

## Supplementary Text

### **The association of metabolic risk factors with income, urbanization, and western diet: statistical methods and considerations**

All of our graphical and statistical analyses are based on a Bayesian multiple imputation approach. Specifically, the Bayesian statistical model for estimating risk factor levels borrowed information based on a hierarchy of countries within subregions and regions, across time and age groups, and using a small set of country-specific covariates. These covariates included the country-level characteristics considered in this paper's analyses, namely metrics of national income, urbanization, and western diet. This may appear to introduce circularity and potentially overestimate the association. Below, we provide the statistical justification for this approach and specify how we took into consideration the fact that the risk factor data were estimated using a Bayesian statistical model with covariates. In our explanation below, we conceptually divide our risk factor estimates into those that are essentially "known" based on good data for a given country-year and those that are imputed in the absence of such data; in reality there is a continuum of uncertainty.

First, we note that the covariates in the Bayesian model were chosen with the goal of best predicting country risk factor levels. The predicted risk factor levels used here are based on the posterior predictive distribution from the Bayesian hierarchical model, which conditions on all available information, both risk factor data and explanatory variables. As such, the posterior draws of country risk factor levels are a Bayesian multiple imputation. It is well known in the statistical literature that a correct multiple imputation procedure should condition on all available

information<sup>1</sup>. Further, we note that the imputed country risk factor levels are based on the estimated relationship with covariates and the variability of country risk factor levels around the relationship, hence incorporating the variation around the estimated relationship. In other words, we draw from the posterior predictive distribution, which is the model's estimate of the distribution of the country risk factor levels, and therefore includes all of the appropriate sources of variation.

We can motivate the approach further by considering an example of why it would be incorrect to exclude the country-level characteristics of interest from the Bayesian hierarchical model. Suppose that we exclude a country covariate that is correlated with the risk factor of interest, and that none of the other covariates in the model are correlated with that characteristic. The result will be that our imputed values for missing country risk factor levels will not be correlated with the characteristic. When we produce figures such as Figures 1-3, those countries with data-driven, essentially-known risk factor levels would show a correlation with the characteristic but the imputed values would not, so the overall association would appear weaker than if we knew the true country risk factor levels. Now suppose that the characteristic of interest is not correlated with the risk factor of interest but that we include it in the Bayesian model. In the Bayesian model, we will estimate a near-zero coefficient based on the available country data, and the imputed values will be uncorrelated with the characteristic. Then in the subsequent analyses, neither the data-driven risk factor levels nor the imputed values will be correlated with the characteristic, and there will not be a circularity problem.

Given the uncertainty in the country-specific risk factor levels, including in relation to the covariates, our assessment of associations takes a missing data perspective and is based on a Bayesian multiple imputation approach<sup>1,2</sup>. Specifically, we present the Loess fits, and the correlation and regression coefficients, in Figures 1-4 based on 500 posterior draws from the Bayesian model. Uncertainty intervals were calculated as the 2.5<sup>th</sup> to 97.5<sup>th</sup> percentiles of these 500 draws.

## **Supplementary Table**

**Table S1:** Country data used in Figures 1-4 of the main paper. Data are from a systematic analysis of population-based data, by sex, for 199 countries and territories, as described in detail in previous publications<sup>3-6</sup> and in the main paper.



Country	Population (mil)			Per Capita GDP (2005 int \$)			Percentage of Women Out			SDP (mm\$)			TC (mm\$)			R&D (mm\$)			FDI (mm\$)					
	2005	2006	Change per 1000	2005	2006	Change per 1000	2005	2006	Change per 1000	2005 (2005)	2006 (2005)	Change per 1000 (2005)	2005 (2005)	2006 (2005)	Change per 1000 (2005)	2005 (2005)	2006 (2005)	Change per 1000 (2005)	2005 (2005)	2006 (2005)	Change per 1000 (2005)			
	2005	2006	Change per 1000	2005	2006	Change per 1000	2005	2006	Change per 1000	2005 (2005)	2006 (2005)	Change per 1000 (2005)	2005 (2005)	2006 (2005)	Change per 1000 (2005)	2005 (2005)	2006 (2005)	Change per 1000 (2005)	2005 (2005)	2006 (2005)	Change per 1000 (2005)			
Yurt Bani	0.18	0.18	0.00	157	1100	643	0.06	0.40	0.34	137	1100	643	1.73	137	1100	643	1.73	137	1100	643	1.73	137	1100	643
Guinea-Bissau	0.04	0.04	0.00	4225	3142	1083	0.05	0.47	0.42	124	7164	4132	0.05	124	7164	4132	0.05	124	7164	4132	0.05	124	7164	4132
Tajik	0.10	0.10	0.00	1035	4207	3172	0.12	0.24	0.12	1035	4207	3172	1.11	1035	4207	3172	1.11	1035	4207	3172	1.11	1035	4207	3172
Tanzania	0.12	0.12	0.00	1178	2102	924	0.11	0.14	0.03	1178	2102	924	0.11	1178	2102	924	0.11	1178	2102	924	0.11	1178	2102	924
Aruba	0.02	0.02	0.00	233	238	5	0.29	0.38	0.09	233	238	5	0.29	233	238	5	0.29	233	238	5	0.29	233	238	5
North Macedonia	0.16	0.16	0.00	1519	1976	457	0.24	0.27	0.03	1519	1976	457	0.24	1519	1976	457	0.24	1519	1976	457	0.24	1519	1976	457
Maldives (Maldives)	0.06	0.06	0.00	3393	3392	1	0.65	0.63	0.02	3393	3392	1	0.65	3393	3392	1	0.65	3393	3392	1	0.65	3393	3392	1
France	1.00	1.00	0.00	2076	4334	2258	0.37	0.49	0.12	131	4121	2810	-0.12	131	4121	2810	-0.12	131	4121	2810	-0.12	131	4121	2810
Finland	0.48	0.48	0.00	14704	15501	797	0.64	0.68	0.04	14704	15501	797	0.64	14704	15501	797	0.64	14704	15501	797	0.64	14704	15501	797
France New Caledonia	0.10	0.10	0.00	105	2214	2109	0.43	0.44	0.01	105	2214	2109	0.43	105	2214	2109	0.43	105	2214	2109	0.43	105	2214	2109
Latvia	0.21	0.21	0.00	1446	2001	555	0.34	0.34	0.00	1446	2001	555	0.34	1446	2001	555	0.34	1446	2001	555	0.34	1446	2001	555
Uruguay	0.10	0.10	0.00	2460	2430	-30	0.19	0.13	-0.06	2460	2430	-30	0.19	2460	2430	-30	0.19	2460	2430	-30	0.19	2460	2430	-30
Togo	0.21	0.21	0.00	1700	1070	630	0.48	0.47	0.01	1700	1070	630	0.48	1700	1070	630	0.48	1700	1070	630	0.48	1700	1070	630
Venezuela	0.15	0.15	0.00	1476	4872	3396	0.27	0.14	-0.14	1476	4872	3396	0.27	1476	4872	3396	0.27	1476	4872	3396	0.27	1476	4872	3396
Algeria and Morocco	0.01	0.01	0.00	1495	1492	-3	0.44	0.75	0.31	1495	1492	-3	0.44	1495	1492	-3	0.44	1495	1492	-3	0.44	1495	1492	-3
Burkina Faso	0.12	0.12	0.00	1017	1016	-1	0.42	0.79	0.37	1017	1016	-1	0.42	1017	1016	-1	0.42	1017	1016	-1	0.42	1017	1016	-1
Belarus	0.46	0.46	0.00	1266	2070	804	0.42	0.37	-0.05	1266	2070	804	0.42	1266	2070	804	0.42	1266	2070	804	0.42	1266	2070	804
Belgium	0.46	0.46	0.00	1266	2070	804	0.42	0.37	-0.05	1266	2070	804	0.42	1266	2070	804	0.42	1266	2070	804	0.42	1266	2070	804
Bolivia (Plurinational)	0.11	0.11	0.00	1018	7187	6169	0.44	0.47	0.03	1018	7187	6169	0.44	1018	7187	6169	0.44	1018	7187	6169	0.44	1018	7187	6169
Burkina Faso	0.10	0.10	0.00	1017	1016	-1	0.42	0.79	0.37	1017	1016	-1	0.42	1017	1016	-1	0.42	1017	1016	-1	0.42	1017	1016	-1
Burkina Faso	0.11	0.11	0.00	1018	1016	-2	0.42	0.79	0.37	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2
Burkina Faso	0.11	0.11	0.00	1018	1016	-2	0.42	0.79	0.37	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2
Burkina Faso	0.11	0.11	0.00	1018	1016	-2	0.42	0.79	0.37	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2
Burkina Faso	0.11	0.11	0.00	1018	1016	-2	0.42	0.79	0.37	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2
Burkina Faso	0.11	0.11	0.00	1018	1016	-2	0.42	0.79	0.37	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2
Burkina Faso	0.11	0.11	0.00	1018	1016	-2	0.42	0.79	0.37	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2
Burkina Faso	0.11	0.11	0.00	1018	1016	-2	0.42	0.79	0.37	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2
Burkina Faso	0.11	0.11	0.00	1018	1016	-2	0.42	0.79	0.37	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2
Burkina Faso	0.11	0.11	0.00	1018	1016	-2	0.42	0.79	0.37	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2
Burkina Faso	0.11	0.11	0.00	1018	1016	-2	0.42	0.79	0.37	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2
Burkina Faso	0.11	0.11	0.00	1018	1016	-2	0.42	0.79	0.37	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2
Burkina Faso	0.11	0.11	0.00	1018	1016	-2	0.42	0.79	0.37	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2
Burkina Faso	0.11	0.11	0.00	1018	1016	-2	0.42	0.79	0.37	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2
Burkina Faso	0.11	0.11	0.00	1018	1016	-2	0.42	0.79	0.37	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2
Burkina Faso	0.11	0.11	0.00	1018	1016	-2	0.42	0.79	0.37	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2
Burkina Faso	0.11	0.11	0.00	1018	1016	-2	0.42	0.79	0.37	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2
Burkina Faso	0.11	0.11	0.00	1018	1016	-2	0.42	0.79	0.37	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2
Burkina Faso	0.11	0.11	0.00	1018	1016	-2	0.42	0.79	0.37	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2
Burkina Faso	0.11	0.11	0.00	1018	1016	-2	0.42	0.79	0.37	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2
Burkina Faso	0.11	0.11	0.00	1018	1016	-2	0.42	0.79	0.37	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2
Burkina Faso	0.11	0.11	0.00	1018	1016	-2	0.42	0.79	0.37	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2
Burkina Faso	0.11	0.11	0.00	1018	1016	-2	0.42	0.79	0.37	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2
Burkina Faso	0.11	0.11	0.00	1018	1016	-2	0.42	0.79	0.37	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2
Burkina Faso	0.11	0.11	0.00	1018	1016	-2	0.42	0.79	0.37	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2
Burkina Faso	0.11	0.11	0.00	1018	1016	-2	0.42	0.79	0.37	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2
Burkina Faso	0.11	0.11	0.00	1018	1016	-2	0.42	0.79	0.37	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2
Burkina Faso	0.11	0.11	0.00	1018	1016	-2	0.42	0.79	0.37	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2	0.42	1018	1016	-2
Burkina Faso	0.11	0.11	0.00	1018	1016	-2	0.42	0.79	0.37	1018	1													

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# Maternal and perinatal outcomes among nulliparous adolescents in low- and middle-income countries: a multi-country study

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**Objective** To investigate the risk of adverse pregnancy outcomes and caesarean section among adolescents in low- and middle-income countries.

**Design** Secondary analysis using facility-based cross-sectional data from the World Health Organization (WHO) Global Survey on Maternal and Perinatal Health.

**Setting** Twenty-three countries in Africa, Latin America, and Asia.

**Population** Women admitted for delivery in 363 health facilities during 2–3 months between 2004 and 2008.

**Methods** We constructed multilevel logistic regression models to estimate the effect of young maternal age on risks of adverse pregnancy outcomes.

**Main outcome measures** Risk of adverse pregnancy outcomes among young mothers.

**Results** A total of 78 646 nulliparous mothers aged  $\leq 24$  years and their singleton infants were included in the analysis. Compared with

mothers aged 20–24 years, adolescents aged 16–19 years had a significantly lower risk of caesarean section (adjusted OR 0.75, 95% CI 0.71–0.79). When the analysis was restricted to caesarean section indicated for presumed cephalopelvic disproportion, the risk of caesarean section was significantly higher among mothers aged  $\leq 15$  years (aOR 1.27, 95% CI 1.07–1.49) than among those aged 20–24 years. Higher risks of low birthweight and preterm birth were found among adolescents aged 16–19 years (aOR 1.10, 95% CI 1.03–1.17; aOR 1.16, 95% CI 1.09–1.23, respectively) and  $\leq 15$  years (aOR 1.33, 95% CI 1.14–1.54; aOR 1.56, 95% CI 1.35–1.80, respectively).

**Conclusions** Adolescent girls experiencing pregnancy at a very young age (i.e.  $<16$  years) have an increased risk of adverse pregnancy outcomes.

**Keywords** Adolescent pregnancy, caesarean section, low- and middle-income countries, low birthweight, perinatal mortality, preterm birth.

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## Introduction

Pregnancy and childbirth are the leading causes of death in adolescent girls in low- and middle-income countries,<sup>1</sup> and obstetric risk is highest by far in sub-Saharan Africa.<sup>2</sup> It is estimated that about 15 million adolescents aged 15–19 years give birth each year, and more than 90% of these births occur in low- and middle-income countries.<sup>1</sup> In 2007, the number of births per 1000 women aged 15–19 years was as high as 121 in sub-Saharan Africa, and

74 in Latin America and the Caribbean, and in many parts of the world the decline in adolescent birth rates has stagnated since 2000.<sup>3</sup>

Pregnancy during adolescence has been associated with higher risks of adverse pregnancy outcomes such as low birthweight, preterm delivery, and perinatal and maternal death.<sup>4,5</sup> However, pregnant adolescents are more likely to be socially deprived: they are more likely to be poorer, less educated, and single, and to have fewer antenatal care visits than older mothers.<sup>4–6</sup> Hence, the contribution of young



age itself to the risk of adverse pregnancy outcomes among adolescents is difficult to estimate, as the risk may be at least partly attributable to the unfavourable sociodemographic characteristics of adolescent mothers.<sup>7</sup>

Despite the fact that most adolescent pregnancies occur in low- and middle-income countries, large studies from such countries are scarce, and most of these studies have not taken into account the confounding effect of sociodemographic factors.<sup>8–10</sup> We therefore conducted an analysis of data from the Global Survey on Maternal and Perinatal Health, which was a large multi-country study carried out in 24 mainly low- and middle-income countries in Africa, Latin America, and Asia, to assess the effect of young maternal age on pregnancy outcomes after adjustment for sociodemographic characteristics.

## Methods

### Study design

A secondary analysis of data from the World Health Organization (WHO) Global Survey on Maternal and Perinatal Health was conducted. Methodological details of this survey have been published elsewhere.<sup>11,12</sup> Briefly, the survey was a multi-country, facility-based, cross-sectional study. A stratified multistage cluster sampling design was used to obtain a sample of countries and health facilities worldwide. The survey was implemented in 24 countries and 373 health facilities. In each country, the capital city was included in the sample. In addition, two provinces were randomly selected from other administrative areas. The countries included in the survey were from three continents: Africa (Algeria, Angola, Democratic Republic of Congo, Niger, Nigeria, Kenya, and Uganda), Latin America (Argentina, Brazil, Cuba, Ecuador, Mexico, Nicaragua, Paraguay, and Peru), and Asia (Cambodia, China, India, Japan, Nepal, the Philippines, Sri Lanka, Thailand, and Vietnam). Only health institutions that reported at least 1000 deliveries per year and were capable of performing caesarean sections were eligible to participate. A random sample of up to seven institutions from each country was selected. All women admitted for delivery during a fixed recruitment period were included in the survey. The period of recruitment (data collection) was arbitrary, defined as 3 months for institutions with up to 6000 deliveries per year, and 2 months for those with more than 6000 deliveries. The survey was conducted between 2004 and 2005 in Africa and Latin America, and between 2007 and 2008 in Asia.

### Data collection

Data were collected for institutions and individuals. Data for individuals were directly extracted from the patient records by trained medical staff before maternal hospital

discharge or within 7 days of delivery. Maternal age referred to age in completed years at the time of delivery. Maternal weight in Africa and Latin America was measured at the last antenatal care visit, whereas in Asia it was measured upon maternal admission for delivery. Gestational age at birth was defined as the number of completed weeks of gestation based on the estimated delivery date in the clinical records. Consistent with previous studies,<sup>13,14</sup> the operational definition of caesarean section indicated for cephalopelvic disproportion (CPD) in our study was based on presumed CPD, and included caesarean sections indicated for dystocia, failure to progress, and failed vacuum extraction or forceps delivery, but excluded those indicated for fetal distress, breech and other types of malpresentation, and failed induction. Maternal and early neonatal deaths were defined as intra-hospital deaths that occurred on or before the eighth day postpartum and seventh day after delivery, respectively. Stillbirths included both macerated and fresh stillbirths.

Institutional data were collected on a standard form by the hospital coordinators, in consultation with the director or head of obstetrics. Data on the provision of maternal and perinatal care were obtained, including: laboratory tests; anaesthesiology resources; services provided for intrapartum care, delivery, and care of the newborn baby; and the presence or absence of basic emergency medical and obstetric care facilities, intensive care units, and human training resources.

### Statistical analysis

The study population was restricted to nulliparous women because of the small number of multiparous younger mothers and the strong correlation between parity and maternal age. Only mothers who had a singleton neonate of birthweight  $\geq 500$  g or gestational age  $\geq 22$  weeks – if the birthweight was missing – were included in the analysis, as a birthweight or gestational age outside this range is considered a miscarriage.<sup>15</sup> Age was categorised as  $\leq 15$ , 16–19, and 20–24 years, and, similar to previous studies,<sup>4,8,16,17</sup> those over 25 years of age were excluded from the analysis. Japan was excluded from the analysis as our aim was to focus on low- and middle-income countries.

Region-wise descriptive analyses were conducted to account for the heterogeneity between regions, as the quality of medical services and the social and cultural backgrounds of adolescent mothers were expected to differ by region. The region-wise characteristics of mothers in the three age groups were compared using chi-square tests.

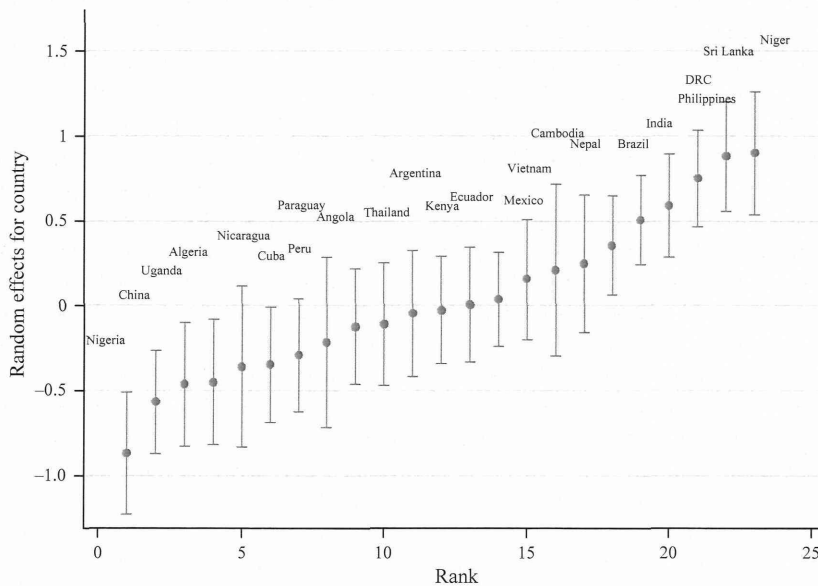
To estimate the effect of young maternal age on the risks of caesarean section, caesarean section indicated for CPD, low birthweight ( $< 2500$  g), preterm delivery ( $< 37$  completed weeks of gestation), and perinatal death (early intra-hospital death or stillbirth), we constructed multilevel

logistic regression models with random effects for facilities and countries. The significance of the random effects was determined using a likelihood ratio test by comparing models nested within models with additional levels.<sup>18</sup> The variability of outcomes was assessed, and caterpillar plots of the random-effect estimates for each country are shown for low birthweight only (Figure 1). For the analyses, four models are presented. In order to understand the independent roles of biological versus environmental factors in the association between adolescent pregnancy and adverse birth outcomes, adjustment was made for country and facility variables in the first model, and individual variables such as maternal education, marital status, and antenatal care visits in the second. For analyses on caesarean section, caesarean section indicated for CPD, low birthweight, and perinatal mortality, further adjustment was made for maternal height (short maternal height being defined as <1.50 m) and gestational age at birth in the third and fourth models. Individual- and facility-level variables were available in the survey data, whereas country-level variables were obtained from the World Bank Development Indicators and *Lancet* series on maternal and child mortality.<sup>19</sup> Country variables included in the model were gross national income (GNI) *per capita*, classified according to the World Bank categorisation as low (\$935 or less), lower-middle (\$936–3705) and upper-middle (\$3706–11 455), maternal mortality ratio (MMR) per 100 000 live births, and early neonatal mortality (ENM) per 1000 live births. The facility capacity index score was considered as a facility-level variable, and was used to reflect the level of

services available in each of the facilities and to summarise the capacity of an institution to provide obstetric care.<sup>20</sup> The analyses were not adjusted for maternal body mass index (BMI) because of variation in the timing of maternal weight measurements among countries. Data on maternal morbidities such as eclampsia, diabetes, severe anaemia (defined as haemoglobin, HB < 7 g/dl), sexually transmitted infections, and HIV infection were available, and the multiple regression analyses were only adjusted for those associated with maternal age in the univariate analysis, in order to restrict the number of confounding factors included in the final models. For multilevel logistic regression analyses on caesarean section and caesarean section indicated for CPD, facilities with no provision for caesarean section delivery, and countries with > 40% missing data on maternal height (Angola, 42.3%; Kenya, 87.5%; Brazil, 68.1%), were excluded. Statistical analysis was performed in STATA/MP 12.0 (Stata Corp. LP, College Station, TX, USA), and *P* < 0.05 was considered to be statistically significant.

## Results

The WHO Global Survey on Maternal and Perinatal Health collected data on a total of 290 610 deliveries. A total of 119 551 mothers and their infants were retained in the analysis after exclusion of data from Japan, multiparous births, multiple births, and infants with birthweight <500 g or gestational age <22 weeks, if birthweight was missing. Table 1 presents the distribution of women by age group.



**Figure 1.** Random-effect estimations for low birthweight: country-level effects in rank order, with approximate 95% confidence intervals. DRC, Democratic Republic of Congo.