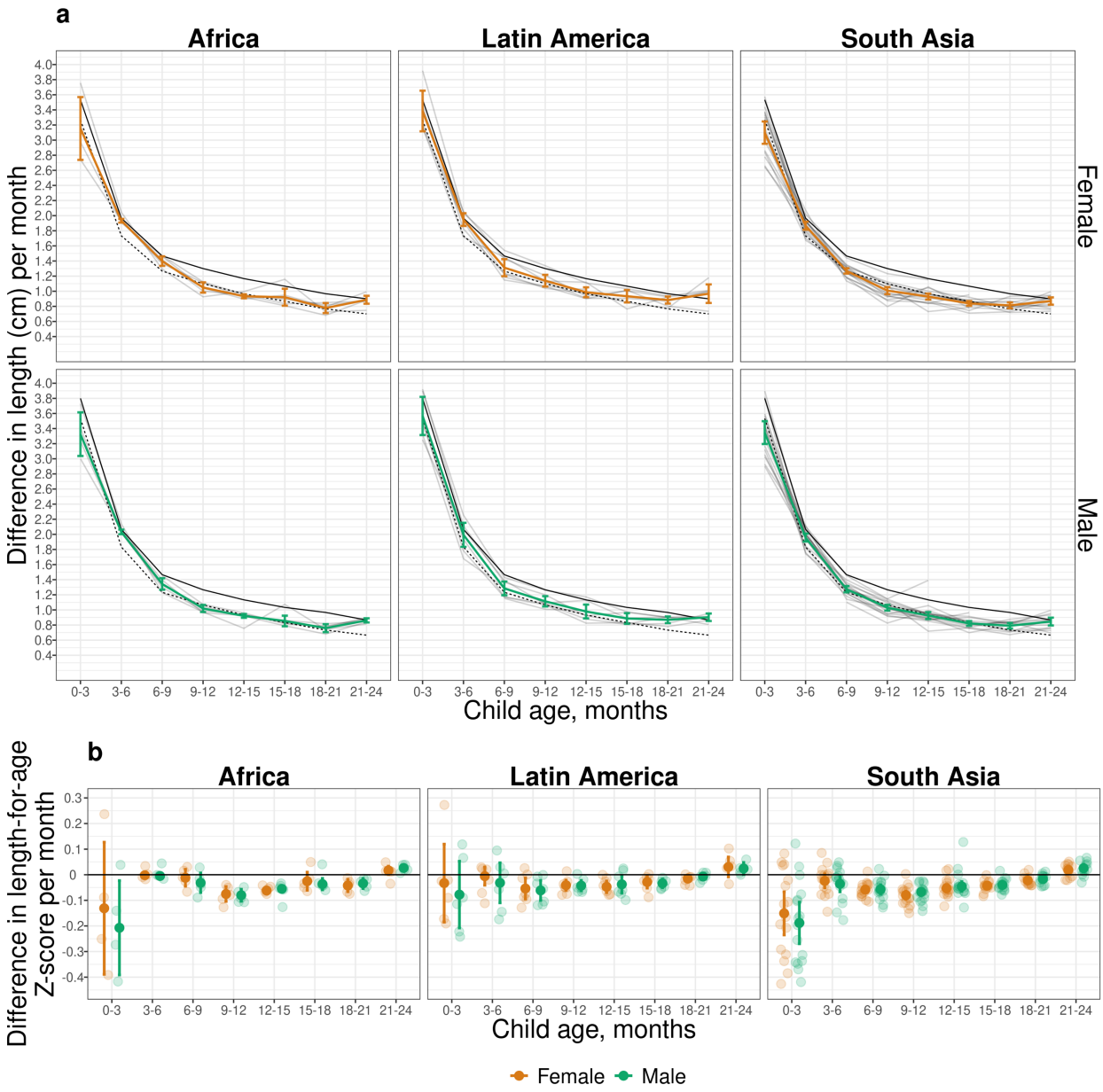
Extended Data Figure 7 | Parametric mean, standard deviation, and Pearson's index of skewness estimates by age and cohort. Estimates were obtained from linear models with skew-elliptical error terms fit using maximum likelihood estimation. Includes 412,458 measurements from 52,640 children in 32 cohorts.

medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint
(which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity.
It is made available under a CC-BY 4.0 International license .

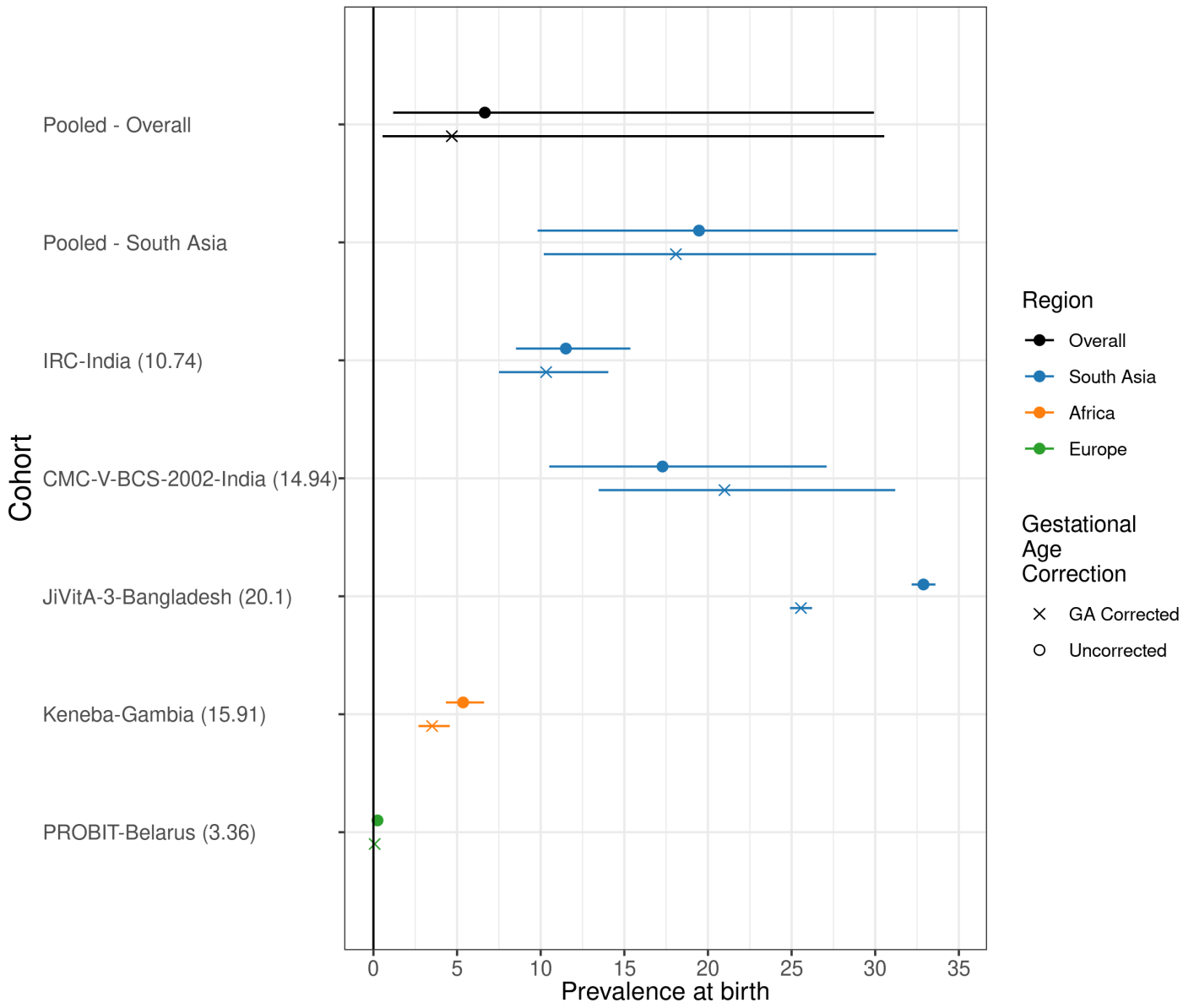


Extended Data Figure 8 | Distribution of LAZ at subsequent measurements after stunting reversal. Includes data from 21 cohorts in 10 countries with at least monthly measurement (N = 11,424 children). All panels contain data up to age 15 months because in most cohorts, measurements were less frequent above 15 months.

medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint
(which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity.
It is made available under a CC-BY 4.0 International license .



Extended Data Figure 9 | Linear growth velocity by age and sex stratified by region. a) Within-child difference in length in centimeters per month stratified by age, sex, and region. Dashed black line indicates 25th percentile of the WHO Growth Velocity Standards; solid black line indicates the 50th percentile. Colored lines indicate and vertical bars indicate 95% confidence intervals for *ki* cohorts. Light gray lines indicate cohort-specific linear growth velocity curves. (**b**) Within-child difference in length-for-age Z-score per month by age, sex, and region. Smaller partially transparent points indicate cohort-specific estimates. Results shown in all panels were derived from 32 *ki* cohorts in 14 countries that measured children at least quarterly (n = 52,640 children).


Pooled - Overall
Pooled - South Asia
IRC-India (10.74)
CMC-V-BCS-2002-India (14.94)
JiVitA-3-Bangladesh (20.1)
Keneba-Gambia (15.91)
PROBIT-Belarus (3.36)
Cohort
0
5
10
15
20
25
30
35
Prevalence at birth
Region
Overall
South Asia
Africa
Europe
Gestational Age Correction
GA Corrected
Uncorrected

Extended Data Figure 10 | Comparison of 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) for 37,218 measurements in 5 cohorts. The number in the parentheses following each cohort name indicates the prevalence of pre-term birth in each cohort. The corrections are using the Intergrowth standards and are implemented using the R *growthstandards* package (https://ki-tools.github.io/growthstandards/). Overall, the stunting 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. Gestational age was estimated based on mother's recall of the last menstrual period in the Jivita-3, IRC, and CMC-V-BCS-2002 cohorts, was based on the Dubowitz method (newborn exam) in the Keneba cohort, and was based on ultrasound measurements in the PROBIT trial.

Extended Data Table 1| Summary of *ki* cohorts

Region, Study ID	Country	Study Years	Design	Children Enrolled*	Anthropometry measurement ages (months)	Total measurements*	Primary References
South Asia							
Biomarkers for EE	Pakistan	2013-2015	Prospective cohort	379	Birth, 1, 2, ..., 18	8484	Iqbal et al 2018 Nature Scientific Reports[1]
Resp. Pathogens	Pakistan	2011 - 2014	Prospective cohort	284	Birth, 1, 2, ..., 17	3177	Ali et al 2016 Journal of Medical Virology[2]
Growth Monitoring Study	Nepal	2012 - Ongoing	Prospective cohort	698	Birth, 1, 2, …, 24	13465	Not yet published
MAL-ED	Nepal	2010 - 2014	Prospective cohort	240	Birth, 1, 2, …, 24	5703	Shrestha et al 2014 Clin Infect Dis[3]
CMC Birth Cohort, Vellore	India	2002 - 2006	Prospective cohort	373	Birth, 0.5, 1, 1.5, ..., 24	8709	Gladstone et al. 2011 NEJM[4]
MAL-ED	India	2010 - 2012	Prospective cohort	251	Birth, 1, 2, ..., 24	5702	John et al 2014 Clin Infect Dis[5]
Vellore Crypto Study	India	2008 - 2011	Prospective cohort	410	Birth, 1, 2, ..., 24	9771	Kattula et al. 2014 BMJ Open[6]
CMIN 93	Bangladesh	1993 - 1996	Prospective Cohort	277	Birth, 3, 6, ..., 24	5363	Pathela et al 2007 Acta Paediatrica[7]
TDC	India	2008-2011	Quasi-experimental	160	Birth, 1, 2, ..., 24	3593	Sarkar et al. 2013 BMC Public Health [8]
MAL-ED	Bangladesh	2010 - 2014	Prospective cohort	265	Birth, 1, 2, ..., 24	5604	Ahmed et al 2014 Clin Infect Dis[9]
PROVIDE RCT	Bangladesh	2011 - 2014	Individual RCT	700	Birth, 6, 10, 12, 14. 17, 18, 24, 39, 40, 52, 53 (weeks)	9207	Kirkpatrick et al 2015 Am J Trop Med Hyg[10]

Food Suppl RCT	India	1995 - 1996	Individual RCT	418	Baseline, 6, 9, 12	2232	Bhandari et al 2001 J Nutri[11]
Optimal Infant Feeding	India	1999 - 2001	Cluster RCT	472	Birth, 3, 6, ..., 18	2948	Bhandari et al 2004 J Nutri[12]
NIH Birth Cohort	Bangladesh	2008 - 2009	Prospective Cohort	629	Birth, 3, 6, ..., 12	6215	Korpe et al. 2016 PLOS NTD[13]
JiVitA-4 Trial	Bangladesh	2012 - 2014	Cluster RCT	1434	6, 9, 12, 14, 18	9344	Christian et al 2015 IJE[14]
JiVitA-3 Trial	Bangladesh	2008 - 2012	Cluster RCT	13475	Birth, 1, 3, 6, 12, 24	53453	West et al JAMA 2014[15]
NIH Cryptosporidium Study	Bangladesh	2014 - 2017	Prospective cohort	758	Birth, 3, 6, ..., 24	6914	Steiner et al 2018 Clin Infect Dis[16]
Africa							
MAL-ED	Tanzania	2009 - 2014	Prospective cohort	262	Birth, 1, 2, ..., 24	5713	Mduma et al 2014 Clin Infect Dis[17]
Tanzania Child 2	Tanzania	2007 - 2011	Individual RCT	2396	1, 2, ..., 20	29565	Locks et al Am J Clin Nutr 2016[18]
MAL-ED	South Africa	2009 - 2014	Prospective cohort	314	Birth, 1, 2, ..., 24	6163	Bessong et al 2014 Clin Infect Dis[19]
MRC Keneba	Gambia	1987 - 1997	Cohort	2915	Birth, 1, 2, ..., 24	40275	Schoenbuchner et al. 2019, AJCN[20]
ZVITAMBO Trial	Zimbabwe	1997 - 2001	Individual RCT	14074	Birth, 6 wks, 3, 6, 9, 12	71928	Malaba et al 2005 Am J Clin Nutr[21]
Lungwena Child Nutrition RCT	Malawi	2011 - 2014	Individual RCT	840	Birth, 1-6 wk, 6, 12 18	4336	Mangani et al. 2015, Mat Child Nutr[22]
iLiNS-Zinc Study	Burkina Faso	2010 - 2012	Cluster RCT	797	9, 12, 15, 18	1471	Hess et al 2015 Plos One[23]

CMIN GB94	Guinea Bissau	1994 - 1997	Prospective Cohort	870	Enrollment and every 3 months after	6451	Valentiner-Branth 2001 Am J Clin Nutr[24]
Latin America							
MAL-ED	Peru	2009 - 2014	Prospective cohort	303	Birth, 1, 2, ..., 24	6142	Yori et al 2014 Clin Infect Dis[25]
CONTENT	Peru	2007 - 2011	Prospective cohort	215	Birth, 1, 2, ..., 24	8339	Jaganath et al 2014 Helicobacter[26]
Bovine Serum RCT	Guatemala	1997 - 1998	Individual RCT	315	Baseline, 1, 2, ...,8	2545	Begin et al. 2008, EJCN[27]
MAL-ED	Brazil	2010 - 2014	Prospective cohort	233	Birth, 1, 2, ..., 24	4858	Lima et al 2014 Clin Infect Dis[28]
CMIN Brazil89	Brazil	1989-2000	Prospective Cohort	119	Birth, 1, 2, ..., 24	889	Moore et al. 2001 Int J Epidemiol.[29]
CMIN Peru95	Peru	1995 - 1998	Prospective Cohort	224	Birth, 1, 2, ..., 24	3979	Checkley et al. 2003 Am J Epidemiol.[30]
CMIN Peru89	Peru	1989 - 1991	Prospective Cohort	210	Birth, 1, 2, ..., 24	2742	Checkley et al. 1998 Am J Epidemiol.[31]
Europe							
PROBIT Study	Belarus	1996 - 1997	Cluster RCT	8127	1, 2, 3, 6, 9, 12	58649	Kramer et al 2001 JAMA[32]
*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.

	CMC-V-BCS-2002, India	CMIN Bangladesh 93	CMIN Brazil 89	CMIN Guinea-Bissau 94	CMIN Peru 89	CMIN Peru 95	CONTENT, Peru	EE, Pakistan	GMS-Nepal	Guatemala BSC
	(N=373)	(N=280)	(N=119)	(N=885)	(N=210)	(N=224)	(N=215)	(N=380)	(N=698)	(N=315)
Sex										
Female	187 (50.1%)	122 (43.6%)	62 (52.1%)	443 (50.1%)	100 (47.6%)	96 (42.9%)	109 (50.7%)	185 (48.7%)	328 (47.0%)	162 (51.4%)
Male	186 (49.9%)	158 (56.4%)	57 (47.9%)	442 (49.9%)	110 (52.4%)	128 (57.1%)	106 (49.3%)	195 (51.3%)	370 (53.0%)	153 (48.6%)
Birthweight										
Mean (SD)	2910 (434)	2560 (967)	3270 (477)	3330 (541)	3550 (492)	3690 (367)	3070 (323)	2640 (506)	2660 (423)	
Maternal age										
Mean (SD)	24.1 (4.11)							30.0 (3.99)	24.0 (5.09)	25.2 (6.21)
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)
Number of rooms										
4+	14 (3.75%)						78 (36.3%)		323 (46.3%)	
1	202 (54.2%)						44 (20.5%)		49 (7.02%)	
2	106 (28.4%)						54 (25.1%)		145 (20.8%)	
3	51 (13.7%)						39 (18.1%)		181 (25.9%)	
Number of children <5yrs										
1										
2+										
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%)	

	IRC, India	JiVitA-3, Bangladesh	JiVitA-4, Bangladesh	Keneba, Gambia	LCNI-5, Malawi	MAL-ED, Bangladesh	MAL-ED, Brazil	MAL-ED, India	MAL-ED, Nepal	MAL-ED, Peru	MAL-ED, South Africa
	(N=410)	(N=28300)	(N=5449)	(N=2954)	(N=840)	(N=265)	(N=233)	(N=251)	(N=240)	(N=303)	(N=314)
Sex											
Female	185 (45.1%)	13785 (48.7%)	2728 (50.1%)	1426 (48.3%)	421 (50.1%)	136 (51.3%)	113 (48.5%)	138 (55.0%)	110 (45.8%)	143 (47.2%)	159 (50.6%)
Male	225 (54.9%)	14515 (51.3%)	2721 (49.9%)	1528 (51.7%)	419 (49.9%)	129 (48.7%)	120 (51.5%)	113 (45.0%)	130 (54.2%)	160 (52.8%)	155 (49.4%)
Birthweight											
Mean (SD)	2890 (448)	2550 (428)	2990 (823)	2970 (421)		2800 (412)	3340 (483)	2890 (442)	2980 (390)	3130 (430)	3130 (464)
Maternal age											
Mean (SD)	23.7 (3.68)	21.4 (5.27)		27.4 (7.16)	26.8 (7.87)	24.8 (4.99)	24.8 (5.53)	23.9 (4.10)	26.4 (3.76)	24.2 (6.06)	26.4 (6.86)
Maternal weight											
Mean (SD)		43.7 (6.13)			50.9 (6.66)	49.6 (8.54)	61.9 (11.8)	50.4 (9.37)	56.3 (8.27)	55.5 (8.95)	67.5 (14.9)
Maternal education (years)											
Mean (SD)	5.06 (4.61)	5.06 (3.82)	7.51 (4.82)		3.54 (3.34)	5.63 (2.58)	9.18 (2.81)	7.88 (3.17)	8.77 (3.44)	7.81 (2.79)	10.3 (1.94)
Number of rooms											
4+	17 (4.17%)	1181 (4.18%)	286 (5.26%)			12 (4.96%)	127 (60.5%)	25 (10.6%)	131 (55.5%)	139 (51.1%)	196 (76.3%)
1	185 (45.3%)	16754 (59.3%)	3196 (58.8%)			152 (62.8%)	4 (1.90%)	84 (35.7%)	52 (22.0%)	19 (6.99%)	14 (5.45%)
2	170 (41.7%)	7605 (26.9%)	1389 (25.6%)			50 (20.7%)	20 (9.52%)	78 (33.2%)	31 (13.1%)	52 (19.1%)	22 (8.56%)
3	36 (8.82%)	2723 (9.63%)	562 (10.3%)			28 (11.6%)	59 (28.1%)	48 (20.4%)	22 (9.32%)	62 (22.8%)	25 (9.73%)
Number of children <5yrs											
1	89 (21.7%)	18200 (64.4%)			391 (48.2%)						
2+	321 (78.3%)	10066 (35.6%)			421 (51.8%)						
Improved sanitation											
1		19609 (69.4%)	4191 (77.1%)		3 (0.369%)	204 (84.3%)	206 (98.1%)	108 (46.4%)	235 (99.6%)	65 (24.7%)	4 (1.60%)
0		8655 (30.6%)	1242 (22.9%)		810 (99.6%)	38 (15.7%)	4 (1.90%)	125 (53.6%)	1 (0.424%)	198 (75.3%)	246 (98.4%)
Food security level											
Food Secure		8711 (50.0%)	2751 (50.9%)			161 (83.0%)	3 (2.33%)	190 (89.6%)	94 (73.4%)	27 (23.9%)	132 (56.7%)
Mildly Food Insecure		5793 (33.3%)	1951 (36.1%)			4 (2.06%)	11 (8.53%)	5 (2.36%)	15 (11.7%)	29 (25.7%)	19 (8.15%)
Food Insecure		2910 (16.7%)	703 (13.0%)			29 (14.9%)	115 (89.1%)	17 (8.02%)	19 (14.8%)	57 (50.4%)	82 (35.2%)

	MAL-ED, Tanzania	NIH-Birth, Bangladesh	NIH-Crypto, Bangladesh	PROBIT, Belarus	PROVIDE, Bangladesh	ResPak, Pakistan	SAS-CompFeed, India	SAS-FoodSuppl, India	Tanzania Child 2	TDC, India	ZVITAMBO, Zimbabwe
	(N=262)	(N=629)	(N=758)	(N=17046)	(N=700)	(N=284)	(N=1535)	(N=418)	(N=2400)	(N=160)	(N=14104)
Sex											
Female	133 (50.8%)	297 (47.2%)	381 (50.3%)	8217 (48.2%)	332 (47.4%)	136 (47.9%)	702 (45.7%)	223 (53.3%)	1184 (49.3%)	75 (46.9%)	6847 (48.5%)
Male	129 (49.2%)	332 (52.8%)	377 (49.7%)	8829 (51.8%)	368 (52.6%)	148 (52.1%)	833 (54.3%)	195 (46.7%)	1216 (50.7%)	85 (53.1%)	7257 (51.5%)
Birthweight											
Mean (SD)	3180 (452)	2710 (414)	2800 (410)	3440 (419)	2780 (371)	2930 (525)	2750 (516)		3230 (474)	2910 (450)	2970 (456)
Maternal age											
Mean (SD)	28.4 (6.67)	25.0 (5.32)	24.3 (4.68)	24.9 (4.92)	24.7 (4.65)		23.6 (4.08)	25.0 (4.63)	26.4 (5.04)		24.5 (5.30)
Maternal weight											
Mean (SD)	55.7 (9.11)	48.0 (8.51)	52.1 (9.17)	66.2 (12.5)	49.3 (9.41)		47.6 (7.05)		62.2 (11.7)		60.0 (11.1)
Maternal education (years)											
Mean (SD)	6.17 (1.79)	3.76 (3.45)	5.77 (3.63)	13.0 (1.40)	4.33 (3.62)		4.42 (4.52)	1.25 (2.70)	7.90 (2.27)		9.66 (1.95)
Number of rooms											
4+	108 (43.2%)		95 (12.5%)		23 (3.29%)					5 (3.13%)	
1	13 (5.20%)		368 (48.5%)		507 (72.4%)					91 (56.9%)	
2	63 (25.2%)		191 (25.2%)		108 (15.4%)					49 (30.6%)	
3	66 (26.4%)		104 (13.7%)		62 (8.86%)					15 (9.38%)	
Number of children <5yrs											
1			541 (71.4%)		512 (73.1%)				1640 (68.6%)		
2+			217 (28.6%)		188 (26.9%)				749 (31.4%)		
Improved sanitation											
1		242 (38.5%)	655 (87.7%)		58 (96.7%)						
0		387 (61.5%)	92 (12.3%)		2 (3.33%)						
Food security level											
Food Secure		95 (15.1%)	453 (59.8%)								
Mildly Food Insecure		492 (78.2%)	219 (28.9%)								
Food Insecure		42 (6.68%)	86 (11.3%)								

medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint
(which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity.
It is made available under a CC-BY 4.0 International license .

Extended Data Table 3| Countries and survey years included in the analysis of Demographic and Health Survey data

Africa	
Gambia	2013
Malawi	2015-2016
Tanzania	2015-2016
South Africa	2016
Zimbabwe	2015
South Asia	
Bangladesh	2014
India	2015-2016
Nepal	2016
Pakistan	2017-2018
Latin America	
Brazil	1996
Guatemala	2014-2015
Peru	2012

References

1. Iqbal, N. T. *et al.* Promising Biomarkers of Environmental Enteric Dysfunction: A Prospective Cohort study in Pakistani Children. *Sci. Rep.* **8**, 2966 (2018).
2. Ali, A. *et al.* Respiratory viruses associated with severe pneumonia in children under 2 years old in a rural community in Pakistan. *J. Med. Virol.* **88**, 1882–1890 (2016).
3. Shrestha, P. S. *et al.* Bhaktapur, Nepal: The MAL-ED Birth Cohort Study in Nepal. *Clin. Infect. Dis.* **59**, S300–S303 (2014).
4. Gladstone, B. P. *et al.* Protective Effect of Natural Rotavirus Infection in an Indian Birth Cohort. *N. Engl. J. Med.* **365**, 337–346 (2011).
5. John, S. M. *et al.* Establishment of the MAL-ED Birth Cohort Study Site in Vellore, Southern India. *Clin. Infect. Dis.* **59**, S295–S299 (2014).

medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint
(which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity.
It is made available under a CC-BY 4.0 International license .

6. Kattula, D. *et al.* The first 1000 days of life: prenatal and postnatal risk factors for morbidity and growth in a birth cohort in southern India. *BMJ Open* **4**, e005404 (2014).

7. Pathela, P. *et al.* Diarrheal illness in a cohort of children 0-2 years of age in rural Bangladesh: I. Incidence and risk factors: Risk factors for diarrhea in Bangladeshi children. *Acta Paediatr.* **95**, 430–437 (2007).

8. Sarkar, R. *et al.* Burden of childhood diseases and malnutrition in a semi-urban slum in southern India. *BMC Public Health* **13**, 87 (2013).

9. Ahmed, T. *et al.* The MAL-ED Cohort Study in Mirpur, Bangladesh. *Clin. Infect. Dis.* **59**, S280–S286 (2014).

10. Kirkpatrick, B. D. *et al.* The "Performance of Rotavirus and Oral Polio Vaccines in Developing Countries" (PROVIDE) Study: Description of Methods of an Interventional Study Designed to Explore Complex Biologic Problems. *Am. J. Trop. Med. Hyg.* **92**, 744–751 (2015).

11. Bhandari, N. *et al.* Food Supplementation with Encouragement to Feed It to Infants from 4 to 12 Months of Age Has a Small Impact on Weight Gain. *J. Nutr.* **131**, 1946–1951 (2001).

12. Bhandari, N. *et al.* An Educational Intervention to Promote Appropriate Complementary Feeding Practices and Physical Growth in Infants and Young Children in Rural Haryana, India. *J. Nutr.* **134**, 2342–2348 (2004).

13. Korpe, P. S. *et al.* Natural History of Cryptosporidiosis in a Longitudinal Study of Slum-Dwelling Bangladeshi Children: Association with Severe Malnutrition. *PLoS Negl. Trop. Dis.* **10**, (2016).

14. Christian, P. *et al.* Effect of fortified complementary food supplementation on child growth in rural Bangladesh: a cluster-randomized trial. *Int. J. Epidemiol.* **44**, 1862–1876 (2015).

15. West, K. P. *et al.* Effect of Maternal Multiple Micronutrient vs Iron–Folic Acid Supplementation on Infant Mortality and Adverse Birth Outcomes in Rural Bangladesh: The JiVitA-3 Randomized Trial. *JAMA* **312**, 2649–2658 (2014).

medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint
(which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity.
It is made available under a CC-BY 4.0 International license .

16. Steiner, K. L. *et al.* Species of Cryptosporidia Causing Subclinical Infection Associated With Growth Faltering in Rural and Urban Bangladesh: A Birth Cohort Study. *Clin. Infect. Dis. Off. Publ. Infect. Dis. Soc. Am.* **67**, 1347–1355 (2018).

17. Mduma, E. R. *et al.* The Etiology, Risk Factors, and Interactions of Enteric Infections and Malnutrition and the Consequences for Child Health and Development Study (MAL-ED): Description of the Tanzanian Site. *Clin. Infect. Dis.* **59**, S325–S330 (2014).

18. Locks, L. M. *et al.* Effect of zinc and multivitamin supplementation on the growth of Tanzanian children aged 6–84 wk: a randomized, placebo-controlled, double-blind trial12. *Am. J. Clin. Nutr.* **103**, 910–918 (2016).

19. Bessong, P. O., Nyathi, E., Mahopo, T. C. & Netshandama, V. Development of the Dzimauli Community in Vhembe District, Limpopo Province of South Africa, for the MAL-ED Cohort Study. *Clin. Infect. Dis.* **59**, S317–S324 (2014).

20. Schoenbuchner, S. M. *et al.* The relationship between wasting and stunting: a retrospective cohort analysis of longitudinal data in Gambian children from 1976 to 2016. *Am. J. Clin. Nutr.* doi:10.1093/ajcn/nqy326.

21. Malaba, L. C. *et al.* Effect of postpartum maternal or neonatal vitamin A supplementation on infant mortality among infants born to HIV-negative mothers in Zimbabwe. *Am. J. Clin. Nutr.* **81**, 454–460 (2005).

22. Mangani, C. *et al.* Effect of complementary feeding with lipid-based nutrient supplements and corn–soy blend on the incidence of stunting and linear growth among 6- to 18-month-old infants and children in rural Malawi. *Matern. Child. Nutr.* **11**, 132–143 (2015).

23. Hess, S. Y. *et al.* Small-Quantity Lipid-Based Nutrient Supplements, Regardless of Their Zinc Content, Increase Growth and Reduce the Prevalence of Stunting and Wasting in Young Burkinabe Children: A Cluster-Randomized Trial. *PLOS ONE* **10**, e0122242 (2015).

medRxiv preprint doi: https://doi.org/10.1101/2020.06.09.20127001; this version posted October 21, 2021. The copyright holder for this preprint
(which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity.
It is made available under a CC-BY 4.0 International license .

24. Valentiner-Branth, P. *et al.* Community-based controlled trial of dietary management of children with persistent diarrhea: sustained beneficial effect on ponderal and linear growth. *Am. J. Clin. Nutr.* **73**, 968–974 (2001).

25. Yori, P. P. *et al.* Santa Clara de Nanay: The MAL-ED Cohort in Peru. *Clin. Infect. Dis.* **59**, S310–S316 (2014).

26. Jaganath, D. *et al.* First Detected Helicobacter pylori Infection in Infancy Modifies the Association Between Diarrheal Disease and Childhood Growth in Peru. *Helicobacter* **19**, 272–279 (2014).

27. Bégin, F., Santizo, M.-C., Peerson, J. M., Torún, B. & Brown, K. H. Effects of bovine serum concentrate, with or without supplemental micronutrients, on the growth, morbidity, and micronutrient status of young children in a low-income, peri-urban Guatemalan community. *Eur. J. Clin. Nutr.* **62**, 39–50 (2008).

28. Lima, A. A. M. *et al.* Geography, Population, Demography, Socioeconomic, Anthropometry, and Environmental Status in the MAL-ED Cohort and Case-Control Study Sites in Fortaleza, Ceará, Brazil. *Clin. Infect. Dis.* **59**, S287–S294 (2014).

29. Moore, S. R. *et al.* Early childhood diarrhoea and helminthiases associate with long-term linear growth faltering. *Int. J. Epidemiol.* **30**, 1457–1464 (2001).

30. Checkley, W., Epstein, L. D., Gilman, R. H., Cabrera, L. & Black, R. E. Effects of acute diarrhea on linear growth in Peruvian children. *Am. J. Epidemiol.* **157**, 166–175 (2003).

31. Checkley, W. *et al.* Effects of Cryptosporidium parvum infection in Peruvian children: growth faltering and subsequent catch-up growth. *Am. J. Epidemiol.* **148**, 497–506 (1998).

32. Kramer, M. S. *et al.* Promotion of Breastfeeding Intervention Trial (PROBIT): A Randomized Trial in the Republic of Belarus. *JAMA* **285**, 413–420 (2001).