

Short Maternal Stature Increases Risk of Small-for-Gestational-Age and Preterm Births in Low- and Middle-Income Countries: Individual Participant Data Meta-Analysis and Population Attributable Fraction^{1–3}

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Abstract

Background: Small-for-gestational-age (SGA) and preterm births are associated with adverse health consequences, including neonatal and infant mortality, childhood undernutrition, and adulthood chronic disease.

Objectives: The specific aims of this study were to estimate the association between short maternal stature and outcomes of SGA alone, preterm birth alone, or both, and to calculate the population attributable fraction of SGA and preterm birth associated with short maternal stature.

Methods: We conducted an individual participant data meta-analysis with the use of data sets from 12 population-based cohort studies and the WHO Global Survey on Maternal and Perinatal Health (13 of 24 available data sets used) from low- and middle-income countries (LMIC). We included those with weight taken within 72 h of birth, gestational age, and maternal height data ($n = 177,000$). For each of these studies, we individually calculated RRs between height exposure categories of <145 cm, 145 to <150 cm, and 150 to <155 cm (reference: ≥ 155 cm) and outcomes of SGA, preterm birth, and their combination categories. SGA was defined with the use of both the International Fetal and Newborn Growth Consortium for the 21st Century (INTERGROWTH-21st) birth weight standard and the 1991 US birth weight reference. The associations were then meta-analyzed.

Results: All short stature categories were statistically significantly associated with term SGA, preterm appropriate-for-gestational-age (AGA), and preterm SGA births (reference: term AGA). When using the INTERGROWTH-21st standard to define SGA, women <145 cm had the highest adjusted risk ratios (aRRs) (term SGA—aRR: 2.03; 95% CI: 1.76, 2.35;

preterm AGA—aRR: 1.45; 95% CI: 1.26, 1.66; preterm SGA—aRR: 2.13; 95% CI: 1.42, 3.21). Similar associations were seen for SGA defined by the US reference. Annually, 5.5 million term SGA (18.6% of the global total), 550,800 preterm AGA (5.0% of the global total), and 458,000 preterm SGA (16.5% of the global total) births may be associated with maternal short stature.

Conclusions: Approximately 6.5 million SGA and/or preterm births in LMIC may be associated with short maternal stature annually. A reduction in this burden requires primary prevention of SGA, improvement in postnatal growth through early childhood, and possibly further intervention in late childhood and adolescence. It is vital for researchers to broaden the evidence base for addressing chronic malnutrition through multiple life stages, and for program implementers to explore effective, sustainable ways of reaching the most vulnerable populations. *J Nutr* 2015;145:2542–50.

Keywords: small-for-gestational-age, chronic malnutrition, neonatal health, maternal health, maternal height

Introduction

The WHO recently declared a global target of reducing the number of infants born at a low birth weight (LBW)³¹ (<2500 g) by 30% by the year 2025 (1). A total of 20 million LBW infants are born each year, a large majority of those births occurring in low- and middle-income countries (LMIC) (2). LBW babies comprise those who did not grow properly (intrauterine growth restricted) and those who were born too soon (preterm birth). Small-for-gestational-age (SGA) is defined as weighing below the 10th percentile of a sex-specific, population-based birth weight reference curve for gestational age (3), and is a common proxy for intrauterine growth restriction. SGA and preterm birth have been linked to increased risk of neonatal and infant mortality, as well as long-term health consequences such as neurocognitive impairment and adult chronic disease (4–7). The 2014 Lancet Every Newborn Series (8) called for more research into effectively reducing the health burden associated with the 32.4 million SGA (9) and 13.7 million preterm infants (5) born each year in LMIC.

To prevent suboptimal fetal development, it is important to understand the mechanisms leading to SGA and preterm birth. Previously reported risk factors include maternal acute malnutrition (10), morbidities (e.g., gestational diabetes, pre-eclampsia/eclampsia, and infections) (11), and reproductive health-related exposures (young/advanced age, low/high parity, and short birth

intervals) (12, 13). Several studies have also reported maternal chronic protein-energy malnutrition as being associated with these adverse newborn outcomes (10, 14). If chronic malnutrition is indeed associated with these 2 neonatal outcomes, the aforementioned goal of reducing LBW births will go hand in hand with another WHO goal of reducing the number of stunted children <5 y of age by 40% between 2010 and 2025 (1).

One goal of the Child Health Epidemiology Reference Group SGA/Preterm Birth Working Group was to investigate the association between short maternal stature and SGA and preterm birth, and to calculate the population attributable fraction (PAF) of SGA and preterm births associated with short maternal stature. Unlike previous meta-analyses on this topic, we use the same height cutoffs as those used in national health surveys that report prevalence of short stature. This allows us to have consistent exposure categories across the pooled studies and to calculate PAFs for LMIC. In addition, we attempt to distinguish the associations between SGA and preterm by differentiating the newborns by those who are SGA only, preterm only, both, or neither. Our findings will help inform strategies to reduce not only neonatal mortality and morbidities, but also adverse intergenerational health consequences associated with SGA and/or preterm birth.

Methods

We conducted individual participant data meta-analysis (15) by first estimating associations in the individual studies with standardized exposure and outcome measures, and then conducting a meta-analysis of the associations.

Data sets for RR estimation. Twenty studies from LMIC containing data on gestational age and neonatal weight were identified for a separate study (4). Briefly, the study examined associations between SGA/preterm birth and neonatal and infant mortality. The data sets required gestational age, birth weight, and systematic vital status follow-up through 28 d after delivery. The protocol for data identification is described in more detail in a separate publication (4). For this analysis, we used the 12 data sets that also collected maternal height data. We did

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³ Supplemental Tables 1–9, Supplemental Figures 1–3, Supplemental Texts 1 and 2, and Supplemental Appendix 1 are available from the “Online Supporting Material” link in the online posting of the article and from the same link in the online table of contents at <http://jn.nutrition.org>.

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³¹ Abbreviations: AGA, appropriate-for-gestational-age; aRR, adjusted risk ratio; DHS, demographic and health survey; INTERGROWTH-21st, International Fetal and Newborn Growth Consortium for the 21st Century; LAC, Latin America and the Caribbean; LBW, low birth weight; LMIC, low- and middle-income countries; MDG, Millennium Development Goal; PAF, population attributable fraction; SGA, small-for-gestational-age; STEPS, Stepwise approach to Surveillance; WHO, WHO Global Survey on Maternal and Perinatal Health.

not expect systematic differences between the studies that contributed height data and those that did not [4 of 8 data sets from Asia, 3 of 7 data sets from Africa, and 1 of 4 data sets from Latin America and the Caribbean (LAC) not included], although it should be noted that the exclusion of one of the LAC data sets left data only from Brazil for the region. The SGA and preterm birth prevalence ranged from 15% to 56% and 7% to 22%, respectively, in the included data sets and 7% to 62% and 3% to 28%, respectively, in the excluded data sets. The investigators were asked to conduct the analysis with the use of standardized templates or to provide their data set to the core working group for analysis. We also analyzed data from the WHO Global Survey on Maternal and Perinatal Health (WHOGS), a multinational facility-based survey (16). These data were collected retrospectively from hospital medical records. For each country surveyed, facilities from the capital city and 2 randomly selected provinces were sampled. In a previous Child Health Epidemiology Reference Group analysis (9), the WHOGS data sets were restricted to facilities with high-quality and representative SGA and preterm prevalence data; facilities were excluded if they had a small sample size (<500 births/facility), implausible preterm rates (>40% or <3%), or implausible low birth weight rates (<1%). Japan (a high-income country) was excluded, leaving 23 data sets. To improve representativeness, we further limited the WHO data sets to those countries that had high facility delivery rates, because all WHO data were taken from facilities. We included countries that had national-level facility delivery rates >70% (17) during the years the WHOGS was conducted (2004–2008), leaving 13 data sets.

Exposure variable. Maternal height was categorized into the 4 groups used by major health surveys, including the Demographic and Health Surveys (DHSs): <145 cm, 145 to <150 cm, 150 to <155 cm, and ≥155 cm (as the reference group). Height was categorized rather than examined as a continuous variable to enable calculation of the PAF with the use of nationally representative data on prevalence of short stature.

Outcome variables. We defined SGA as a birth weight below the 10th percentile of a sex-specific birth weight distribution by gestational age. We calculated SGA with the use of 2 different distributions. We first calculated SGA with the use of the International Fetal and Newborn Growth Consortium for the 21st Century (INTERGROWTH-21st) birth weight standard, a description of birth weight in fetuses in 8 countries that experienced optimal growth. This standard includes gestational ages 33–42 completed weeks. Separately, we also used the US 1991 birth weight reference (3) to define SGA, because it captured a wider gestational age range of 20–44 completed weeks and allowed us to examine the entire birth cohort represented in our data. The US 1991 reference is the most often cited birth weight reference (18), and it allowed us to compare our results to the existing literature. The reference differs from the aforementioned standard in that this is a description of birth weight in the population, not a description of optimal birth weight. We also examined the outcome of severe SGA (below the 3rd percentile). For the 1991 US reference, the 3rd percentile is not available in the published literature; thus, the 3rd percentile cutoff value was taken from the 2000 US birth weight reference (19). To calculate SGA, we only used weights taken within 72 h of birth to minimize misclassification. We defined preterm birth as gestational age <37 completed weeks. We also created 4 mutually exclusive outcome categories combining SGA and preterm birth to investigate how short stature is distinctly associated with the 2 outcomes. The categories were term appropriate-for-gestational-age (AGA) (weighing above the 10th percentile of a reference population; term AGA is the comparison group), term SGA, preterm AGA, and preterm SGA.

Maternal height exposure distribution. Data on the distribution of height of women of reproductive age by country were obtained through nationally representative surveys, including DHSs, the Stepwise approach to Surveillance (STEPS) survey on chronic disease risk factors (20), and other national surveys. We excluded data collected before the year 2000. For countries with multiple sources of data, the sources were prioritized by most recent year and then by following a hierarchy: DHSs, STEPS, and other surveys. Exceptions to this criterion were made based on data availability. For countries without data, regional averages were used. More details can be found in Supplemental Text 1.

Analysis. For each study, Poisson regression with robust error variance was used to calculate RRs for the exposures and outcomes (21). The Poisson models were used after log-binomial models did not converge in several individual studies. Unadjusted and adjusted associations were estimated for each study. The adjusted analyses controlled for the following variables (as available): parity (0, 1–2, and ≥3 live births), maternal age (<18, 18–<35, and ≥35 y), maternal education (no education, 1–9 y, and ≥10 y), antenatal care visits (<4 compared with ≥4 visits), and maternal signs of urinary tract infection. Categorical variables were used for parity and age to differentiate the potential adverse effects of nulliparity/high parity and also young/advanced age. Sensitivity analysis was conducted by additionally controlling for pre-/early-pregnancy BMI among the data sets with relevant information.

For the meta-analysis, we conducted a meta-analysis of the adjusted risk ratios (aRRs), which is what we present throughout the text. A priori, we decided to use random-effects models with DerSimonian-Laird pooled RRs and 95% CIs (22), under the assumption that the studies included in the meta-analysis were not functionally equivalent (23). We calculated global estimates, as well as Millennium Development Goal (MDG) regional estimates (Africa, Asia, LAC). We conducted a metaregression with the use of the metareg command in Stata to explore heterogeneity of the RRs by region. We also conducted sensitivity analyses by separating the risk estimates of the prospective birth cohort studies and the WHOGS data. The metan command in Stata was used for the meta-analyses. We deemed $\alpha < 0.05$ as statistically significant.

We calculated the PAFs of term SGA, preterm AGA, and preterm SGA births associated with maternal short stature. The PAF represents the proportion of these outcomes that would be reduced/averted if exposure risk is brought to a theoretical minimum level.

We used the height distribution in women of reproductive age from the NHANES (2011–2012) as the theoretical minimum risk level (<145 cm = 0.57% of women <145 cm, 3.03% of women 145 to <150 cm, 9.66% of women 150 to <155 cm, and 86.74% of women ≥155 cm) (24). Although healthier populations do exist, we used the US distribution as the counterfactual that allowed for greater comparisons with existing literature. PAFs were calculated for each country, then multiplied by the number of SGA/preterm neonates born annually in the country (2010 estimates) (5, 9) to calculate the number that could be averted. Details on how uncertainty ranges were derived can be found in Supplemental Text 2. The data were then summarized by MDG region. Stata (version 13) was used for the analyses.

Results

Included studies. We identified 12 prospective cohort studies from LMIC, with 4 studies from Asia (25–28), Africa (29–32), and the Americas (33–36), respectively (Table 1). The studies included 40,375 live births, of which 36,803 (91.2%) had maternal height, gestational age, and birth weight (taken within 72 h of birth) data. Details of the studies can be found in Table 1 and Supplemental Table 1. Methods of gestational age assessment differed across studies and are also listed in Table 1. Among the 13 WHOGS data sets, 140,197 live births had maternal height, gestational age, and birth weight data (see Supplemental Table 2 for more details).

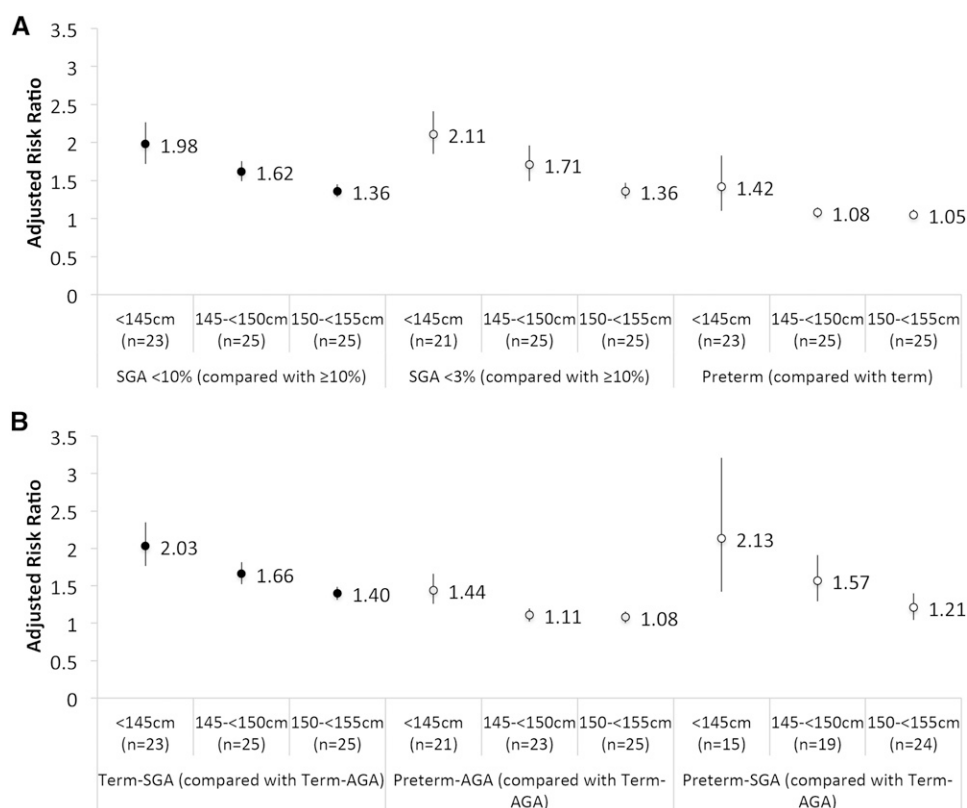
Associations. The associations between height and adverse neonatal outcomes were similar across the 3 regions (Supplemental Table 3 for SGA defined by INTERGROWTH-21st standard; Supplemental Table 4 for SGA defined by US 1999 reference). Metaregressions between each height category and each outcome showed no statistically significant differences in RR by region (data not presented). For that reason, we report global associations here, and use these associations to calculate the PAF. See Supplemental Figures 1–3 for the forest plot of the associations between height <145 cm and term SGA, preterm

TABLE 1 Studies included in the individual participant data meta-analysis¹

Study	Setting	Primary study design	Population represented	Original cohort, Analyzed cohort, ² <i>n</i>	<i>n</i>	NMR LBW	Preterm SGA delivery	Facility Method of gestational age assessment	Women with height <145 cm	Timing of height measurement
Asia										
Nepal (1999) (25)	Rural Sarlahi, Nepal	Cluster RCT of multiple micronutrient supplementation	Recruitment of all pregnant women in study area	4130	3169	42	39	22	56	6 LMP 15.8 First or early second trimester
Nepal (2003) (28)	Dhanusha, Nepal	RCT of antenatal micronutrient supplementation	Antenatal clinic-based recruitment of pregnant women in study area	1106	1050	25	22	7	53	53 Ultrasound 13.5 <20 wk gestation
Philippines (1983) (26)	Urban Cebu, Philippines	Longitudinal health/nutritional survey of infant feeding patterns	Population-based random cluster sample of census	3080	2757	14	11	18	25	34 LMP; Ballard to confirm 12.8 6th–7th month of pregnancy
Thailand (2001) (27)	Bangkok, Thailand	Prospective follow-up of birth cohort	Longitudinal birth cohort of all births in 4 districts	4245	3814	5	8	9	22	99 Best obstetric estimate (LMP, ultrasound, or clinical assessment) 3.2 28 wk gestation
Africa										
Burkina Faso (2004) (30)	Hounde, Burkina Faso	RCT of multiple micronutrient supplementation	Prospective community-based cohort	1373	1049	21	17	16	35	77 Ultrasound 0.2 First or early second trimester
Burkina Faso (2006) (29)	Hounde, Burkina Faso	RCT of maternal fortified food supplementation	Prospective community-based cohort	1316	1061	20	16	18	29	84 Ultrasound 0.1 First or early second trimester
Tanzania (2001) (32)	Urban Dar es Salaam, Tanzania	RCT of multivitamin supplementation	Facility-based antenatal clinics	7752	6846	28	8	17	20	97 LMP 3.5 12–27 wk gestation
Tanzania (2008) (31)	Korogwe, Tanzania	Observational malaria study	Facility-based recruitment, ANC clinics, community follow-up	915	795	33	11	5	22	88 Ultrasound 0.5 ≤24 wk gestation
Americas										
Brazil (1982) (34)	Urban Pelotas city, Rio Grande do Sul, Southern Brazil	Longitudinal birth cohort survey	Population-based; all births in Pelotas hospitals (100% facility delivery)	5914	5808	11	7	6	17	100 LMP 2.2 Immediately after delivery
Brazil (1993) (35)	Urban Pelotas city, Rio Grande do Sul, Southern Brazil	Longitudinal birth cohort survey	Population-based; all births in Pelotas hospitals (100% facility delivery)	5279	5203	7	9	11	19	100 LMP and Dubowitz 0.8 Immediately after delivery
Brazil (2004) (33)	Urban Pelotas city, Rio Grande do Sul, Southern Brazil	Longitudinal birth cohort survey	Population-based; all births in Pelotas hospitals (100% facility delivery)	4287	4287	10	11	16	15	100 LMP and ultrasound, if available; Dubowitz 0.6 3 mo postpartum
Peru (1995) (36)	Urban shantytown, Lima, Peru	RCT of maternal zinc supplementation	Facility-based	978	964	0	4	5	11	100 LMP, clinical indications, and ultrasound, if available 11.6 10–24 wk gestation

¹ All values are percentages except NMR (which is number of neonatal deaths per 1000 live births). Details of the WHO data are available in Supplemental Table 2. ANC, antenatal care; LBW, low birth weight; LMP, (date of) last menstrual period; NMR, neonatal mortality rate; RCT, randomized controlled trial; SGA, small-for-gestational-age.
² With data on maternal height, gestational age, and birth weight taken within 72 h of birth.

FIGURE 1 Pooled adjusted RRs between short maternal stature (<145 cm, 145 to <150 cm, and 150 to <155 cm, reference: ≥ 155 cm) and adverse neonatal outcomes with the use of the INTERGROWTH-21st standard to define SGA. SGA <10%, SGA <3%, and preterm birth (A). Term SGA, preterm AGA, and preterm SGA (B). n = number of studies included in the pooled association. AGA, appropriate-for-gestational-age; INTERGROWTH-21st, International Fetal and Newborn Growth Consortium for the 21st Century; SGA, small-for-gestational-age.



AGA, and preterm SGA births (INTERGROWTH-21st), respectively (other forest plots not presented).

SGA defined by the INTERGROWTH-21st standard and the US 1991 reference showed almost identical RRs. Thus, we present in the text the results for SGA defined by the INTERGROWTH-21st standard only, and in the **Supplemental Appendix 1** for both the INTERGROWTH-21st standard (Supplemental Table 3) and the US 1991 reference (Supplemental Table 4).

Very short stature (<145 cm) had the strongest associations with all adverse neonatal outcomes we examined compared with the reference group of ≥ 155 cm. Height <145 cm had an aRR of 1.98 (95% CI: 1.72, 2.27; $P < 0.001$) for SGA <10% and an aRR of 2.11 (95% CI: 1.85, 2.41; $P < 0.001$) for SGA <3%. Height showed a dose-response relation with the SGA outcomes; the magnitude of the associations became smaller with increasing height (Figure 1, Supplemental Table 3).

Women with height <145 cm had an aRR of 1.42 (95% CI: 1.10, 1.83; $P = 0.006$) with preterm birth (compared with all term births regardless of SGA status). The association for 145 to <150 cm was an aRR of 1.08 (95% CI: 1.01, 1.15; $P = 0.036$) and for 150 to <155 cm, a nonsignificant aRR of 1.05 (95% CI: 0.99, 1.12; $P = 0.09$). There was no clear dose-response relation at the global level between height and the risk of preterm birth (Figure 1, Supplemental Table 3).

All height categories below the reference were statistically significantly associated with risk of term SGA, preterm AGA, and preterm SGA births (compared with term AGA), with women <145 cm having the highest RR (term SGA—aRR: 2.03; 95% CI: 1.76, 2.35; $P < 0.001$; preterm AGA—aRR: 1.44; 95% CI: 1.26, 1.66; $P = 0.011$; preterm SGA—aRR: 2.13; 95% CI: 1.42, 3.21; $P = 0.031$) (Figure 1, Supplemental Table 3). Although the CIs overlapped, the magnitude of the associations decreased for all 3 of these outcomes as height increased.

The analyses were stratified by population-based birth cohort studies and the WHOIS (Supplemental Tables 5 and 6). The association between short maternal stature and SGA was weaker in the WHOIS data than in the cohort studies. For preterm birth, the population-based cohort study data and WHOIS data produced similar results.

Only 9 of our data sets had pre- or early pregnancy maternal weight; controlling for early pregnancy BMI in these data sets did not result in substantial changes in RRs (data not presented). We also conducted a sensitivity analysis, removing the 2 studies that had >20% missing data (25, 30), and we saw no major change in the association (data not presented).

Prevalence of short stature in women of reproductive age.

Of 138 LMIC, nationally representative data (collected in the year 2000 or after) for women of reproductive age were available from 80 countries. The data were obtained from DHSs ($n = 52$), STEPS ($n = 24$), the China Health and Nutrition Survey, the Indonesia Family Life Survey, the Mexico National Health and Nutrition Survey, and the Thailand National Health Examination Survey (Supplemental Table 7). The 80 countries represent >80% of women of reproductive age in LMIC with the use of UN World Population Prospects estimates from 2010 (37).

Across the MDG subregional averages, the prevalence of <155 cm ranged from 19.8% in the Caucasus and Central Asia to 68.5% in Southern Asia, with a median of 32.4%. The prevalence of <145 cm ranged from 0.7% in the Caucasus and Central Asia to 10.7% in Southern Asia, with a median of 2.3% (Figure 2, Supplemental Table 8). Figure 2 also includes the NHANES prevalence to allow for visualization of the counterfactual we used to calculate PAR.

Population attributable fraction. With the use of the INTERGROWTH-21st standard, the proportion of term SGA

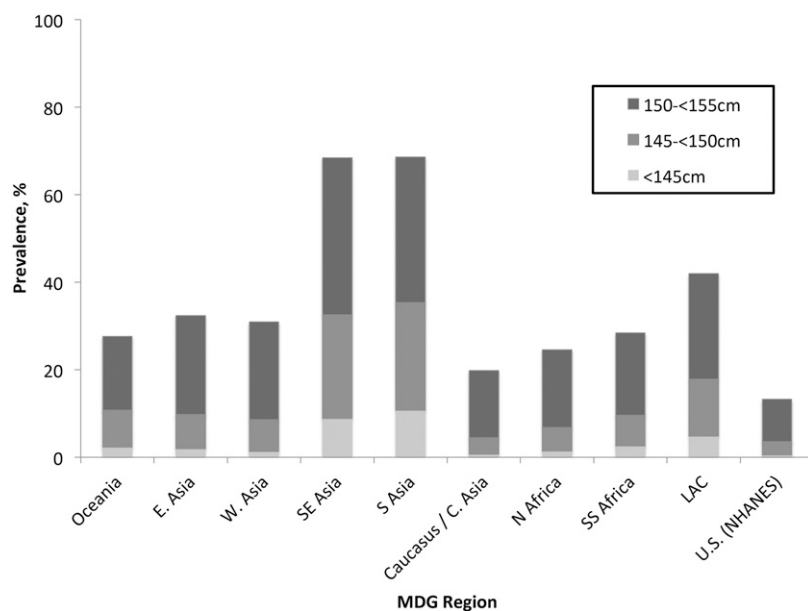


FIGURE 2 Height distribution in women of reproductive age by UN Millennium Development Goal subregions, with NHANES data used as the theoretical minimum. Data derived from 80 nationally representative surveys (52 demographic and health surveys, 24 stepwise approach to surveillance surveys, and 4 others). C, Central; E, Eastern; LAC, Latin America and the Caribbean; MDG, Millennium Development Goal; N, Northern; S, South; SE, Southeast; SS, Sub-Saharan; W, Western.

associated with maternal short stature ranged from 3.4% in the Caucasus and Central Asia to 24.3% in Southern Asia. In total, 5.5 million (95% CI: 5.2 million, 5.8 million) term SGA births were associated with maternal short stature, or 18.6% of the global total (95% CI: 17.4%, 19.7%).

The proportion of preterm AGA births associated with maternal short stature ranged from 0.7% in the Caucasus and Central Asia to 7.9% in Southern Asia. In total, 550,800 (95% CI: 360,400, 719,200) preterm AGA births were associated with maternal short stature, or 5.0% of the global total (95% CI: 3.3%, 6.6%) (Table 2).

Finally, the proportion of preterm SGA associated with maternal short stature ranged from 2.8% in the Caucasus and Central Asia to 23.3% in Southeast Asia. In total, 457,500 (95% CI: 380,600, 526,900) preterm SGA births were associated with maternal short stature, or 16.5% of the global total (95% CI: 13.7%, 18.9%) (Table 2).

South Asia had the largest total number of term SGA (16.2 million), preterm AGA (4.0 million), and preterm SGA (1.2 million) births. Of these, 3.9 million term SGA, 315,000 preterm AGA, and 268,000 preterm SGA babies were associated with maternal short stature (Table 2). National PAF estimates are available in **Supplemental Table 9**. India had the largest absolute number of all 3 outcomes associated with short maternal stature, followed by Pakistan, Bangladesh, and Indonesia.

Discussion

Our study found evidence of statistically significant associations between short maternal stature and term SGA, preterm AGA, and preterm SGA birth outcomes, respectively. Close to 6.5 million SGA and/or preterm births in LMIC may be attributed to factors that are associated with short maternal stature. SGA and preterm births have a higher risk of adverse health consequences, including neonatal and infant mortality (4), childhood undernutrition (6), and adulthood chronic disease (7). In light of the INTERGROWTH-21st study findings that show that optimal fetal growth at the population level is similar across the globe, this highlights a greater need to address fetal growth restriction in low-resource settings.

The associations and PAFs we present here should be interpreted as either having a direct causal link with short stature and/or operating through underlying factors that are highly associated or correlated with short stature. The association between short stature and SGA and/or preterm birth could be a function of residual confounding. For instance, short stature may be correlated with acute malnutrition, low socioeconomic status, or poor access to or quality of antenatal care. Although we controlled for available confounders in our analysis, we expect that the associations still may be driven partly by factors external to maternal height and chronic malnutrition. We controlled for maternal BMI in a subset of studies and saw no major changes in the associations. One possible biological mechanism linking short stature directly to SGA/preterm birth is low uterine volume and/or small pelvic size (38). Small uterine volume is considered to restrict fetal growth (39), and Kramer et al. (38) hypothesized that earlier filling of the pelvis could lead to early spontaneous labor. Shorter women, through chronic malnutrition, also may be more susceptible to infections during pregnancy (40), thus having a higher risk of adverse newborn outcomes. There is also some literature suggesting that placental epigenetic modifications contribute to intrauterine growth (41) and also to adulthood height determination (42); such potentially transgenerational factors may play a role as well.

The need for health intervention in LMIC to improve height attainment has been highlighted in various publications. Silventoinen (43) states that in low-resource settings, a larger percentage of height variation within the population is attributable to the environment over genetics, and this author highlights nutrition and disease as the main environmental contributors to attained height. The association between socioeconomic status and height diminishes in a population as standard of living increases. Subramanian et al. (44, 45) also reported the association between socioeconomic status and attained height as being a consistent pattern across LMIC. Other studies have also reported changes in population height with economic development (46), which likely serves as a proxy for adverse nutritional and disease exposures. For example, in Brazil, between 1974 and 2007, the national prevalence of stunting dropped from 59.0% to 11.2% in the lowest income quintile and 12.1% to 3.3% in the highest income quintile, a 33 y span during which Brazil saw major reductions in inequality indexes (47).

TABLE 2 Number and percentage of small-for-gestational-age and preterm births attributable to short maternal stature, US population as counterfactual¹

UN MDG subregion	Term SGA births, <i>n</i>	Term SGA births attributed to		Preterm AGA birth, <i>n</i>	Preterm AGA birth attributed to maternal short stature, <i>n</i> (95% CI)		PAF, % (95% CI)	Preterm SGA birth, <i>n</i>		Preterm SGA birth attributed to maternal short stature, <i>n</i> (95% CI)		PAF, % (95% CI)
		maternal short stature, <i>n</i> (95% CI)	PAF, % (95% CI)		short stature, <i>n</i> (95% CI)	to maternal short stature, <i>n</i> (95% CI)						
Caucasus and Central Asia	207,000	7100 (6400, 7900)	3.4 (3.1, 3.8)	117,500	880 (250, 1500)		0.7 (0.2, 1.2)	33,800		940 (630, 1200)		2.8 (1.9, 3.7)
Eastern Asia	900,900	76,500 (70,500, 82,200)	8.5 (7.8, 9.1)	980,800	21,100 (11,200, 30,100)		2.1 (1.1, 3.1)	281,400		21,200 (16,200, 25,900)		7.5 (5.8, 9.2)
Latin America and the Caribbean	1,180,000	178,200 (166,500, 189,600)	15.1 (14.1, 16.1)	735,300	34,000 (22,200, 44,600)		4.6 (3.0, 6.1)	194,100		28,700 (23,800, 33,300)		14.8 (12.2, 17.2)
Northern Africa	295,900	19,200 (17,700, 20,700)	6.5 (6.0, 7.0)	217,500	3500 (1900, 5000)		1.6 (0.9, 2.3)	41,700		2,300 (1800, 2900)		5.6 (4.4, 6.8)
Oceania	51,000	6700 (6200, 7200)	13.2 (12.2, 14.1)	15,200	450 (250, 630)		2.9 (1.6, 4.1)	4400		500 (400, 570)		11.3 (9.4, 13.1)
Southeast Asia	2,336,400	564,100 (530,300, 596,700)	24.1 (22.7, 25.5)	1,163,400	89,200 (59,500, 115,500)		7.7 (5.1, 9.9)	334,000		77,500 (65,300, 88,300)		23.2 (19.5, 26.4)
South Asia	16,213,600	3,939,700 (3,703,400, 4,166,300)	24.3 (22.8, 25.7)	4,008,800	314,800 (214,200, 402,800)		7.9 (5.3, 10.0)	1,150,300		267,600 (226,400, 304,000)		23.3 (19.7, 26.4)
Sub-Saharan Africa	7,525,300	640,100 (593,000, 684,800)	8.5 (7.9, 9.1)	3,304,700	79,100 (47,200, 108,300)		2.4 (1.4, 3.3)	632,000		50,300 (39,800, 60,300)		8.0 (6.3, 9.5)
Western Asia	958,200	82,200 (75,500, 88,800)	8.6 (7.9, 9.3)	379,400	8000 (3700, 11,800)		2.1 (1.0, 3.1)	108,800		8,500 (6500, 10,400)		7.8 (5.9, 9.6)
Total LMIC	29,668,300	5,513,900 (5,169,600, 5,844,200)	18.6 (17.4, 19.7)	10,922,600	550,800 (360,400, 719,200)		5.0 (3.3, 6.6)	2,780,500		457,500 (380,600, 526,900)		16.5 (13.7, 18.9)

¹ The numbers of observations (*n*) were rounded to the closest 100, but PAFs were calculated before rounding. AGA, appropriate-for-gestational-age; LMIC, low- and middle-income countries; MDG, Millennium Development Goal; PAF, population attributable fraction; SGA, small-for-gestational-age.

Our study contributes unique data by creating mutually exclusive combination categories of preterm and/or SGA, allowing us to differentiate maternal stature's associations with each of these outcomes. We found that short stature has a stronger association with SGA birth than with preterm birth.

Although the exposure and outcome definitions were not exactly comparable, our associations were similar to those reported in previous literature. The WHO Collaborative Study of Maternal Anthropometry and Pregnancy Outcomes meta-analysis reported a pooled crude OR of 1.9 (95% CI: 1.8, 2.0) for SGA birth [with the use of a different US standard reference distribution (48) from the one we used] and 1.2 (95% CI: 1.1, 1.2) for preterm birth, comparing the lowest to highest quartile of height in each data set (10). The meta-analysis in that study did not use adjusted associations, and its use of quartile cutoffs for height did not allow for PAF calculation. The Knowledge Synthesis Group's systematic review reported an association between short stature and SGA births (2 studies; crude pooled OR 1.39, 95% CI: 1.15, 1.68) and inconsistencies in association for preterm birth (14). The pooled crude RR for preterm birth was 1.23 (95% CI: 1.11, 1.37), but the adjusted data available in some of the included studies showed no statistical significance. Also, the definitions of SGA and short stature were not standardized across the included studies; the height cutoffs of "short stature" ranged from <155 cm to <173 cm.

There may be the potential to intervene across an individual's lifespan to prevent maternal stunting. Existing literature has stressed the "1000 d" principle, emphasizing exposures in utero and at ≤ 2 y of age as the main drivers of child development and linear growth (49). SGA neonates have a higher risk of childhood stunting (6), which subsequently has been associated with adulthood stunting. A Guatemalan study that followed birth cohorts through their own pregnancies also reported maternal birth size and birth length as predictive of offspring birth size and birth length, even after controlling for maternal weight or height at the time of pregnancy (50). There is also literature reporting that girls born SGA have smaller uterine volume in adolescence (51). Systematic reviews have reported a 34% reduction with protein-energy supplementation (52) and a 13% reduction with micronutrient supplementation (compared with iron and folate supplementation) in the odds of SGA births (53). However, there is low coverage, inequities in benefit (e.g., better-off women benefiting more), and weak evidence of health impact when using supplementation programs to impact height (54). Most programs also have been conducted in Africa, despite the higher burden of stunting and SGA births in Asia. There are also potential concerns pertaining to protein-energy supplementation in South Asia; supplementation leading to larger fetal size but no changes to attained maternal height could potentially increase rates of cephalopelvic disproportion and obstructed labor. A recent systematic review reported increases in birth weight and no increased risk of neonatal mortality and stillbirths with protein-energy supplementation, but only included one study from South Asia (52).

There is an increasing focus on the potential for intervention in adolescence to reduce stunting, as promoted by the UNICEF Subcommittee on Nutrition through the Lifecycle. There has been minimal research conducted in later childhood or in adolescence to examine if and to what degree growth trajectories can be altered. Importantly, interventions would need to result in increased stature without inducing overweight or early menarche. A recently published study notes that even in the

absence of intervention, individuals can experience catch-up growth between 2 y of age and midchildhood and also between midchildhood and early adulthood (55). This evidence argues for investing in further research on childhood and adolescent interventions to improve linear growth.

There are several limitations to our analysis. We did not explore height as a continuous variable. In many countries, national height prevalence data were only available in the categories we report here. Furthermore, we needed RRs by height categories to subsequently calculate the PAF. We expect maternal height to shift during pregnancy because of spinal compression and pedal changes. However, we expect minimal impact on our results, because this should minimally alter the height distributions as categorized in 5 cm increments. Because of the lack of data, we were unable to explore exposures such as infections and weight gain and outcomes such as stillbirth. For several studies, gestational age was obtained using the date of last menstrual period. Although most studies conducted active pregnancy surveillance, we still expected some discrepancy between true and calculated gestational age. We expected our uncertainty intervals for the PAFs to be narrower than they should be, because the uncertainty associated with the national height distribution estimates was not taken into account. Finally, nationally representative data on prevalence of maternal short stature, SGA birth, and/or preterm birth were not available for every country and had to be extrapolated from available data.

In sum, ~6.5 million preterm and/or SGA births in LMIC annually may be associated with short maternal stature. A reduction in this burden requires primary prevention of SGA births, an improvement in postnatal growth through early childhood, and possibly further intervention in late childhood and adolescence. We also found dose-response associations between stature and adverse neonatal outcomes, suggesting that even an incremental change could lead to a health impact. The WHO has declared goals of reducing the number of LBW newborns by 30% and stunted children <5 y of age by 40% between 2010 and 2025 (1). To meet these and other post-MDG neonatal and child health goals, it is vital for researchers to broaden the evidence base for addressing chronic malnutrition through multiple life stages, and for program implementers to explore effective, sustainable ways of reaching the most vulnerable populations.

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