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Regional trends in birth weight in low- and middle-income countries 2013–2018

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Abstract

Background: Birth weight (BW) is a strong predictor of neonatal outcomes. The purpose of this study was to compare BWs between global regions (south Asia, sub-Saharan Africa, Central America) prospectively and to determine if trends exist in BW over time using the population-based maternal and newborn registry (MNHR) of the Global Network for Women's and Children's Health Research (Global Network).

Methods: The MNHR is a prospective observational population-based registry of six research sites participating in the Global Network (2013–2018), within five low- and middle-income countries (Kenya, Zambia, India, Pakistan, and Guatemala) in three global regions (sub-Saharan Africa, south Asia, Central America). The birth weights were obtained for all infants born during the study period. This was done either by abstracting from the infants' health facility records or from direct measurement by the registry staff for infants born at home. After controlling for demographic characteristics, mixed-effect regression models were utilized to examine regional differences in birth weights over time.

Results: The overall BW means were higher for the African sites (Zambia and Kenya), 3186 g (SD 463 g) in 2013 and 3149 g (SD 449 g) in 2018, as compared to Asian sites (Belagavi and Nagpur, India and Pakistan), 2717 g (SD 450 g) in 2013 and 2713 g (SD 452 g) in 2018. The Central American site (Guatemala) had a mean BW intermediate between the African and south Asian sites, 2928 g (SD 452) in 2013, and 2874 g (SD 448) in 2018. The low birth weight (LBW) incidence was highest in the south Asian sites (India and Pakistan) and lowest in the African sites (Kenya and Zambia). The size of regional differences varied somewhat over time with slight decreases in the gap in birth weights between the African and Asian sites and slight increases in the gap between the African and Central American sites.

Conclusions: Overall, BW means by global region did not change significantly over the 5-year study period. From 2013 to 2018, infants enrolled at the African sites demonstrated the highest BW means overall across the entire study period, particularly as compared to Asian sites. The incidence of LBW was highest in the Asian sites (India and Pakistan) compared to the African and Central American sites.

Trial registration: The study is registered at clinicaltrials.gov. ClinicalTrials.gov Trial Registration: NCT01073475.

Keywords: Birth weight, Global network, Low birth weight, Neonatal mortality, Newborns
low- and low-middle-income countries (LMICs), BWs are not always measured, and when measured, they are often obtained and recorded inaccurately. Ideally, BW is measured within the first hours after delivery, before significant postnatal weight loss has occurred [1].

A newborn is defined as having normal BW if weight at birth is ≥2500 g. Low birth weight (LBW), as defined by the World Health Organization (WHO), is a weight at birth that is less than 2500 g (up to and including 2499 g). Infants with BW < 2500 g are further categorized into low birth weight (LBW), 1500–2499 g; very low birth weight (VLBW), 1000–1499 g; and extremely low birth weight (ELBW) < 1000 g [1]. There is an inverse relationship between BW and mortality; newborns with LBW have a higher risk of neonatal mortality and are also at risk for stunting, poor neurodevelopment, and adult-onset diseases [2–4]. Worldwide, an estimated 15–20% of all newborns weigh <2500 g at birth [5]. This translates to more than 20 million births a year. The WHO has a goal to reduce the LBW rate by 30% by the year 2025 [6]. In certain regions, there has been an increase in the incidence of LBW deliveries [7]. LMICs carry the highest burden of LBW infants. In 2015, three-quarters of the world’s LBW newborns were born in three regions: south Asia (47%), eastern and southern Africa (13%) and west and central Africa (12%) [5].

In the recent past, data from high-income countries such as the United States and the United Kingdom recorded an increasing trend in mean BW, with a concurrent decrease in the prevalence of LBW [8, 9]. This finding prompts the question as to whether a similar trend is occurring in LMICs. Exploring temporal trends in BW are important to health care policymakers, especially if there are changes in or regression in medical care or nursing practices, or patterns related to health service access [10]. For example, lack of, or late access to comprehensive antenatal care, which is common in LMICs [11], is correlated with a higher risk of pregnancy and newborn complications, including LBW. Improving rates of prenatal care is associated with decreases in the risk of premature birth and LBW [12].

A major challenge in monitoring the incidence of LBW is that about 60% of newborn babies in LMICs are not weighed nor have BW recorded [5]. Population-based survey data often rely on retrospective maternal recall and modeled estimates, with statistical methods to adjust for underreporting and misreporting of BW. By contrast, the Global Network prospectively collects BW data in a population-based maternal and newborn health registry (MNHR) in six sites within five LMICs from sub-Saharan Africa (Kenya and Zambia), south Asia (Belgavi and Nagpur India; Pakistan), and Central America (Guatemala) [13]. The purpose of this study was to examine trends and regional variation of documented BW and LBW categories over time and to explore possible factors related to those trends in the Global Network MNHR.

Methods
We performed a longitudinal cohort analysis of all infants born to mothers enrolled in the MNHR of the Global Network between 2013 and 2018. For the analysis, all deliveries with a measured BW, obtained between day 0 and day 7 were included. We excluded multiple births, miscarriages, medically terminated pregnancies, and pregnancies of women living outside the predefined study cluster (Fig. 1). We also excluded from our analyses clusters within sites that started after 2013, or were closed prior to 2018.

For infants born in a health facility, the weight recorded by facility personnel was abstracted from the medical record. For infants born at home, study personnel visited the home and obtained the weight. These weights were measured by the study personnel, or in the case of Kenya by the village elder trained for the task using standard scales [14]. It is however important to note that, in most sites, accurate gestational estimation was not possible, and therefore not included in the analysis. Thus, it is not possible to say whether the birthweights were appropriate for gestational age or not.

Data analysis
We summarized maternal and neonatal demographic characteristics by year of enrollment. To examine possible demographic changes over time, we compared the characteristics of neonates born in 2013 to those in 2018, using t tests for continuous variables and chi-square tests for categorical variables.

Means and standard deviations (SDs) for BW were computed by region and year. In addition, to account for possible demographic differences across the regions, we computed adjusted mean BWs by region and year, controlling for the following demographic characteristics: maternal age, education, parity, weight, height, infant sex, and time between birth and weight measurement. To compute the adjusted means, we fit a linear mixed-effect regression model of BW by region, year, and region by year interaction, controlling for demographic characteristics and including sampling cluster as a random effect. In addition, we tested for interactions between year and demographic characteristics to determine if birth weights changed for different demographic subgroups over time. In Kenya, maternal height was not routinely measured between 2013 and 2017, hence for this and other missing values on control variables (i.e., demographic characteristics), multiple imputation techniques was utilized. Analysis performed with
and without imputations were similar. Given the large sample sizes, we had a high level of statistical power, and therefore, even very small effects were found to be statistically significant. To determine whether significant changes in mean birth weights from 2013 to 2018 were meaningful, we examined Cohen’s d as a measure of effect size for which values of 0.2–0.4 are considered small effects, 0.5–0.7 are medium effects, and 0.8 or higher are large effects. All analyses were conducted using SAS version 9.4.

Ethical consideration
This study was reviewed and approved by all participating sites’ ethics review committees/boards including review boards at each U.S. partner university and the data coordinating center (RTI International). All women provided informed consent for participation in the study, including data collection and the follow-up visits.

Results
Between 2013 and 2018, we enrolled 355,625 pregnant women in the MNHR. Of these, 1% (N = 3254) were lost to follow up. Of the 291,085 deliveries captured in the MNHR within the study period, 265,130 (91%) met inclusion criteria (Fig. 1). Of the singleton deliveries (267,697), only 1% (2567) did not have a recorded birth weight in the MNHR.

Maternal demographic by region
As shown in Table 1, maternal age was generally similar across regions, with Central American women in our sample being slightly older than African or Asian women. African women had slightly higher percentages of women with primary or secondary schooling. African women were heavier, especially compared to Asian women, and taller, especially as compared to Central American women.

Birth weight difference by time period and region
Eighty five percent of infants in the sample were weighed within two days after birth. Mean BW by region and year are shown in Table 2. Mean changes in BW (grams) from 2013 to 2018 by region were: Africa (36.51, SD = 456.00); Asia (3.86, SD = 451.30); and Central America (53.07, SD = 450.20). Change in birth weight over time was not statistically significant for Asia (p = 0.389). While the changes in mean BW from 2013 to 2018 were statistically significant for Africa and Central America (p < 0.001), these changes did not reach the threshold for even a small effect based on Cohen’s d, suggesting that BW generally remained stable over time: Africa (d = 0.08), Asia (d = 0.01), and Central America (d = 0.12).

Birth weights of African newborns were consistently greater than that of Central American infants, which were likewise greater than BWs of Asian neonates. This pattern remained when BW was adjusted for region, year, and maternal demographics, although the size of the mean differences between regions changed slightly over time (Fig. 2).

Birth weight categories by region
Consistent with the pattern seen for mean BW, the African sites had the highest percentage of normal BW
(95.8%), hence the lowest percentage of all low BW categories (3.9% LBW, 0.3% VLBW, and 0.1% ELBW; Fig. 3). The Central American site was intermediate, with 84.4% normal BW and 15.6% across all LBW categories, and the Asian regional site had the lowest percentage of normal BW (79.8%) and highest percentages of births in all LBW categories (20.2%; Fig. 3).

Discussion
We examined trends, and regional differences in mean BW, between 2013 and 2018, of all newborns from six sites in five LMICs enrolled in the Global Network MNHR. Overall, after controlling for maternal demographic characteristics, there appeared to be a consistent pattern of regional differences across the time period. The mean BW was generally found to be highest in the African regional site (Zambia and Kenya) as compared to the other regional sites, of South Asia (India and Pakistan) and Central America (Guatemala). Across the study period, there were slight changes observed in the size of these disparities over time, with the gap between the African and Asian sites decreasing, and the gap between the African and Central American sites increasing. These observations, however, may not be generalizable to the regions on whole, since the presence of the registry in these clusters may have exerted an influence (Hawthorne effect) on pregnancy outcomes over time.

The highest annual LBW rates were recorded in the Asian sites at 20.2% (18.6%, 1.1%, and 0.5% for LBW, VLBW and ELBW respectively). This is consistent with a 2019 UNICEF report, in which the LBW rate in South Asia was 28%. However, the prevalence of LBW in Latin America was reported to be 8.7%, which was almost half of what our study reports [5]. Similar findings have also been reported in the WHO multicenter Growth Reference Study [15]. The LBW rate in the African sites in our study was 4%. This result is similar to the proportion (3.5%) reported in the Intergrowth 21st study [16], but

Table 1 Demographic characteristics by region

| Characteristic                        | Africa (N=85,551) | Asia (N=122,349) | Central America (N=57,230) | Africa vs. Asia Mean/% diff p value | Africa vs. CA Mean/% diff p value | Asia vs. CA Mean/% diff p value |
|--------------------------------------|-------------------|------------------|----------------------------|-----------------------------------|----------------------------------|---------------------------------|
| Maternal age (years), Mean (SD)      | 24.43 (6.09)      | 24.81 (4.24)     | 26.01 (5.65)               | −0.38 < 0.001                     | 1.58 < 0.001                     | −1.20 < 0.001                   |
| Maternal age (years), N (%)          |                   |                  |                            |                                   |                                  |                                 |
| 11–19                                | 20,101 (24)       | 7165 (6)         | 9772 (17)                 | 18 < 0.001                        | 7 < 0.001                        | −11 < 0.001                     |
| 20–35                                | 60,198 (70)       | 112,716 (92)     | 41,572 (73)               | −22 < 0.001                       | −3 < 0.001                       | 19 < 0.001                      |
| 36+                                  | 5149 (6)          | 2454 (2)         | 5883 (10)                 | 4 < 0.001                         | < 0.001                          | −8 < 0.001                      |
| Nulliparous, N (%)                   | 26,529 (31)       | 76,189 (37)      | 17,039 (30)               | −6 < 0.001                        | 1 < 0.001                        | 7 < 0.001                       |
| Education, N (%)                     |                   |                  |                            |                                   |                                  |                                 |
| No formal education                  | 3902 (5)          | 36,886 (30)      | 7583 (13)                 | −25 < 0.001                       | −8 < 0.001                       | 17 < 0.001                      |
| Primary/secondary education          | 77,313 (90)       | 73,006 (60)      | 46,323 (81)               | 30 < 0.001                        | 9 < 0.001                        | −21 < 0.001                     |
| University                           | 4230 (5)          | 12,394 (10)      | 3323 (6)                  | −5 < 0.001                        | −1 < 0.001                       | 4 < 0.001                       |
| Maternal weight (kgs), Mean (SD)     | 60.19 (9.51)      | 46.68 (8.05)     | 56.70 (9.48)              | 13.51 < 0.001                     | 3.49 < 0.001                     | −10.02 < 0.001                  |
| Maternal height (cm), Mean (SD)      | 158.74 (6.72)     | 152.93 (5.65)    | 147.10 (5.45)             | 5.81 < 0.001                      | 11.64 < 0.001                    | 5.83 < 0.001                    |
| Male infant, N (%)                   | 43,179 (50)       | 63,443 (52)      | 29,175 (51)               | −2 < 0.001                        | −1 < 0.001                       | 0.052 1 < 0.001                |
| Facility birth, N (%)                | 65,281 (76)       | 108,573 (89)     | 33,135 (58)               | −13 < 0.001                       | −18 < 0.001                      | 31 < 0.001                      |
| Number of days between birth and birth weight measurement, Mean (SD) | 0.32 (1.04) | 0.51 (0.97) | 1.07 (1.89) | −0.19 < 0.001 | −0.75 < 0.001 | −0.56 < 0.001 |
differs from 13% reported in the 2019 UNICEF report [5]. A possible explanation for this difference is that the data used for the UNICEF report were obtained from multiple sources and subjected to modeling. Up to 28% of the births in the UNICEF study had no weight recorded, with the highest rates of missing BW data reported to have occurred in Africa, where the rate of missing birthweight data was estimated to be over 50% [5]. By contrast, in the Global Network’s prospective, population-based MNHR from 2013 to 2018, 85% of the newborns were weighed at or within 2 days of birth.

Usually, the causes of LBW deliveries are multifactorial. Genetic and environmental factors play a significant role. Parity, low socioeconomic status, marital status, maternal age, nutritional status, maternal body mass index (BMI), maternal health status, smoking, alcohol intake, and prevailing infections such as from malaria have all been associated with BW outcomes [16–19]. There exist regional differences in the prevalence of certain diseases, such as malaria, which has been reported to increase the odds of weighing were also observed; African sites weighed newborns closer to time of birth as compared to the Asian and Central American sites. The time a newborn weight is obtained may affect the measured on the same day, immediately after birth.

One limitation of our study is that not all BWs were measured on the same day, immediately after birth. The time a newborn weight is obtained may affect the recorded BW. However, in our study, this limitation is attenuated. The vast majority of all babies included in the analysis were weighed within 48 h of birth, and, for the entire sample, birthweights were acquired within one week of delivery. However, regional differences in time of weighing were also observed; African sites weighed the newborns closer to time of birth as compared to the Asian and Central American regional sites.

An additional potential source of bias in the results is the population of women who were entered into the study, but were lost to follow-up before the birth of the infant and measurement of BW. Our rates for loss-to-follow-up were quite low (1%); however, it is possible that premature and LBW infants are over-represented among infants lost to follow-up, resulting in bias.

| Year | Africa | Asia | Central America | Africa vs. Asia | Africa vs. CA | Asia vs. CA |
|------|--------|------|----------------|----------------|--------------|------------|
|      | Mean (SD) | Mean (SD) | Mean (SD) | Mean diff. (SD) | p value | Mean diff. (SD) | p value | Mean diff. (SD) | p value |
| 2013 | 3186 (13) | 2717 (15) | 2928 (18) | 469 (45) | <0.001 | 258 (459) | <0.001 | −211 (451) | <0.001 |
| 2014 | 3172 (14) | 2730 (17) | 2922 (18) | 441 (46) | <0.001 | 249 (453) | <0.001 | −192 (465) | <0.001 |
| 2015 | 3168 (15) | 2717 (18) | 2909 (18) | 451 (47) | <0.001 | 258 (466) | <0.001 | −193 (481) | <0.001 |
| 2016 | 3148 (16) | 2716 (17) | 2897 (44) | 432 (47) | <0.001 | 251 (455) | <0.001 | −181 (465) | <0.001 |
| 2017 | 3149 (17) | 2714 (16) | 2889 (46) | 434 (46) | <0.001 | 260 (462) | <0.001 | −174 (461) | <0.001 |
| 2018 | 3149 (17) | 2713 (15) | 2874 (44) | 436 (46) | <0.001 | 275 (448) | <0.001 | −161 (451) | <0.001 |

Adjusted means obtained from models with the following variables: year, region, year × region interaction, maternal age, parity, year × parity interaction, education, maternal weight, maternal height, infant sex, and time between birth and weight measurement.
towards larger infants in the measured and reported population. Also, stillbirth and early neonatal deaths were likely to have their birthweights estimated instead of measured.

Observer errors have been reported in some studies of BW, as a result of digit preference. As an example, weights ending in 5 (five) or 0 (zero) tend to be preferred, as well as weights of multiples of 100. This is especially problematic when a continuous BW variable is categorized. For instance, an infant with a measured BW of 2492 g may be recorded as 2500, and hence categorized as a normal BW rather than LBW. Digit preference and rounding errors may result in over or underestimation, and therefore may affect observed BW trends [26]. Some infant weighing scales also tend to have readings to the nearest 50 g or nearest 100 g, and this may underestimate the LBW rates. In our cohort, the process of obtaining
and documenting birth weight is subject to this potential error.

A final limitation of our study is that the data were prospectively obtained from relatively small, discrete geographical areas (clusters) within each country. Hence, the data may not be representative of the country or region as a whole. However, as compared to other methods and data sources (e.g., Demographic Health Surveys) we enrolled an extremely large number of participants, prospectively, and followed standard procedures in obtaining and documenting weight, across sites, throughout the study period.

Conclusions
In a prospective, population-based, longitudinal cohort study of birthweight among three global regions, the observed BW means had no significant changeover time in aggregate or by region. In addition, the BW means recorded for African sites, as compared to the Asian sites, remained consistently higher.

The LBW rate was consistently higher in the Asian sites as compared to the African sites. The incidence of LBW observed for the two African sites in the MNHR was lower than that reported for other global estimates.

As compared to past regional estimates of BW, those obtained in the current study were determined from a very large sample of actual birthweights measured within sevendays of delivery. BW is impacted by a variety of complex maternal and environmental characteristics; future investigations should focus on determining the mechanistic underpinnings of regional and site differences in BW observed in this study.

Abbreviations
BW: Birth weight; ELBW: Extremely low birth weight; GN: Global Network for Women's and Children's Health Research; LBW: Low birth weight; LMIC: Low-middle-income country; MNHR: Maternal and newborn health registry; SD: Standard deviation; VLBW: Very low birth weight; WHO: World Health Organization.

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Authors’ contributions
IK participated in the data collection, drafted the manuscript and finalized the manuscript; OE revised, reviewed and and approved the manuscript; CM performed statistical analysis reviewed and approved the manuscript; SB study coordination, reviewed and approved the manuscript; PN participated in data collection study coordination; reviewed and approved the manuscript; AP participated in study design and coordination, reviewed and approved the manuscript; PH study design and coordination, reviewed and approved the manuscript, SS study design, coordination, reviewed and approved the manuscript, RG participated in study design, coordination, review and approval of the manuscript, SS participated in study design, coordination, review and approval of the manuscript; RJ participated in study design, coordination, review and approval of the manuscript; RJ participated in study design, coordination, review and approval of the manuscript; AL participated in study design, coordination, review and approval of the manuscript; NF participated in study design, coordination, review and approval of the manuscript; EC coordination of the study, review of manuscript and approval, WA participated in study design, coordination, review and approval of the manuscript; MB participated in study design, coordination review and approval of manuscript, MK participated in study design coordination, review and approval of the manuscript, JL participated in data management, statistical analysis, review and approval of manuscript; EM participated in data management, review and approval of the manuscript, FE participated in study design, coordination review and approval of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials
The dataset generated and analyzed during this study is not yet publicly available due to ongoing data analysis but it will be available in the NIH/EDAT data and specimen Hub. Request for data prior to public release will be handled by the author.

Ethics approval and consent to participate
At each site, institutional review boards or ethics committees approved the study. All women provided written informed consent before the start.

Consent for publication
The article was approved for publication by NICHD through its clearance mechanism.

Competing interests
The authors have no competing interest.

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