REVIEW

Low birth weight, very low birth weight and extremely low birth weight in African children aged between 0 and 5 years old: a systematic review

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Low birth weight (LBW < 2500), very low birth weight (VLBW < 1500), extremely low birth weight (ELBW < 1500) infants are at high risk for growth failure that result in delayed development. Africa is a continent that presents high rates of children born with LBW, VLBW and ELBW particularly sub-Saharan Africa. To review the existing literature that explores the repercussions of LBW, VLBW and ELBW on growth, neurodevelopmental outcome and mortality in African children aged 0–5 years old. A systematic review of peer-reviewed articles using Academic Search Complete in the following databases: PubMed, Scopus and Scholar Google. Quantitatives studies that investigated the association between LBW, VLBW, ELBW with growth, neurodevelopmental outcome and mortality, published between 2008 and 2015 were included. African studies with humans were eligible for inclusion. From the total of 2205 articles, 12 articles were identified as relevant and were subsequently reviewed in full version. Significant associations were found between LBW, VLBW and ELBW with growth, neurodevelopmental outcome and mortality. Surviving VLBW and ELBW showed increased risk of death, growth retardation and delayed neurodevelopment. Post-neonatal interventions need to be carried out in order to minimize the short-term effects of VLBW and ELBW.

Introduction

Africa is a continent that has high rates of children born with low birth weight, particularly sub-Saharan Africa and recent studies have shown a high rate of mortality.[1–3] Low birth weight (LBW) is defined as a birth weighing 500 g but below 2500 g irrespective of gestational age.[4–6] At the extreme end of LBW, a distinction is made of very LBW (VLBW), depicting infants <1500 g and extremely LBW (ELBW), depicting infants <1000 g.[7] VLBW and ELBW infants are at high risk for growth failure and co-morbidities that result in delayed neurodevelopment and academic achievement.[8–10]

It is estimated that in sub-Saharan Africa, LBW represents 14.3% that is almost twice of the rate of European countries.[11] A study performed in Congo showed that rates of LBW children were 164 per 1000 live births in Kama, and 270 per 1000 in Kipaka.[12] In Jimma, southwestern of Ethiopia, it was found a prevalence of 22.5% LBW around 145 newborn infants.[13] In Zimbabwe, a study found a prevalence of 12.9% of LBW children.[14] Because there is a high percentage of LBW in Sub-Saharan Africa, it is important to assess the impact during the stages of growth of those children.

Growth evaluation during the neonatal period is determined by the changes in anthropometric measurements and the body weight gain is a valuable guide to indicate an adequate growth.[15] The change in the body weight during the neonatal period of LBW children is characterized by an initial loss of ~8–15% in the first 7 days of life followed by a recovery that occurs around 10–21 postnatal day.[16] The body weight loss in the postnatal period is higher in VLBW and ELBW children than normal children.[16] Growth retardation or failure to recover body weight may occur due several factors that may be medical, nutritional or environmental.[11] This delay in growth or failure in the body weight regain may have consequences in adulthood.

VLBW and ELBW are associated with motor difficulties or developmental coordination disorders.[17,18] Insufficient attention has been paid to the prevention and control of LBW in Africa, particularly programs that target VLBW and ELBW infants. Data are required to advocate intervention studies in Africa. Thus, the main goal of the present study was to analyze the repercussions of the low, very low and extreme low birth weight in Africa. This review will focus on studies that associate birth weight with the growth, neurodevelopmental parameters and mortality of African children.

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Methods

Search strategy

A systematic review was carried out in the PubMed, scopus and scholar Google databases, using combinations of the following keywords: Africa, low birth weight, growth, neurodevelopment, mortality, children (PubMed); low birth weight, mortality, African children, growth, motor neurodevelopment (scopus and scholar Google).

Inclusion and exclusion criteria

Articles were included in this review should be published in English language between January 2008 and September 2015. The characteristics of articles were: Africans, humans, LBW, VLBW, ELBW associated with growth, non-infectious diseases and neurological disturbs. Original articles and available articles as full text were also criteria of inclusion. It was used as exclusion criteria: review articles, articles related to AIDS-HIV and infection diseases, alcohol, cigarettes, animals. Studies that linked LBW, VLBW and ELBW with supplementation of any medication, disease of sexual transmission, and domestic violence during pregnancy were excluded. Studies with other countries than African countries were excluded. Articles without abstract and out of the study period were excluded. Newborns were classified as low birth weight (LBW < 2500 g), very low birth weight (VLBW < 1500 g), and extremely low birth weight (ELBW < 1000 g).

Selection process

The flow diagram in Fig. 1 displays the process for selecting the studies of this review. The titles and abstracts were screened by two authors. The initial search resulted in a total of 1755 articles, of which 1691 were excluded after the title and abstract were read. These 1691 articles were mostly articles related to AIDS-HIV and infection diseases, alcohol, supplementation with medication, disease of sexual transmission and domestic violence during pregnancy. Full texts of 64 articles were read, and a further 52 excluded due to ineligibility, leaving 12 papers appropriate for this review.

Data abstraction

The relevant information from the studies are shown in three tables. All authors reviewed the summary of each study. Tables 1–3 summarize studies that examined the associations among LBW, VLBW and ELBW with growth (Table 1), neurodevelopmental outcome (Table 2) and mortality (Table 3). The tables included information about the country of study, design, sample characteristics, objectives, methodology, and findings of each study.

Results

Association between LBW, VLBW and ELBW with growth

Five different studies[11,19–22] analyzed the association between LBW, VLBW and ELBW with growth and regain of body weight and length (Table 1). A longitudinal study verified that gestational age is negatively correlate with initial weight loss and growth and positively correlated with the body weight regain.[19] Two cohort studies (prospective and retrospective) were performed in South Africa and compared body weight and length, head circunferance and growth velocity at diferent gestational ages [average for gestational age (AGA) and small for
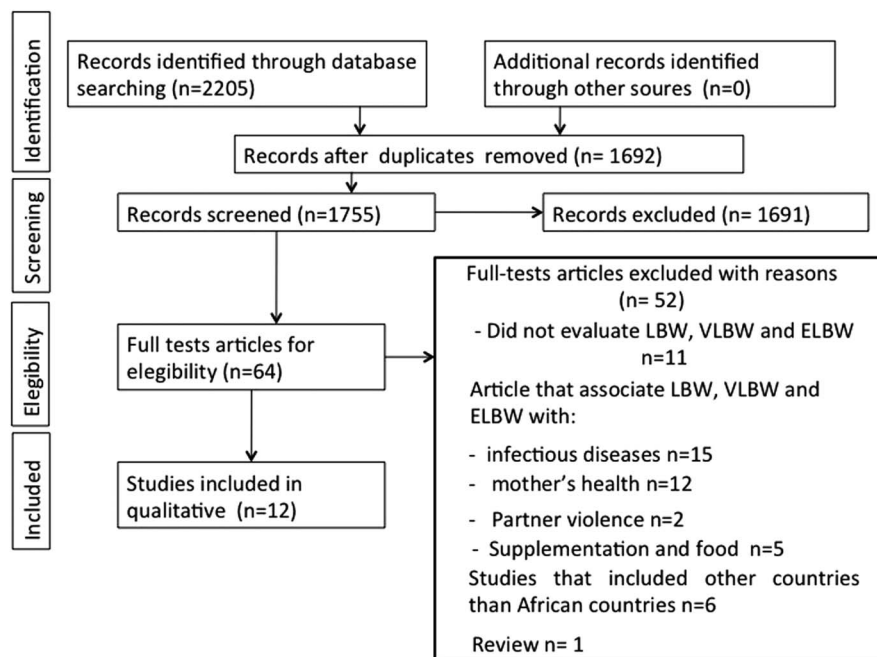

Fig. 1. Flow of studies included in the review.

Table 1. *List of studies that examined the repercussion of low birth weight (LBW), very low birth weight (VLBW) and excessive low birth weight (ELBW) with the indicators of growth*

Reference country	Participant characteristic: study design	Study aim	Measurement of growth achieved	Findings
Njokanma et al.[19] Nigeria	n = 89 preterm, 46 term. Age range 40 weeks Preterm grouped (Groups I, II, III, IV and V) 26/28, 29/30, 31/32, 33/34 and 35/36 weeks. Observational cohort longitudinal study	To describe the growth of ELBW, VLBW, LBW and NBW	Body weight, length and occipito-frontal circumference of 89 preterm, LBW, appropriate-for-dates infants were monitored from birth until 53 post-conceptional weeks. Growth velocities were compared with 46 terms	Initial weight loss, age at regaining birth weight and growth rate in the early postnatal weeks were inversely related to gestational age. Subsequent weight gain was directly related to gestational age. Between birth and 40 weeks post conception, growth rates for different gestational age groups were 129 to 207 g/week (weight), 0.78 to 0.93 cm/week (length) and 0.62 to 0.65 cm/week (head circumference). After 40 weeks, the corresponding rates were 188 to 238 g/week, 0.86 to 0.96 cm and 0.48 to 0.50 cm/week, respectively
Mackay et al.[20] South Africa	n = 139 VLBW (<1500 g) Age range 3 months. Prospective cohort study	To assess the growth of a cohort of VLBW infants in Johannesburg	Growth parameters, including body weight, length and head circumference were recorded at each visit by the same nursing sister	At 12 months in variable weight, AGA showed higher values than SGA (9.01 ± 1.31 v. 7.71 ± 1.26, $P = 0.004$). In lengths AGA showed higher values than SGA (72.51 ± 3.39 v. 68.9 ± 4.23, $P = 0.007$). No difference was found between AGA and SGA in head circumference. (45.71 ± 1.16 v. 45.08 ± 1.54, $P = 0.19$)
Namiiro et al.[11] Uganda	n = 235 Age range 21 days VLBW; ≤1500 g = 88, >1500 g = 147 Cross sectional study	To determine what proportion of LBW infants had not regained their birth weight by 21 days of age after discharge from the Special Care Unit of Mulago hospital, Kampala	Anthropometric measurements (weight, length and head circumference) and physical examination were carried out and recorded	Of the 235 LBW infants, 113 (48.1%) did not regain their birth weight by 21 days. Hospital stay of more than 7 days ($P = 0.001$) and initiation of first feed of more than 48 h (0.034) were the significant factors that contributed to failure to regain birth weight among the study participants
Olusanya et al.[21] Nigeria	n = 142 Age range 45 days VLBW Cohort study	To determine the pattern and predictors of growth velocity in early infancy in a resource-poor setting	Growth or weight velocity (GV) for each infant was computed based on three methods: (1) two-point birth weight (BW) Model: net weight gain over the time interval divided by the time interval and BW, or estimated GV = $[1000 \times (Wn - W1)]/[(Dn - D1) \times BW]$. 2) two-point average weight (AW) Model: net weight gain over the time interval divided by the time interval and average weight, or estimated GV = $[1000 \times (Wn - W1)]/\{(Dn - D1) \times [(W1 + Wn)/2]\}$ 3) Exponential (Expo) Model: estimated GV = $[1000 \times Ln(Wn/W1)]/(Dn - D1)$	High weight velocity was strongly associated with lower birth weight ($P < 0.001$) indicative of 'catch up' growth as well as with higher gestational age ($P < 0.001$)
Lango et al.[22] South Africa	n = 51 Age range = 56 days ELBW [The median birth weight of the cohort was 875 (640–995) g]. Retrospective cohort study	To describe the growth velocity of a cohort of ELBW infants and to compare with internationally acceptable benchmarks	Growth velocity (GV) was determined from weekly weights starting from day 7 using the two-point system as shown below: GV = $[1000 \times (Wn - W1)]/\{(Dn - D1) \times [(W1 + Wn)/2]\}$	No difference between AGA and SGA $P = 0.52$. The overall mean (s.d.) growth velocity was 14 (2.9) g/kg/day. In this cohort of ELBW infants, growth velocity was within the range currently deemed acceptable by international consensus

WHO, World Health Organization; AGA, appropriate for gestational age; SGA, small for gestational age; P value determined using the unpaired t-test; $P < 0.005$. W = body weight in grams, D1, beginning of the time interval; Dn, end of the time interval, in days; NBW, normal birth weight.

Table 2. *List of studies that examined the repercussion of low birth weight (LBW), very low birth weight (VLBW) and excessive low birth weight (ELBW) with neurodevelopmental outcomes*

Reference country	Participant characteristic: study design	Study aim	Measures of psychological distress	Findings
Burger et al.[23] South Africa	n = 115 Age range = during 12 months ELBW and VLBW ⩽ 1250 g Prospective descriptive study	To assess the predictive validity of general movements during the fidgety movements' period in VLBW and ELBW infants admitted to TCH in Cape Town, South Africa	A light-sensitive digital video camera (JVCGR-DV4000) was used to record the infants' spontaneous movement patterns at 12 weeks corrected age (CA). The (PDMS-2), and the AIMS were used to assess the infants' fine and gross motor development at 12 months CA. A physician performed a complete neurological examination, according to the procedure recommended by Amiel-Tisonand Gosselin	A significant relationship was found (P < 0.01) between fidgety movement outcome and the infants' final motor outcome at 12 months corrected age.
Gladstone et al.[24] Malawi	n = 840 Age range 2 years Group 1 preterm BW < 37 weeks Group 2 term BW 37–41 weeks Prospective cohort study and questionnaire Longitudinal	To assess four specific outcomes post neonatal survival, morbidity, growth, and development in a community-based sample of infants born after spontaneous preterm delivery in rural sub-Saharan Africa	Development and disability were assessed using the TQQ and the MDAT. MDAT was used to assess children in two ways: through a pass/fail scoring system and through a numerical scoring system applied to each of four domains of development	Preterm infants more often screened positively for disability on the Ten Question Questionnaire (P = 0.002). They also had higher rates of developmental delay on the MDAT at 18 months (P = 0.009). In terms of overall pass/fail on the MDAT, more children in the preterm group compared with the term group failed in the MDAT at each stage of assessment: at 12 mo [6.7 v. 2.9% (P = 0.216)], at 18 mo [22.8 v. 10.9% (P = 0.009)], and at 24 months [12.8 v. 10.7% (P = 0.274)]. Significant differences were also found specifically at 18 mo for language development (P = 0.033)

BW, birth weight; TCH, Tygerberg Children's Hospital; PDMS-2, Peabody Developmental Motor Scale, second edition; AIMS, Alberta Infant Motor Scale; TQQ, Ten Question Questionnaire; MDAT, Malawi Developmental Assessment Tool.

Table 3. *List of studies that examined the repercussion of low birth weight (LBW), very low birth weight (VLBW) and excessive low birth weight (ELBW) and mortality*

Reference country	Participant characteristic: study design	Study aim	Method	Finding
Ahlsen et al.[25] Malawi	n = 1496 Age range 5 months LBW <2500 VLBW (1000–1499) ELBW <1000 Prospective descriptive study	To demonstrate the short-term survival of infants with LBW nursed in BH and KCH in Lilongwe, Malawi	Included babies that were admitted to the nurseries. Survival was defined as alive on discharge from either the nursery or postnatal ward. Excluded were babies with severe congenital mal formations, birth weight <600 g and babies with unknown outcome. The data were collected from the maternity registers, nursery admission books, duty report books and all available obstetric case records	Survival was 7% for ELBW infants, 52% for VLBW and 90% for LBW
Ballot et al.[26] South Africa	n = 562 VLBW (1000–1499) ELBW <1000 g Retrospective cohort study	To compare morbidity and mortality in VLBW infants in two period, 2013 with similar data from 2006/2007	Two similar studies with ELBW, VLBW in two period 2013 and 2006/2007 examined the survival infants	Survival in 2013 was similar to that in 2006/2007 (73.4 v. 70.2%, P = 0.27). However, survival in neonates who weighed 750–900 g significantly improved from 20.4% in 2006/2007 to 52.4% in 2013 (P = 0.001)
Hong et al.[27] Egypt	n = 11,361 Age range 5 years LBW <2500 Observational cohort study longitudinal	To examine the risk of infant mortality among LBW children controlling for other risk factors of infant mortality	Data from the 2000 Egypt Demographic and Health Survey (EDHS) was used. It is based on the information of 11,361 children born during the 5 years before the survey. The EDHS collected demographic, socioeconomic and health of mother's child	Higher birth order; shorter birth interval; lack of prenatal care, safe sources of drinking-water and hygienic toilet facilities; living in urban residence and upper Egypt rural region were associated with a higher risk of infant mortality. The multivariate model indicated that low-birth-weight children were about three times more likely to die in infancy than other children (hazard ratio = 2.89, 95% CI: 2.33–3.58) independent of other risk factors
Rylance et al.[2] Malawi	n = 268 Age range 6 months VLBW and ELBW ⩽1500 g Observational cohort study longitudinal	To study early mortality outcome in VLBW infants admitted to the neonatal nursery, Queen Elizabeth Central Hospital, Blantyre and determine duration of hospital stay of surviving infants and their attendance for recommended follow-up	Data were extracted detailing birth weight, date of birth, sex, mode of delivery, singleton or multiple birth, estimated gestation, source of referral, maternal HIV status, antiretroviral administration for PMTCT and survival to discharge. Gestation was estimated by the SR using the Ballard score	42% (112/268) of VLBW infants survived to discharge. Survival significantly increased with increasing birth weight (11% for infants weighing ⩽1000 g v. 53% for those >1000 g, P < 0.001), and greater gestation (19% for infants, <32 weeks v. 68% for ⩾32 weeks, P < 0.001). Most deaths (88%, 137/156) occurred within the first week, 58% of them (91/156) within 48 h of admission. Surviving infants with a birth weight of 1001–1500 g stayed in hospital for a mean 21 days (range 5–44) and those weighing ⩽1000 g at birth (eight) stayed for a mean 47 days (range 35–64). A total of 108 infants were discharged from hospital, 87 of whom (81%) attended at least one follow-up visit, 62 of whom (57%) completed the recommended follow-up attendance
Sania et al.[3] Tanzania	n = 7725 LBW <2500 Age range 18 months randomized trial	To examine the associations of neonatal and infant mortality with preterm birth and IUGR, and to estimate the pPAR% of neonatal and infant mortality due to preterm birth and IUGR	Participants were HIV-negative pregnant women and their infants enrolled in Dar es Salaam, Tanzania. Gestational age calculated from date of last menstrual period was used to define preterm, and SG was used as proxy for IUGR. Survival of infants was ascertained at monthly follow-up visits. Cox proportional hazard models were used to estimate the associations of preterm and SGA with neonatal and infant mortality	Compared to term and AGA, RR of neonatal mortality among preterm-AGA was 2.6 [95% CI 1.8, 3.9], RR among term-SGA was 2.3 [95% CI 1.6, 3.3], and the highest risk was among the preterm-SGA babies (RR 15.1 [95% CI 8.2, 27.7]). Severe SGA was associated with more than fourfold higher risk of neonatal mortality 4.2 [2.8, 6.2] and SGA was associated with a doubling of neonatal mortality compared with AGA infants

BMI, body mass index; BH, Bwaila Hospital; KCH, Kamuzu Central Hospital; CMJAH, Charlotte Maxeke Johannesburg Academic Hospital; PMTCT, Prevention of mother-to-child transmission; SR, Senior clinician; IUGR, Intrauterine growth restriction; p PAR%, partial population attributable risk per cent; AGA, appropriately sized babies; RR, relative risks.

gestational age (SGA)].[20,22] In Uganda, from 235 LBW infants evaluated, 113 (48.1%) remained with their body weight until 21 postnatal days[11] and high body weight velocity, as an indicative of *catch up* growth, was found in LBW Nigerian children.[21]

Association between LBW, VLBW and ELBW with neurodevelopmental outcomes

Table 2 presents the two prospective studies that investigated the relationship between VLBW and ELBW with neurodevelopmental outcomes.[23,24] A significant relationship was found between fidgety movement outcome and the ELBW and VLBW infants' final motor outcome at 12 months.[23] Preterm infants (VLBW) are more often screened positively for disability on the Ten Question Questionnaire, presented developmental delay on the MDAT and language development.[24]

Association between LBW, VLBW and ELBW with mortality

Table 3 presents five studies that associated LBW, VLBW and ELBW with mortality.[2,3,25–27] Survival significantly increased with increasing birth weight and time of gestation.[2,25] Survival in two period of study (2013 and 206/2007) was similar, but for ELBW, the rate of survival increased from 20.4% (in 2006/2007) to 52.4% (in 2013).[26] In an observational longitudinal study with Egyptian children, LBW children were about three times more likely to die in infancy than other children independent of socioeconomic risk factors.[27] Gestational age was associated with more than four-fold higher risk of neonatal mortality according to a randomized trial study in Tanzania.[3]

Discussion

The findings of the relationship between birth weight and growth were relatively consistent across studies. The studies of this review presented some limitations, such as, lack of detailed information regarding length of hospital stay and time to regain birth weight. The studies had no control over timing of discharge and scheduling of follow-up dates. Since all recorded informations were obtained from the mother and the available medical records, recall bias and incomplete documentation, respectively, may have affected the results. Gestational age estimates were based on hospital records derived from parental accounts of last menstrual period which may be prone to errors.

Significant associations were found between LBW, VLBW and ELBW with lower values of growth, body weight and length regain, and *catch up* growth.[11,19,20] Accordingly, LBW and intrauterine growth retardation were significantly associated with growth impairment,[28] and the growth rate of VLBW infants is characterized by early suboptimal growth followed by a period of *catch up* growth.[29] Rapid *catch up* growth is advantageous with respect to improved neurodevelopmental outcomes, fewer psychosocial problems in later childhood and lower risk of persistent short stature but may be associated with an increased risk of childhood obesity and other metabolic complications.[29,30] SGA is an independent risk factor of persistent short stature, excessive fat mass gain during infancy and metabolic disease in later life.[31] The developmental origin of health and disease (DOHaD) hypothesis suggests that SGA children have a higher risk of developing metabolic syndrome later in adult life.[32] Epidemiological studies have shown that humans born small- or large-for-gestational-age have a higher likelihood of developing obesity during infancy and adolescence.[19,32–34] Aligned with this proposition, some African countries have shown an increase in the prevalence of obesity during infancy and adolescence, for example Mozambique.[35,36]

Two prospective cohort studies analyzed the neurodevelopmental outcomes of studies and found associations among ELBW and VLBW and developmental delay.[23,24] ELBW are prone to a range of long-term complications in comparison to their born-at-term counterparts.[37,38] These complications include: severe handicap such as cerebral palsy, cognitive impairment, blindness and hearing loss to impairment of short-term memory, strabismus, language delays, learning difficulties and behavioural disorders.[38–40] In addition, infants with neurodevelopmental disabilities can present a secondary musculoskeletal impairments and a decline in mobility and functional abilities.[41] Early intervention, such as, physiotherapic treatment and physical education classes during the first infancy would be able to minimize the short-effects of ELBW and VLBW on neurodevelopment of children.[42,43] The methods of Malawi study, MDTA and TQQ, found interesting results, but more sophisticated tests are necessary to provide more details. The studies follow-up the children only 2 years but the minimum age required for a proper distinction between the normal trajectory, with slow motor development, and an abnormal pattern of development appears to be around 4 years of age.[44]

The current review found the association between LBW, VLBW and ELBW with mortality.[2,3,25–27] To born VLBW and ELBW is the most important cause of neonatal mortality.[45] In a study of 795 mother–infant pairs in rural Malawi, the odds of neonatal mortality among preterm babies was 11 times greater than that of term babies.[46] The studies of this review only investigated the short-term survival of the infants with LBW, VLBW and ELBW. There is no information about long-term survival or morbidity of the infants. Only one study provided information about cases of death,[27] others did not.

Limitations

This review does not provide data on long-term neonatal outcomes. We found studies until the age of 2 or 3 years old. There is an extreme lack of studies with African population that associated LBW, VLBW, ELBW with growth and development during childhood, adolescence and adulthood. In almost all countries, the studies were carried out at the reference hospitals, which have a higher standard of care than most other hospitals in the countries, so it is bias to generalize the results. Gestational age estimation based on the date of last menstrual

period depends on women's recall ability and, therefore, there is a high probability of error. This might lead to differential misclassification in preterm birth leading to an underestimate of the true risk of mortality due to preterm birth. This review analyzed studies only in English language and did not follow-up the articles of other languages.

Conclusion

The results of this review showed that for surviving VLBW and ELBW babies, there is disadvantage with increased risk of death, growth retardation, and developmental delay. The association between LBW, VLBW and ELBW and risk of disturb during growth and development in childhood is considered the most consistent evidence supporting the thrifty phenotype hypothesis proposed by Hales and Barker.[33] Post-neonatal interventions, such as, program of nutritional recovery, physiotherapist care and habitual physical activity in the school age need to be carried out which might improve outcomes in this group of VLBW and ELBW. In addition, hospitals must take this problems seriously increasing access to quality prenatal care.

Acknowledgments

Conflicts of Interest

None.

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