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Is birth weight associated with blood pressure among African children and adolescents? A systematic review

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There is substantial evidence of an inverse association between birth weight and later blood pressure (BP) in populations from high-income countries, but whether this applies in low-income countries, where causes of low birth weight are different, is not certain. Objective: We conducted a review of the evidence on the relationship between birth weight and BP among African children and adolescents. Medline, EMBASE, Global Health and Web of Science databases were searched for publications to October 2016. Papers reporting the relationship between birth weight and BP among African children and adolescents were assessed. Bibliographies were searched for further relevant publications. Selected papers were summarized following the preferred reporting items for systematic review and meta-analysis (PRISMA) guidelines. In total, 16 papers from 13 studies conducted in nine African countries (Nigeria, Republic of Seychelles, Gambia, Democratic Republic of Congo, Cameroon, South Africa, Algeria, Zimbabwe and Angola) were reviewed. Eight studies were cohorts, while five were cross-sectional. The relationship between birth weight and later BP varied with age of the participants. Studies in neonates showed a consistently positive association, while predominantly inverse associations were seen among children, and studies in adolescents were inconsistent. Based on the limited number of studies identified, the relationship between birth weight and later BP may vary with age in African children and adolescents. Not all studies adequately controlled for confounding, notably gender or age. Whether the inverse relationship between birth weight and BP in later life observed in Western settings is also seen in Africa remains unclear.

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Key words: Africa, birth weight, blood pressure, systematic review

Introduction

A strong geographical correlation between infant mortality (from 1921 to 1925) and adult ischaemic heart disease (IHD) mortality (from 1968 to 1978) was observed by Barker and Osmond. They postulated that factors which increased the risk of death during infancy also increased susceptibility to IHD among those who survived infancy, and later, showed that birth pressure (BP) in adulthood was positively related to placenta weight but inversely associated with birth weight. They suggested that poor fetal nutrition indicated by intrauterine growth restriction and low birth weight was associated with this increased susceptibility to IHD.

Subsequently, several studies [mainly from high-income countries (HICs)] have investigated the relationship between birth size parameters (e.g. birth weight, head circumference, placenta size) and later cardiovascular disease risk (mainly BP), with birth weight the most widely studied parameter. Results from several of these studies have shown an inverse association between birth weight and BP later in life. A smaller number of studies have reported positive or no association between birth weight and later BP. For example, positive associations have been reported among UK neonates and Chinese children, whereas birth weight was not associated with BP among American adolescents. The relationship between birth weight and later BP differed by gender among UK adolescents: a negative association was seen in the males but a positive association in the females. Systematic reviews have reported that, on average, systolic blood pressure (SBP) drops by 2–4 mmHg for every kilogram increase in birth weight. These reviews have predominantly comprised of studies among adults from HICs.

In HICs the prevalence of low birth weight varies between 5 and 8%. Low birth weight is more common in Africa (7% in Nigeria, 8% Uganda, 11% Zambia, 17% Zimbabwe and Benin, and 28% Ethiopia) and on average African populations have lower birth weights when compared with European populations. In HICs, low birth weight is predominantly due to prematurity (most commonly as a result of maternal smoking in pregnancy), whereas, in developing countries, low birth weight for gestational age constitutes most of the low birth weight infants. The causes of low birth weight differ between rural, tropical Africa and developed or non-tropical settings: for example, malaria (an important cause of low birth weight) is restricted to the tropics and prophylactic antimalarial drugs in pregnancy reduce the risk of low birth weight. We hypothesized that the relationship between birth weight and BP in African settings might differ from that commonly observed in HICs.
The role of birth weight in the later development of BP is important to African countries: these have a high burden of malnutrition, low birth weight, and raised BP. Early life interventions that reduce maternal malnutrition and extremes of birth weight (both low and high) may thus control childhood BP (before clinical manifestation of disease) and could be vital in the prevention of high BP in adulthood. Birth weight records for adults in many African countries and the low accuracy of maternally recalled birth weight limits prospects for studying the relationship between birth weight and BP in adulthood. However, the emergence of a number of birth cohorts (with birth records) in Africa provides opportunities to investigate the relationship between birth weight and BP among African children and adolescents. Childhood BP predicts BP in early adulthood, thus studies of the relationship between birth weight and BP among children are important in the identification of at-risk groups for targeted interventions early in life. We conducted a qualitative assessment of the direction and consistency of the relationship between birth weight and BP among African children and adolescents using a systematic review of existing literature.

Methods

A literature search covering publications up to 15 October 2016 with no restriction on start date was performed using Medline, EMBASE, Global Health and Web of Science databases. The search was performed on combinations of the keywords: (hypertension OR blood pressure) AND (birth weight) AND (paediatric OR child OR young people OR youth OR juvenile OR adolescent OR youngster OR pubescent OR teenage OR new-born OR minor OR infant) AND (Africa OR individual names of countries in Africa).

Original papers on the relationship between birth weight and BP among children and or adolescents, between ages 0 and 19 years and resident in Africa were reviewed. No restrictions on language or publication dates were applied. Publications on children and or adolescents of African ancestry not residing in Africa were excluded. Papers on the same participants were considered as one study. If more than one paper reported on the same participants at the same age, the most complete paper was included in the review. Papers reporting on the same participants were included and reviewed separately if they reported on the relationship between birth weight and BP at different ages. No additional information was sought from authors. Reference lists of the included papers were searched for additional relevant publications.

Search results were exported to Endnote reference management software (Thomson Reuters, version ×7) and duplicates removed. Two independent authors (S.L. and E.W.) assessed titles and abstracts for inclusion in the full-text review and then assessed full-text articles for inclusion in the data synthesis. Inconsistencies were discussed and consensus reached at each stage of the selection process.

Data were extracted independently by two authors (S.L. and E.W.) using standardized data extraction sheets on the year of publication, year of birth, location, age of participants, study design, number of participants, exclusion criteria, study aim, mean birth weight, source of birth weight data, BP measurement procedure, mean BP [SBP and, or, diastolic blood pressure (DBP)], relationship between birth weight and BP and how this was assessed, and whether there was adjustment for confounders. Information was recorded as presented in the original publication, except where the overall mean BP or birth weight was missing; in this case, where possible the overall mean was calculated from any stratum-specific means presented. Studies were assessed for selection bias and adjustment for confounding. Meta-analysis was not performed due to diversity in studies included in the review, in terms of their design, analysis, source population and covariates controlled for in the analysis. Guidelines from the preferred reporting items for systematic review and meta-analysis (PRISMA) were followed.

Results

A total of 990 published abstracts were retrieved from four databases, of these 366 duplicates were removed, leaving 624 abstracts for review (Fig. 1). Of these, 562 were excluded and of the remaining 62 papers that were subjected to full-text review, 46 were excluded. Of the 46 papers excluded, two papers were duplicates (reported on the same participants at the same age) of one of the included papers. Thus, 16 papers from 13 studies describing, but not necessarily focussing on, the relationship between birth weight and BP were included in the final review and data extraction (Fig. 1).

Of the 16 papers reviewed, six were from West Africa, six Southern Africa, two Central Africa, one East Africa and one North Africa. Four papers from Southern Africa were from the same cohort but presented data on BP at different ages of follow-up. Four papers reported results in neonates (0–28 days), four in children (1–9 years), four in adolescents (10–19 years) and four in both children and adolescents.

The papers were published between 1989 and 2016. The main characteristics of the reviewed papers are shown in Table 1. Briefly, all papers included both males and females. The number of participants ranged from 157 to 2743 individuals per paper, with five papers reporting on more than 1000 participants. Seven papers had less than 500 participants. Two of the reviewed papers did not present quantitative information on the relationship between birth weight and BP. Eleven of the papers (from eight studies) described results from cohorts, while five papers reported results from cross-sectional studies.

Except for one paper, in which the source of participants was unclear, participants were recruited from schools (n = 5), hospitals (n = 4) and communities (n = 6; representing three studies). Preterm children were excluded in seven papers: all four of the hospital-based
studies, one school-based and one community-based. Twins were excluded in six papers (representing three studies). Children who were small for gestational age or who weighed <2.5 kg at birth were excluded from three papers; one in neonates, one in children and one in children and adolescents. There was variability in the study aims of the papers included: only six described assessing the association between birth weight and BP as one of their main aims.

Table 2 summarizes birth weight and BP measurements and values, statistical analysis methods and the relationship between birth weight and BP in the reviewed papers.

**Birth weight ascertainment**

Birth weight was either measured and recorded immediately after birth (predominantly in the cohort studies), or extracted from birth or child health card records. In one study, parentally recalled birth weight was used when birth records were missing (in an unknown number of participants). Mean birth weight varied from 2.4 to 3.4 kg.

**BP assessment**

BP procedures were relatively similar across studies. All studies used automated devices, except for one study, which used the sphygmomanometer machine. Eleven papers reported a resting period (from 5 to 20 min) before proceeding with measuring the BP. In four studies, measurements were taken on the left arm, whereas in six studies measurements were on the right arm; the remaining studies did not include this information.

BP was measured in triplicates in the majority of papers (n = 12) with one paper reporting single measurement, two reporting double measurement and one reporting five measurements. The rest period between consecutive BP measurements varied from 1 to 3 min.

Of the 12 papers that measured BP in triplicate, five used the mean of all three measurements in data analysis, five used the
<table>
<thead>
<tr>
<th>Authors</th>
<th>Year of publication</th>
<th>Year of birth</th>
<th>Place, country</th>
<th>Age at BP assessment</th>
<th>Study size</th>
<th>Study type</th>
<th>Source of subjects</th>
<th>Reason for exclusion</th>
<th>Study aim</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ayoola</td>
<td>2011</td>
<td>NM</td>
<td>Ibadan, Nigeria</td>
<td>1–3 days</td>
<td>436</td>
<td>Cohort</td>
<td>Hospital</td>
<td>Preterm, twins, metabolic defects, congenital abnormalities or severe birth trauma, babies of women with HIV, STDs, hypertension or diabetes</td>
<td>Evaluate the impact of maternal malaria on new-born BP</td>
</tr>
<tr>
<td>Chiolero</td>
<td>2011</td>
<td>1984–1997</td>
<td>Republic of Seychelles</td>
<td>5.5, 9.1, 12.5, 15.5 years</td>
<td>2743</td>
<td>Cohort</td>
<td>School</td>
<td>Not mentioned</td>
<td>Assess the association between BW, weight change, and current BP across the entire age span of childhood and adolescence</td>
</tr>
<tr>
<td>Hawkesworth</td>
<td>2009</td>
<td>1989–1994</td>
<td>West Kiang, Gambia</td>
<td>11–17 years</td>
<td>1267</td>
<td>Cohort</td>
<td>Community</td>
<td>Preterm, implausible BP reading, ambiguity on treatment allocation</td>
<td>Investigate the effect of maternal protein-energy supplementation on BP in adolescence</td>
</tr>
<tr>
<td>Longo-Mbenza</td>
<td>1999</td>
<td>1980–1991</td>
<td>Kinshasa, DRC</td>
<td>5–16 years, mean 11 years</td>
<td>2409</td>
<td>CS</td>
<td>School</td>
<td>Preterm birth, small for gestational age</td>
<td>Examine the possible association between LBW and hypertension later in life</td>
</tr>
<tr>
<td>Margetts</td>
<td>1991</td>
<td>1980–1988</td>
<td>Rural, Gambia</td>
<td>1–9 years</td>
<td>675</td>
<td>Cohort</td>
<td>Community</td>
<td>Febrile illnesses</td>
<td>Relate BP levels in children to their mother’s weight in pregnancy</td>
</tr>
<tr>
<td>Sadoh</td>
<td>2010</td>
<td>NM</td>
<td>Benin City, Nigeria</td>
<td>1–4 days</td>
<td>473</td>
<td>CS</td>
<td>Hospital</td>
<td>Preterm, abnormal APGAR score, congenital abnormality, admission to neonatal unit, babies of mothers with pre-eclampsia or diabetes</td>
<td>Determine the association between maternal and neonatal factors with BP at birth</td>
</tr>
<tr>
<td>Salvi</td>
<td>2010</td>
<td>1986–1990</td>
<td>Medlili, Algeria</td>
<td>15–19 years</td>
<td>568</td>
<td>CS</td>
<td>School</td>
<td>Major disabilities, significant heart disease, renal or liver disease</td>
<td>Assess the association of current body weight and birth weight with BP values in school children living in Algerian Sahara</td>
</tr>
<tr>
<td>Law</td>
<td>2000</td>
<td>1989–1993</td>
<td>Sagamu, Nigeria</td>
<td>3–6 years, mean 4.4 years</td>
<td>293</td>
<td>Cohort</td>
<td>NM</td>
<td>Preterm, weighing less than 2.5 kg</td>
<td>Determine how reduced fetal growth is related to raised BP in countries where chronic malnutrition is common</td>
</tr>
<tr>
<td>Woelk</td>
<td>1998</td>
<td>1987–1989</td>
<td>Harare, Zimbabwe</td>
<td>Mean 6.5 years</td>
<td>583</td>
<td>Cohort</td>
<td>School</td>
<td>Twins, not born in Harare</td>
<td>Determine whether poor uterine growth may be associated with increased BP and subsequent hypertension in adulthood</td>
</tr>
</tbody>
</table>
Determine the factors associated with pulse wave velocity values and propose preliminary reference values in pre-pubertal Angolan school children.

Determine BP values in apparently healthy term newborns in the first 48 h of life and evaluate the factors affecting BP at birth.

Evaluate SBP variations in newborns.

Examine the relationship between BW and BP at 5 years in a cohort of South African children.

Examine the association between early growth and BP trajectories and assess the influence of height on the association between early growth and BP trajectories.

Understand the relationship between household and neighbourhood SES with SBP.

Investigate how linear growth and weight gain relative to linear growth in childhood and adulthood are related to health and human capital outcomes in young adults.

BP, blood pressure; BW, birth weight; DRC, Democratic Republic of Congo; CS, cross-sectional study; LBW, low birth weight; NM, not mentioned; SBP, systolic blood pressure; SES, socioeconomic status.

*Papers from the same cohort (Birth to Twenty cohort).
Table 2. Main results from the studies included in the systematic review

<table>
<thead>
<tr>
<th>Authors</th>
<th>Mean BW</th>
<th>Source of BW data</th>
<th>Mean BP (mmHg)</th>
<th>Procedure for BP measurement</th>
<th>Relationship between BW and BP</th>
<th>Adjusting factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ayoola</td>
<td>2.9 kg</td>
<td>Hospital birth records</td>
<td>SBP = 71.0 DBP = 36.1</td>
<td>With the child comfortable on the mother’s lap for 5 min or asleep, three BP measurements with a minute’s interval between successive measurements were taken on the left arm using a DataScope monitor. Mean of the last two readings was used for analysis</td>
<td>Positive BW–BP association. SBP increased by 8.35 mmHg/kg increase in BW (95% CI: 4.36, 12.35, ( P &lt; 0.001 )). DBP increased by 3.07 mmHg/kg increase in BW (95% CI: 0.26, 5.88, ( P = 0.032 ))</td>
<td>Gestational age, baby length, maternal malaria, age, weight, height, BP, gravidity, antenatal visits</td>
</tr>
<tr>
<td>Chiolero</td>
<td>3.1 kg</td>
<td>Medical records</td>
<td>Could not be determined</td>
<td>After 5 min rest, two BP measurements were taken on the right arm with a minute’s interval between each using automated devices (OmmronM5; Ommron, UK). Mean of the two measurements was used for analysis</td>
<td>No overall BW–BP association. BW was not associated with SBP or with DBP, with exception of girls at 12.5 years among whom BW was inversely associated with SBP (( \beta = 0.9, 95% \text{ CI}: -1.6, -0.1, ( P = 0.026 )) and DBP (( \beta = -0.7, 95% \text{ CI}: -1.3, -0.1, ( P = 0.028 ))</td>
<td>Current weight</td>
</tr>
<tr>
<td>Hawkesworth</td>
<td>2.9 kg</td>
<td>Birth records</td>
<td>SBP = 110.5 DBP = 64.7</td>
<td>Measured in triplicate using the automated Ommron 7051 T device (Ommron), following manufacturer’s instruction. Mean of the three measurements was used for analysis</td>
<td>No association between BW and BP, ( \beta = -0.001, 95% \text{ CI}: -0.002, 0.000, ( P = 0.06 ))</td>
<td>Age, current body size, sex, gestational age, birth season</td>
</tr>
<tr>
<td>Longo-Mbenza</td>
<td>2.4 kg</td>
<td>Parental recall, medical records</td>
<td>Could not be determined</td>
<td>With child in a sitting position and relaxed for 20 min, five BP measurements were obtained using an automatic device (HEM-705 CP; Ommron, Tokyo, Japan). Not clear which measurements were used in the analysis</td>
<td>BW inversely correlated with BP. With ( r = -0.1, P &lt; 0.001 ) for SBP and ( r = -0.1, P &lt; 0.05 ) for DBP. LBW had twice the odds of hypertension OR = 2.0, 95% CI: 0.9, 8.2, ( P &lt; 0.01 ) for SBP and OR = 2.3, 95% CI: 0.6, −11.5, ( P &lt; 0.01 ) for DBP *</td>
<td>NM</td>
</tr>
<tr>
<td>Margetts</td>
<td>3.0 kg</td>
<td>Birth records</td>
<td>1 year: SBP = 89.3 DBP = 56.2, 9 years: SBP = 102.7 DBP = 63.9</td>
<td>After 5 min in a sitting position or on the mother’s knee in the young children, BP was measured twice on the right arm using an automated device (Dinamap model: 18465X). Not clear which measurements were used in the analysis</td>
<td>BW not associated with SBP at any age</td>
<td>NM</td>
</tr>
<tr>
<td>Sadoh</td>
<td>3.2 kg</td>
<td>Hospital birth records</td>
<td>SBP = 69.2</td>
<td>Measured 1 h after feeds between 11:00 and 13:30 using a Dinamap 8100 monitor (Critikon, Tampa Fla) device, when the baby was asleep or awake and calm. Three BP measurements were obtained within 3 min of each other on the right arm. Mean of three BP readings was used in the analysis</td>
<td>Positive BW–BP association. BW was correlated with SBP (( r = 0.235, P = 0.001 )), SBP rose by 3.61 mmHg/0.5 kg increase in birth weight</td>
<td>NM</td>
</tr>
<tr>
<td>Salvi</td>
<td>3.4 kg</td>
<td>Obstetric records in local hospitals</td>
<td>SBP = 118.1 DBP = 69.9</td>
<td>Three BP measurements with 3-min interval between successive measurements were taken on the left arm, after 10-min rest in a sitting position. An automated oscillometric device (Ommron 705 T; Ommron) was used. Average of the three measurements was used for the analysis</td>
<td>No correlation between BW and SBP ( (\beta = 0.4, 95% \text{ CI}: -2.1, 2.9) )</td>
<td>Multivariate analysis was not done</td>
</tr>
<tr>
<td>Law</td>
<td>3.2 kg</td>
<td>Birth records</td>
<td>SBP = 101.6</td>
<td>After 5 min rest, three BP measurements were taken on the left arm using automated BP machines (Dinamap model 8100) with a 1 min interval between consecutive measurements. Mean of the three measurements was used for the analysis</td>
<td>No association between BW and SBP ( (\beta = 0.4, 95% \text{ CI}: -2.1, 2.9) )</td>
<td>Gender, observer, child’s status, (crying or not) current weight and cuff size</td>
</tr>
<tr>
<td>Name</td>
<td>Birth Weight</td>
<td>Birth Method</td>
<td>SBP</td>
<td>DBP</td>
<td>Notes</td>
<td></td>
</tr>
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<td>-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Woelk</td>
<td>3.0 kg</td>
<td>Birth records</td>
<td>SBP = 108.3</td>
<td>DBP = 62.1</td>
<td>With child sitting quietly, BP was measured in the morning on the right arm. Three measurements were taken 2 min apart using a Dinamap model 8100 BP. The average of the last two BP readings was used for analysis.</td>
<td></td>
</tr>
<tr>
<td>Silva</td>
<td>3.2 kg</td>
<td>Birth records</td>
<td>SBP = 102</td>
<td>DBP = 62</td>
<td>No correlation between BW and SBP. After resting for 5–10 min in a sitting position, three consecutive BP measurements were taken on the left arm with 2 min intervals using an automatic sphygmomanometer (model HEM-742; OMRON, Nanjing, China). Mean of last two readings was used for analysis.</td>
<td></td>
</tr>
<tr>
<td>Nwokoye</td>
<td>2.5–4.0 kg</td>
<td>Hospital birth records</td>
<td>Day 1, SBP = 63.3</td>
<td>DBP = 36.8</td>
<td>Positive correlation between BW and SBP. For BW, birth weight; BP, blood pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; CI, confidence interval; LBW, low birth weight; OR, odds ratio; NM, not mentioned; SES, socioeconomic status; r, correlation coefficient; β, linear regression coefficient.</td>
<td></td>
</tr>
<tr>
<td>Youmbissi</td>
<td>3.2 kg</td>
<td>Hospital birth records</td>
<td>SBP = 65.1</td>
<td>DBP = 40.0</td>
<td>Positive correlation between BW and SBP. After 10–15 min rest, a single BP measurement was taken on the right arm when the infant was awake and quiet or asleep and in spine position using an oscillometric machine (Dinamap 8100)</td>
<td></td>
</tr>
<tr>
<td>Levi£</td>
<td>3.1 kg</td>
<td>Birth records</td>
<td>SBP = 108.0</td>
<td>DBP = 62.6</td>
<td>Inverse association between BW and SBP. After 10-min rest, BP was measured in triplicate using a Dinamap vital signs Monitor (1846SX). The lowest DBP with its matching SBP were used in the analysis.</td>
<td></td>
</tr>
<tr>
<td>Kagura</td>
<td>3.1 kg</td>
<td>Birth records</td>
<td>SBP = 114.8</td>
<td>DBP = 71.4</td>
<td>Positive correlation between BW and SBP. After 5–10 min rest, three BP measurements were taken using a digital (Omron M6; Omron) device with a rest of several minutes between successive measurements. The average of the last two measurements was used for analysis.</td>
<td></td>
</tr>
</tbody>
</table>

**Notes:**
- 95% CI and P-value reported as in paper but are inconsistent.
- Mean birth weight not reported and could not be calculated (determined).
- Papers from the same study group (Birth to Twenty cohort).
mean of the last two measurements, one used the lowest DBP (with matching SBP) and one was unclear. For the paper where BP was measured five times and one of the two papers where BP was measured in duplicate, it was unclear which measurements or combination thereof were used for data analysis. In the other paper where BP was measured in duplicate, the mean of the two measurements was used in the analysis.

Among neonates, mean SBP varied from 65.1 to 71.0 mmHg and in children and adolescents from 89.3 to 118.1 mmHg. Mean DBP varied from 36.1 to 63.9 mmHg in neonates and between 56.2 and 71.4 mmHg among children and adolescents. Mean SBP and DBP generally increased with age over the course of childhood and adolescence, this was especially apparent in the four papers that reported results from the same cohort study at different ages.

**Birth weight and BP relationship**

The relationship between birth weight and SBP varied across papers; seven papers reported no association, nine an inverse association, one a positive association, and three a positive association. Among the neonates, three out of four papers reported a positive association while one reported no association. Of the four papers in children, two reported inverse associations and two no association. The papers on children and adolescents predominately found inverse associations (three out of four papers) while among adolescents, three papers found no association and one an inverse association.

Of the seven papers with participant size less than 500 individuals, three papers reported no association between birth weight and SBP, one an inverse association and three a positive association. Studies with larger participant sizes (greater than 500 individuals) more likely to report inverse associations. Of the nine studies with participant size over 500, three reported no association between birth weight and SBP, five an inverse association and one reported a positive association.

In three of the six papers reporting inverse associations, analyses were conducted at different ages and, or, separately for males and females, with inverse associations only seen among particular subgroups (girls at 12.5 years, boys only, and analyses from other subgroups showing no evidence of association.

Analysis approaches used to assess the relationship between birth weight and BP were diverse, varying from simple correlation analysis with no adjustment for potential confounders, to more complex group-based trajectory modelling approaches. Multivariable analysis, adjusting for potential confounder(s) [often including age, sex or body size (weight or height)] was conducted in eight papers, of these five reported an inverse association, two no association and one a positive association. In comparison, of the eight papers that did not undertake adjustment for confounders, one reported an inverse association between birth weight and SBP, five reported no association and two a positive association.

The relationship between birth weight and DBP was described in eight papers; a positive association was seen in two papers, inverse association in two papers and no association was reported in four papers. Of these eight papers, two were in neonates, two in children, three in children and adolescents, and one in adolescents only.

**Discussion**

Overall, this systematic review of existing literature showed varied results. We identified 16 papers from 13 studies addressing the question of whether the inverse relationship between birth weight and BP in later life seen in Western settings is also present in Africa. The relatively small number of studies and their heterogeneity in design and analysis prohibits definitive conclusions. However, we found some evidence to suggest that the relationship between birth weight and SBP in Africa varies with the participants’ age; positive associations were seen in neonates and inverse associations mainly in children. Among adolescents, the relationship was either inverse or showed no evidence of association. Only a few papers reported on the relationship between birth weight and DBP, with most papers reporting no relationship between birth weight and DBP.

This review supports an earlier review by Law that did not include any of the papers reviewed herein (only two of the papers included in the present review had been published at the time of the Law review, and of these Margetts et al. was excluded for missing quantitative information while Youmbissi et al. was not mentioned). The Law review reported inconsistencies in the relationship between birth weight and BP, especially among adolescents. Generally, inverse associations were among children and positive associations in neonates, inconsistencies could be due to differences in age, sample sizes and statistical analysis approaches. Interestingly, results from the cohort studies included in our review, that measured BP at more than one-time point (different ages), did not show evidence of increasing strength of the association between birth weight and BP with age as reported by the earlier review.

Studies in neonates consisted mainly of less than 500 participants and reported positive associations. Studies with smaller participant numbers are more likely to be underpowered to detect real associations, but also to produce spurious positive or negative associations. However, this may not be a factor for the results among neonates, which are consistent.

The relationship between birth weight and BP among adolescents has been reported in previous reviews as either inconsistent or inverse with smaller effects than observed among (pubescent) children. Similarly, this review found an inconsistent relationship between birth weight and BP among adolescents, while the relationship among younger children was generally inverse. The positive relationship observed in neonates is as expected, with the duration between birth and BP assessment too short to allow for any impact of subsequent weight trajectory. Explanations for the changing relationships...
among children and adolescents are uncertain, but could possibly relate to different growth patterns, for example, catch-up growth among those of low birth weight, and hormonal changes occurring at adolescence.12,58

Adjustment for possible confounding factors varied and was often incomplete. Consistent with previous reviews, which mainly included papers from HICs, studies adjusting for current body size (weight and/or height) were more likely to report an inverse relationship59,60 than those that did not make such an adjustment. Adjusting for current size has been noted to lead to a stronger inverse relationship between birth weight and BP compared with results without such adjustments.6 In most of the reviewed papers, that reported estimates adjusted for current size, unadjusted estimates for the effect of birth weight on BP were not reported. Therefore, we were unable to establish whether adjusting for current weight leads to stronger inverse relationships in these populations. The interpretation of findings adjusting for current weight is complex6,59 because current weight may be seen as a confounder or mediator of the effect of birth weight on BP.6

Several mechanisms such as obesity, salt-sensitivity, renin–angiotensin system and endothelial activation are important in the pathophysiology of hypertension. None of the reviewed papers investigated the role of these factors and their impact on BP. Recent evidence suggests that the relationship between birth weight and BP could be U shaped,61 highlighting the importance of both reduced and excessive nutrition in utero. It was not possible to examine this hypothesis from the papers reviewed. Compared with birth weight, other measures such as birth body mass index or pendular index may more accurately reflect the birth size, but none of the studies reviewed included these measures.

Studies were subject to selection bias as individuals most likely to be low birth weight (such as preterm and twins) were excluded in many studies. This could have led to an underestimation of the effect of birth weight on BP. Furthermore, characteristics (such as maternal hypertension, parasitic infections, socioeconomic status (past or current) that influence birth weight and may also be associated with BP in offspring were not adjusted for in these studies. Hence, estimates were subject to residual confounding. It remains uncertain what role (if any) such factors have in the relationship between birth weight and subsequent BP in children or adolescents.

Inconsistencies seen between reviewed papers are less likely to be due to differences in BP measurement procedures, as studies followed a similar approach. For nearly all papers, there was an initial rest period (before starting BP procedure) and between successive BP measurements, automated devices were used and analysis was based on the average of two or three measurements. In the majority of studies, early life information including birth weight was prospectively collected thus studies were less prone to misclassification and recall bias.

Generally, studies reviewed came from all the African regions but with a strong representation of West Africa and Southern Africa. East Africa and North Africa had the least number of papers (one each) reviewed. The only paper from East Africa reported on an island population, thus there were no results on the mainland population of East Africa.

In conclusion, relatively few studies have investigated the relationship between birth weight and BP later in life in Africa. The relationship between birth weight and BP varied depending on the age of the participants. Our review emphasizes the need for larger studies on the relationship between birth weight and later BP from Africa, applying appropriate control of potential confounding factors. Accumulating evidence on raised BP in Africa and understanding the impact of growth in early life and of prenatal exposures on BP later in life is key in identifying at-risk groups and developing early life interventions to reduce BP risk in later life.

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Ethical Standards
Review was based on published manuscripts thus ethical approvals were not required.

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Conflicts of Interest
None.

References


