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Nutrition, growth, and other factors associated with early cognitive and motor development in Sub-Saharan Africa – a scoping review

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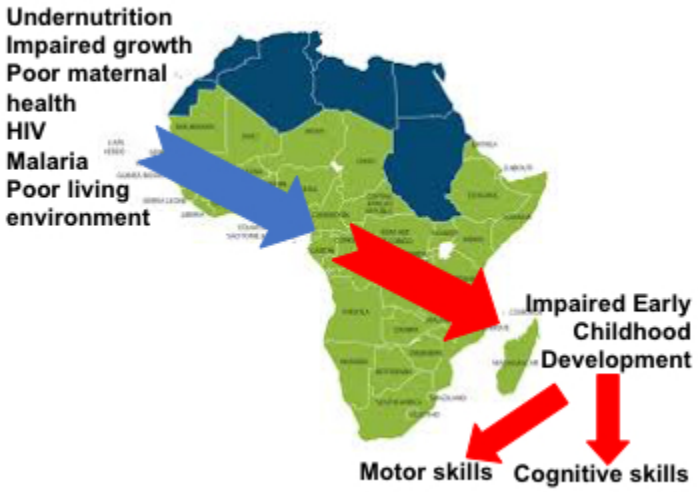

Figure 1. Graphical abstract
Poverty, poor maternal health, malnutrition and exposure to infectious disease blights the development of cognitive and motor skills in children living in Sub-Saharan Africa. This scoping review considers factors which hinder development of early cognitive and motor skills, and subsequent achievement of potential. The methodological limitations of conducting research using Western methods in this region are significant and more robust approaches are required to address this critical issue.

189x150mm (54 x 54 DPI)

Nutrition, growth, and other factors associated with early cognitive and motor development in Sub-Saharan Africa – a scoping review

Abstract

Background: Food insecurity, poverty, and exposure to infectious disease are well-established drivers of malnutrition in children in Sub-Saharan Africa. Early development of cognitive and motor skills – the foundations for learning – may also be compromised by the same or additional factors that restrict physical growth. However, little is known about factors associated with early child development in this region, which limits the scope to intervene effectively. To address this knowledge gap, we compared studies that have examined factors associated with early cognitive and/or motor development within this population.

Methods: Predetermined criteria were used to examine four publication databases (PsychInfo, Embase, Web of Science, and Medline) and identify studies considering the determinants of cognitive and motor development in children aged 0-8 years in Sub-Saharan Africa.

Results: 51 quantitative studies met the inclusion criteria, reporting on 30% of countries across the region. Within these papers, factors associated with early child development were grouped into five themes: Nutrition, Growth and Anthropometry, Maternal Health, Malaria and HIV, and Household. Food security and dietary diversity were associated with positive developmental outcomes, whereas exposure to HIV, malaria, poor maternal mental health, poor sanitation, maternal alcohol abuse, and stunting were indicators of poor cognitive and motor development.

Discussion: This synthesis of research findings shows across Sub-Saharan Africa, factors which restrict physical growth also hinder development of early cognitive and motor skills, but additional factors also influence early developmental outcomes. It also reviews methodological limitations of conducting research using Western methods in sub-Saharan Africa.

Introduction

According to the World Health Organisation (WHO) early child development spans the ages of 0-8 years. This is a critical and formative period in a child's life when the brain is developing rapidly and core cognitive and motor skills, the foundations for later learning[1], are being acquired. It is estimated that 250 million, or 43% of children living in low-to-middle-income countries fail to reach their full cognitive and educational potential[2]. The vast majority of these children live in Sub-Saharan Africa[1] where there is also a high prevalence of stunting[1] and malnutrition[3]. Many low-income countries in Sub-Saharan Africa are burdened with high rates of maternal, infant, and childhood mortality as well as undernutrition. These are driven by various factors including but not limited to: lack of maternal education, poor sanitation, exposure to human immunodeficiency virus (HIV), and low rates of exclusive breastfeeding[4]. Coupled with economic and gender inequalities, factors which operate in the first 8 years of life result in many children failing to achieve their educational potential. A prolonged history of poor and unequal early child development and learning is shown across Sub-Saharan Africa,[5] which impacts on the long-term economic growth and welfare of the population. Early child development encompasses several aspects of development including physical, cognitive, psychosocial, and motor development. Factors that impact on development, such as nutrition, play an important role in developmental delay. A combination of adverse health environments (e.g. undernutrition and repeated infection) during key periods of development, and inadequate provision and uptake of schooling, maintains a cycle of poor cognitive and physical development, poverty, and inequality, which inevitably passes to subsequent generations.

Cohort and longitudinal studies can examine relationships between nutritional status, prevalence of disease, maternal deprivation, and access to health care, and how these factors are associated with child growth and development over sustained periods of time[6]. Accordingly, recent years have seen an increase in cohort and longitudinal studies in low-to-middle-income country settings, including Sub-Saharan Africa. Increasingly, these studies are considering outcomes on cognitive and motor development – the foundations for learning – that can have long-term sequelae[7,8], but for Sub-Saharan Africa there is currently a lack of clear consensus on which factors have a detrimental or positive influence.

This scoping review considers factors associated with early child development in Sub-Saharan African countries. Though of limited usefulness in terms of providing quantitative data relating to specific research questions, scoping reviews are an ideal tool to determine the

range or coverage of literature on a given topic and explore emerging evidence. They give a clear indication of the volume of studies available as well as an overview of their focus. This review focused solely on cognitive and motor development as these are foundational skills that underpin educational potential and scholastic achievement[9-11]. Considering only cohort and longitudinal studies, the review assessed multiple factors that might influence cognitive and motor development in children under the age of 8 years, with a strong focus on the first two years of life. Enhancing understanding of how early nutrition and other environmental factors influence early child development is important for countries across Sub-Saharan Africa to break the cycle of poor cognitive and motor development which limits educational potential and attainment. By assessing current evidence, this scoping review aimed to identify key factors that are associated with early development of foundational skills that are core to later learning[1,12].

Method

This review aimed to scope previous and current cohort and longitudinal studies conducted across Sub-Saharan Africa that had examined cognitive and motor development across early childhood.

Inclusion criteria

Type of studies

Published and peer-reviewed quantitative studies were examined, including cohort and longitudinal studies with experimental and observational designs.

Type of population

Studies examining children aged between 0-8 years were reviewed. If a wider age range was reported, age-specific findings were extracted and reported separately.

Phenomena of interest

This review focused on factors that influence cognitive and/ or motor development in Sub-Saharan countries as these are foundational for later learning potential.

Type of Outcome

The primary outcome was the measurement of cognitive and/or motor development and the factors that influence these developmental processes. For inclusion, studies were required to

provide clear details on the measurements used (outcome variables and controls), ideally including details on how measures were adapted for low-to-middle-income country contexts. However, if no such adaptation contexts were mentioned, studies were still included to examine the extent to which Western measures of early child development were employed.

Context

This review included studies conducted in Sub-Saharan Africa or that included at least one site within Sub-Saharan Africa. Sub-Saharan Africa is defined as the geographical area of the continent of Africa that lies south of the Sahara and includes 46 countries.

Exclusion criteria

Qualitative studies, mixed methods studies, literature reviews, unpublished and grey literature were excluded. Studies were also excluded if they did not specify the precise location, details of measurement of cognitive and motor development, or did not report separate findings between age groups if including older children. Studies that did not use a longitudinal or cohort design were also excluded. The inclusion and exclusion criteria are summarised in Table 1.

Search strategy

Four databases (PsychInfo, Embase, Web of Science, Medline) were searched from inception to extract published studies. Following the search of these main databases and removal of duplicates, an initial search and preliminary analysis was conducted of the subject headings (MeSH) and text words related to early child development contained in the title and abstract.

The search strategy comprised a combination of key words (e.g. 'Early Child Development', 'Sub Saharan Africa') and controlled vocabulary (e.g. 'health', 'growth'). A full search strategy for Medline (MEDLINE In-Process & Non-Indexed Citations and OVID MEDLINE 1946 to present-Ovid) is detailed in Supplementary Table 1, as an example. The search was first performed on the 18th of December 2018 and conducted again on the 8th of October 2019. Date and language limits were not imposed.

Reference lists of all selected papers that met the inclusion criteria were hand searched to check for additional studies.

Study selection

Following the search, all identified citations were uploaded into Endnote and duplicates were removed. The review authors independently screened the titles and abstracts for assessment

against the search inclusion criteria. Full texts were obtained for all titles that appeared to meet the inclusion criteria.

A main review author (BF) screened and assessed the full text reports in detail against the inclusion criteria (see Table 1). Studies that did not meet the inclusion criteria were excluded. A record of excluded studies, including reasons for exclusion, is provided in the PRISMA flow diagram[13] (Figure 1).

Data extraction and outcomes

Data extraction

One reviewer (BF) extracted data from the included studies, informed by a standardised data extraction tool for quantitative studies (JBI- MAStARI[14]) and this was checked by a second reviewer (LO). The extracted data included specific details relating to the inclusion criteria (see Table 1), which address the main aim of this scoping review.

Outcomes

The main outcome was the exploration of measurement of cognitive and motor development in young children aged 0-8 years in Sub-Saharan African countries and the factors influencing them. Multiple types of factors reported in the selected studies were evaluated, such as child health, growth, and development. These factors were grouped into themes within the synthesis phase and subsequently grouped into factors associated with the acquisition of early cognitive and motor skills.

Assessment of methodological quality

Following quality assessment reviews guidelines[15], two review authors (BF and LO) critically appraised all selected studies for methodological quality using standardised quality appraisal tools for quantitative studies) (JBI Critical appraisal checklist for case studies, JBI Critical appraisal checklist for cohort studies, JBI RCTs appraisal tool [8]). These instruments assess the quality of evidence across studies with different designs, including but not limited to criteria, such as sampling strategy, analysis, transparency, and interpretation. Any disagreement between reviewers was resolved through discussion. Studies were stratified in Table 2 according to the result of the quality assessment. Study quality score did not affect inclusion in the review; all studies that met the inclusion criteria were subjected to data extraction and synthesis.

Following Kmet, Lee and Cook's[8] guidelines, an original quality score from 0 to 1 was calculated for each study. Scores were then classified from low (0 - 0.44), moderate (0.45 - 0.69), and high (0.70 - 1.00). Study quality was assessed by the two reviewers (BF and LO). Initial agreement between reviewers was 89% overall and all disagreements were resolved through discussion. Some variation in quality was shown across 51 studies included in this review. The average quality score was 0.67, which was comprised of 28 studies that received a high-quality rating, 19 studies that received a moderate-quality rating, and four studies that received a low-quality rating.

Data synthesis

Two reviewers (BF and LO) conducted the syntheses in a sequential order. One reviewer (BF) developed the synthesis and the second reviewer (LO) checked the findings. Any disagreements were discussed (initial agreement of 80%) and a mutual resolution was found. Once data was extracted in descriptive form, and according to JBI scoping review guidelines, quantitative synthesis was generated and summarised in thematic statements[14]. There was a high level of heterogeneity within the included studies which precluded statistical pooling of extracted data. Consequently, an inductive approach of a narrative synthesis of the extracted data was deemed most appropriate. Configuration of all themes generated a set of statements that represent the final aggregation.

Factors extracted for this review that were found to influence early cognitive and motor development were categorised into five main themes, these being: Nutrition, Growth and Anthropometry, Maternal Health, Malaria and HIV, and Household and other factors.

Results

Study selection

The study selection process is illustrated in Figure 1. In total, 51 studies published between 1991 and 2019 met the inclusion criteria. Of these 29 (57%, 11 in 2017, 10 in 2018 and 4 in 2020) were published after 2016, when The Lancet published a special edition of research papers focused on this topic.

Table 2 summarises the extracted data for each study included in the review. Amongst the included studies, a range of 14 Sub-Saharan countries were represented with 12 studies

originating from South Africa, eight from Ethiopia, six from Tanzania, five from Malawi, four from Kenya, three each from Ghana and Zambia, two each from Uganda, Botswana, and Benin, and one each from Gambia, Sudan, Rwanda and Congo. A range of methodologies were reported in the studies included in this review: most were prospective or longitudinal cohort studies and four randomised control trials were also included. There was high variability in sample size, ranging from 85 to 4205. In addition, attrition varied at follow-up from 0% to 95.3%. Twenty-seven (53%) of the 51 studies included in this scoping review reported change of numbers in at least one point of follow up; the rest of the studies did not include data on participants lost to follow up. Of the 27 studies that reported on follow up, a mean attrition of 47.8% (SD = 26.2%) was found (note: for the 5 studies that reported on more than one point or group at follow-up, mean attrition was calculated and used to determine the grand mean). For most studies, limited information, if any, was given as to why loss at follow up occurred. More details are provided in Table 2.

Measures used in assessing cognition and motor development

Amongst the studies included in this review, a wide range of tools were used to assess cognitive and motor development, making it difficult to generalise findings (Table 3). The most common assessment tool used was the Bayley Scale of Infant Development (BSID), which was employed in 20 of the 51 (39%) studies reviewed.

Data extraction and summary of results

Results revealed many factors associated with early cognitive and motor development. These factors were grouped into five main overarching categories. These categories were interlinked, reflecting a multi-level framework, and demonstrating that no individual category could explain differences in early cognitive and motor development across Sub-Saharan Africa.

The five main categories of factors highlighted by this review include: Nutrition, Growth and Anthropometry, Maternal Health, Malaria and HIV, and Household.

Nutrition

The first group of factors influencing early cognitive and motor development related to infant and maternal nutrition. Principally, studies looked into the effect of nutrition and nutrients[16-20], and vitamin supplements[21-24].

Studies reporting on the influence of food consumption on early child development showed that children living in households that experienced food insecurity in the first two years of life had low gross motor, communication, and personal social scores[18]. Conversely, dietary diversity, child iron status, and early nutritional interventions that increased birth weight and growth in the first two years were associated with improved growth, language skills, and motor development[19].

Less than optimal micronutrient status was a strong focus on the influence of nutrition on early child development, but most studies[21-24] found no impact of nutrient supplementation (zinc, multivitamin, iron and ferritin) on young children. Two studies investigating the differences between groups of infants taking zinc and vitamin supplements in Zambia[22] and Tanzania[21] found no difference in motor and cognitive development compared to placebo controls. Similarly, Mireku and colleagues (2016) demonstrated that prenatal iron deficiency and low neonatal ferritin were not associated with poor cognitive or gross motor function, although a negative relationship between gross motor function and children's haemoglobin concentration was reported[24]. Cognitive development and linear growth at age 4-6 years was also reported by Ocansey et al. (2019) to be significantly associated with haemoglobin concentration at 18 months[25], but unlike Mireku et al (2016), Ocansey et al. (2019) found no association with motor development. A randomised control trial (RCT) exploring prenatal supplementation with vitamin A and zinc[21] reported no developmental benefits in children of women consuming the supplement.

Growth and anthropometry

Growth and anthropometry encompass many different aspects of children's physical health. Many studies evaluated the influence of children's physical health on their early cognitive and motor development. While some studies focused on stunting and growth[10,14,21-25], others focused more specifically on anthropometry at birth[31-34]. Most studies found a strong relationship between restricted physical growth and poor early cognitive and motor outcomes.

Stunting is defined as the impaired linear growth of children who experience poor nutrition or repeated infection[2]. Stunting and impaired growth were shown to be strong predictors of poor cognitive and motor development[16,20,30,34]. In exploring the long-term effect of stunting, Crookston and colleagues (2013) demonstrated that height-for-age was positively associated with mathematics achievement, reading comprehension, and receptive vocabulary. Children persistently stunted between early and late childhood faced more adverse outcomes at school

compared to those who were never stunted[29]. Moreover, children who recovered from stunting showed persistently low cognitive test performance that was commensurate with the performance of children who remained stunted[26], demonstrating a long-term impact of early stunting into later childhood. Whilst these studies largely supported a negative influence of stunting on developmental measures, one study based in Tanzania showed weight-for-age and weight-for-length scores were positively associated with gross motor scores, but not for other measures of motor and cognitive skills[28].

Anthropometry at birth was explored in relation to long-term early child development. Length-for-age scores at birth and at 6 and 18 months were associated with cognitive, but not motor development in children aged 4-6 years in Ghana[25]. High fat mass in the first 48 hours of birth predicted high global developmental scores[31]. A study based in South Africa showed that very low birth weight was not predictive of neurodevelopmental outcomes[32]. Infants born preterm (<37 weeks gestation) in Malawi had a high rate of developmental delay at 18 months, which was inversely associated with gestational age[33].

Maternal Factors

Maternal factors were investigated primarily in relation to maternal mental wellbeing. General maternal health and mental disorders[30-33], post-traumatic stress disorder (PTSD)[31], and foetal alcohol spectrum disorder (FASD)[40] were discussed as factors affecting outcomes in early childhood.

Accumulated exposures to maternal risk factors, for example, low socio-economic status (SES) and domestic violence, were shown to have a stronger association with child cognitive and motor development, compared to common maternal mental health disorders, such as depression or anxiety[37]. Infants with FASD in South Africa were shown to have impaired performance on all scales of mental development of the BSID[40]. Several maternal protective and risk factors were associated with cognitive and motor developmental outcomes. For example, maternal education and SES were shown to ~~the~~ be protective factors whereas maternal anaemia in pregnancy, depression, partner violence, and HIV infection were shown to ~~the~~ be risk factors[41]. Maternal weight and diet also influenced neurobehavioural and motor performance at birth and at 6 months. Greater maternal dietary quality was associated with better infant motor performance[17].

While common maternal mental health disorders influenced child absenteeism and school dropout, it did not affect child academic achievement[36]. Other factors such as mother's access

to antenatal care were found to be related to improved child cognitive development[30,36]. Meanwhile, low maternal height, delivery characteristics (e.g. oxytocin administration) were associated with cognitive and development outcomes at 15 months[38]. Maternal PTSD was associated with poor fine motor and poor adaptive motor development in children[39]. Finally, greater caregiver/child stimulation was found to predict higher child cognitive scores and maternal completion of primary school was associated with higher child motor and cognitive scores[43].

Malaria and HIV

Studies included in this review also considered the relationships between child development and malaria or HIV (5 studies on malaria and 11 studies on HIV). Malaria studies focused primarily on cognitive development[44-47] while HIV studies incorporated both cognitive and motor development[29,42-52].

Studies investigating the impact of malaria on early child development have produced inconsistent findings. Bangirana and colleagues (2014) reported that Ugandan infants with cerebral malaria and severe malarial anaemia had lower scores in cognitive ability, attention and associative memory at 12 months than their control peers. Similarly, exposure to the malaria parasite in early childhood was associated with lower tolerance of the testing procedure of the cognitive tasks at 6 years[46]. When tested at 5 years of age, children with malaria in a cohort study based in Malawi[47] showed on average a 6-month delay in motor, language and social development. Despite this, no difference in age-expected attainment was found for cognitive skills compared to control[45].

Studies on HIV have consistently demonstrated impairment of cognitive and motor functions in children and infants with HIV[29,47] showing delayed attainment of developmental milestones[48], including gross motor skills[54] and neurodevelopment deficits[49] compared to uninfected children. Leroux and colleagues (2018) reported delays in cognitive and motor development but highlighted no delays in expressive language scores at 18 months. The effects of HIV infection on development can be overcome with treatment. Three studies investigated the outcomes of HIV care and demonstrated that infected infants and children who received HIV care achieved similar cognitive and motor scores to uninfected children at 6, 12 and 24 months[56-58].

Children can also be exposed to HIV in utero without becoming infected. Studies of HIV-exposed uninfected infants have yielded inconsistent results. Whilst, Brahmbatt and

colleagues (2014) found that HIV exposure alone was associated with impaired receptive language skill in children and generally poor early child development, other studies found no difference in cognitive and motor development of infants and children exposed to HIV and their non-exposed peers[44,45,49].

Household and other factors

Many household factors were found to be associated with early child development. This highlights the importance of the environment that children grow up in for supporting the acquisition of cognitive and motor skills. Studies investigating household factors have examined SES[10,23,37,53], sanitation and water[14,54], access to antenatal care[35], orphanage[61], and insecticide exposure[62].

Investigations into the effect of SES on early child development have produced mixed findings, which might reflect differences in how SES is conceptualised and measured in different contexts and different countries. One study reported no effect of SES (measured by a household asset index) on early child development but rather area of residence (established by geographical area) was associated with early developmental outcomes[16]. In contrast, other studies demonstrated that SES (measured by a socio-economic questionnaire and household wealth) was linked to child language development[59] and cognitive scores at 15 months of age[28].

Access to improved water (i.e. piped water, public tap or standpipe, tube well or borehole, protected dug well, protected spring, and rainwater collection) at 1 year of age was associated with higher language scores in children at 5 and 8 years[60] and access to a flush-toilet in the home/village environment was associated with higher cognitive and motor scores in children aged 18-36 months compared to those where a flush-toilet was not available[20].

Attendance at antenatal care by mothers was shown to have a positive association with cognitive development at age 5[35]. Whilst orphaned infants showed impairments in psychomotor development at admission (1 month old), over 85% of orphaned children showed age-appropriate development by 18 months[61].

Finally, a study investigating exposure to insecticide showed no significant relationship with cognitive development[62]. Other factors also investigated in some of the studies included the influence of twin birth[63], ethnicity[64], early mental development[65], and birth asphyxia[66] on early child development. These studies demonstrated that twin birth was associated with delayed attainment of motor development milestones[57], and factors linked to ethnicity such as

family stability and income were positively associated with motor and language development[58]. Moreover, poor mental development at age one was associated with poor cognitive development at age 5[59]. Regular treatment of asphyxia after birth was associated with good cognitive scores at three years of age. Prado et al. (2018)[13] also considered the influence of access to play materials and activities with caregivers on early language and motor development and showed a positive association of these factors on growth and language development.

Discussion

The aim of this review was to scope published literature reporting on factors associated with early cognitive and motor development in Sub-Saharan Africa. A detailed understanding of these factors is a prerequisite for design of future longitudinal cohort studies and interventions targeted at improving the lives of children living across this region. A clear need for focussed research in this area was revealed. In total, only 51 studies have been published in the past 28 years (between 1991 and 2019) which met the inclusion criteria, with the majority of studies (90%) being published in the past 10 years. The recent rise in studies focusing on this topic demonstrates increasing awareness of the need to enhance understanding of factors influencing development of foundational skills that underpin later learning potential[67]. This is a critical step for countries to be able to meet the 2030 United Nations Sustainable Development Goals.

Only 14 (30%) of the 46 countries comprising the Sub-Saharan Africa region were included in the 51 studies that met the inclusion criteria for this scoping review. The absence of relevant studies from the remaining 37 countries of Sub-Saharan Africa, demonstrates an alarming lack of knowledge about factors influencing early cognitive and motor development across more than 70% of the region. Whilst the factors identified in this scoping review may apply to other countries in the region, this needs confirmation from quantitative longitudinal cohort studies. The results of this scoping review are therefore important for guiding future research.

The 51 studies included in this review identified multiple factors that broadly addressed five key themes, namely Nutrition, Growth and Anthropometry, Maternal Factors, Malaria and HIV, and Household. Although these factors may operate in isolation, it is likely that they will interact with a multiplicative effect to influence on the development of early cognitive

and motor skills. This emphasises the importance of adopting a multi-level conceptual framework of early child development across Sub-Saharan Africa that describes the complexity by which different factors influence early developmental outcomes that underpin potential to succeed at primary school.

Childhood nutrition, growth, and maternal health were the factors with the most frequently reported influence on early child development, with infectious diseases such as HIV and malarial infection also playing a key role. Whilst infectious diseases such as tuberculosis, gastrointestinal infections or measles are common in Sub-Saharan Africa, the studies in this review only investigated the influence of Malaria and HIV on development, demonstrating a significant lack of research in the influence of other infectious diseases in Sub-Saharan Africa. There is a well-established interrelationship between nutrition and infectious disease which is often driven by SES, and has been shown to influence physical growth, stunting and wasting. Maternal health and nutrition during pregnancy is a key driver of growth outcomes for children[4]. The papers identified in this scoping review indicate that this is also the case for early cognitive and motor development. Maternal nutrition and lack of specific nutrients for mothers, during pregnancy and early years were also shown to have long-term impact on child development. This has been recognised previously in randomised control trials considering the influence of iron deficiency on cognitive and motor development[68]. Less than optimal maternal nutrition and health directly influences children's health and growth which are also related to early cognitive and motor development. The broader literature on nutrient deficiency and cognitive development suggests that the window of time for intervention is limited and cognitive deficits at an early age have lasting effects on brain development[69]. However, the studies included in this review demonstrated limited positive effects of supplementation of micronutrients. While maternal and child health encompassed the main factors affecting early child development highlighted by this review, it is also important to note that household and other factors also need to be considered. This review showed that household determinants, such as access to sanitised water or access to antenatal care, influence cognitive and motor development in Sub-Saharan Africa, in a similar way to the risks of stunting and wasting.

Methodological considerations were also emphasised by this review. Sample size and attrition were highly variable across studies, which raises concerns about data security and limits the extent to which comparisons across studies can be drawn. Of the studies that reported on attrition, on average 47.8% of the original sample was lost at follow up. Future

research should take this into account when recruiting new participants to ensure sufficient statistical power at follow-up.

Many studies relied on the use of psychometric tools validated for Western populations for measuring early cognitive and motor development in Sub-Saharan African countries. The use of assessment tools used in Western cultures has been shown to be somewhat problematic[72]. Motor and cognitive development need to be assessed in relation to cultural and environmental factors. For instance, motor assessment in Western countries include developmental stages such as climbing steps which is not necessarily relevant in some low-to-middle-income settings where steps are not a prevalent feature of many family homes. Adapting these tools by excluding such tasks is not necessarily appropriate, so using a culturally relevant tool, such as the Malawi Development Assessment Tool[73] for studies conducted in Malawi for instance, might be more fitting.

The Bayley Scale of Infant Development (BSID) was the most frequently used psychometric tool used to assess early child development in the studies covered by this review. This measure is recognised internationally as one of the most comprehensive tools to assess children from as young as one month old and with the latest version of this tool, BSID-III, it is possible to obtain detailed information even from non-verbal children as to their level of functioning. However, while the BSID is considered a valid and reliable measure of early child development for Western populations, there are a number of practical barriers to use in Sub-Saharan contexts, including the high cost for materials, the need for specially trained administrators and the relatively long administration time[74]. Furthermore, the use of the BSID and other Western assessments is often inadequate in developing countries [75]. The BSID was developed in the US, a Western, high-income country, and may not translate to low-to-middle-income country contexts[72]. Furthermore, the use of norm-referenced scores based on high-income-country contexts are not valid in low-income countries and may lead to children being misclassified as having developmental delay[76] and produce misleading results. Adapting psychometric tools to be culturally appropriate for low-to-middle-income contexts can overcome this problem. Hanlon et al. (2016)[77] successfully adapted the BSID for use in rural Ethiopia by translating and modifying the test materials, instructions and concepts measured. There are several emerging assessment tools that have been specially designed for use in low-to-middle-income countries. For example, the Intergrowth 21st Neurodevelopmental Assessment (Inter-NDA) is a holistic and objective measure of early child development that has been trialled in a broad range of 13 countries (none in Sub-

Saharan Africa) and validated against the BSID-III. The Inter-IDA items have been specially designed to be culture-free and easy and reliable to administer by non-specialists in low-to-middle-income contexts[78].

Country-specific distributions can be used to identify children 'at risk' with greater ecological validity than comparing to Western norms. Whilst this relative method of identifying children at risk would enable comparison between countries, it is important to note that absolute levels of ability might differ across countries. This would result in some children being identified as at risk for poor early outcomes in some countries, who would not be classified at risk in other countries where the distribution of scores was lower, and vice versa. Direct comparison of test performance across countries is only meaningful when both the average (mean/median) and distribution of test scores is similar. ~~We recommend that measures of early child development that have been developed and norm-referenced for Western, high-income, countries are validated by low-income countries before adopting them as an outcome measure in studies examining early child development. This can determine the extent to which they are suitable for administration in specific country contexts without adaptation. Depending on the results of the validation study, adaptation to test materials might be required before they are considered appropriate for use in a given context and before population distribution data is obtained.~~

This scoping review has demonstrated that birth cohort and longitudinal studies are a viable method for investigating a range of multi-level factors in early childhood in Sub-Saharan Africa. Ongoing birth cohort studies are also considering a wider range of determinants of early child development than have been studies previously. For example, the Drakenstein Child Health Study follows a multi-level, ecological approach to understand cognitive, socio-emotional and neuropsychological child development[79]. The Malnutrition and Enteric Disease Study (MAL-ED) multi-site birth cohort study is also examining child development and language acquisition from birth to 24 months in eight low-to-middle-income countries[80,81]. Consistent with previous research, data from the MAL-ED project in Tanzania showed child weight-for-age, weight-for-length, SES and female gender were associated with cognitive and motor development [28]. However, Donald et al.[79], Caulfield et al.[80], and Murray-Kolb et al.[81] all highlight important issues surrounding measurement and data collection in low-to-middle-income contexts, which can impact on results.

Future research should further investigate the multiple factors highlighted in this review, taking into consideration the cultural and environmental setting of different study sites. While

maternal and child health factors are prominent areas of research, the findings from this review are somewhat contradictory. Future research should aim to gain a clearer understanding of why this is and how factors such as HIV or nutrition affect early child development. This would allow for better targeted interventions and guidelines to be implemented to mitigate risk of childhood morbidity and underachievement at school.

As the number of cohort studies being conducted in other low-to-middle-income countries increases, there could be potential for cross-cultural comparisons. This could further inform theoretical and practical understandings of generic factors that are associated with early child development in low-to-middle-income country contexts compared to country-specific factors. Studies in Latin America, for example, show that specific nutrient deficiency (iron) influence early child development[82] and the meta-analysis by Ip et al. (2017)[83] of randomised control trials of nutritional supplements showed improved cognitive function in children in several developing countries, including Bangladesh, Chile, China, Colombia, Guatemala, India, Indonesia, Jamaica, Mexico, Nepal, Pakistan, Peru, Thailand, Vietnam, as well as several nations in Sub-Saharan Africa. However, in the context of uncontrolled observational studies, findings from a wide representation of multiple types of backgrounds and study sites might not be generalisable over all contexts. The sample of studies included for this scoping review was skewed by a strong prevalence of studies from South-Africa (12 out of 51), and mainly from urban sites, which might not reflect the conditions of other countries and settings.

~~*Limitations*~~

This scoping review has highlighted several factors that influence early cognitive and motor development in infants born across Sub-Saharan Africa. Despite the serious consequences of poor early child development on an individual's potential and a country's economic growth, surprising few studies have focussed on this important issue. Many studies reported on one particular factor, and there was variability across findings, so it is difficult to generalise results until a more comprehensive evidence base exists. Drawing firm conclusions was a challenge for this review due to variabilities in reporting, methodology and quality of the literature. As such, the results from this scoping review should be treated as early indications of how different factors influence early cognitive and motor skills, until further studies are available to enable general trends to be established through replication and reproducible findings. ~~The studies reviewed here also show high variability in sample size and attrition, which can bias findings, especially with small samples and high levels of attrition. In addition, there is variability across studies in the conceptualisation and measurement of~~

~~different factors and skills, which makes drawing conclusions difficult. To enable generalisation within and across countries, studies need to adopt a consistent conceptual framework and ideally utilise the same tasks to measure early cognitive and motor skill, with appropriate norms. As development is a dynamic process that changes over time, a finding at one point in time is not necessarily indicative of outcomes at a later point in development. Downstream effects mean that secondary impairments can emerge later in the developmental pathway for functions that are reliant on the development of a specific function acquired at an earlier age.~~

~~To address these limitations, longitudinal monitoring is required across the first 8 years in life, and beyond. Cohort studies are needed, ideally from pregnancy or birth, across the early childhood period to enable a greater understanding of factors that influence early cognitive and motor skill to be determined. These are difficult to conduct largely because they require acquisition of big datasets across a long period of time and are thus costly. Nevertheless, longitudinal pregnancy or birth cohort studies are the best methodology for addressing this issue. Benefits might also be gained from utilising applied statistical techniques that enable different datasets to be combined in a meaningful manner. These techniques are starting to emerge from the work of big data scientists and have the potential to be transformational when applied to understanding factors that influence the process of early child development across Sub-Saharan Africa. Accordingly, we call upon funding agencies to invest in these methods, if we are to gain a better understanding of what causes poor developmental outcomes in early childhood, how best to intervene, and ultimately how to prevent the cycle of poverty that mars these countries.~~ *Recommendations for future research*

This review has uncovered a number of significant omissions and inconsistencies in the evidence base relating to early life influences on cognitive and motor development. To enable generalisation within and across countries, studies need to adopt a consistent conceptual framework and ideally utilise the same tasks to measure early cognitive and motor skill, with appropriate norms. As development is a dynamic process that changes over time, a finding at one point in time is not necessarily indicative of outcomes at a later point in development. Downstream effects mean that secondary impairments can emerge later in the developmental pathway for functions that are reliant on the development of a specific function acquired at an earlier age. ~~To address these limitations,~~ Llongitudinal monitoring is required across the first 8 years in life, and beyond. Cohort studies are needed, ideally from pregnancy or birth, across the early childhood period to enable a greater understanding of factors that influence early

cognitive and motor skill to be determined. These are difficult to conduct largely because they require acquisition of big datasets across a long period of time and are thus costly. Nevertheless, longitudinal pregnancy or birth cohort studies are the best methodology for addressing this issue. Benefits might also be gained from utilising applied statistical techniques that enable different datasets to be combined in a meaningful manner. These techniques are starting to emerge from the work of big data scientists and have the potential to be transformational when applied to understanding factors that influence the process of early child development across Sub-Saharan Africa. Accordingly, we call upon funding agencies to invest in these methods, if we are to gain a better understanding of what causes poor developmental outcomes in early childhood, how best to intervene, and ultimately how to prevent the cycle of poverty that mars these countries.

We further recommend that measures of early child development that have been developed and norm-referenced for Western, high-income, countries are validated by low-income countries before adopting them as an outcome measure in studies examining early child development. This can determine the extent to which they are suitable for administration in specific country contexts without adaptation. Depending on the results of the validation study, adaptation to test materials might be required before they are considered appropriate for use in a given context and before population distribution data is obtained.

~~To address these limitations, longitudinal monitoring is required across the first 8 years in life, and beyond. Cohort studies are needed, ideally from pregnancy or birth, across the early childhood period to enable a greater understanding of factors that influence early cognitive and motor skill to be determined. These are difficult to conduct largely because they require acquisition of big datasets across a long period of time and are thus costly. Nevertheless, longitudinal pregnancy or birth cohort studies are the best methodology for addressing this issue. Benefits might also be gained from utilising applied statistical techniques that enable different datasets to be combined in a meaningful manner. These techniques are starting to emerge from the work of big data scientists and have the potential to be transformational when applied to understanding factors that influence the process of early child development across Sub-Saharan Africa. Accordingly, we call upon funding agencies to invest in these methods, if we are to gain a better understanding of what causes poor developmental outcomes in early childhood, how best to intervene, and ultimately how to prevent the cycle of poverty that mars these countries.~~

Conclusion

In conclusion, this scoping review has highlighted many important factors to take into consideration when conducting research in low-to-middle-income country contexts. The complex relationship between early nutrition, growth, infectious disease and poverty in determining early child development is clear, highlighting the importance of well-designed and targeted interventions to improve cognitive function, educational attainment and achievement of potential. ~~Methodological factors, such as attrition rates or the use of specific assessment tools, are important considerations in conducting research in low-to-middle-income countries.~~ Factors affecting early child development highlight the need for a multi-level approach, including maternal health, child health and household determinants.

~~Due to the wide range of studies included, the wide difference in methods, designs and in study qualities, it is difficult to summarise clear conclusions or make strong recommendations from this review.~~ The variance found in this review demonstrates a need for more robust and consistent research on this topic. This is needed to gain a more comprehensive understanding of how different factors come to play in early child development in Sub-Saharan Africa and how targeted interventions can address these impacts.

Transparency Declaration

The authors affirm that this manuscript is an honest, accurate, and transparent account of the study being reported. The reporting of this work is compliant with PRISMA guidelines. The lead author affirms that no important aspects of the study have been omitted.

Acknowledgement

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Figure legends

Figure 1 Flow diagram of the study selection processes

~~**Figure 2** Frequency of publications included in the scoping review per year~~

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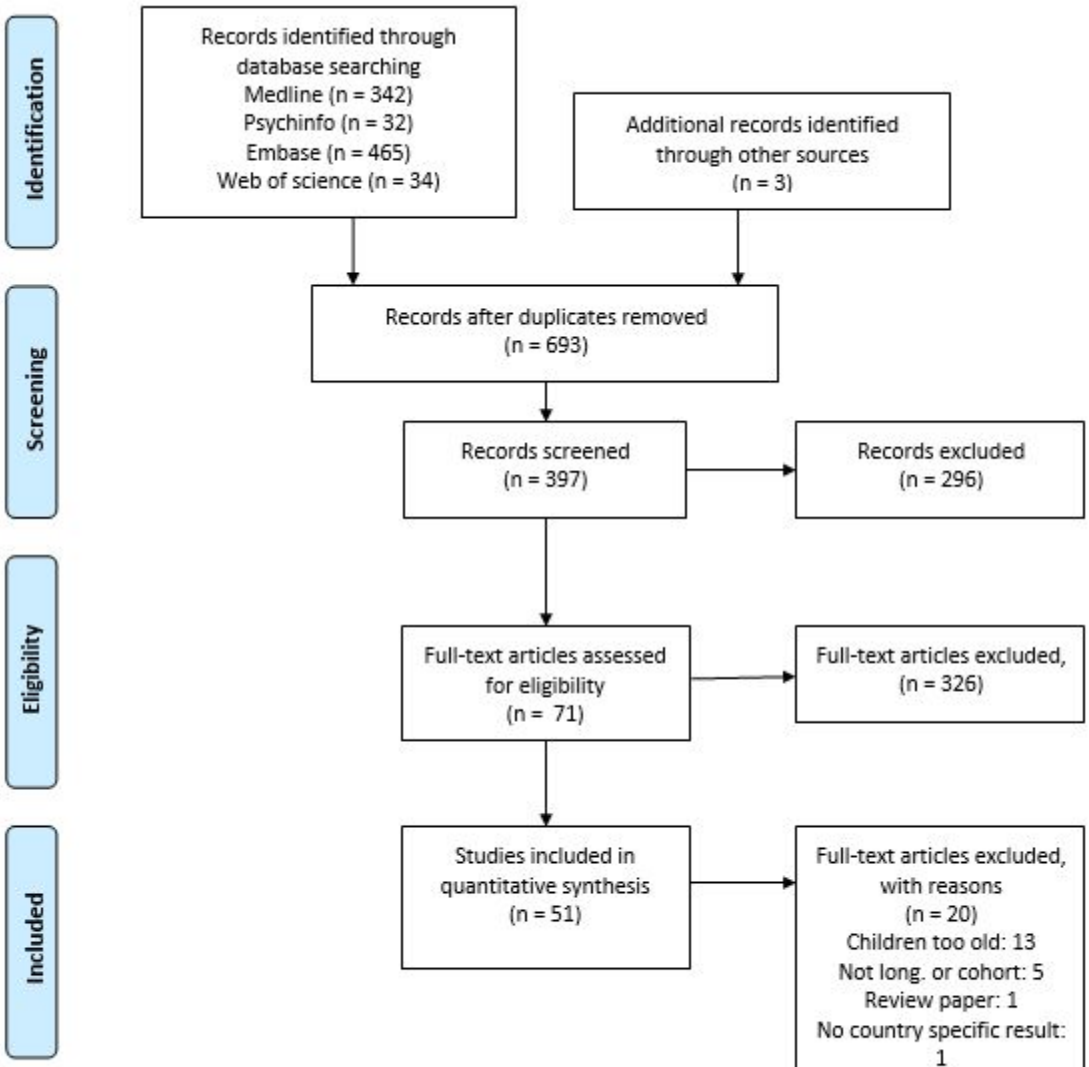
Identification
Screening
Eligibility
Included
Records identified through database searching
Medline (n = 342)
Psychinfo (n = 32)
Embase (n = 465)
Web of science (n = 34)
Additional records identified through other sources (n = 3)
Records after duplicates removed (n = 693)
Records screened (n = 397)
Records excluded (n = 296)
Full-text articles assessed for eligibility (n = 71)
Full-text articles excluded, (n = 326)
Studies included in quantitative synthesis (n = 51)
Full-text articles excluded, with reasons (n = 20)
Children too old: 13
Not long. or cohort: 5
Review paper: 1
No country specific result: 1

Table 1 – Search inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Peer-reviewed cohort, observational and longitudinal studies Sub-Saharan Africa Children aged 0-8 years Cognitive and/or motor development measures	Qualitative or mixed method studies Studies with unspecified locations Studies with unspecified outcome measures Older age groups including children over 8

Table 2- Characteristics and quality ratings of the final included studies

Study and study design	Topic	Exposure Measure	Cognitive/Motor Outcome Measure	Findings	Location	Participants		Quality Rating	Review theme
						Age	Initial N Follow- Up N		
COGNITIVE DEVELOPMENT									
Abera et al (2017, 26) Longitudinal cohort study	Birth weight and cognitive early child development (ECD)	Body composition (FM and FFM) within 48h of birth	Denver Developmental Screening Test (DDST-II)	FFM but not FM was positively associated with higher global development score at age 2 (β 2.48, 95% CI 0.17; 4.79).	Ethiopia	Birth to 2 years	617 enrolled 227 at follow up Attrition = 63.2%	High	Growth and anthro-pometry
Ajayi et al (2017, 10) Prospective cohort study	Health, nutritional status and cognitive ECD	Site, sex, education, child's HIV status, SES, parent education status, haemoglobin and height for age	Grover-Counter Scale of Cognitive Development. Subtests of the Kaufman Assessment Battery for Children (KABC II)	Area of residence and height-for-age ($p<0.05$) were factors affecting cognitive test scores, regardless of attending pre-school. Paternal level of education ($p<0.05$) was also associated with cognitive test scores of children for all three cognitive test results, whereas HIV status, sex and SES were not.	South Africa	Recruited at 4-6 years Tested at 6-8 years	1581 enrolled 1383 at follow up Attrition = 12.5%	Low	Growth and anthro-pometry Environment Nutrition
Ballot et al (2012, 27) Birth cohort study	Very low birth weight and ECD	Very low birth weight	Bayley Scales of Infant and Toddler Development (BSID)	Approximately one third of infants were identified as being at risk (score between 70 and 85) on each subscale. Factors associated with poor outcomes included cystic periventricular leukomalacia (PVL), resuscitation at birth, maternal parity, prolonged hospitalisation and duration of supplemental oxygen. PVL was associated with poor outcome on all three subscales. Birth weight and gestational age were not predictive of neurodevelopmental outcomes.	South Africa	16 months	178 enrolled 106 at follow up Attrition = 40.5%	High	Growth and anthro-pometry
Bangirana et al (2017, 38) Prospective cohort	Malaria and cognitive development	Cerebral malaria (CM): Coma, P. falciparum on blood smear Severe Malarial Anaemia (SMA): P. falciparum on blood smear or children with haemoglobin levels ≤5	Mullen Scales of Early Learning (MSEL), Colour Object Association Test, Early Childhood Vigilance Test	At 12 months, children with CM had lower adjusted scores than community children (CC) in cognitive ability ($p<0.001$), attention ($p<0.05$), and associative memory ($p<0.05$). Children with SMA had lower scores than CC in cognitive ability ($p<0.05$) but not attention or associative memory. Cognitive ability scores in children with CM and SMA did not differ significantly.	Uganda	Between 18 months and 5 years Tested at Baseline, 6 and 12 months later	268 enrolled 221 at follow up Attrition = 17.5%	High	Malaria and HIV
Boivin et al (2018, 52) Prospective cohort study	Antiretroviral exposure and neurodevelop ment	Ante-partum and post-partum to antiretroviral treatment in HIV exposed uninfected children (HEU) and HIV unexposed and uninfected children (HUU)	MSEL and KABC II	At 48 months, MSEL cognitive composite scores were worse for children of mothers who did not remain on triple antiretroviral treatment throughout both the ante-partum and post-partum treatment phases (adjusted means 80.64 [95% CI 77.74-83.54] and 81.34 [78.19-84.48], respectively), compared with those who did remain on triple treatment (adjusted mean 85.93, 95% CI 83.05-88.80; $p=0.0486$ for the comparison of all groups). The KABC-II composite scores (mental processing index) did not differ at 48 or 60 months according to	Malawi and Uganda	12, 24, 48 and 60 months	861 enrolled 738 at 12m; 790 at 24m; 692 at 48m; 445 at 60m; follow up Attrition = 14.3%; 8.2%, 19.6%; 48.3& at 12m, 24m,	High	Malaria and HIV

Table 2- Characteristics and quality ratings of the final included studies

Study and study design	Topic	Exposure Measure	Cognitive/Motor Outcome Measure	Findings	Location	Participants		Quality Rating	Review theme
				exposure (p=0.81 and 0.89, respectively, for comparison of all groups). Scores for MSEL and KABC-II for children of mothers on triple antiretrovirals in both the ante-partum and post-partum treatment phases were similar to those for children in the HIV-unexposed and uninfected reference group at all time points.			48m, and 60m follow up		
Brim et al (2017, 39) Prospective, longitudinal case control study	Malaria and cognitive and psychiatric outcomes	Infants with Retinopathy-positive cerebral malaria (a Blantyre Coma Scale of ≤2, P. falciparum parasitemia) and a control group with no CM	Malawi Developmental Assessment Tool, KABC II	In children younger than 5 years, cases were delayed in motor, language, and social development by approximately 6 months, compared with controls (p<0.001). More significant delays occurred in those with MRI abnormalities at the 1-month follow-up visit. There were no differences between cases and controls in inhibitory self-control, nor in cognitive function in children under 5 years of age.	Malawi	6 months to 5 years tested at baseline and 1 month later	221	High	Malaria and HIV
Casale & Desmond (2016, 21) Longitudinal birth cohort study	Stunting and cognitive function	Stunting status at age 2 and 5 years, Height for age z score (HAZ) ≤ -2 SD form the mean of the reference population	Revised Denver Pre-screening Developmental Questionnaire (R-DPDQ)	Children who recovered from stunting by age 5 still performed significantly worse on cognitive tests than children who did not experience early malnutrition, and almost as poorly as children who remained stunted. These findings suggest that the timing of nutritional inputs in the early years is key in a child's cognitive development.	South Africa – Birth to twenty	Tested at 5 years, recruited at birth	3273 enrolled 2y- 1839 4y– 1858 5y- 1586 between 1019 & 666 based on which controls were included Attrition = 43.8%; 43.2%; 51.5% at 2y, 4y, & 5y follow up	High	Growth and anthro-pometry
Crookston et al (2013, 22) Observational cohort study	Growth and cognitive ECD	HAZ at 1 year and 8 years. Four categories: recovered (stunted at age 1y not at age 8y), faltered (not stunted at age 1y and stunted at age 8y), persistently stunted (stunted at 1 and 8y), or never stunted (not stunted at 1 and 8y).	School attendance, math test, the Early Grade Reading Assessment, Peabody Picture Vocabulary Test (PPVT)	The HAZ (1) was inversely associated with overage for grade and positively associated with mathematic achievement, reading comprehension, and receptive vocabulary. Unpredicted growth from 1 to 8 y of age was also inversely associated with overage for grade (OR range across countries: 0.80–0.84) and positively associated with mathematics achievement (effect-size range: 0.05–0.10), reading comprehension (0.02–0.10), and receptive vocabulary (0.04–0.08).	Ethiopia, India, Peru and Vietnam-young lives	Birth to 8 years Tested at 5 and 8 years	8062 overall 1757 in Ethiopia Attrition = 78.2%	Moderate	Growth and anthro-pometry
Davies et al (2011, 35) Birth cohort study	Developmental delay and foetal alcohol	Foetal alcohol spectrum disorder (FASD). Diagnosis	Griffiths Mental Development scales	Infants and children with FASD performed worse than their non-FASD counterparts over all scales and total developmental quotients. Mean quotients for both groups decline between	South Africa	7-12 months and again	392 enrolled 83 at 17m follow up	High	Maternal factors

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Study and study design	Topic	Exposure Measure	Cognitive/Motor Outcome Measure	Findings	Location	Participants		Quality Rating	Review theme
	spectrum disorder	using Institute of Medicine criteria		assessments across subscales with a particularly marked decline in the hearing and language scale at Time 2 (scores dropping from 110.6 to 83.1 in the non-FASD group and 106.3 to 72.7 in the FASD group; p=0.004).		at 17-21 months	Attrition = 78.8%		
Dearden et al (2017, 54) Prospective cohort study	Household water and sanitation and vocabulary performance	Improved water and sanitation used definition from UNICEF Joint Monitoring Program	PPVT	Access to improved water at 1 year was associated with higher language scores at 5 years (3/4 adjusted associations) and 8 years (4/4 unadjusted associations). Ethiopian children with access to improved water at 1 year had test scores that were 0.26 SD (95% CI 0.17 to 0.36) above children without access at 5 years.	Ethiopia, India, Peru and Vietnam-young lives	Birth to 8 years Tested at 5 and 8 years	7269 overall 1792 in Ethiopia Attrition = 75.3%	High	Environment
Di Cesare & Sabates (2013, 30) Longitudinal birth cohort study	Antenatal care and cognitive ECD	Antenatal care described by WHO recommendation (four visits during pregnancy and a skilled practitioner during birth)	Cognitive development Assessment (CDA)	Positive association between mother's access to antenatal care and children's cognitive development in stunted (β 0.40; p>0.05) and non-stunted children (β 0.56; p<0.05)	Young lives: Ethiopia, India, Peru, and Vietnam	Birth to 5 years	3722 overall 1,807 in Ethiopia Attrition = 51.5%	Moderate	Maternal factors Environment
Douglas et al (2019, 36) Longitudinal cohort study	WHO maternal guidelines and cognition	Antenatal care described by WHO recommendation (four visits during pregnancy and a skilled practitioner during birth)	CDA, PPVT, Early Grade Reading Assessment (EGRA) and math test	Children of mothers who received the WHO recommended 4+ antenatal care visits or received the WHO recommended first antenatal care visit during the first trimester scored higher on all academic achievement tests. In the multivariable analysis, children of mothers who received 4+ antenatal care visits scored significantly higher on the CDA at ages 4-5 years and Math Test at ages 7-8 years. Children of mothers who received antenatal care in the first trimester scored higher on the CDA at ages 4-5 years. Children of mothers who received both antenatal care in the first trimester and 4+ antenatal care visits scored significantly higher on the CDA at ages 4-5 years and Math Test at both ages 7-8	Ethiopia	From 4-5 years to 8 years Tested at 4-5 and 7-8 years	1914	Moderate	Maternal factors
Eskenazi et al (2018, 56) Birth cohort study	Prenatal Insecticide exposure and neurodevelopment	Maternal exposure to the insecticide dichlorodiphenyltrichloroethane (DDT) and its breakdown product dichlorodiphenyldichloroethylene (DDE). Blood tests pre- and post-natal and pyrethroid metabolites in urine	BSID-III	Exposure to DDT and DDE were not associated with lower scores on the BSID-III. Prenatal exposure to pyrethroids may be associated at 1 year of age with poorer social-emotional development. At 2 years of age, poorer language development was observed with higher prenatal pyrethroid levels.	South Africa	Tested at 1 and 2 years	752 enrolled 665 completed visits at both 1y and 2y and 40 completed one visit at either 1y or 2y Attrition = 11.6% for those that	High	Environment

Table 2- Characteristics and quality ratings of the final included studies

Study and study design	Topic	Exposure Measure	Cognitive/Motor Outcome Measure	Findings	Location	Participants		Quality Rating	Review theme
							completed visits at both 1y and 2y		
Gladstone et al (2011, 28) Community-based stratified cohort study	Preterm birth and developmental outcome - stratified cohort study	Preterm babies born under 37 weeks of gestation	Ten Question Questionnaire, Malawi Development Assessment Tool	Compared to infants born at term: preterm infants were at significantly greater risk of death (hazard ratio 1.79, 95% CI 1.09–2.95); surviving preterm infants were more likely to be underweight (weight-for-age z score; p,0.001) or wasted (weight-for-length z score; p,0.01) with no effect of gestational age at delivery; were more often screened for disability on the Ten Question Questionnaire (p=0.002); and had higher rates of developmental delay on the MDAT at 18 months (p=0.009), with gestational age at delivery increasing this likelihood (p=0.01).	Malawi	Tested at 12, 18 and 24 months	850	Moderate	Growth and anthro-pometry
Hsiao & Richter (2014, 59) Longitudinal birth cohort study	Early mental development and cognitive and behaviour development	Griffiths Mental Development Scales (GMDSs) at age 1 and maternal education	Adapted items of R-PDQ and PDQ-II at age 5	Mental development at 1 year of age significantly predicted preschool outcomes when children were 5 years of age (β 0.19; p<0.01), over and above the contributions of maternal education (β 0.29; p<0.01). Children with the poorest mental development at 1 year of age also had the poorest cognitive and behavioural development at 5 years of age. However, higher levels of maternal education attenuated the negative impacts of early developmental delay on preschool cognitive and behavioural outcomes.	South Africa	Birth to 5 years Tested at 1 and 5 years	167	Low	Environment
Knox et al (2016, 41) Longitudinal birth cohort study	Cerebral malaria and cognitive impairment – longitudinal study	Retinopathy-confirmed cerebral malaria children	Oculomotor tasks, including isuomotor prosaccade and antisaccade tasks, recorded eye movements that are typically associated with persistent or serious impairments in attention and behavioural inhibition.	There were no statistically significant differences between the cerebral malaria and control groups, suggesting that cerebral malaria survivors are not generally at an increased risk of persistent cognitive deficits.	Malawi	54 months for intervention and 117 months for controls - tested over 32 months	47 and 37 for controls	Moderate	Malaria and HIV
Mekonnen et al (2018, 31) Population-based cohort study	Maternal common mental disorders and child education	Maternal common mental disorders (CMD) was measured with SRQ-20	Academic achievement, absenteeism and dropout	After adjusting for potential confounders, exposure to maternal CMD at 7-8 years was associated significantly with school dropout (OR 1.07; 95% CI 1.00 to 1.13, p=0.043) and absenteeism (incidence rate ratio 1.01; 95% CI 1.00 to 1.02 p=0.026) at the end of 2014-15 academic year. There was no association between maternal CMD and child academic achievement.	Ethiopia	7-8 years and 8-9 years	2090	High	Maternal factors

Table 2- Characteristics and quality ratings of the final included studies

Study and study design	Topic	Exposure Measure	Cognitive/Motor Outcome Measure	Findings	Location	Participants		Quality Rating	Review theme
Reynolds et al (2017, 53) Longitudinal cohort study	SES and vocabulary ECD	Household wealth index (housing quality, ownership of consumer durables, and access to services such as electricity, water and sanitation) and parental education	PPVT	Children in the top quartile of household SES were taller and had better language skills than children in the bottom quartile; differences in vocabulary scores between children with high and low SES were also reported. For vocabulary, SES disparities emerged early in life, but patterns were not consistent across age and widen between 5 and 12y in Ethiopia.	Young lives: Ethiopia, India, Peru and Vietnam	At 5, 8 and 12 years	1986 in Ethiopia 1345 at follow up Attrition = 32.3%	Moderate	Environment
Sunny et al (2018, 24) Longitudinal birth cohort study	Stunting and school performance	Anthropometric measures collected at first visit after birth and after 1 year and between the age of 4-8; Height-for age	School outcomes	The effects of stunting on schooling were evident in early childhood but were more pronounced in late childhood. Children who were stunted in early childhood (9.3%) were less likely to perform underage at enrolment, more likely to repeat Standard 1, and were 2–3 times more likely to be overage for their grade by the age of 11, compared to their non-stunted peers. Those persistently stunted between early and late childhood (7.3%) faced the worst consequences on schooling, being three times as likely to enrol late and 3–5 times more likely to be above the age for their grade by the age of 11, compared to those never stunted.	Malawi	Tested at Birth, 11-16 months and 4-8 years	1595 at birth 1239 at 11-16m follow up; 1044 at 4-8 years follow up Attrition = 22.3% & 34.5% at 11-16m & 4-8 year follow up	High	Growth and anthro-pometry
MOTOR DEVELOPMENT									
Benki-Nugent et al (2017, 42) Prospective cohort study	Developmental milestones and HIV - prospective study	HIV-infected infants and control of HIV uninfected and unexposed (HUU) infants	Tests adapted from the DDST-II	HIV-infected infants on ART had delays in attainment of developmental milestones compared to HUU infants: median age at attainment of sitting with support, sitting unsupported, walking with support, walking unsupported, monosyllabic speech and throwing toys were all delayed (all p-values <0.0005). Compared with HUU infants, the subset of HIV-infected infants with both virologic suppression and immune recovery at 6 months had delayed speech (delay: 2.0 months; p=0.0002) and a trend for delayed walking unsupported. Among HIV-infected infants with poor post-ART responses at 6 months (lacking viral suppression and immune recovery) there were greater delays versus HUU infants for walking unsupported (delay: 4.0 months; p=0.0001) and speech (delay: 5.0 months; p<0. 0001).	Kenya	Infants tested 1, 3 and 6 months	73 HIV-infected and 92 HUU	High	Malaria and HIV
Espie et al (2011, 55) Longitudinal cohort study	Psychomotor development in orphans	Children under 1 month of age admitted to an orphanage	Simplified Neonatal Behaviour Assessment Scale (NBAS), Brunet-Lezine Scale and	At admission, 15% of children <1 month had a regulation impairment according to the NBAS, and 33.8% presented with a distressed state (ADBB score >5). More than 85% (129/151)	Sudan	Tested at 2,4,9,12 and 18 months	148 enrolled 7 at 18 months follow up	Moderate	Environment

Table 2- Characteristics and quality ratings of the final included studies

Study and study design	Topic	Exposure Measure	Cognitive/Motor Outcome Measure	Findings	Location	Participants		Quality Rating	Review theme
			Alarm Distress Baby Scale (ADBB)	recovered normal psychomotor development by 18 months.			Attrition = 95.3%		
Goetghebuer et al (2011, 57) Prospective cohort study	Twins and motor developmental delay	Twins and singleton with a birth weight above 2.5kg	Eight motor milestones adapted from the DDST-II	Significant difference between singletons and twins in maintaining head ($p<0.05$), sitting without support ($p<0.05$) and walking ($p<0.05$), with twins having a higher age of milestone achievement. When monozygotic and dizygotic twins were compared, a significant heritability was observed for crawling, sitting, standing and walking, with over 90% of the observed population variance being attributed to genetic rather than environmental factors.	Gambia	Birth to 18 months	84 twin pairs and 72 singletons All singletons were followed up but only 44 twin pairs were followed up at 18 months Attrition = 0% for singletons; 47.6% for twin pairs	Moderate	Environment
Manno et al (2012, 16) Randomised control trial	Micronutrients and mental and psychomotor development	Four treatment groups: Zinc supplement, multivitamins supplement, multivitamin and zinc supplement and placebo	BSID-III and development milestones from test developed by WHO multicentre growth reference study	No significant difference in mean BSID-III scores in any of the five test domains for univariate or multivariate models comparing each of the four treatment groups.	Zambia	6 to 18 months	743 202 received BSID-III at 6, 12 & 18 months Attrition = 72.8%	High	Nutrition
COGNITIVE AND MOTOR DEVELOPMENT									
Allen (1993, 11)	Review- Malnutrition and cognitive and behavioural deficit	Mother's diet: Intake of animal product, zinc, iron, vitamin B12. Maternal weight and fatness, birth weight	Brazelton Neonatal Assessment Scale	Maternal weight and diet during pregnancy appeared to affect infant neurobehavioural performance at birth and in the first 6 months. Maternal dietary intake was also associated with motor development.	Egypt, Kenya and Mexico	Tested at 3, 6, 18, 24 months	Not reported	Low	Nutrition
Blakstad et al (2019, 33) Prospective cohort study	Neurodevelopment and maternal, socioeconomic, delivery, infant nutritional characteristics	Demographic, socioeconomic, delivery characteristics and infant growth measures. HIV exposed and unexposed children	BSID-III	Low maternal height predicted all BSID-III domains in HIV-unexposed children; low maternal education predicted lower cognitive (standardized mean difference, -0.41; 95% CI, -0.74 to -0.08) and lower gross motor scores (standardized mean difference, -0.32; 95% CI, -0.61 to -0.04) in HIV-exposed children. Among delivery characteristics, facility delivery predicted higher cognitive scores (standardized mean difference, 1.36; 95% CI, 0.26-2.46); and oxytocin administration predicted lower fine motor scores (standardized mean difference, -0.48; 95% CI, -0.87 to -0.09) in HIV-exposed children. Higher length-for-age z-scores at 6	Tanzania	From 6 weeks to 24 months Tested at 14-17 months	196 HIV-exposed 226 HIV-unexposed	Moderate	Maternal factors

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Study and study design	Topic	Exposure Measure	Cognitive/Motor Outcome Measure	Findings	Location	Participants		Quality Rating	Review theme
				weeks of age predicted better cognitive (standardized mean difference, 0.15; 95% CI, 0.01-0.29) and expressive language scores (standardized mean difference, 0.16; 95% CI, 0.02-0.29) at 15 months in HIV-exposed infants					
Brahmbhatt et al (2014, 43) Prospective birth cohort study	Neurodevelopment and Antiretroviral therapy	Maternal and Child HIV status	MSEL	Compared to uninfected children and uninfected mothers dyads, HIV-infected children were more likely to have global deficits on all measures of neurodevelopment except gross motor skills, whereas in dyads of HIV infected mothers of HIV uninfected children, there was impairment in receptive language (adj. PRR=2.67, CI: 1·08, 6.60) and early learning composite score (adj. PRR=2.94, CI: 1.11, 7.82). Of the children born to HIV infected mothers, HIV infected children did worse than those unifected only in Visual Reception skills (adj. PRR=2.86; CI: 1.23–6.65). Of the 116 HIV+ children, 44% had initiated ART. Compared to ART duration of <12 months, ART durations 24–60 months was associated with decreased impairments in Fine Motor, Receptive Language, Expressive Language and ELC scores	Uganda	0-6 years	329	Moderate	Malaria and HIV
Chaudhury et al (2017, 45) Prospective birth cohort study	Neurodevelopment and HIV – prospective cohort	HIV exposed uninfected children (HEU) and HIV unexposed and uninfected children (HUU) DNA PCR test	BSID-III, DMC	HEU children performed equally well on neurodevelopmental assessments at 24 months of age compared with HUU children.	Botswana	Birth to 24 months	670 children with BSID-III 723 with DMC	Moderate	Malaria and HIV
Chaudhury et al (2018, 44) Prospective birth cohort study	Neurodevelopment and Antiretroviral exposure – prospective cohort	HIV exposed and uninfected (HEU) children exposed in utero to either ART (antiretroviral therapy) or ZDV (zidovudine monotherapy)	BSID-III, Development Milestones Checklist (DMC)	Neurodevelopmental outcomes at 24 months of age were similar in ART-exposed versus ZDV-exposed HEU children. Adjusted mean Bayley-III scores were similar among ART exposed versus ZDV-exposed, with adjusted mean differences (95% CI): Bayley-III Cognitive:0.3 (-1.4, 0.9); Gross Motor: 0.8 (-0.1, 1.7); Fine Motor: 0.5 (-0.2, 1.3); Expressive Language: 0.7 (-0.3, 1.7); Receptive Language: 0.1 (-0.7, 0.8); Development Milestone Checklist Locomotor: 0.0 (-0.5, 0.6); Fine Motor: 0.3 (-0.3, 0.8); Language: -0.1 (-0.5, 0.4); Personal-Social: 0.2 (-0.7, 1.1).	Botswana	Birth to 24 months	598	Moderate	Malaria and HIV
Donald et al (2019, 37) Population-based birth cohort study	Risks and protective factors of child development	Sociodemographic and environmental variables, child and maternal physical health, substance	BSID-III	Bivariate and multivariable analyses revealed several factors that were associated with developmental outcomes. These included protective factors (maternal education, higher birth weight, and socioeconomic status) and risk	South Africa	Birth to 24 months	1143 at birth 734 at 24m follow up Attrition = 35.8%	High	Maternal factors Malaria and HIV

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Study and study design	Topic	Exposure Measure	Cognitive/Motor Outcome Measure	Findings	Location	Participants		Quality Rating	Review theme
		use and psychosocial measures		factors (maternal anaemia in pregnancy, depression or lifetime intimate partner violence, and maternal HIV infection). Boys consistently performed worse than girls (in cognition [beta = -0.74; 95% CI -1.46 to -0.03, p = 0.042], receptive language [beta = -1.10; 95% CI -1.70 to -0.49, p < 0.001], expressive language [beta = -1.65; 95% CI -2.46 to -0.84, p < 0.001], and fine motor [beta = -0.70; 95% CI -1.20 to -0.20, p = 0.006] scales). There was evidence that child sex interacted with risk and protective factors including birth weight, maternal anaemia in pregnancy, and socioeconomic factors					
Fink et al (2013, 40) Prospective cohort study	Early childhood exposure to Malaria and pre-school development	Cluster-level parasitaemia data was used to construct a village specific measure	Adapted PPVT, physical development, behaviour and socio-emotional development, general fine motor skills	Exposure to the malaria parasite was associated with lower ability to cope with the demand of the cognitive tasks procedure (Z-score difference -1.11, 95% CI -2.43-0.20). No associations were found between malaria exposure and receptive vocabulary or fine-motor skills.	Zambia	6 years	1686 1410 at follow up Attrition = 16.4%	High	Malaria and HIV
Koen et al (2017, 34) Birth cohort study	Maternal posttraumatic stress disorder (PTSD) and infant development	Childhood Trauma Questionnaire, The Intimate Partner Violence Questionnaire and clinical interviews to assess PTSD	BSID-III	Maternal PTSD was significantly associated with poor fine motor (β-1.5; p<0.05) and adaptive behaviour–motor development (β-1.3; p<0.05); the latter remained significant when adjusted for site, alcohol dependence, and infant head-circumference-for-age z-score at birth.	South Africa Drakenstein Child Health Study	Median: 8.9 months	675 enrolled 112 at follow up Attrition = 83.4%	High	Maternal Factors
Le Roux et al (2018, 46) Prospective birth cohort study	Breastfeeding HIV infants and neurodevelopment	HIV-infected women and HEU children	BSID-III	Compared to HIV-unexposed children, HEU children had higher odds of cognitive delay [odds ratio (OR) 2.28 (95% confidence interval (CI)1.13–4.60)] and motor delay [OR 2.10 (95%CI 1.03–4.28)], but not language delay, in crude and adjusted analyses. Preterm delivery modified this relationship for motor development: compared with term HIV-unexposed children, term HEU children had similar odds of delay, preterm HIV-unexposed children had five-fold increased odds of delay (adjusted OR 4.73, 95% CI 1.32;16.91) and preterm HEU children, 16-fold increased odds of delay (adjusted OR 16.35, 95% CI 5.19; 51.54).	South Africa	12 to 18 months	521	High	Malaria and HIV
Locks et al (2017, 15) Randomised control trial	Zinc and multivitamin intervention and early child	Infants randomised to one of four interventions: zinc supplement, multivitamin supplement, zinc and	BSID-III	No significant difference in mean BSID-III scores for any of the five domains in univariate or multivariate models comparing each of the four treatment groups. No significant difference in mean BSID-III scores when comparing children who received zinc supplements versus those who	Tanzania	15 months	2400 of which 247 completed BSID-III	High	Nutrition

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Study and study design	Topic	Exposure Measure	Cognitive/Motor Outcome Measure	Findings	Location	Participants		Quality Rating	Review theme
	development - RCT	multivitamin supplement, or placebo		did not, or in comparisons of children who received multivitamin supplements versus those who did not.					
McDonald et al (2013, 29) Prospective cohort study	HIV and neurodevelopment – prospective cohort RCT	Pregnant women infected with HIV received 1 of 4 regimens of multivitamins through to lactation.	Psychomotor Development Index (PDI) and Mental Development Index (MDI) of BSID-III	Preterm birth, child HIV infection, stunting, and wasting were independently associated with low scores on the PDI and MDI.	Tanzania	Birth to 18 months - tested at 6, 12 and 18 months	1078 enrolled 331 at follow up Attrition = 69.3%	Moderate	Growth and anthro-pometry Malaria and HIV
McGrath et al (2006, 47) Prospective cohort study	Timing of transmission of HIV and neurodevelopment -RCT	Pregnant women with infected HIV received a daily dose of 1 of 4 regimens: vitamin A; multivitamins, excluding vitamin A; multivitamins, including vitamin A; or placebo; through to 18 months.	PDI and MDI of BSID-III	Children who tested HIV-1-positive at birth had significantly higher decreases per month in MDI and PDI than HIV-1negative children; 1.1 [95% confidence interval (95% CI), 0.4, 1.8] for MDI and 1.4 (95% CI 0.0, 2.7) for PDI. Children who tested HIV-1-positive after birth had an additional 0.6 (95% CI 0.1, 1.1) point decrease in MDI per month and a 0.6 (95% CI 0.0, 1.1) higher decrease in PDI each month than HIV-1-negative children. Testing HIV-1-positive at birth was associated with a 14.9 (95% CI 5.0, 44.7) times higher rate of becoming developmentally delayed in mental function, while testing HIV-1-positive after birth was associated with a 3.2 (95% CI 1.6, 6.4) times higher rate than in uninfected children.	Tanzania	Birth to 18 months-tested at 6, 12 and 18 months	1078 enrolled 327 at follow up Attrition = 69.7%	High	Malaria and HIV
Milner et al (2018, 12) Longitudinal panel study	Food insecurity (timing, intensity and duration) and child development	Household Food Insecurity Access Scale	Subscales of the Ages and Stages Questionnaire: Inventory (ASQ:I) were used to assess 3 domains of child development: gross motor, communication, and personal social skills	Children in households that experienced greater aggregate food insecurity over the past 2 years (intensity) had significantly lower gross motor (β -0.14; p=0.045), communication (β -0.16; p =0.023), and personal social skills (β -0.20; p<0.05) Z-scores than children with greater food security. Children with more time exposed to food insecurity (duration) had significantly lower gross motor (β -0.050; p=0.10), communication (β -0.042; p=0.057), and personal social skills (β -0.037; p=0.76) Z-scores than children with less time exposed to food insecurity.	Kenya	Children under 2 years. Visited 5 times over 24 months	309 enrolled 304 at follow up Attrition = 1.6%	Low	Nutrition
Mireku et al (2015, 18) Prospective cohort study	Prenatal Haemoglobin (Hb), and early cognitive and motor development	Blood sample to measure Hb concentration	MSEL	A significant negative quadratic relationship between infant gross motor function and Hb concentration at first and second antenatal care visits.	Benin	1 year	828 enrolled 636 at follow up Attrition = 23.2%	High	Nutrition
Mireku et al (2016, 17) Prospective	Prenatal iron deficiency, neonatal	Blood and stool sample during pregnancy and at	MSEL	Neither prenatal ID nor CBSF concentration was associated with poor cognitive or gross motor function of children at age 1 year. CBSF	Benin	1 year	828 enrolled 636 at follow up	High	Nutrition

Table 2- Characteristics and quality ratings of the final included studies

Study and study design	Topic	Exposure Measure	Cognitive/Motor Outcome Measure	Findings	Location	Participants		Quality Rating	Review theme
cohort study	ferritin, and early cognitive and motor development - prospective cohort	birth to measure low cord blood serum ferritin (CBSF) and iron deficiency (ID). Daily iron and folic acid supplement during pregnancy		concentrations were lower among mothers who had ID anaemia (IDA) at delivery compared with non-IDA pregnant women (adjusted mean difference: −0.2 [95% confidence interval: −0.4 to −0.0]).			Attrition = 23.2%		
Molteno et al (1991, 58) Birth cohort study	Development of children of colour	Preschool children of colour. Social background, economic status and physical environment were recorded	Three milestones, sitting unsupported, walking unaided, and saying single words. Specific assessment designed.	At 12 months, development correlated best with family stability. Language development at 30 months was associated with mother's education and family stability and reflected a general lag in verbal skills. By 5 years there was a good correlation between development and social indicators, particularly income and mother's education.	South Africa	Birth to 5 years	187	Low	Environment
Msellati et al (1993, 48) Prospective cohort study	HIV and development	Children born to seropositive mothers and that were either infected with HIV-1, uninfected, or with indeterminate status.	Adaptation of DDST-II and Illingworth's The Development of the Infant and Young Child. Gross motor development, fine motor development, language acquisition and social contacts	The proportion of abnormal neurologic examinations in HIV-infected children varied from 15% to 40% according to age and was always higher than in HIV-uninfected children born to HIV-seropositive and seronegative mothers. The proportion of abnormal examinations in infected children was 12.5% at 6 months, 16% at 12 months, 20% at 18 months, and 9% at 24 months of age and was more frequent than in HIV-uninfected children. Developmental delay was principally due to significantly lower gross motor scores.	Rwanda	Tested at 6, 12, 18 and 24 months	436 (218 HIV and 218 non-HIV)	Moderate	Malaria and HIV
Ocansey et al (2019, 19) Follow up of a randomised control trial	Growth, haemoglobin concentration association with cognitive and motor development	Birth length and linear growth (LAZ) at three postnatal periods and haemoglobin concentration (Hb)	NIH Toolbox 9-Hole Pegboard NEPSY-II body part naming and identification and comprehension of instructions, paired-associate learning and recall task and block design	Cognitive development at 4-6 years was significantly associated with LAZ at birth (beta = 0.12, 95% CI = 0.05, 0.19), DELTALAZ from 6 to 18 months (beta = 0.16, 95% CI = 0.04, 0.28), and Hb at 18 months (beta = 0.13, 95% CI = 0.06, 0.20), but not with DELTALAZ during 0-6 months, DELTALAZ from 18 months to 4-6 years, Hb at 6 months, or Hb at 4-6 years. No evidence of associations with motor or social-emotional development were found.	Ghana	Birth to 4-6 years Tested at 6 months, 18 months and 4-6 years	966 710 for the LAZ sample 617 for the Hb sample	High	Nutrition
Pitchik et al (2018, 20) Prospective cohort study	Motor and cognitive development, early life nutrition and parenting practices.	Height and weight of children, questionnaire assessing caregiver stimulation and verbal and physical punishment. Mothers prenatal supplementation of zinc and vitamin A	Early Tanzanian version of the Caregiver Reported Early Childhood Development Index (CREDI)	Children born to mothers having received prenatal vitamin A had significantly lower reported motor scores, -0.29 SD, 95% CI [-0.54, -0.04], p = 0.03, as compared with children whose mothers did not receive vitamin A. There was no significant effect of prenatal zinc intake on any development domain. Greater caregiver-child stimulation was associated with 0.38 SD, 95% CI [0.14, 0.63], p < 0.01, better cognitive/language scores, whereas children who	Tanzania	20-39 months	198	High	Maternal factors Nutrition

Table 2- Characteristics and quality ratings of the final included studies

Study and study design	Topic	Exposure Measure	Cognitive/Motor Outcome Measure	Findings	Location	Participants		Quality Rating	Review theme
				experienced both verbal and physical punishment had 0.29 SD, 95% CI [-0.52, -0.05], p = 0.02, lower scores in socioemotional development. Maternal completion of primary school was associated with higher reported motor and cognitive/language development. Further, children of mothers who were <155 cm tall had lower cognitive and language scores.					
Prado et al (2017, 13) Prospective cohort study	Predictors of language and motor development	Sociodemographic information. Blood samples for assessment of malaria and haemoglobin status. Saliva sample to assess stress levels. SRQ-20. Infant feeding practices. HOME inventory	Ghana and Malawi-Kilifi Developmental Inventory and MacArthur Bates Communicative Development Inventory Burkina Faso- DMC	Out of 42 indicators of the 34 factors examined, 6 were associated with 18-month language and/or motor development in 3 or 4 cohorts: child linear and ponderal growth, variety of play materials, activities with caregivers, dietary diversity, and child haemoglobin/iron status.	Ghana, Malawi, and Burkina Faso	18 months	4205	Moderate	Nutrition
Ribe et al (2018, 23) Prospective cohort study	Determinant of early cognitive development	Gender, WAMI index, HOME score, weight-for-age z-score, length-for-age z-score and head circumference-for age z-score	BSID-III	Univariate regression analysis, weight-for-age and weight-for-length z-scores at 6 months were significantly associated with Bayley gross motor score at 15-months, but not with other Bayley scores at 15-months. Length-for-age z-scores at 6 months were not significantly associated with Bayley scores at 15-months. Socio-economic status, measured by a set of assets and monthly income, was significantly associated with Bayley cognitive score at 15-months.	Tanzania	Tested at birth, 6 and 15 months	262 enrolled 137 at follow up Attrition = 47.7%	Moderate	Growth and anthro-pometry
Servili et al (2010, 32) Population-based cohort study	Maternal Common Mental Disorder (CMD) and early cognitive development	Maternal CMD using SRQ-20. Cofounding variables: SES, parental education levels, marital discord, pregnancy time point, episodes of malaria, social support, maternal height and weight, maternal prolonged labour, infant nutritional status.	Adapted BSID-III (no time limit, no stairs questions, translated)	Antenatal maternal CMD symptoms were associated with poor infant motor development (β-0.20; 95% CI: -0.37 to -0.03), but this became non-significant after adjusting for confounding variables. Postnatal CMD symptoms were not associated with any domain of infant development. There was evidence of a dose-response relationship between the number of time-points at which the mother had high levels of CMD symptoms (SRQ ≥ 6) and impaired infant motor development (β -0.80; 95%CI -2.24, 0.65 for ante- or postnatal CMD only, β -4.19; 95% CI -8.60, 0.21 for ante- and postnatal CMD, compared to no CMD; test-for-trend c213.08(1), p < 0.001). Although this association became non-significant in the fully adjusted model, the β coefficients were unchanged indicating that the relationship was not confounded. In multivariable analyses, low socio-economic status and low	Ethiopia	Birth to 12 months	521 enrolled 199 at follow up Attrition = 61.8%	Moderate	Maternal factors

Table 2- Characteristics and quality ratings of the final included studies

Study and study design	Topic	Exposure Measure	Cognitive/Motor Outcome Measure	Findings	Location	Participants		Quality Rating	Review theme
				infant weight-for-age were associated with significantly low scores on both motor and cognitive developmental scales. Maternal experience of physical violence was significantly associated with impaired cognitive development.					
Springer et al (2018, 49) Prospective cohort study	HIV and neurodevelopmental outcomes	HIV uninfected infants of HIV infected (HUU) and HIV uninfected (HEU) mothers	BSID-III, Alarm Distress Baby Scale	Performance on the BSID did not differ in any of the domains between HEU and HUU infants.	South Africa	11 to 14 months	96 (58 HUU and 38 HEU)	High	Malaria and HIV
Strehlau et al (2016, 50) Prospective cohort study	HIV and neurodevelopmental delay	HIV infected infants before starting ART and after viral suppression had been achieved.	Ages and Stages Questionnaires	Compared with pre-ART, better outcomes were reported at time of viral suppression with a lower proportion of children failing the gross motor (31.5% vs. 13%, p=0.0002), fine motor (21.3% vs. 10.2%, p=0.017), problem solving (26.9% vs. 9.3%, p=0.0003) and personal–social (19.6% vs. 7.4%, p=0.019) domains. However, there was no change in the communication domain (14.8% vs. 12.0%, p=0.6072).	South Africa	Under 2 years	323 enrolled 195 at follow up Attrition = 39.6%	High	Malaria and HIV
Sudfeld et al (2015, 14) Randomised control trial	Malnutrition and early cognitive development	Length and weight of children. 6 items from the UNICEF Multiple Indicator Cluster Survey Early Child Development	Adapted BSID-III	Height-for-age z score (HAZ) was associated with cognitive, communication, and motor development z scores across the observed range in this population (all p values for linear relation <0.05). Each unit increase in HAZ was associated with +0.09 (95% CI:0.05, 0.13), +0.10 (95% CI:0.07, 0.14), and +0.13 (95% CI:0.09, 0.16) higher cognitive, communication, and motor development z scores, respectively. The relation of weight-for-height z score (WHZ) was nonlinear with only wasted children (WHZ <22) experiencing deficits (p values for nonlinear relation <0.05). Wasted children had 20.63 (95% CI:20.97, 20.29), 20.32 (95% CI:20.64, 0.01), and 20.54 (95% CI: 20.86, 20.23) deficits in cognitive, communication, and motor z scores. Tall maternal stature and flush toilet use were associated with high cognitive and motor z scores, whereas being born small for gestational age was associated with a 20.16 (95% CI: 20.30, 20.01 z score deficit in cognition.	Tanzania	18 to 36 months	1036	High	Growth and anthro-pometry Nutrition
Van Rie et al (2009, 51) Prospective cohort study	HIV care and neurodevelopment	HIV-infected children, HIV-uninfected children, HIV exposed children and control children.	BSID-III in young children, PPVT motor scale and Snijders-Oomen Nonverbal Intelligence Test for older	After one year of care, HIV-infected children achieved mean motor and cognitive scores that were similar to HIV uninfected children. Overall, HIV-infected children experienced accelerated motor development but similar gains in cognitive development compared to control children.	Congo	18 to 71 months, tested at baseline, 6 and 12 months later	70 HIV infected 90 HIV uninfected children	Moderate	Malaria and HIV

Table 2- Characteristics and quality ratings of the final included studies

Study and study design	Topic	Exposure Measure	Cognitive/Motor Outcome Measure	Findings	Location	Participants		Quality Rating	Review theme
Wallander et al (2014, 60) Observational cohort study	Early developmental intervention and early cognitive development	Early development Intervention program on children with birth asphyxia that required resuscitation. Home visits every 2 weeks over 36 months. Treatment dose: Home visit dose and program implementation dose	PDI and MDI of BSID-III	Higher home visits dose was significantly associated with higher MDI (mean for dose quintiles 1-2 combined = 97.8, quintiles 3-5 combined = 103.4, p<0.001). Higher treatment dose was also generally associated with greater mean PDI, but the relationships were non-linear. Location, sociodemographic, and child health variables were associated with treatment dose.	India, Pakistan, Zambia	36 months	540 enrolled 145 at follow up in all countries Attrition = 73.1%	High	Environment
Whaley et al (1998, 25) Longitudinal study	Predictors of early cognitive development	Size measurements, weight, height, and arm circumference measured at birth and monthly thereafter.	Adapted BSID At age 5: Verbal Meaning Test and Raven's Progressive Matrices	Shorter and lighter infants were less sociable at 6 months than infants who were taller and maintained heavier weights. Infants with smaller arms circumferences displayed lower motor scores at 6 months and lower mental scores at 30 months.	Kenya	6, 30 months and 5 years	247 at 6m 137 at 30m 108 at 5y Attrition = 44.5% & 56.3% at 30m & 5y follow-up	Moderate	Growth and anthro-pometry

Abbreviations:

ART – Antiretroviral Therapy
CBSF – Cord Blood Serum Ferritin
CC – Community Children
CHIV – Chile HIV
CM – Cerebral Malaria
CMD - Common Mental Disorders
DDE - Dichlorodiphenyldichloroethylene
DDT - Dichlorodiphenyltrichloroethane
ECD – Early Childhood Development
ELC – Early Learning Composite Score
FASD – Foetal Alcohol Spectrum Disorder
FM - Fat Mass
FFM – Fat-Free Mass
HAZ - Height-for-age Z-scores
Hb - Haemoglobin
HEU – HIV Exposed and Uninfected
HIV - Human Immunodeficiency Virus
HUU – HIV Uninfected and Unexposed
ID – Iron Deficiency
MHIV – Maternal HIV
MRI - Magnetic Resonance Imaging
PTSD – Post Traumatic Stress Disorder
PVL – Periventricular Leukomalacia
RCT – Randomised Controlled Trial
SES – Social Economic Status
SMA – Severe malarial Anaemia
WAMI – Work and Meaning Inventory
ZDV - Zidovudine Monotherapy

Measures

ADBB – Alarm Distress Baby Scale
ASQ:I – Ages and Stages Questionnaire Inventory
BSID – Bayley Scales of Infant and Toddler Development
CDA – Cognitive Development Assessment
DDST – Denver Developmental Screening Test
DMC – Development Milestones Checklist
KABC – Kaufman Assessment Battery for Children
MDI – Mental Development Index
MSEL – Mullen Scales of Early Learning
NBAS – Neonatal Behaviour Assessment scale
PDI – Psychomotor Development Index
PPVT - Peabody Picture Vocabulary Test
R-DPDQ – Revised Denver Pre-screening Developmental Questionnaire
SRQ-20 – Self Reporting Questionnaire

Table 3 Summary of measures used in the studies included in the scoping review

Available Assessments	Number of studies using this tool
Ages and Stages Questionnaire: Inventory	2
Bayley Scale of Infant Development (BSID)	2
BSID-II	1
BSID-III	17
Brazelton Neonatal Assessment scale	1
Brunet-Lezine Scale and Alarm Distress Baby Scale	1
Caregiver Reported Early Childhood Development Index	1
Cognitive Development Assessment Test	2
Denver Developmental Screening Test	4
Development Milestones Checklist	1
Early Childhood Vigilance Test	1
Griffiths Mental Development Scales	1
Grover-Counter Scale of Cognitive Development	1
Kaufman Assessment Battery for Children	3
Kilifi Developmental Inventory	1
Malawi Development Assessment Tool	2
MacArthur Communicative Developmental Inventory	1
Mullen Scales of Early Learning	5
Neonatal Behaviour Assessment Scale	1
NEPSY	1
NIH Toolbox	1
Peabody Picture Vocabulary Test	6
Revised-Denver Pre-screening Development Questionnaire	2

Supplementary Table 1- example of search strategy in Medline

MEDLINE- 18.12.2018

Database: Ovid MEDLINE(R) and In-Process & Other Non-Indexed Citations <1946 to November 30, 2018>

Search Strategy:

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1 exp Child Development/ (55661)

2 (child* or infant or infants).mp. (2736049)

3 exp CHILD/ (1796839)

4 exp INFANT/ (1079561)

5 2 or 3 or 4 (2736049)

6 (health or growth or weight or height or circumference or stunting or "birth weight" or "breast feeding" or "birth order" or "gestational age" or sex or skeletal or malnutrition or "chronic illness" or disabilit* or immuni*).mp. (6368165)

7 exp Cognition/ (143485)

8 (cognition or "cognitive function" or "cognitive development").mp. (192650)

9 7 or 8 (247840)

10 6 and 9 (65837)

11 5 and 10 (15264)

12 1 or 11 (67792)

13 exp "AFRICA SOUTH OF THE SAHARA"/ or exp AFRICA/ (240427)

14 (africa or "sub saharan africa").mp. (139988)

15 13 or 14 (276741)

16 12 and 15 (1152)

17 exp LONGITUDINAL STUDIES/ (118946)

18 exp COHORT STUDIES/ (1798914)

19 (longitunidal or cohort).mp. (525208)

20 17 or 18 or 19 (1973472)

21 16 and 20 (303)

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Nutrition, growth, and other factors associated with early cognitive and motor development in Sub-Saharan Africa – a scoping review

Abstract

Background: Food insecurity, poverty, and exposure to infectious disease are well-established drivers of malnutrition in children in Sub-Saharan Africa. Early development of cognitive and motor skills – the foundations for learning – may also be compromised by the same or additional factors that restrict physical growth. However, little is known about factors associated with early child development in this region, which limits the scope to intervene effectively. To address this knowledge gap, we compared studies that have examined factors associated with early cognitive and/or motor development within this population.

Methods: Predetermined criteria were used to examine four publication databases (PsychInfo, Embase, Web of Science, and Medline) and identify studies considering the determinants of cognitive and motor development in children aged 0-8 years in Sub-Saharan Africa.

Results: 51 quantitative studies met the inclusion criteria, reporting on 30% of countries across the region. Within these papers, factors associated with early child development were grouped into five themes: Nutrition, Growth and Anthropometry, Maternal Health, Malaria and HIV, and Household. Food security and dietary diversity were associated with positive developmental outcomes, whereas exposure to HIV, malaria, poor maternal mental health, poor sanitation, maternal alcohol abuse, and stunting were indicators of poor cognitive and motor development.

Discussion: This synthesis of research findings shows across Sub-Saharan Africa, factors which restrict physical growth also hinder development of early cognitive and motor skills, but additional factors also influence early developmental outcomes. It also reviews methodological limitations of conducting research using Western methods in sub-Saharan Africa.

Introduction

According to the World Health Organisation (WHO) early child development spans the ages of 0-8 years. This is a critical and formative period in a child's life when the brain is developing rapidly and core cognitive and motor skills, the foundations for later learning[1], are being acquired. It is estimated that 250 million, or 43% of children living in low-to-middle-income countries fail to reach their full cognitive and educational potential[2]. The vast majority of these children live in Sub-Saharan Africa[1] where there is also a high prevalence of stunting[1] and malnutrition[3]. Many low-income countries in Sub-Saharan Africa are burdened with high rates of maternal, infant, and childhood mortality as well as undernutrition. These are driven by various factors including but not limited to: lack of maternal education, poor sanitation, exposure to human immunodeficiency virus (HIV), and low rates of exclusive breastfeeding[4]. Coupled with economic and gender inequalities, factors which operate in the first 8 years of life result in many children failing to achieve their educational potential. A prolonged history of poor and unequal early child development and learning is shown across Sub-Saharan Africa,[5] which impacts on the long-term economic growth and welfare of the population. Early child development encompasses several aspects of development including physical, cognitive, psychosocial, and motor development. Factors that impact on development, such as nutrition, play an important role in developmental delay. A combination of adverse health environments (e.g. undernutrition and repeated infection) during key periods of development, and inadequate provision and uptake of schooling, maintains a cycle of poor cognitive and physical development, poverty, and inequality, which inevitably passes to subsequent generations.

Cohort and longitudinal studies can examine relationships between nutritional status, prevalence of disease, maternal deprivation, and access to health care, and how these factors are associated with child growth and development over sustained periods of time[6]. Accordingly, recent years have seen an increase in cohort and longitudinal studies in low-to-middle-income country settings, including Sub-Saharan Africa. Increasingly, these studies are considering outcomes on cognitive and motor development – the foundations for learning – that can have long-term sequelae[7,8], but for Sub-Saharan Africa there is currently a lack of clear consensus on which factors have a detrimental or positive influence.

This scoping review considers factors associated with early child development in Sub-Saharan African countries. Though of limited usefulness in terms of providing quantitative data relating to specific research questions, scoping reviews are an ideal tool to determine the

range or coverage of literature on a given topic and explore emerging evidence. They give a clear indication of the volume of studies available as well as an overview of their focus. This review focused solely on cognitive and motor development as these are foundational skills that underpin educational potential and scholastic achievement[9-11]. Considering only cohort and longitudinal studies, the review assessed multiple factors that might influence cognitive and motor development in children under the age of 8 years, with a strong focus on the first two years of life. Enhancing understanding of how early nutrition and other environmental factors influence early child development is important for countries across Sub-Saharan Africa to break the cycle of poor cognitive and motor development which limits educational potential and attainment. By assessing current evidence, this scoping review aimed to identify key factors that are associated with early development of foundational skills that are core to later learning[1,12].

Method

This review aimed to scope previous and current cohort and longitudinal studies conducted across Sub-Saharan Africa that had examined cognitive and motor development across early childhood.

Inclusion criteria

Type of studies

Published and peer-reviewed quantitative studies were examined, including cohort and longitudinal studies with experimental and observational designs.

Type of population

Studies examining children aged between 0-8 years were reviewed. If a wider age range was reported, age-specific findings were extracted and reported separately.

Phenomena of interest

This review focused on factors that influence cognitive and/ or motor development in Sub-Saharan countries as these are foundational for later learning potential.

Type of Outcome

The primary outcome was the measurement of cognitive and/or motor development and the factors that influence these developmental processes. For inclusion, studies were required to

provide clear details on the measurements used (outcome variables and controls), ideally including details on how measures were adapted for low-to-middle-income country contexts. However, if no such adaptation contexts were mentioned, studies were still included to examine the extent to which Western measures of early child development were employed.

Context

This review included studies conducted in Sub-Saharan Africa or that included at least one site within Sub-Saharan Africa. Sub-Saharan Africa is defined as the geographical area of the continent of Africa that lies south of the Sahara and includes 46 countries.

Exclusion criteria

Qualitative studies, mixed methods studies, literature reviews, unpublished and grey literature were excluded. Studies were also excluded if they did not specify the precise location, details of measurement of cognitive and motor development, or did not report separate findings between age groups if including older children. Studies that did not use a longitudinal or cohort design were also excluded. The inclusion and exclusion criteria are summarised in Table 1.

Search strategy

Four databases (PsychInfo, Embase, Web of Science, Medline) were searched from inception to extract published studies. Following the search of these main databases and removal of duplicates, an initial search and preliminary analysis was conducted of the subject headings (MeSH) and text words related to early child development contained in the title and abstract.

The search strategy comprised a combination of key words (e.g. 'Early Child Development', 'Sub Saharan Africa') and controlled vocabulary (e.g. 'health', 'growth'). A full search strategy for Medline (MEDLINE In-Process & Non-Indexed Citations and OVID MEDLINE 1946 to present-Ovid) is detailed in Supplementary Table 1, as an example. The search was first performed on the 18th of December 2018 and conducted again on the 8th of October 2019. Date and language limits were not imposed.

Reference lists of all selected papers that met the inclusion criteria were hand searched to check for additional studies.

Study selection

Following the search, all identified citations were uploaded into Endnote and duplicates were removed. The review authors independently screened the titles and abstracts for assessment

against the search inclusion criteria. Full texts were obtained for all titles that appeared to meet the inclusion criteria.

A main review author (BF) screened and assessed the full text reports in detail against the inclusion criteria (see Table 1). Studies that did not meet the inclusion criteria were excluded. A record of excluded studies, including reasons for exclusion, is provided in the PRISMA flow diagram[13] (Figure 1).

Data extraction and outcomes

Data extraction

One reviewer (BF) extracted data from the included studies, informed by a standardised data extraction tool for quantitative studies (JBI- MAStARI[14]) and this was checked by a second reviewer (LO). The extracted data included specific details relating to the inclusion criteria (see Table 1), which address the main aim of this scoping review.

Outcomes

The main outcome was the exploration of measurement of cognitive and motor development in young children aged 0-8 years in Sub-Saharan African countries and the factors influencing them. Multiple types of factors reported in the selected studies were evaluated, such as child health, growth, and development. These factors were grouped into themes within the synthesis phase and subsequently grouped into factors associated with the acquisition of early cognitive and motor skills.

Assessment of methodological quality

Following quality assessment reviews guidelines[15], two review authors (BF and LO) critically appraised all selected studies for methodological quality using standardised quality appraisal tools for quantitative studies) (JBI Critical appraisal checklist for case studies, JBI Critical appraisal checklist for cohort studies, JBI RCTs appraisal tool [8]). These instruments assess the quality of evidence across studies with different designs, including but not limited to criteria, such as sampling strategy, analysis, transparency, and interpretation. Any disagreement between reviewers was resolved through discussion. Studies were stratified in Table 2 according to the result of the quality assessment. Study quality score did not affect inclusion in the review; all studies that met the inclusion criteria were subjected to data extraction and synthesis.

Following Kmet, Lee and Cook's[8] guidelines, an original quality score from 0 to 1 was calculated for each study. Scores were then classified from low (0 - 0.44), moderate (0.45 - 0.69), and high (0.70 - 1.00). Study quality was assessed by the two reviewers (BF and LO). Initial agreement between reviewers was 89% overall and all disagreements were resolved through discussion. Some variation in quality was shown across 51 studies included in this review. The average quality score was 0.67, which was comprised of 28 studies that received a high-quality rating, 19 studies that received a moderate-quality rating, and four studies that received a low-quality rating.

Data synthesis

Two reviewers (BF and LO) conducted the syntheses in a sequential order. One reviewer (BF) developed the synthesis and the second reviewer (LO) checked the findings. Any disagreements were discussed (initial agreement of 80%) and a mutual resolution was found. Once data was extracted in descriptive form, and according to JBI scoping review guidelines, quantitative synthesis was generated and summarised in thematic statements[14]. There was a high level of heterogeneity within the included studies which precluded statistical pooling of extracted data. Consequently, an inductive approach of a narrative synthesis of the extracted data was deemed most appropriate. Configuration of all themes generated a set of statements that represent the final aggregation.

Factors extracted for this review that were found to influence early cognitive and motor development were categorised into five main themes, these being: Nutrition, Growth and Anthropometry, Maternal Health, Malaria and HIV, and Household and other factors.

Results

Study selection

The study selection process is illustrated in Figure 1. In total, 51 studies published between 1991 and 2019 met the inclusion criteria. Of these 29 (57%, 11 in 2017, 10 in 2018 and 4 in 2020) were published after 2016, when The Lancet published a special edition of research papers focused on this topic.

Table 2 summarises the extracted data for each study included in the review. Amongst the included studies, a range of 14 Sub-Saharan countries were represented with 12 studies

originating from South Africa, eight from Ethiopia, six from Tanzania, five from Malawi, four from Kenya, three each from Ghana and Zambia, two each from Uganda, Botswana, and Benin, and one each from Gambia, Sudan, Rwanda and Congo. A range of methodologies were reported in the studies included in this review: most were prospective or longitudinal cohort studies and four randomised control trials were also included. There was high variability in sample size, ranging from 85 to 4205. In addition, attrition varied at follow-up from 0% to 95.3%. Twenty-seven (53%) of the 51 studies included in this scoping review reported change of numbers in at least one point of follow up; the rest of the studies did not include data on participants lost to follow up. Of the 27 studies that reported on follow up, a mean attrition of 47.8% (SD = 26.2%) was found (note: for the 5 studies that reported on more than one point or group at follow-up, mean attrition was calculated and used to determine the grand mean). For most studies, limited information, if any, was given as to why loss at follow up occurred. More details are provided in Table 2.

Measures used in assessing cognition and motor development

Amongst the studies included in this review, a wide range of tools were used to assess cognitive and motor development, making it difficult to generalise findings (Table 3). The most common assessment tool used was the Bayley Scale of Infant Development (BSID), which was employed in 20 of the 51 (39%) studies reviewed.

Data extraction and summary of results

Results revealed many factors associated with early cognitive and motor development. These factors were grouped into five main overarching categories. These categories were interlinked, reflecting a multi-level framework, and demonstrating that no individual category could explain differences in early cognitive and motor development across Sub-Saharan Africa.

The five main categories of factors highlighted by this review include: Nutrition, Growth and Anthropometry, Maternal Health, Malaria and HIV, and Household.

Nutrition

The first group of factors influencing early cognitive and motor development related to infant and maternal nutrition. Principally, studies looked into the effect of nutrition and nutrients[16-20], and vitamin supplements[21-24].

Studies reporting on the influence of food consumption on early child development showed that children living in households that experienced food insecurity in the first two years of life had low gross motor, communication, and personal social scores[18]. Conversely, dietary diversity, child iron status, and early nutritional interventions that increased birth weight and growth in the first two years were associated with improved growth, language skills, and motor development[19].

Less than optimal micronutrient status was a strong focus on the influence of nutrition on early child development, but most studies[21-24] found no impact of nutrient supplementation (zinc, multivitamin, iron and ferritin) on young children. Two studies investigating the differences between groups of infants taking zinc and vitamin supplements in Zambia[22] and Tanzania[21] found no difference in motor and cognitive development compared to placebo controls. Similarly, Mireku and colleagues (2016) demonstrated that prenatal iron deficiency and low neonatal ferritin were not associated with poor cognitive or gross motor function, although a negative relationship between gross motor function and children's haemoglobin concentration was reported[24]. Cognitive development and linear growth at age 4-6 years was also reported by Ocansey et al. (2019) to be significantly associated with haemoglobin concentration at 18 months[25], but unlike Mireku et al (2016), Ocansey et al. (2019) found no association with motor development. A randomised control trial (RCT) exploring prenatal supplementation with vitamin A and zinc[21] reported no developmental benefits in children of women consuming the supplement.

Growth and anthropometry

Growth and anthropometry encompass many different aspects of children's physical health. Many studies evaluated the influence of children's physical health on their early cognitive and motor development. While some studies focused on stunting and growth[10,14,21-25], others focused more specifically on anthropometry at birth[31-34]. Most studies found a strong relationship between restricted physical growth and poor early cognitive and motor outcomes.

Stunting is defined as the impaired linear growth of children who experience poor nutrition or repeated infection[2]. Stunting and impaired growth were shown to be strong predictors of poor cognitive and motor development[16,20,30,34]. In exploring the long-term effect of stunting, Crookston and colleagues (2013) demonstrated that height-for-age was positively associated with mathematics achievement, reading comprehension, and receptive vocabulary. Children persistently stunted between early and late childhood faced more adverse outcomes at school

compared to those who were never stunted[29]. Moreover, children who recovered from stunting showed persistently low cognitive test performance that was commensurate with the performance of children who remained stunted[26], demonstrating a long-term impact of early stunting into later childhood. Whilst these studies largely supported a negative influence of stunting on developmental measures, one study based in Tanzania showed weight-for-age and weight-for-length scores were positively associated with gross motor scores, but not for other measures of motor and cognitive skills[28].

Anthropometry at birth was explored in relation to long-term early child development. Length-for-age scores at birth and at 6 and 18 months were associated with cognitive, but not motor development in children aged 4-6 years in Ghana[25]. High fat mass in the first 48 hours of birth predicted high global developmental scores[31]. A study based in South Africa showed that very low birth weight was not predictive of neurodevelopmental outcomes[32]. Infants born preterm (<37 weeks gestation) in Malawi had a high rate of developmental delay at 18 months, which was inversely associated with gestational age[33].

Maternal Factors

Maternal factors were investigated primarily in relation to maternal mental wellbeing. General maternal health and mental disorders[30-33], post-traumatic stress disorder (PTSD)[31], and foetal alcohol spectrum disorder (FASD)[40] were discussed as factors affecting outcomes in early childhood.

Accumulated exposures to maternal risk factors, for example, low socio-economic status (SES) and domestic violence, were shown to have a stronger association with child cognitive and motor development, compared to common maternal mental health disorders, such as depression or anxiety[37]. Infants with FASD in South Africa were shown to have impaired performance on all scales of mental development of the BSID[40]. Several maternal protective and risk factors were associated with cognitive and motor developmental outcomes. For example, maternal education and SES were shown to ~~the~~ be protective factors whereas maternal anaemia in pregnancy, depression, partner violence, and HIV infection were shown to ~~the~~ be risk factors[41]. Maternal weight and diet also influenced neurobehavioural and motor performance at birth and at 6 months. Greater maternal dietary quality was associated with better infant motor performance[17].

While common maternal mental health disorders influenced child absenteeism and school dropout, it did not affect child academic achievement[36]. Other factors such as mother's access

to antenatal care were found to be related to improved child cognitive development[30,36]. Meanwhile, low maternal height, delivery characteristics (e.g. oxytocin administration) were associated with cognitive and development outcomes at 15 months[38]. Maternal PTSD was associated with poor fine motor and poor adaptive motor development in children[39]. Finally, greater caregiver/child stimulation was found to predict higher child cognitive scores and maternal completion of primary school was associated with higher child motor and cognitive scores[43].

Malaria and HIV

Studies included in this review also considered the relationships between child development and malaria or HIV (5 studies on malaria and 11 studies on HIV). Malaria studies focused primarily on cognitive development[44-47] while HIV studies incorporated both cognitive and motor development[29,42-52].

Studies investigating the impact of malaria on early child development have produced inconsistent findings. Bangirana and colleagues (2014) reported that Ugandan infants with cerebral malaria and severe malarial anaemia had lower scores in cognitive ability, attention and associative memory at 12 months than their control peers. Similarly, exposure to the malaria parasite in early childhood was associated with lower tolerance of the testing procedure of the cognitive tasks at 6 years[46]. When tested at 5 years of age, children with malaria in a cohort study based in Malawi[47] showed on average a 6-month delay in motor, language and social development. Despite this, no difference in age-expected attainment was found for cognitive skills compared to control[45].

Studies on HIV have consistently demonstrated impairment of cognitive and motor functions in children and infants with HIV[29,47] showing delayed attainment of developmental milestones[48], including gross motor skills[54] and neurodevelopment deficits[49] compared to uninfected children. Leroux and colleagues (2018) reported delays in cognitive and motor development but highlighted no delays in expressive language scores at 18 months. The effects of HIV infection on development can be overcome with treatment. Three studies investigated the outcomes of HIV care and demonstrated that infected infants and children who received HIV care achieved similar cognitive and motor scores to uninfected children at 6, 12 and 24 months[56-58].

Children can also be exposed to HIV in utero without becoming infected. Studies of HIV-exposed uninfected infants have yielded inconsistent results. Whilst, Brahmbatt and

colleagues (2014) found that HIV exposure alone was associated with impaired receptive language skill in children and generally poor early child development, other studies found no difference in cognitive and motor development of infants and children exposed to HIV and their non-exposed peers[44,45,49].

Household and other factors

Many household factors were found to be associated with early child development. This highlights the importance of the environment that children grow up in for supporting the acquisition of cognitive and motor skills. Studies investigating household factors have examined SES[10,23,37,53], sanitation and water[14,54], access to antenatal care[35], orphanage[61], and insecticide exposure[62].

Investigations into the effect of SES on early child development have produced mixed findings, which might reflect differences in how SES is conceptualised and measured in different contexts and different countries. One study reported no effect of SES (measured by a household asset index) on early child development but rather area of residence (established by geographical area) was associated with early developmental outcomes[16]. In contrast, other studies demonstrated that SES (measured by a socio-economic questionnaire and household wealth) was linked to child language development[59] and cognitive scores at 15 months of age[28].

Access to improved water (i.e. piped water, public tap or standpipe, tube well or borehole, protected dug well, protected spring, and rainwater collection) at 1 year of age was associated with higher language scores in children at 5 and 8 years[60] and access to a flush-toilet in the home/village environment was associated with higher cognitive and motor scores in children aged 18-36 months compared to those where a flush-toilet was not available[20].

Attendance at antenatal care by mothers was shown to have a positive association with cognitive development at age 5[35]. Whilst orphaned infants showed impairments in psychomotor development at admission (1 month old), over 85% of orphaned children showed age-appropriate development by 18 months[61].

Finally, a study investigating exposure to insecticide showed no significant relationship with cognitive development[62]. Other factors also investigated in some of the studies included the influence of twin birth[63], ethnicity[64], early mental development[65], and birth asphyxia[66] on early child development. These studies demonstrated that twin birth was associated with delayed attainment of motor development milestones[57], and factors linked to ethnicity such as

family stability and income were positively associated with motor and language development[58]. Moreover, poor mental development at age one was associated with poor cognitive development at age 5[59]. Regular treatment of asphyxia after birth was associated with good cognitive scores at three years of age. Prado et al. (2018)[13] also considered the influence of access to play materials and activities with caregivers on early language and motor development and showed a positive association of these factors on growth and language development.

Discussion

The aim of this review was to scope published literature reporting on factors associated with early cognitive and motor development in Sub-Saharan Africa. A detailed understanding of these factors is a prerequisite for design of future longitudinal cohort studies and interventions targeted at improving the lives of children living across this region. A clear need for focussed research in this area was revealed. In total, only 51 studies have been published in the past 28 years (between 1991 and 2019) which met the inclusion criteria, with the majority of studies (90%) being published in the past 10 years. The recent rise in studies focusing on this topic demonstrates increasing awareness of the need to enhance understanding of factors influencing development of foundational skills that underpin later learning potential[67]. This is a critical step for countries to be able to meet the 2030 United Nations Sustainable Development Goals.

Only 14 (30%) of the 46 countries comprising the Sub-Saharan Africa region were included in the 51 studies that met the inclusion criteria for this scoping review. The absence of relevant studies from the remaining 37 countries of Sub-Saharan Africa, demonstrates an alarming lack of knowledge about factors influencing early cognitive and motor development across more than 70% of the region. Whilst the factors identified in this scoping review may apply to other countries in the region, this needs confirmation from quantitative longitudinal cohort studies. The results of this scoping review are therefore important for guiding future research.

The 51 studies included in this review identified multiple factors that broadly addressed five key themes, namely Nutrition, Growth and Anthropometry, Maternal Factors, Malaria and HIV, and Household. Although these factors may operate in isolation, it is likely that they will interact with a multiplicative effect to influence on the development of early cognitive

and motor skills. This emphasises the importance of adopting a multi-level conceptual framework of early child development across Sub-Saharan Africa that describes the complexity by which different factors influence early developmental outcomes that underpin potential to succeed at primary school.

Childhood nutrition, growth, and maternal health were the factors with the most frequently reported influence on early child development, with infectious diseases such as HIV and malarial infection also playing a key role. Whilst infectious diseases such as tuberculosis, gastrointestinal infections or measles are common in Sub-Saharan Africa, the studies in this review only investigated the influence of Malaria and HIV on development, demonstrating a significant lack of research in the influence of other infectious diseases in Sub-Saharan Africa. There is a well-established interrelationship between nutrition and infectious disease which is often driven by SES, and has been shown to influence physical growth, stunting and wasting. Maternal health and nutrition during pregnancy is a key driver of growth outcomes for children[4]. The papers identified in this scoping review indicate that this is also the case for early cognitive and motor development. Maternal nutrition and lack of specific nutrients for mothers, during pregnancy and early years were also shown to have long-term impact on child development. This has been recognised previously in randomised control trials considering the influence of iron deficiency on cognitive and motor development[68]. Less than optimal maternal nutrition and health directly influences children's health and growth which are also related to early cognitive and motor development. The broader literature on nutrient deficiency and cognitive development suggests that the window of time for intervention is limited and cognitive deficits at an early age have lasting effects on brain development[69]. However, the studies included in this review demonstrated limited positive effects of supplementation of micronutrients. While maternal and child health encompassed the main factors affecting early child development highlighted by this review, it is also important to note that household and other factors also need to be considered. This review showed that household determinants, such as access to sanitised water or access to antenatal care, influence cognitive and motor development in Sub-Saharan Africa, in a similar way to the risks of stunting and wasting.

Methodological considerations were also emphasised by this review. Sample size and attrition were highly variable across studies, which raises concerns about data security and limits the extent to which comparisons across studies can be drawn. Of the studies that reported on attrition, on average 47.8% of the original sample was lost at follow up. Future

research should take this into account when recruiting new participants to ensure sufficient statistical power at follow-up.

Many studies relied on the use of psychometric tools validated for Western populations for measuring early cognitive and motor development in Sub-Saharan African countries. The use of assessment tools used in Western cultures has been shown to be somewhat problematic[72]. Motor and cognitive development need to be assessed in relation to cultural and environmental factors. For instance, motor assessment in Western countries include developmental stages such as climbing steps which is not necessarily relevant in some low-to-middle-income settings where steps are not a prevalent feature of many family homes. Adapting these tools by excluding such tasks is not necessarily appropriate, so using a culturally relevant tool, such as the Malawi Development Assessment Tool[73] for studies conducted in Malawi for instance, might be more fitting.

The Bayley Scale of Infant Development (BSID) was the most frequently used psychometric tool used to assess early child development in the studies covered by this review. This measure is recognised internationally as one of the most comprehensive tools to assess children from as young as one month old and with the latest version of this tool, BSID-III, it is possible to obtain detailed information even from non-verbal children as to their level of functioning. However, while the BSID is considered a valid and reliable measure of early child development for Western populations, there are a number of practical barriers to use in Sub-Saharan contexts, including the high cost for materials, the need for specially trained administrators and the relatively long administration time[74]. Furthermore, the use of the BSID and other Western assessments is often inadequate in developing countries [75]. The BSID was developed in the US, a Western, high-income country, and may not translate to low-to-middle-income country contexts[72]. Furthermore, the use of norm-referenced scores based on high-income-country contexts are not valid in low-income countries and may lead to children being misclassified as having developmental delay[76] and produce misleading results. Adapting psychometric tools to be culturally appropriate for low-to-middle-income contexts can overcome this problem. Hanlon et al. (2016)[77] successfully adapted the BSID for use in rural Ethiopia by translating and modifying the test materials, instructions and concepts measured. There are several emerging assessment tools that have been specially designed for use in low-to-middle-income countries. For example, the Intergrowth 21st Neurodevelopmental Assessment (Inter-NDA) is a holistic and objective measure of early child development that has been trialled in a broad range of 13 countries (none in Sub-

Saharan Africa) and validated against the BSID-III. The Inter-IDA items have been specially designed to be culture-free and easy and reliable to administer by non-specialists in low-to-middle-income contexts[78].

Country-specific distributions can be used to identify children 'at risk' with greater ecological validity than comparing to Western norms. Whilst this relative method of identifying children at risk would enable comparison between countries, it is important to note that absolute levels of ability might differ across countries. This would result in some children being identified as at risk for poor early outcomes in some countries, who would not be classified at risk in other countries where the distribution of scores was lower, and vice versa. Direct comparison of test performance across countries is only meaningful when both the average (mean/median) and distribution of test scores is similar. ~~We recommend that measures of early child development that have been developed and norm-referenced for Western, high-income, countries are validated by low-income countries before adopting them as an outcome measure in studies examining early child development. This can determine the extent to which they are suitable for administration in specific country contexts without adaptation. Depending on the results of the validation study, adaptation to test materials might be required before they are considered appropriate for use in a given context and before population distribution data is obtained.~~

This scoping review has demonstrated that birth cohort and longitudinal studies are a viable method for investigating a range of multi-level factors in early childhood in Sub-Saharan Africa. Ongoing birth cohort studies are also considering a wider range of determinants of early child development than have been studies previously. For example, the Drakenstein Child Health Study follows a multi-level, ecological approach to understand cognitive, socio-emotional and neuropsychological child development[79]. The Malnutrition and Enteric Disease Study (MAL-ED) multi-site birth cohort study is also examining child development and language acquisition from birth to 24 months in eight low-to-middle-income countries[80,81]. Consistent with previous research, data from the MAL-ED project in Tanzania showed child weight-for-age, weight-for-length, SES and female gender were associated with cognitive and motor development [28]. However, Donald et al.[79], Caulfield et al.[80], and Murray-Kolb et al.[81] all highlight important issues surrounding measurement and data collection in low-to-middle-income contexts, which can impact on results.

Future research should further investigate the multiple factors highlighted in this review, taking into consideration the cultural and environmental setting of different study sites. While

maternal and child health factors are prominent areas of research, the findings from this review are somewhat contradictory. Future research should aim to gain a clearer understanding of why this is and how factors such as HIV or nutrition affect early child development. This would allow for better targeted interventions and guidelines to be implemented to mitigate risk of childhood morbidity and underachievement at school.

As the number of cohort studies being conducted in other low-to-middle-income countries increases, there could be potential for cross-cultural comparisons. This could further inform theoretical and practical understandings of generic factors that are associated with early child development in low-to-middle-income country contexts compared to country-specific factors. Studies in Latin America, for example, show that specific nutrient deficiency (iron) influence early child development[82] and the meta-analysis by Ip et al. (2017)[83] of randomised control trials of nutritional supplements showed improved cognitive function in children in several developing countries, including Bangladesh, Chile, China, Colombia, Guatemala, India, Indonesia, Jamaica, Mexico, Nepal, Pakistan, Peru, Thailand, Vietnam, as well as several nations in Sub-Saharan Africa. However, in the context of uncontrolled observational studies, findings from a wide representation of multiple types of backgrounds and study sites might not be generalisable over all contexts. The sample of studies included for this scoping review was skewed by a strong prevalence of studies from South-Africa (12 out of 51), and mainly from urban sites, which might not reflect the conditions of other countries and settings.

~~*Limitations*~~

This scoping review has highlighted several factors that influence early cognitive and motor development in infants born across Sub-Saharan Africa. Despite the serious consequences of poor early child development on an individual's potential and a country's economic growth, surprising few studies have focussed on this important issue. Many studies reported on one particular factor, and there was variability across findings, so it is difficult to generalise results until a more comprehensive evidence base exists. Drawing firm conclusions was a challenge for this review due to variabilities in reporting, methodology and quality of the literature. As such, the results from this scoping review should be treated as early indications of how different factors influence early cognitive and motor skills, until further studies are available to enable general trends to be established through replication and reproducible findings. ~~The studies reviewed here also show high variability in sample size and attrition, which can bias findings, especially with small samples and high levels of attrition. In addition, there is variability across studies in the conceptualisation and measurement of~~

~~different factors and skills, which makes drawing conclusions difficult. To enable generalisation within and across countries, studies need to adopt a consistent conceptual framework and ideally utilise the same tasks to measure early cognitive and motor skill, with appropriate norms. As development is a dynamic process that changes over time, a finding at one point in time is not necessarily indicative of outcomes at a later point in development. Downstream effects mean that secondary impairments can emerge later in the developmental pathway for functions that are reliant on the development of a specific function acquired at an earlier age.~~

~~To address these limitations, longitudinal monitoring is required across the first 8 years in life, and beyond. Cohort studies are needed, ideally from pregnancy or birth, across the early childhood period to enable a greater understanding of factors that influence early cognitive and motor skill to be determined. These are difficult to conduct largely because they require acquisition of big datasets across a long period of time and are thus costly. Nevertheless, longitudinal pregnancy or birth cohort studies are the best methodology for addressing this issue. Benefits might also be gained from utilising applied statistical techniques that enable different datasets to be combined in a meaningful manner. These techniques are starting to emerge from the work of big data scientists and have the potential to be transformational when applied to understanding factors that influence the process of early child development across Sub-Saharan Africa. Accordingly, we call upon funding agencies to invest in these methods, if we are to gain a better understanding of what causes poor developmental outcomes in early childhood, how best to intervene, and ultimately how to prevent the cycle of poverty that mars these countries.~~ *Recommendations for future research*

This review has uncovered a number of significant omissions and inconsistencies in the evidence base relating to early life influences on cognitive and motor development. To enable generalisation within and across countries, studies need to adopt a consistent conceptual framework and ideally utilise the same tasks to measure early cognitive and motor skill, with appropriate norms. As development is a dynamic process that changes over time, a finding at one point in time is not necessarily indicative of outcomes at a later point in development. Downstream effects mean that secondary impairments can emerge later in the developmental pathway for functions that are reliant on the development of a specific function acquired at an earlier age. ~~To address these limitations,~~ Llongitudinal monitoring is required across the first 8 years in life, and beyond. Cohort studies are needed, ideally from pregnancy or birth, across the early childhood period to enable a greater understanding of factors that influence early

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Conclusion

In conclusion, this scoping review has highlighted many important factors to take into consideration when conducting research in low-to-middle-income country contexts. The complex relationship between early nutrition, growth, infectious disease and poverty in determining early child development is clear, highlighting the importance of well-designed and targeted interventions to improve cognitive function, educational attainment and achievement of potential. ~~Methodological factors, such as attrition rates or the use of specific assessment tools, are important considerations in conducting research in low-to-middle-income countries.~~ Factors affecting early child development highlight the need for a multi-level approach, including maternal health, child health and household determinants.

~~Due to the wide range of studies included, the wide difference in methods, designs and in study qualities, it is difficult to summarise clear conclusions or make strong recommendations from this review.~~ The variance found in this review demonstrates a need for more robust and consistent research on this topic. This is needed to gain a more comprehensive understanding of how different factors come to play in early child development in Sub-Saharan Africa and how targeted interventions can address these impacts.

Transparency Declaration

The authors affirm that this manuscript is an honest, accurate, and transparent account of the study being reported. The reporting of this work is compliant with PRISMA guidelines. The lead author affirms that no important aspects of the study have been omitted.

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Figure legends

Figure 1 Flow diagram of the study selection processes

~~**Figure 2** Frequency of publications included in the scoping review per year~~

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