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Predictors and outcomes of low birth weight in Lusaka, Zambia

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Abstract

Objective—To determine factors associated with low birth weight (LBW) in an urban Zambian cohort and investigate risk of adverse outcomes for LBW neonates.

Methods—The present retrospective cohort analysis used data recorded between February 2006 and December 2012 for singletons and first-born twins delivered in the public health system of Lusaka, Zambia. Routine clinical data and generalized estimating equations were used to examine covariates associated with LBW (<2500 g) and describe outcomes of LBW.

Results—In total, 200 557 neonates were included, 21 125 (10.5%) of whom had LBW. Placental abruption, delivery before 37 weeks, and twin pregnancy were associated with LBW in multivariable analysis (P<0.01 for all). Compared with neonates weighing more than 2500 g, those with LBW were at higher risk of stillbirth (adjusted odds ratio [AOR] 8.6, 95% confidence interval [CI] 6.5–11.5), low Apgar score (AOR 5.7, 95% CI 4.6–7.2), admission to the neonatal intensive care unit (AOR 5.4, 95% CI 3.5–8.3), and very early neonatal death (AOR 6.2, 95% CI 3.7–10.3).

Conclusion—LBW neonates are at increased risk of adverse outcomes, including stillbirth and neonatal death, independent of pregnancy duration at delivery and multiple pregnancy. These findings underscore the need for early, comprehensive, and high-quality prenatal care.

Keywords

Low birth weight; Neonatal death; Obstetrics; Perinatal outcomes; Stillbirth; Sub-Saharan Africa

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Conflict of interest

The authors have no conflicts of interest.

1. Introduction

Most cases of low birth weight (LBW; <2500 g) result from preterm birth (either spontaneous or indicated), intrauterine growth restriction, or, less commonly, congenital anomalies. LBW neonates—particularly those born prematurely—are at risk of mortality, severe morbidity, and developmental problems [1], which could in turn have long-term effects on health during adulthood and on socioeconomic outcomes, including education and income [2]. Despite improvements in newborn and child health indicators over the past two decades [3], LBW births remain common, particularly in low- and middle-income countries (LMICs) [4], where approximately 10%–20% of neonates meet the criteria for LBW [1].

Globally, LBW is associated with various maternal and obstetric factors, such as malnutrition and poor weight gain, infection (including malaria and HIV), prepartum hemorrhage, chronic hypertension and hypertensive disorders of pregnancy, diabetes, abnormal placentation, multiple pregnancy, and preterm birth [5]. Some of these factors are modifiable through early and comprehensive prenatal care. Examples include nutritional supplementation, screening and treatment for infectious diseases, progesterone for the prevention of recurrent preterm birth, and smoking cessation. Socioeconomic factors—including education, income, and inequality—and access to prenatal care are also important determinants of pregnancy outcomes and birth weight [6,7]. Because of its association with multiple markers of poor health and limited access to care, LBW has long been considered an important public health indicator [1]. However, published data from Sub-Saharan African cohorts remain scarce. The use of birth weight rather than pregnancy duration as an outcome measure is particularly relevant in LMIC settings, where it is difficult to accurately determine the length of pregnancy because women often present for care late in pregnancy [8], and obstetric ultrasonography is not commonly available or is not used to establish the estimated delivery date [9]. As a result, distinguishing between intrauterine growth restriction and preterm birth is often challenging.

The aims of the present study were to determine factors associated with LBW among Zambian women receiving care in an urban public health system and to investigate whether LBW neonates were at higher risk of adverse perinatal outcomes compared with neonates weighing 2500 g or more at birth.

2. Materials and methods

The present retrospective cohort analysis used prenatal, delivery, and postnatal data from the public Maternal, Newborn, and Child Health (MNCH) system in Lusaka, Zambia, recorded between February 1, 2006, and December 31, 2012. Ethics approval for the present analysis was obtained from the University of Zambia Biomedical Research Ethics Committee (Lusaka, Zambia) and the institutional review board of the University of North Carolina at Chapel Hill (Chapel Hill, NC, USA). Because this was a secondary analysis of routinely collected clinical data, a waiver of consent was granted by the ethics committees.

Lusaka—Zambia's capital and largest city—has an extensive network of primary health clinics where MNCH services are mostly provided free from user fees. Primary health

clinics are staffed by midwives and nurses, who provide prenatal, delivery, and postnatal services to low-risk women and neonates. High-risk pregnancies are referred to the University Teaching Hospital in Lusaka and attended by general medical officers, obstetrician–gynecologists, pediatricians, and other specialists. Clinical MNCH data are captured in an electronic medical record known as the Zambia Perinatal Records System (ZEPRS) [8], which was introduced in 2006.

The analysis included singletons and first-born twins delivered in a primary health clinic or at the University Teaching Hospital for whom the pregnancy duration estimate was deemed "reliable" and for whom a minimum complement of delivery information (date of birth, birth weight, and birth outcome) was recorded in ZEPRS. Because ultrasonography is not commonly used to determine a woman's estimated delivery date in Zambia, clinical dating criteria—last menstrual period (LMP) and symphysis–fundal height—were applied to estimate the pregnancy duration. Women were included only if their LMP had been recorded and if, when appropriate, the estimated pregnancy duration based on the symphysis–fundal height did not differ by more than 3 weeks from that estimated by the LMP method. Mothers with twins were counted once and only the birth weight of the first twin was considered. The analysis was limited to viable deliveries, defined as a pregnancy duration of 28 weeks or more and a birth weight of 1000 g or more, as is customary in the Zambian setting.

The present study had two objectives. The first was to determine demographic, socioeconomic, and/or obstetric factors associated with LBW in singleton and twin pregnancies. The second was to quantify the relative risk of adverse perinatal outcomes in LBW neonates compared with neonates weighing more than 2500 g.

For the first objective, the primary outcome measure was LBW. The following information was obtained from ZEPRS: maternal age, parity, obstetric history (prior stillbirth and prior preterm birth), medical history (pregestational hypertension [systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg] and pregestational diabetes), and prenatal care (pregnancy duration at first visit, singleton or twin pregnancy, body mass index, hemoglobin concentration, syphilis serostatus, HIV serostatus, hypertension, and placental abruption). Perinatal HIV infection was confirmed by cross-referencing ZEPRS data with the electronic database at the laboratory that had performed the neonatal HIV test. Pregnancy duration was calculated by combining information on LMP and symphysis–fundal height, if appropriate. Predictors of LBW were investigated in both univariable and multivariable analyses using generalized estimating equations to account for clustering. Variables for inclusion in the multivariable model were selected a priori. Crude and adjusted odds ratios were calculated with accompanying 95% confidence intervals.

For the second objective, LBW neonates and those weighing more than 2500 g were compared, and crude and adjusted odds were estimated for five adverse outcomes: stillbirth, Apgar score less than 7 at 1 minute of life, admission to the neonatal intensive care unit (NICU), very early neonatal death (death within 24 hours), and perinatal HIV transmission within the first 6 weeks of life. In a multivariable analysis, each outcome model was adjusted for the variables included in the multivariable predictors model (maternal age, parity, prior stillbirth, prior preterm birth, pregestational diabetes, pregnancy duration at first

prenatal care visit, multiple pregnancy, body mass index, hemoglobin concentration, syphilis serostatus, HIV serostatus, hypertension during the current pregnancy, placental abruption, and pregnancy duration at delivery). The HIV transmission model was also adjusted for the maternal antiretroviral regimen. Once again, a generalized estimating equation modeling approach was adopted and odds ratios were calculated with accompanying 95% confidence intervals.

Statistical analyses were performed using Stata version 12 (Statacorp, College Station, TX, USA). $P<0.05$ was considered statistically significant.

3. Results

During the study period, 244 986 pregnancies were registered in Lusaka's public MNCH system and recorded in ZEPRS. A total of 44 429 (18.1%) pregnancies were excluded from the analysis; therefore, 200 557 singleton or first-born twin deliveries were eligible for inclusion in the analysis cohort (Figure 1).

The median maternal age was 25 years and most women were multiparous (Table 1). Consistent with results previously reported by our group [8], most women presented for their first prenatal care visit in the second trimester. The median body mass index at the first prenatal care visit was in the healthy range. Baseline prenatal care laboratory tests included hemoglobin, syphilis, and HIV testing. Overall, 9616 (10.0%) women were anemic with a hemoglobin concentration of less than 100 g/L, 4761 (2.4%) had a positive rapid plasma reagin test for syphilis, and 42 995 (21.4%) were HIV seropositive.

With respect to the obstetric history, 3221 (2.3%) women reported a stillbirth in a prior pregnancy and 5564 (4.0%) had a history of preterm birth (Table 1). A history of hypertension before pregnancy was reported by 2250 (1.1%) women, and 215 (0.1%) reported a diagnosis of pregestational diabetes. Hypertension during prenatal care or delivery was diagnosed in 13 473 (6.7%) women and placental abruption in 122 (0.1%).

A total of 21 125 (10.5%) neonates in the present cohort met the criteria for LBW. There were 3626 stillbirths and 590 very early neonatal deaths, corresponding to a crude stillbirth rate of 18 per 1000 deliveries and a crude rate of very early neonatal death of 3 per 1000 live births.

The results of the univariable and multivariable analyses of factors associated with LBW are presented in Table 2. In multivariable analysis, extremes of maternal age (<20 years, ≥30 years), primiparity, prior stillbirth, prior preterm birth, pregestational diabetes, initial prenatal care visit during the second or third trimester, low body mass index, anemia, syphilis, HIV infection, and hypertension during the current pregnancy were all associated with increased odds of delivering an LBW neonate.

Additionally, the odds of LBW were five times higher among pregnancies complicated by placental abruption than among pregnancies in which placental abruption was not diagnosed (Table 2). Compared with neonates born between 37 and 42 weeks of pregnancy, those born between 28 and 34 weeks of pregnancy had six-fold higher odds of LBW, whereas those

born at 35 or 36 weeks had two-fold higher odds (Table 2). Most importantly, the odds of LBW were more than 34 times higher in twins than in singletons (Table 2), with twins comprising 1.4% of all neonates in the analysis and 9.6% of LBW neonates.

In the multivariable analysis of perinatal outcomes associated with LBW, the adjusted odds of stillbirth were 8.6 times higher among LBW neonates than among neonates weighing more than 2500 g (Table 3). Moreover, LBW neonates were substantially more likely than neonates weighing more than 2500 g to have a low Apgar score and to be admitted to the NICU (Table 3). They also had six-fold increased odds of very early neonatal death (Table 3). However, LBW did not seem to increase the risk of mother-to-child HIV transmission at approximately 6 weeks of life (Table 3).

4. Discussion

The present cohort study provides important perinatal findings from the largest district health system in Zambia. Nearly 11% of neonates in the present cohort met the criteria for LBW. Notably, on the basis of a multivariable analysis, pregnancies complicated by placental abruption were five times more likely to result in LBW than were uncomplicated pregnancies. Delivery before 37 weeks of pregnancy increased the risk of LBW by a factor of two (delivery at 35–36 weeks) to six (delivery at 28–34 weeks). Most worrisome was the finding that the odds of LBW were more than 34 times higher in twins than in singletons, independent of the pregnancy duration at delivery. This is particularly concerning in a setting where twins are also at high risk for stillbirth, neonatal death, and other adverse outcomes [10,11], and in view of the increasing rate of twin pregnancies globally [12].

The prevalence of LBW observed in the present cohort is consistent with Demographic and Health Survey data from 2013–2014 [13], which estimate that 9% of neonates in Zambia are born weighing less than 2500 g. Several of the maternal and obstetric risk factors associated with LBW in the present analysis, including prior stillbirth and preterm birth, hypertension, placental abruption, and anemia, are also consistent with the published literature [14–16].

The present study sought to quantify the extent to which neonates with LBW experienced adverse outcomes. These neonates were at markedly higher risk for stillbirth, a low Apgar score, NICU admission, and very early neonatal death when compared with neonates with a birth weight of 2500 g or more. These findings provide further evidence that although prenatal care attendance in Zambia is high (>95%) [13], a redoubling of effort is required to ensure complete coverage of prenatal and obstetric services as well as initiation of prenatal care early in pregnancy [17]. Increased clinical suspicion and the introduction of routine ultrasonography are also needed for pregnancy dating, early identification of twin pregnancies, and the monitoring of growth-restricted fetuses and other high-risk pregnancies [18,19] in LMIC settings. Furthermore, routine neonatal resuscitation has been demonstrated to improve outcomes for both term and preterm neonates in low-resource settings [20], including in Zambia [21]. If implemented fully and correctly, simple resuscitation algorithms, such as the Helping Babies Breathe protocol [22], are powerful tools to reduce neonatal morbidity and mortality—as are interventions such as kangaroo care (comprising skin-to-skin warming, breastfeeding, and bonding) [23] and cord care [24].

The strengths of the present analysis include the large size of the cohort and the use of "real-world" clinical data from a large public sector health system. The outcome variable of LBW is also highly relevant for a low-resource setting such as Zambia, because ultrasonography is not commonly used either to confirm pregnancy dating or to monitor fetal growth. The finding that some 39% of deliveries were categorized as occurring before 37 weeks seems implausible, and reconfirms the decision to use LBW—rather than preterm birth—as the primary outcome measure.

The study also has several limitations. First, because routine clinical records were used, it was not possible to explore additional risk factors and to control for potential confounders such as tobacco, alcohol, and illicit drug use, violence and injury, income, healthcare decision making, food security, middle-upper-arm circumference, malaria, helminth infections, tuberculosis, sexually transmitted infections, and other medical comorbidities. Second, and again because routine clinical records were used, the adverse perinatal outcomes that could be examined only represent a subset of those that may be of interest. Notably, it was not possible to investigate neonatal morbidity, 7- and 28-day mortality, or neurodevelopmental outcomes in the present cohort. Third, because deliveries in Zambia occurring at less than 28 weeks and/or with a birth weight of less than 1000 g are routinely considered spontaneous abortions and these fetuses are not routinely resuscitated, the present analysis could underestimate adverse outcomes in extremely premature neonates and those with a very low birth weight. Fourth, some very early neonatal deaths may have been misclassified as stillbirths, a practice we have observed in Zambia. Such misclassification would result in an overestimation of stillbirths and an underestimation of neonatal deaths.

In conclusion, 11% of the neonates born in Lusaka's public health system met the criteria for LBW and these newborns were at markedly increased risk for adverse outcomes, including stillbirth, a low Apgar score, NICU admission, and very early neonatal death. Placental abruption, delivery before 37 weeks, and twin pregnancy increased the risk of LBW substantially. Taken together, these results underscore a need for early, comprehensive, and high-quality prenatal care. They also indicate a role for accurate pregnancy dating and growth monitoring with ultrasonography, particularly for high-risk pregnancies. Finally, the expansion of coverage of simple and effective neonatal interventions, such as routine resuscitation, kangaroo care, and cord care, is critical to reducing the risk of morbidity and mortality for neonates with LBW in Zambia and other low-resource settings.

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Synopsis

Low birth weight affects 11% of deliveries in urban Zambia and is associated with adverse perinatal outcomes, including stillbirth and neonatal death.

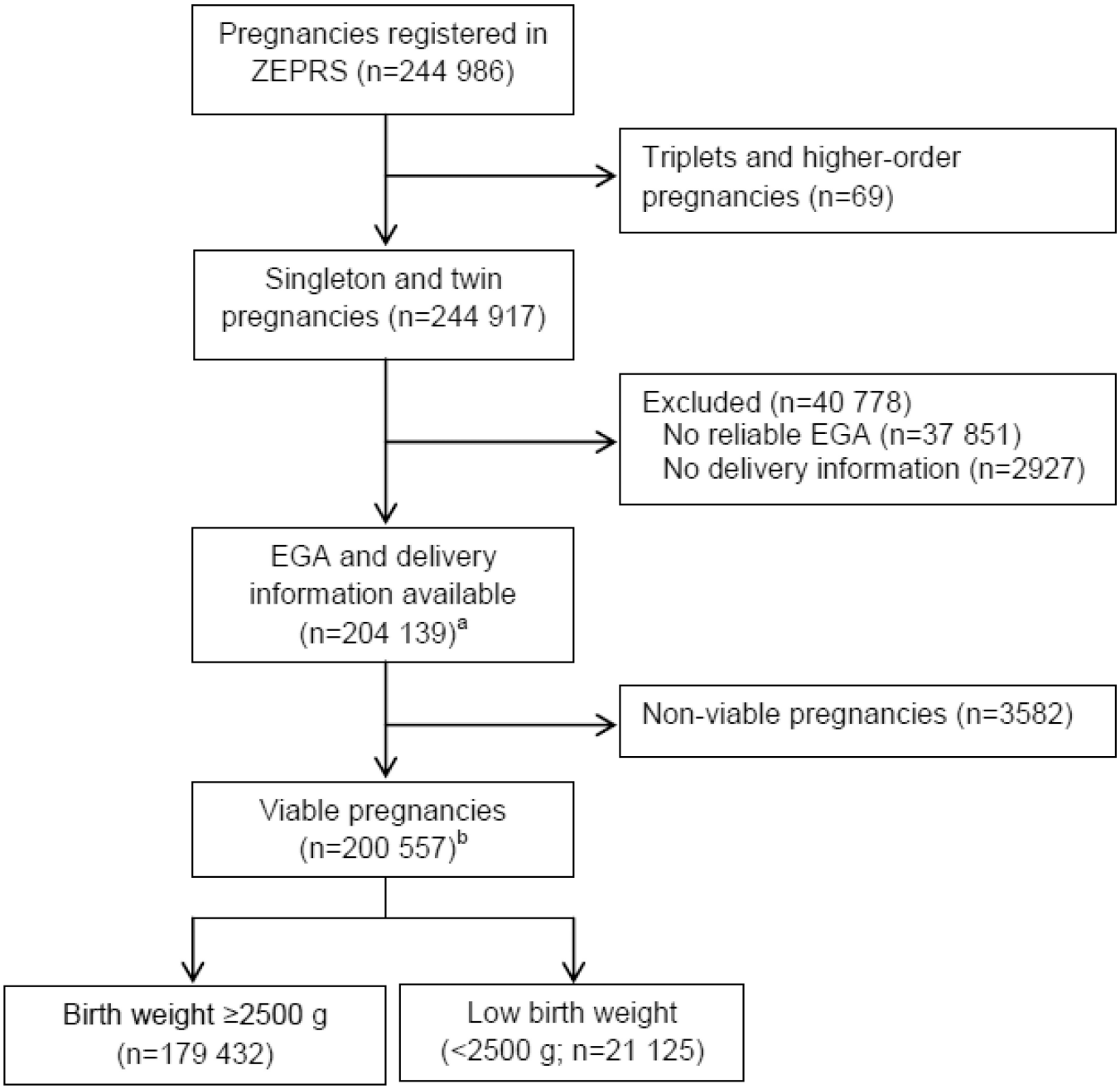

Figure 1.

Flow of patients through the study. Abbreviations: ZEPRS, Zambia Perinatal Records System; EGA, estimated gestational age. [a] For twin deliveries, information for first-born twin included. [b] Pregnancy duration ≥28 weeks and birth weight ≥1000 g.

Table 1

Maternal and newborn characteristics[a,b]

Variable	Total cohort (n=200 557)	Birth weight ≥2500 g (n=179 432)	Birth weight <2500 g (n=21 125)	*P* value
Maternal age, y	25 (20–29)	25 (21–29)	24 (20–29)	<0.001[c]
<20	38 062 (19.0)	32 786 (18.3)	5276 (25.0)	<0.001[d]
20–24	61 673 (30.8)	55 402 (30.9)	6271 (29.7)	
25–30	52 288 (26.1)	47 492 (26.5)	4796 (22.7)	
≥30	48 534 (24.2)	43 752 (24.4)	4782 (22.6)	
Parity	1 (0–3)	1 (0–3)	1 (0–2)	<0.001[c]
Primiparous	62 205 (31.0)	53 513 (29.8)	8692 (41.1)	<0.001[d]
Pregnancy duration at 1st prenatal care visit, wk	22 (18–26)	22 (18–26)	22 (18–26)	<0.001[c]
<14	11 565 (5.8)	10 235 (5.7)	1330 (6.3)	<0.001[d]
14–23	106 603 (53.2)	94 896 (52.9)	11 707 (55.4)	
≥24	82 389 (41.1)	74 301 (41.4)	8088 (38.3)	
Baseline body mass index[e]	24 (21–26)	24 (22–26)	23 (21–25)	<0.001[c]
<20	13 588 (6.8)	11 454 (6.4)	2134 (10.1)	<0.001[d]
20–24	60 776 (30.3)	53 583 (29.9)	7193 (34.0)	
≥25	57 438 (28.6)	52 752 (29.4)	4686 (22.2)	
Missing	68 755 (34.3)	61 643 (34.4)	7112 (33.7)	
Prior stillbirth[f]	3221/138 352 (2.3)	2798/125 919 (2.2)	423/12 433 (3.4)	<0.001[d]
Prior preterm birth[f]	5564/138 352 (4.0)	4702/125 919 (3.7)	862/12 433 (6.9)	<0.001[d]
Twin pregnancy	2860 (1.4)	824 (0.5)	2036 (9.6)	<0.001[d]
Hypertension during prenatal care or delivery	13 473 (6.7)	11 509 (6.4)	1964 (9.3)	<0.001[d]
Pregestational hypertension				
Yes	2250 (1.1)	1991 (1.1)	259 (1.2)	<0.001[d]
No	156 985 (78.3)	140 689 (78.4)	16 296 (77.1)	
Unknown	41 322 (20.6)	36 752 (20.5)	4570 (21.6)	
Pregestational diabetes				
Yes	215 (0.1)	188 (0.1)	27 (0.1)	<0.001[d]
No	163 879 (81.7)	146 820 (81.8)	17 059 (80.8)	
Unknown	36 463 (18.2)	32 424 (18.1)	4039 (19.1)	
Placental abruption	122 (0.1)	72 (<0.1)	50 (0.2)	<0.001[d]
Baseline hemoglobin, g/L	116 (107–125)	116 (107–125)	116 (105–124)	<0.001[c]
<80	1124 (0.6)	904 (0.5)	220 (1.0)	<0.001[d]
80–90	8492 (4.2)	7247 (4.0)	1245 (5.9)	

Variable	Total cohort (n=200 557)	Birth weight ≥2500 g (n=179 432)	Birth weight <2500 g (n=21 125)	*P* value
≥100	86 359 (43.1)	77 394 (43.1)	8965 (42.4)	
Unknown	104 582 (52.1)	93 887 (52.3)	10 695 (50.6)	
Baseline syphilis by rapid plasma reagin				
Reactive, not treated	1489 (0.7)	1304 (0.7)	185 (0.9)	<0.001[d]
Reactive, treated	3272 (1.6)	2844 (1.6)	428 (2.0)	
Nonreactive	138 025 (68.8)	123 940 (69.1)	14 085 (66.7)	
Not done/documented	57 771 (28.8)	51 344 (28.6)	6427 (30.4)	
Baseline HIV serostatus				
Infected	42 995 (21.4)	37 046 (20.6)	5949 (28.2)	<0.001[d]
Uninfected	151 553 (75.6)	136 991 (76.3)	14 562 (68.9)	
Unknown	6009 (3.0)	5395 (3.0)	614 (2.9)	
Antiretrovirals given during prenatal care/delivery [g]				
None	1011/42 995 (2.4)	814/37 046 (2.2)	197/5949 (3.3)	<0.001[d]
Nevirapine	6059/42 995 (14.1)	5069/37 046 (13.7)	990/5949 (16.6)	
Zidovudine	23 941/42 995 (55.7)	21 060/37 046 (56.8)	2881/5949 (48.4)	
Highly active antiretroviral therapy	11 984/42 995 (27.9)	10 103/37 046 (27.3)	1881/5949 (31.6)	
Pregnancy duration at delivery, wk	37 (35–39)	38 (35–39)	35 (32–37)	<0.001[c]
28–34	28 407 (14.2)	20 634 (11.5)	7773 (36.8)	<0.001[d]
35–36	49 751 (24.8)	43 655 (24.3)	6096 (28.9)	
37–42	108 613 (54.2)	102 041 (56.9)	6572 (31.1)	
43–44	13 786 (6.9)	13 102 (7.3)	684 (3.2)	

[a] Values are given as median (range), number (percentage), or number/total number, unless indicated otherwise.

[b] Mothers with twins are accounted for only once and only the birth weight of the first twin is considered. Prior stillbirth, prior preterm birth, hypertension during prenatal care or delivery, and placental abruption are coded as yes/not yes variables and therefore do not have any missing values.

[c] Wilcoxon rank-sum test.

[d] Pearson χ^2 test.

[e] Calculated as weight in kilograms divided by the square of height in meters.

[f] Denominators exclude primiparas.

[g] Includes women with HIV infection only.

Table 2

Risk factors for low birth weight[a]

Variable	Univariable analysis		Multivariable analysis	
	Crude odds ratio (95% confidence interval)[b]	*P* value	Adjusted odds ratio (95% confidence interval)[c]	*P* value
Maternal age, y				
<20	1.6 (1.3–1.9)	<0. 001	1.3 (1.1–1.5)	0.01
20–24	1.1 (1.0–1.3)	0.041	1.1 (0.9–1.2)	0.397
25–30	1.0	1.0		
≥30	1.1 (1.1–1.1)	<0.001	1.3 (1.1–1.4)	<0.001
Primiparous	1.7 (1.4–2.0)	<0.001	1.8 (1.6–2.0)	<0.001
Pregnancy duration at 1st prenatal care visit, wk				
<14	1.0		1.0	
14–24	1.0 (0.9–1.0)	0.126	1.3 (1.1–1.4)	0.004
>24	0.8 (0.8–0.9)	0.003	1.5 (1.2–1.8)	<0.001
Baseline BMI[d]				
<20	1.4 (1.3–1.5)	<0.001	1.5 (1.3–1.7)	<0.001
20–24	1.0		1.0	
≥25	0.7 (0.6–0.7)	<0.001	0.7 (0.6–0.7)	<0.001
Prior stillbirth	1.3 (1.2–1.4)	<0.001	1.5 (1.3–1.7)	<0.001
Prior preterm birth	1.6 (1.4–1.8)	<0.001	1.6 (1.4–1.9)	<0.001
Twin pregnancy	23.1 (19.1–27.9)	<0.001	34.4 (28.9–41.0)	<0.001
Hypertension during PNC or delivery	1.5 (1.2–1.8)	<0.01	1.6 (1.4–2.0)	<0.001
Pregestational hypertension	1.1 (0.9–1.4)	0.333	1.2 (1.0–1.5)	
Pregestational diabetes	1.2 (1.0–1.6)	0.112	1.9 (1.1–3.1)	0.013
Placental abruption	5.9 (4.6–7.6)	<0.001	5.2 (2.8–9.4)	<0.001
Baseline hemoglobin, g/L				
<80	2.1 (1.7–2.6)	<0.001	1.6 (1.3–1.9)	<0.001
80–90	1.5 (1.4–1.6)	<0.001	1.2 (1.1–1.4)	0.008
≥100	1.0	1.0		
Baseline syphilis by rapid plasma reagin				
Reactive, not treated	1.3 (1.1–1.4)	0.003	0.9 (0.7–1.2)	0.409
Reactive, treated	1.3 (1.2–1.5)	<0.001	1.0 (0.8–1.3)	0.893
Nonreactive	1.0		1.0	
Positive HIV serostatus at baseline	1.5 (1.5–1.6)	<0.001	1.5 (1.4–1.7)	<0.001
Antiretrovirals given during prenatal care/delivery				
None	1.8 (1.5–2.1)	<0.001	–	
Nevirapine	1.4 (1.2–1.7)	<0.001	–	
Zidovudine	1.0		–	
Highly active antiretroviral therapy	1.4 (1.3–1.4)	<0.001	–	
Pregnancy duration at delivery, wk				

Variable	Univariable analysis		Multivariable analysis	
	Crude odds ratio (95% confidence interval)[b]	*P* value	Adjusted odds ratio (95% confidence interval)[c]	*P* value
28–34	5.9 (4.0–8.6)	<0.001	6.3 (4.3–9.4)	<0.001
35–36	2.2 (1.9–2.5)	<0.001	2.2 (1.8–2.7)	<0.001
37–42	1.0		1.0	
43–44	0.8 (0.7–0.9)	<0.001	0.7 (0.6–0.7)	<0.001

Abbreviations: BMI, body mass index; CI, confidence interval; HAART, highly active antiretroviral therapy; NS, not significant; NVP, nevirapine; OR, odds ratio; PNC, prenatal care; RPR, rapid plasma reagin; ZDV, zidovudine.

[a] Missing and unknown values are excluded from the analysis.

[b] Calculated from univariable logistic regression of the effect of each factor on odds of low birth weight.

[c] Calculated from multivariable logistic regression of the effect of low birth weight on each of the outcomes, adjusting for all risk factors shown except antiretroviral regimen. The sample size for the complete-case analysis adjusted regression 41 595.

[d] Calculated as weight in kilograms divided by the square of height in meters.

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Table 3

Pregnancy outcomes[a,b]

Outcome	Birth weight ≥2500 g (n=179 432)	Birth weight <2500 g (n=21 125)	Univariable analysis		Multivariable analysis	
			Crude odds ratio (95% confidence interval)[c]	*P* value	Adjusted odds ratio (95% confidence interval)[d]	*P* value
Stillbirth						
No	177 629/179 432 (99.0)	19 302/21 125 (91.4)	1.0		1.0	
Yes	1803/179 432 (1.0)	1823/21 125 (8.6)	9.3 (7.0–12.4)	<0.001	8.6 (6.5–11.5)	<0.001
Apgar score <7 at 1 minute						
No	160 627/164 638 (97.6)	16 550/18 995 (87.1)	1.0		1.0	
Yes	4011/164 638 (2.4)	2445/18 995 (12.9)	5.9 (4.5–7.7)	<0.001	5.7 (4.6–7.2)	<0.001
Admission to the neonatal intensive care unit						
No	178 411/179 432 (99.4)	20 290/21 125 (96.0)	1.0		1.0	
Yes	1021/179 432 (0.6)	835/21 125 (4.0)	7.2 (4.8–10.8)	<0.001	5.4 (3.5–8.3)	<0.001
Very early neonatal death (<24 h)						
No	177 335/177 629 (99.8)	19 009/19 305 (98.5)	1.0		1.0	
Yes	294/177 629 (0.2)	296/19 305 (1.5)	9.4 (6.1–14.6)	<0.001	6.2 (3.7–10.3)	<0.001
HIV transmission by 6 weeks of life [e]						
No	9535/10 111 (94.3)	1119/1212 (92.3)	1.0		1.0	
Yes	576/10 111 (5.7)	93/1212 (7.7)	1.4 (1.0–1.7)	0.005	1.1 (0.7–1.7)	0.64

[a]Values given as number/total number (percentage) unless indicated otherwise.

[b]Missing values excluded from the analysis. Stillbirth: crude OR n=200 557, adjusted OR n=76 292; Apgar score <7: crude OR n=183 633, adjusted OR n=69 733; admission to the neonatal intensive care unit: crude OR n=200 557, adjusted OR n=76 292; very early neonatal death: crude OR n=196 934, adjusted OR n=74 876; HIV transmission by 6 weeks of life: crude OR n=11 323, adjusted OR n=4499.

[c] Calculated from univariable logistic regression of the effect of low birth weight on each of the outcomes.

[d] Calculated from multivariable logistic regression of the effect of low birth weight on each of the outcomes, adjusting for all risk factors shown in Table 2 except antiretroviral regimen. Odds ratios for covariates have been omitted for presentation purposes.

[e] Limited to mothers known to have HIV infection.