A systematic review of cerebral palsy in African paediatric populations

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Declaration

I declare that this thesis has been composed solely by myself and that it has not been submitted, in whole or in part, in any previous application for a degree. Except where stated otherwise by reference or acknowledgment, the work presented is entirely my own.

Dr Serini Murugasen

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“To win the respect of intelligent people and the affection of children, to earn the appreciation of honest critics and endure the betrayal of false friends; to appreciate beauty, to find the best in others, to leave the world a bit better, whether by a healthy child, a garden patch or a redeemed social condition; to know even one life has breathed easier because you have lived. This is to have succeeded.” – Ralph Waldo Emerson

Abstract

Introduction Most knowledge on cerebral palsy (CP) comes from studies of North American and European populations. Translating this information into African contexts is difficult and flawed due to the dearth of information on CP in the region.

Objective To review the literature on the prevalence, aetiology, co-morbidities, therapies and functional outcomes of African children with CP over a 20-year period.

Methods PubMed, SCOPUS and Web of Science databases were searched for original research on children with CP aged <18 years published from 2000-2020. 1452 articles underwent a primary and secondary survey against explicit inclusion and exclusion criteria, with the final 58 articles reviewed by all 3 authors prior to quality assessment and data extraction.

Results Prevalence of CP ranged from 0.8-10 per 1000 children, with most studies reporting a prevalence of 2-3 per 1000 children, but with concerns around case identification and undercounting. Almost half these children had identifiable risk factors in the perinatal period but up to 26% had no identifiable risk factor. Hypoxic ischaemic encephalopathy and kernicterus were important risk factors for CP in Africa. Spasticity was the most common clinical subtype and up to two-thirds of children with CP had at least one co-morbidity. Hospital-based populations had a larger proportion of more severely impaired children compared to the community, but all children had a disproportionately low level of access to assistive devices or rehabilitation services. Children with CP showed functional improvement with interventions compared to controls. Caregivers struggle significantly with multiple barriers to accessing services.

Conclusion The true prevalence of CP in Africa remains uncertain, but African children have a different risk factor profile and higher levels of impairment and co-morbidities compared to the global North. Significant barriers prevent these children from accessing optimal care.

Contents

Introduction

The term “cerebral palsy” refers to a heterogenous group of conditions arising from a static, non-progressive insult to the developing foetal or infant brain. The primary pathology is motor dysfunction – involving tone, posture and movement – with clinical expression changing over time as the central nervous system matures, expected developmental milestones change and sequelae of the primary features develop (1). Cerebral palsy (CP) may negatively impact function in other areas of development as well, such as speech and self-care. It is also associated with a high number of co-morbidities such as seizure disorders, other neurodevelopmental disorders and intellectual disability (2).

The cited global prevalence of CP is 2 per 1000 live births (3–5) with an extensive list of antenatal risk factors including prematurity, low birth weight, intrauterine infection, maternal smoking/alcohol/obesity, hypoxic ischaemic encephalopathy, intrauterine growth restriction, multiple pregnancy, pre-eclampsia and abruptio placentae (6,7). Genetic susceptibility was historically thought to be uncommon but the advent of new sequencing techniques reveals it may play a bigger role in conferring vulnerability than previously appreciated (8). Initially, the prevalence of CP rose as the survival of children with CP improved (9). However, over the last two decades, the prevalence in preterm infants has decreased and has been stable in term and late preterm infants (10,11) - likely due to improved antenatal and perinatal care in high-income countries (HICs).

The majority of our knowledge on the prevalence, aetiology, co-morbidities and outcomes for children with CP comes from studies in North American and European populations (3–6,10,11). African countries face challenges unique to our continent and to each individual country that impact on all facets of this condition and make translating this information into African contexts difficult and flawed.

In many African countries, there is a broad understanding of the conditions encompassed by the term “cerebral palsy”– partly due to local resources and the main point of contact with the health system, e.g. traditional healer versus medical officer versus specialist. In practice, CP is commonly used to refer to all motor disability syndromes as diagnosis is often made by

health practitioners with limited paediatric experience, perinatal history and/or diagnostic facilities (12). Across Africa, postnatal causes of CP play a much larger role compared to other parts of the world (13–17). As a result, some African countries consider deficits resulting from postnatal insults up to age five rather than two years as CP, which widens the range of the reported CP prevalence among African populations to 2-10 per 1000 live births (13,18,19). In low and middle-income countries (LMICs), birth asphyxia/perinatal hypoxia, kernicterus and neonatal infections are the most common antenatal risk factors (18,20,21) versus prematurity and low birth weight in Europe and USA (3,5,10).

There appears to be a larger proportion of more severely disabled children in both hospital and older community-based populations (13,15,17,22–24): spastic diplegia and spastic hemiplegia are the predominant clinical phenotype in HICs versus spastic quadriplegia in LMICs (14,16,22,25). There appears to be a similar reported pattern of co-morbidities for children with CP in Africa, including seizure disorders and intellectual disability (15,22,26), but greater impairment in their physical and psychosocial health when compared with international counterparts (24). This greater burden of disability may be due to delayed presentation and/or limited number of appropriately trained professionals or limited access to diagnostic imaging, medication, supportive services or early intervention programmes. The results may be further confounded by existing reports reflecting largely hospital-based populations.

It is important to acknowledge the role of stigma as well as geographical and financial barriers in accessing appropriate health and education services that many children with disabilities and their families face in Africa. Consequently, standard guidelines for diagnosis and intervention for CP (27) may not be easily translated into resource-poor settings (12). Longitudinal studies in African populations looking at locally-derived, culturally-sensitive and effective interventions are lacking.

Previously, there was a global focus on a biomedical model of impairment and targeting “normality” as the end point when discussing people with disabilities, as reflected in the World Health Organization's (WHO) 1980 International Classification of Impairment, Disability and Handicap (28). In 2001, the WHO released the International Classification of

Functioning, Disability and Health (ICF) which tried to shift the lens on disability towards conceptualising it as four interconnected domains (body functions and structures, activities and participation, environmental factors, and personal factors) that emphasise a biopsychosocial model of functioning rather than focusing on deficits (29). However, research on CP in Africa still appears focused on functional impairment rather than considering the interplay with participation, environment and personal factors, which may identify modifiable factors that offer opportunities for intervention (29).

A 2014 systematic review by Donald *et al* sought to synthesise the available literature at that time on the prevalence, aetiology, comorbidities, outcomes, screening tools and therapies for children with CP in Africa (30). They identified 38 relevant English-language publications across this range of topics for inclusion. The review highlighted several gaps in knowledge and concerns around study methodology: true prevalence of CP due to varied definitions and populations sampled; appropriate adjustment for confounding and bias and lack of a control group in studies on aetiology; the impact of selection bias using hospital cohorts and the paucity of information on coordinated care and interventions for children with multiple co-morbidities. Since then, studies from both population and hospital cohorts have provided new insights into the condition across the continent. For example, the prevalence of CP in the general population in Uganda may be more similar to that seen in HICs (2.7-2.9 [95% CI 2.2-3.6] per 1000 children) with unilateral spastic hemiplegia rather than bilateral spastic quadriplegia as the predominant clinical subtype and most children having only mild impairment (13). In Botswana, a hospital-based study of children with CP found that while birth complications and postnatal infection were statistically significantly associated with CP, prematurity was not and maternal HIV infection just achieved statistical significance (25). These results provide both new information on, as well as further confirmation of, the varying presentations of CP in Africa. As such, an updated systematic review of the literature on CP in Africa is warranted.

Aims

Primary aim

- To review the existing literature over the last 20 years on cerebral palsy in African countries available via peer-reviewed journals

Secondary aims

- To provide estimates of prevalence of cerebral palsy on the African continent
- To summarise the information on aetiology/risk factors, clinical subtypes, co-morbidities and functional outcomes of cerebral palsy in Africa
- To discuss the use of imaging, therapeutic services and interventions for children with cerebral palsy in Africa, and the barriers to accessing healthcare
- To provide individual/societal context to the experience of children with cerebral palsy in Africa

Methods

The protocol for this systematic review was first approved by the Stellenbosch University Human Research Ethics Committee (HREC) in December 2020 (HREC Reference No: S20/10/272), with progress reports submitted in 2021. The protocol was also registered with PROSPERO, an international prospective register of systematic reviews produced by the University of York Centre for Reviews and Dissemination, on 9 September 2021 with ID CRD42021270979 (https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=270979)

Search strategy

PubMed, Web of Science and SCOPUS online databases were selected based on expert advice that they were reputed to have the largest indexed African content. The databases were searched between January 2021 and July 2021 using defined search strings that were built sequentially to include multiple MeSH and key words to maximise return of results for all articles containing research on cerebral palsy in developing countries. See Appendix A for details of search strategy for each database.

A search of the PubMed database on 28 February 2021 returned 1165 results which were exported immediately to a reference manager for later review. Subsequent sequential searches of the SCOPUS and Web of Science databases returned an additional 139 and 148 new results each on 16 June 2021 and 8 July 2021 respectively, which were exported to the same reference manager for later review (Figure 1).

Primary, secondary and tertiary survey of results

The titles and abstracts of all 1452 results underwent primary review by the author (SM) against inclusion and exclusion criteria as listed below:

Inclusion criteria

- Timeframe or publication date range: 1 January 2000 to 30 June 2020
- Language and national context: English or English translation available; study conducted in African country
- Content of the paper: cerebral palsy explicitly mentioned as a reported condition in the full text of the study
- Study population defined as children aged ≤18 years at outset of study or time of intervention
- Explicit methodology for both observational studies and interventional studies,
- Factors investigated: prevalence, clinical subtypes, aetiology, co-morbidities, mortality, functionality (e.g. Gross Motor Functional Classification System), imaging and therapeutic interventions

Exclusion criteria

- Published outside of stipulated time frame
- Full text not available in English
- Non-African country
- Adult-only study population i.e. patients aged 18 years or older at the outset of the study
- Causes of developmental delay/disability other than cerebral palsy or unspecified
- Editorial, review, commentary, case series, conference presentations, thesis dissertation i.e. grey literature

The details of studies that were excluded were entered into a spreadsheet listing the author, digital object identifier (DOI) or PubMed unique identifier number (PMID) and reason for exclusion (Table 1). Studies were excluded first if they involved research conducted outside Africa, or else according to another exclusion criterion as applicable if they were conducted in Africa.

Table 1: Reasons for exclusion from systematic review

Reason for exclusion	Number excluded
Outside Africa	333
Global developmental delay or type of developmental disability not specified	146
Neurodevelopmental disorder other than cerebral palsy	208
Unrelated to topic of systematic review	447
(Systematic) review	62
Case study/series	39
Programme report/study protocol	22
Editorial/opinion piece	72
Adult study population	37
Full text not available in English	6
Non-human study population	7
Grey literature	4
Total studies excluded	***1383***

69 studies, both qualitative and quantitative, met inclusion criteria after the primary survey. The full text of all 69 articles was sourced and reviewed by the primary author SM against inclusion and exclusion criteria again. Both supervisors PS and KD reviewed 34 and 35 articles respectively against the same inclusion and exclusion criteria, such that all articles were reviewed by two individuals during the secondary survey. A meeting was held with all 3 reviewers to reach a consensus over the final 58 articles that are included in this review with reasons for exclusion during the secondary and tertiary surveys listed below (Table 2). A new criterion – total number of study participants with CP <10 – was added at this stage as the reviewers agreed that such small sample populations were unlikely to provide any meaningful results.

Table 2: Reasons for exclusion during secondary and tertiary surveys

Reason for exclusion	Number of studies
Outside Africa	0
Global developmental delay or type of developmental disability not specified	1
Neurodevelopmental disorder other than cerebral palsy	0
Unrelated to topic of systematic review	1
(Systematic) review	1
Case study/series	0
Programme report/study protocol	1
Editorial/opinion piece	0
Adult study population	2
Full text not available in English	1
Non-human study population	0
Grey literature	0
Total number of study participants with CP <10	4
Total studies excluded	***11***

Quality assessment and data extraction

All 58 articles underwent a quality assessment by SM (Appendix B). Quality assessment criteria were derived based on the Joanna-Briggs Institute checklists for each study design (https://jbi.global/critical-appraisal-tools) and applied to the 54 quantitative studies (Table 3).

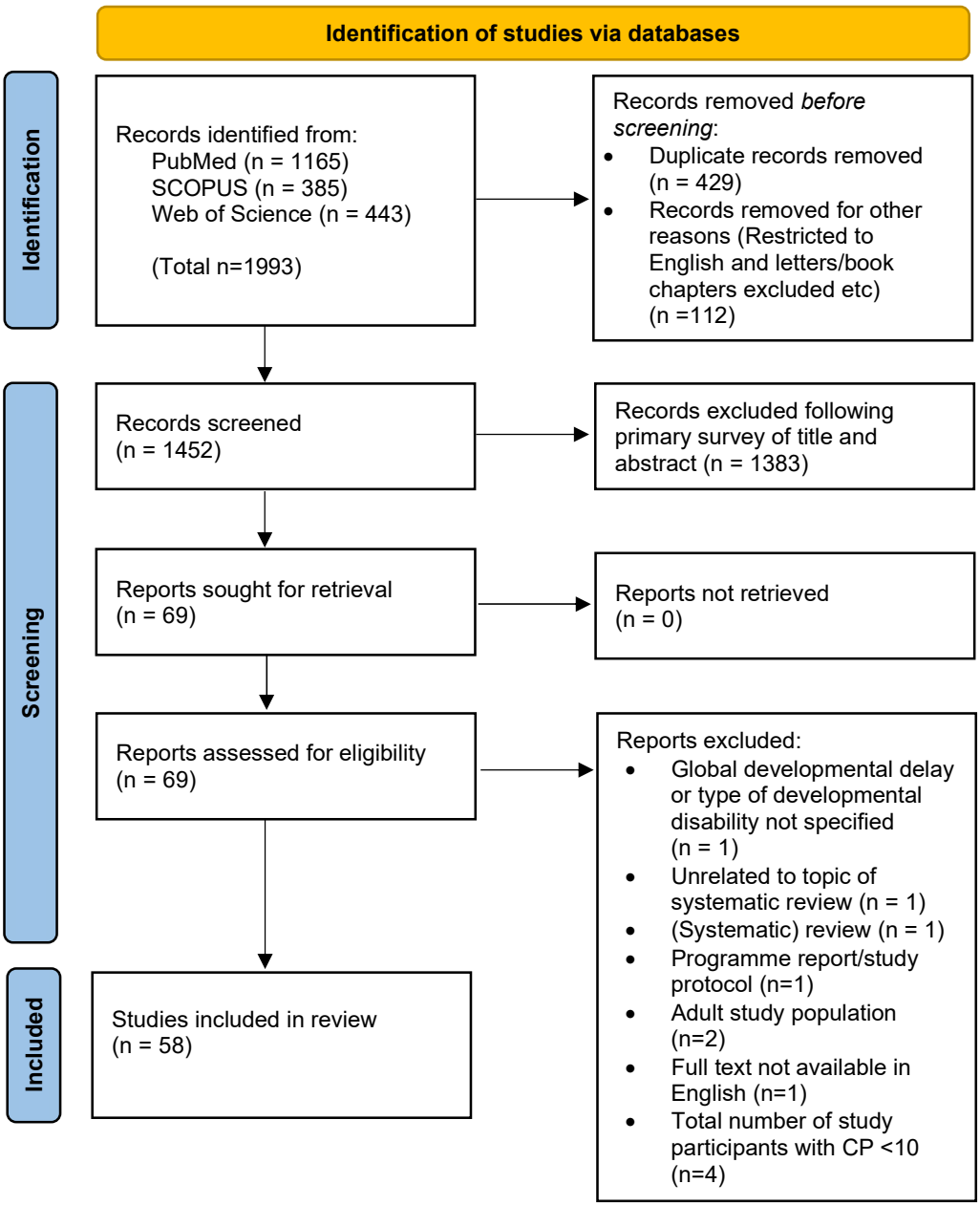
Table 3: Quality assessment criteria for each primary study

Criterion	High quality	Medium quality	Low quality
Design	Prospective observational study OR randomised controlled trial	Retrospective observational study OR cross-sectional analyses	Case series, editorial, commentary, thesis dissertations
Ascertainment of exposure	Clear diagnostic criteria for cerebral palsy OR Direct measurement of proposed aetiology for CP	Children with existing diagnosis of CP at outset of study	Children with any form of developmental delay that may be attributable to CP as well as other disorders
Ascertainment of outcome	Direct measurement of outcome by specific criteria, blinded assessment and follow-up more than 2 years	Indirect measurement of outcome (e.g. sourced from medical records or databases), assessment preferably blinded and follow-up less than 2 years but longer than a year	Self-reported measures of outcome or unblinded assessment and follow-up less than one year duration
Control for confounding	Adjustment for at least 2 confounders	Adjustment for at least 1 confounder	No adjustment for confounders

The remaining 4 qualitative articles were reviewed against the Critical Skills Appraisal Programme 2018 Qualitative Checklist (31) to assess their quality (Appendix C).

The full text of 54 quantitative articles were reviewed by SM and data extracted into summary tables which were used to report the final results of this review (Appendix D). Tests of statistical significance are reported when used by the cited studies. The qualitative studies are reported separately to give personal/societal context to the results from the quantitative studies.

Figure 1: PRISMSA flow diagram for selection of studies via database search



Results

Summary of search strategy results

A total of 1452 articles were returned by the original search strategies for PubMed, SCOPUS and Web of Science databases. Following primary survey of the 1452 titles and abstracts by SM, the full text of 69 articles underwent secondary survey by SM and either supervisor (PS or KD). A total of 58 articles were selected for the final review – 54 quantitative and 4 qualitative. Of the 54 quantitative studies, 34 were cross-sectional studies, 7 were case-control studies, 6 were cohort studies and 7 were intervention studies.

There is a range of African countries represented in this review (Table 4); however, all 4 qualitative research studies included were conducted in South Africa.

Table 4: Number of studies per country

Country	Region	Number of studies
Egypt	Northern	7
Sudan	Northern	1
Uganda	Eastern	10
Zimbabwe	Eastern	1
Tanzania	Eastern	2
Malawi	Eastern	1
Nigeria	Western	16
Ghana	Western	1
Benin	Western	1
South Africa	Southern	15
Botswana	Southern	3

The major themes examined were aetiology/risk factors; prevalence; clinical subtypes; co-morbidities; anthropometry/malnutrition; functional outcomes (measured by a defined and validated scoring system); mortality, imaging, barriers to accessing care and therapeutic interventions. The 54 quantitative studies were examined for summary measures for these themes, with many studies contributing to more than one theme (Table 5). The 4 qualitative studies were used to provide commentary on the individual/societal context of cerebral palsy among African children.

Table 5: Contributing quantitative studies for each major theme

Theme	Contributing number of studies
Prevalence and burden of disease	7 + 8
Aetiology/risk factors	19
Clinical subtypes	18
Co-morbidities	20
Malnutrition/nutritional status	5
Functional outcomes	12
Referral for therapy/use of assistive devices/school attendance	6
Effect of therapeutic interventions	9
Barriers to accessing healthcare	3
Mortality	3
Imaging	3

Prevalence and burden of disease

The reported prevalence of CP among community-based studies ranged from 0.8 to 10 per 1000 children, and was relatively consistent across countries: 0.8 per 1000 children in rural Malawi (32); 2.3 per 1000 (95% CI 2-2.5/1000) among Nigerian children (33), 1 per 1000 (34) and 2 per 1000 (95% CI 1.48–2.59/1000) (35) among Egyptian children, 2.7 per 1000 (95% CI

2.2–3.3/1000) among Ugandan children (13). After adjustment for attrition in the Ugandan study, the prevalence increased to 2.9 per 1000 children (95% CI 2.4–3.6/1000) (13). However, in rural South Africa, community-based prevalence of CP ranged from 3 per 1000 children (26) to 10 per 1000 children (19), despite both studies using community-based screening with the "Ten Questions" Questionnaire to identify children in the study areas with any type of disability, followed by formal assessment and confirmation of diagnosis by the study team.

CP makes a large contribution to the burden of disease from neurological conditions in Africa. Eight studies in this review looked at the proportion of children with CP in various hospital-based settings, recruiting participants from clinics predominantly for neurological disorders (36–41), but also included one clinic for neuromuscular disorders (42) and an emergency centre (43). The reported proportion of children with CP among these clinics ranged from 4% (42) to 55.3% of children attending (41). A cross-sectional Egyptian study found that, of the children with an existing diagnosis presenting to the emergency department of a tertiary hospital over a 1 year period, 13.3% had CP (43).

Aetiology/risk factors

Possible aetiologies listed for CP across all the African countries represented in the review included antenatal, peripartum, and postnatal factors, including intrapartum hypoxic events, prematurity, postnatal infections, stroke, antenatal infections, bilirubin encephalopathy, blood dyscrasias, congenital brain malformations, genetic disorders, metabolic disorders and trauma, although some children did not have an identifiable risk factor (15,22,46–54,25,33,35,37,39,40,44,45). A study of Nigerian children seen at a tertiary hospital neurology clinic reported the majority of children as having risk factors from the perinatal period (46.3% versus neonatal 24.4% versus post neonatal 18.3% versus prenatal 7.3%) (47), which was consistent with the findings of a South African study of children also seen at a tertiary hospital neurology clinic (48). However, among Ugandan children at a tertiary hospital clinic, prematurity and antenatal risk factors accounted for the majority of children

with CP (13.3% and 27.2% respectively) (22). The proportion of children with CP with no identifiable risk factors was as high as 26% even in hospital-based populations (15).

Neonatal hypoxic ischaemic encephalopathy (NHIE) and bilirubin encephalopathy were important risk factors for CP in the African context. In one prospective cohort study of survivors of NHIE in South Africa, the proportion of children with CP was reported as 15.5% amongst those with NHIE versus 0% in the unexposed group ($p<0.001$) (44). Although there appeared to be an increasing proportion of children with CP with increasing severity of NHIE, this did not achieve statistical significance ($p=0.566$), nor did the use of therapeutic hypothermia appear significantly associated with subsequent diagnosis of CP ($p=0.11$) (44). The proportion of children with CP among survivors of neonatal bilirubin encephalopathy was reported as 86.4% in a Nigerian cross-sectional study (53). Low birth weight and prematurity did not appear to be as important risk factors in African studies. A case-control study in Botswana using a hospital-based population found significant associations of CP with birth complications (adjusted odds ratio (aOR) 11.8, 95% CI 2.2-63.5, p= 0.004); postnatal infection (aOR 80.2, 95%CI 2.3-2782.4, p= 0.015); and maternal HIV (aOR 13.2, 95%CI 1.0-171.6, p= 0.05), although gestational age ≤32 weeks was not significantly associated with CP in that study (aOR 13.1, 95% CI 0.8-198.1, p= 0.06) (25). Similarly, a prospective cohort study of very low birth weight infants at a tertiary hospital in South Africa reported the proportion of survivors with CP as only 3.7% (54).

Clinical subtypes of cerebral palsy

There was variability in the clinical subtypes of CP reported by studies on the topic, reflecting the evolving classification system over the review period. Clinical subtypes reported included spastic (hemiplegic, diplegic or quadriplegic), dystonic/dyskinetic, choreoathetoid, ataxic, mixed, hypotonic/atonic and unclassified. Current terminology for clinical subtypes is derived from the Survey of Cerebral Palsy in Europe (SCPE) and describes CP according to 4 subtypes i.e. spastic, dyskinetic, ataxic and non-classifiable, with further division of spastic into unilateral versus bilateral and dyskinetic into dystonic versus choreo-

athetotic (2). It was not possible to adapt the terminology used in the included studies consistently to reflect the SCPE version and so results are reported according to the original subtype terminology of each study.

The majority of studies reported spasticity as the most common subtype (13,15,41,45–47,49–51,22,25,33–35,37,38,40), with the proportion of children with spastic subtypes ranging up to 86% (13). However, a cross-sectional study at a South African tertiary hospital neurology clinic reported more children with a mixed subtype: 39% versus 30% (48). The proportion of children with non-classified CP varied among studies, constituting up to 22.2% of participants (41).

More extensive limb involvement was associated with poorer baseline function as measured by the Gross Motor Classification System (GMFCS): Egyptian children with spastic hemiplegia functioned at GMFCS I-III level whereas children with spastic quadriplegia were classified as GMFCS IV-V ($p<0.001$) (34).

There was reported variation of clinical subtype by aetiology and age. Among Ugandan children, 100% of children born <37 weeks had spastic quadriplegia, compared to children with intrapartum-related encephalopathy, of whom 88% had spastic quadriplegia, 7% spastic hemiplegia and 5% dyskinetic subtype (51). In the same study, of children with a history of neonatal sepsis, 93% had spastic quadriplegia and 7% spastic hemiplegia, versus children with CNS infections, of whom 75% had spastic quadriplegia, 17% spastic hemiplegia and 8% dyskinetic subtype (51). A small Nigerian cross-sectional study of children at a tertiary hospital neurology clinic found no significant association between CP subtype and mode of delivery ($p=0.175$) or presence of antenatal care ($p=0.14$) (40). In a Ugandan community-based cohort, the dyskinetic subtype was more common in children aged 2–7 years than in children aged 8–17 years (13% versus 5% respectively), whereas spastic hemiplegia was less common in the younger versus older age groups (43% versus 50% respectively) (13).

Co-morbidities

The range of co-morbidities reported among studies was largely consistent across countries (15,22,41,45–48,50,55–58,26,32,34–37,39,40), and included epilepsy, visual impairment, hearing impairment, communication disorders, feeding difficulties, intellectual disability, orthopaedic complications, malnutrition and high risk of infections. A cross-sectional study in Uganda reported significant differences in the distribution of co-morbidities between clinical subtypes ($\chi^2(4) = 21.51$, $p<0.001$), gross motor function levels (χ^2 (2) = 14.98, p=0.001) and fine motor function levels (χ^2 (2) = 25.60, $p<0.001$) (22). Co-morbidities were reported as more common with increasing topographical involvement (p = 0.024) (40). Similarly, a cross-sectional study in South Africa reported that type of CP (p=0.008), intellectual impairment (p=0.027) and orthopaedic complications (p=0.003) were correlated with a higher GMCSF level (48). Many children suffered from more than one co-morbidity: in a cross-sectional population-based study in Uganda, 32% of children with CP had no associated co-morbidities, 37% had one associated co-morbidity, and 31% had two or more associated co-morbidities (55).

Epilepsy or seizure disorders were the most commonly investigated and reported co-morbidity among studies (15,22,50,55,58,34,35,37,39,40,46–48). The proportion of children with seizure disorders ranged from 11% (37) to 68% (55), with treatment gaps as high as 61% reported (55). The presence of seizures was significantly associated with CP subtype, GMFCS level and age ($p<0.05$ for all) in a cross-sectional study in Benin (50) and with history of neonatal seizures (p=0.001) and presence of spastic unilateral hemiplegia (p=0.013) in a cross-sectional study in Nigeria (46). The latter study in Nigeria also reported that 40% of children experienced neonatal seizures and 74% the first seizure in their first year of life (46). Hospital-based studies in Nigeria (46) and South Africa (48) reported generalised tonic-clonic seizures as the most common subtype (58% and 67%, respectively) whereas a community-based study in Uganda reported 64.3% of children had complex partial seizures, with non-athetoid CP significantly more common in children with complex partial seizures versus other seizure types (17.8% compared with 2.1%, $p<0.01$)(58).

Intellectual disability (ID) was also reported as common among children with CP (15,26,50,55,32,34,35,37,39,40,47,48) with the proportion of children with ID as high as 86% (95% CI = 73%–91%) in one hospital-based study in Botswana (15). In rural South Africa, 8.4% of children with ID also had CP, with the proportion of children with CP apparently increasing according to severity of ID: 25.6% of children with severe ID versus 4.6% of children with mild ID (26). Cognitive impairment was not associated with age, subtype or GMFCS level ($p>0.05$) in a cross-sectional study of 114 children in Benin (50); however, a hospital-based study of 68 children in Botswana did find a significant association with GMFCS level ($p<0.05$), although there was no association with aetiology or inpatient status ($p>0.05$) (15). The latter study was supported by a cross-sectional study in Uganda that reported 41% prevalence of ID in those with GMFCS levels I–II versus 89% of those with GMFCS levels IV–V (55). A study of Egyptian children with CP also reported that each grade higher on the GMFCS was associated with 2.5 and 1.5-fold increased risk for cognitive impairment and epilepsy, respectively ($p=0.01$) (34).

A few studies chose to focus on specific co-morbidities among children with CP. Lagunju *et al* found that the prevalence of ocular abnormalities was 28.2% among 149 children aged ≤13 years with CP seen at a tertiary hospital clinic in Nigeria (45). Almost two-thirds (61.9%) of the children had total blindness, 31.0% were partially blind and 7.1% had normal vision (45). The cause of visual impairment was optic atrophy in 50.0%, strabismus in 50.0% and cortical visual impairment in 47.7% (45). A larger proportion of children with spastic quadriplegia had associated visual impairment when compared to other CP subtypes (39.5% versus 17.8%; $\chi^2=6.18$, $p=0.01$) (45). Munyumu *et al* found that the prevalence of sleep disorders was 32% (95% CI 24.0-39.7) among 135 children with CP aged 2-12 years recruited from the paediatric neurology clinic of a tertiary hospital in Uganda (56). Statistically significant associations were found between sleep disorders and bilateral spastic cerebral palsy (aOR 11.2, 95% CI 2.1 – 59.0, $p=0.004$), GMFCS V (aOR 13.2, 95%CI 3.7 – 47.0, $p = < 0.001$), GMFCS IV (aOR 12.9, 95%CI 2.0– 82.3, $p = 0.007$), Manual Ability Classification System (MACS) V (aOR 11.2, 95% CI 2.2 – 56.4, $p = 0.004$) and epilepsy (aOR 3.9, 95% CI 1.4 – 10.9, $p = 0.011$) (56). Nwaneri *et al* found that the prevalence of intestinal helminthiasis was 32.2% among children with CP in a case-control study of 155 children with neurological

disorders as a tertiary hospital neurology clinic in Nigeria (57). Behaviours more commonly found in children with CP infected with helminths versus uninfected children with CP included nail-biting, sucking of fingers and encopresis, with nail-biting and encopresis significantly associated with increased prevalence of intestinal helminthiasis (p≤0.03) (57).

Functional outcomes

Various studies measured functional outcome by standardised and validated tools such as the GMFCS, MACS and Communication Function Classification System (CFCS) in order to report the range of morbidity among children with CP (13,15,55,59,22,23,33,34,47,48,50,52). Hospital-based studies tended to report a larger proportion of children with more severe gross motor impairments i.e. GMFCS IV-V (15,47,48,50) compared to community-based studies (13,33,55), the discrepancy being as large as 70.7% of children with GMFCS levels IV-V in one Nigerian hospital-based study (47) versus 53% of children with GMFCS level I in one community-based Ugandan study (13).

Many studies also reported varying functional impairments by age, with younger children being more severely affected than older children (13,50,52,55). Two cross-sectional community-based studies in Uganda reported similar associations between age and functional impairment: 36% of children aged 2 to 5 years had severe gross motor impairment (GMFCS levels IV–V) versus 10% children aged 6 to 17 years (p=0.002) (55). Similarly, 48% of children aged 2 to 5 years had severe fine motor impairments (MACS levels IV–V) versus 10% of children aged 6 to 17 years (p=0.01) (55). The second study showed an association between age and the prevalence of CP: the expected number of cases decreased with age which was significantly associated with GMFCS level (estimated coefficient –0·05778, p=0·023) (13). The effect of age was only significant for GMFCS levels IV-V (estimated coefficient –0·2136, p=0·008) i.e. the lower number of older children with CP was driven by a reduction in the number of children with higher GMFCS levels (13). Similarly, in a cross-sectional study in Benin, there was no association between age and GMFCS until children were grouped as “independent walkers” (GMFCS I-II) versus “non-walkers” (GMFCS III-V) (χ^2 (df) 12.27 (3), p= 0.01), where the proportion of severely affected

children decreased with increasing age (50). By contrast, other studies reported improvement in function with age: a cross-sectional study in South Africa reported that age was significantly correlated with the visual perception z-score (VIS-z) (r=0.36 p=0.02), which they attributed to improvement as the participants grew older (52). A prospective cohort study in Nigeria that looked at change in function over one year found an inverse relationship between severity of CP and improvement in motor function (OR 10.5, 95% CI 2.91-37.95, p<0.001) (47).

Various measures of function showed concordance i.e. increasing impairment in one functional domain was associated with similar changes in another domain. Cerebral performance score was highly correlated with GMFCS score (Spearman correlation coefficient = 0.59, P < 0.001) as was overall performance score (Spearman correlation coefficient = 0.83, P < 0.001) in a cross-sectional hospital-based study in Botswana (15). Outcomes on GMFCS, cerebral performance score, and overall performance score did not vary by aetiology (p ≥ 0.5, small numbers for subgroup analyses), or by inpatient versus outpatient status (p = 0.7) (15).

A few studies examined the association between GMFCS and presumed aetiology of CP. A cross-sectional study in South Africa found no significant correlations between birth weight or gestational age and functional outcomes (52). Time of brain injury was significantly associated with higher GMFCS level (estimated coefficient 1·6726, p=0·0085) in a cross-sectional community-based study in Uganda i.e. only a few children with a high GMFCS level were post-neonatal cases (13). Similarly, a cross-sectional study in Benin, drawing from community and hospital clinic-based populations, found that reported complications during delivery were significantly associated with GMFCS level (χ^2(df) 9.3 (4), p= 0.05) (50). By contrast, a study of school-aged children with spastic bilateral diplegia in South Africa did not find a significant correlation between gestational age or birth weight and functional outcome (p>0.05) (52).

One case-control study in South Africa compared functional outcomes of children with spastic bilateral diplegia due to CP versus HIV infection, but found no significant difference

between the HIV-infected and CP groups for GMFCS level (p = 0.2) or tone or muscle strength (p>0.05) (59).

Malnutrition/ nutritional status

Although numerous included studies mentioned malnutrition as a common co-morbidity among children with CP, five studies focused on measures of nutritional status in children with CP (60–64). Overall prevalence of malnutrition among children with CP was high, with one case-control study in Nigeria reporting the proportion of children with CP with undernutrition as 79.3% compared to 45.3% of controls (χ^2: 34.027. P < 0.0001) and 31.1% of the children with CP had severe wasting compared to 1.9% of controls (χ^2: 32.887, P < 0.0001) (60).

Growth was affected across multiple parameters: A cross-sectional study in Uganda reported that 42% (95% CI 33–51%) of children with CP were underweight-for-age (UWFA) and 38% (95% CI 30–46%) were stunted (62). These findings were consistent with a cross-sectional study in Ghana that reported 23% (95% CI 14.2–35.1) of children with CP were UWFA and 40% (CI 28.5–52.6) severely UWFA, as well as 25% (95% CI 16.4– 37.0) being stunted (height-for age between -2 and-3 z-score) and 34% (95% CI 23.6–45.8) severely stunted (height-for-age below -3 z-score) (63). A case-control study in Egypt reported that height-for-age, weight-for-age, head circumference, triceps skin fold and waist circumference were significantly lower in children with CP compared to healthy controls (p<0.04), with a statistically significant reduction in total body water, fat mass, fat free mass, fat percentage and BMR in cases (p<0.01), although there was no difference between groups in terms of BMI, hip circumference, waist-to-hip circumferences ratio, MAC, and subscapular skin fold thickness (64).

Multiple risk factors were found to be statistically significantly associated with malnutrition in multivariate analyses, including GMFCS and socioeconomic status in a case-control study in Botswana (aOR 3.8, 95% CI 1.5-9.6, p=0.006 and aOR 2.1, 95% CI 1.0-4.1, p=0.04,

respectively) (61). A cross-sectional study in Uganda reported that risk of malnutrition was significantly associated with presence of cognitive impairment (aOR 4.5, 95% CI 1.6-12.5, p=0.004); age ≥5 years (aOR 3.4, 95% CI 1.2-9.7, p=0.02) and feeding difficulties in the perinatal period (aOR 3.2, 95% CI 1.3-7.9, p=0.008), with infection in the perinatal period and microcephaly being additional risk factors for being UWFA (aOR 3.6, 95% CI 1.2-10.3, p=0.017 and aOR 2.9, 95% CI 1.1- 7.4, p=0.024, respectively) (62). Both the cross-sectional study in Uganda and a cross-sectional study in Ghana found that severe feeding difficulties conferred an additional risk for malnutrition (62,63). This was consistent with a study in Egypt that found children with more severe gross motor impairment and oromotor dysfunction had increasing markers of malnutrition: children with GMFCS III-V had lower subscapular, triceps skin fold thickness, fat percentage and serum ferritin levels, versus GMFCS I-II ($p<0.001$, 0.035, 0.028 and 0.037, respectively), and children with oromotor dysfunction had significantly lower subscapular and triceps skin fold thicknesses versus those without ($p< 0.01$) (64).

Tomoum *et al* examined biochemical parameters for malnutrition in a case-control study in Egypt and found that, compared to controls, there were statistically significant lower values in haemoglobin concentration, serum ferritin, and serum albumin in children with CP ($p<0.01$) but serum protein and leptin levels were not significantly different (64).

Imaging

Imaging was not readily available for most studies included. The three hospital-based studies that did include imaging findings for CP reported the proportion of children with abnormal findings as 32.7%- 69% (35,48,65) , with changes including brain atrophic changes, white matter changes, corpus callosum agenesis etc (35). A cross-sectional study in Uganda found that, of the 69% of children with abnormal imaging, 53% had a single abnormality and 17% a combination of primary grey and white matter abnormalities (65). A cross-sectional study in South Africa found that periventricular white matter lesions (periventricular leukomalacia etc) were the commonest abnormality at 54%; with congenital brain lesions (lissencephaly, schizencephaly etc) at 6.8% (48). By contrast, the Ugandan study found that

children admitted to hospital following birth were three times more likely to have primary grey matter injury than any of the other neuroimaging patterns (OR 2.8, 95% CI 1.1–7.1, p=0.026) (65).

Mortality

Three studies looked at mortality amongst children with CP in Nigeria (47), Tanzania (66) and Uganda (67), with all three studies reporting excessive premature mortality. In Nigeria, the mean age at death was 18.3 ±(SD =6.5) months, with 100% of children dying at home (47). In Tanzania, CP accounted for 11.1% of deaths due to a neurological disorder among children < 5 years and 18.2% among children aged 5–19, with a cause-specific mortality fraction of 0.40% (95% CI: 0.10–0.70) in children aged ≤5 years (66).

Namaganda *et al* conducted a prospective cohort study of 97 children with CP aged 2–17 years enrolled in 2015 and followed to 2019, who were compared with 41 319 age-matched children from the general population in the Iganga-Mayuge Health and Demographic Surveillance System of Uganda (67). The study reported a mortality rate ratio (MRR) of 29.0 (95% CI 17.1–49.1; p<0.0001) in the CP cohort, with the general population as the reference (67). The standardised mortality rate (MR) was 3455 per 100 000 person-years (95% CI 2212–6519) for the CP cohort versus 137 per 100 000 person years (95% CI 117–159) in the general population, with a standardized MRR of 25.3 (67). The most commonly recorded immediate causes of death in children with CP were anaemia secondary to malaria or malnutrition (40%), malaria (33%), pneumonia (17%) and meningitis (13%) (67). Among children with CP, the survival probability was not significantly different between age groups (p = 0.28) or sexes (p = 0.15) or with associated impairments/seizures (p = 0.213), but was significantly lower in children with severe malnutrition (p = 0.037), and risk of death was almost 4 times higher in children with severe malnutrition (HR 3.7; p = 0.052) (67). The MR was higher in children with GFMCS IV-V (8718 deaths per 100 000 person-years) than GMFCS I-II (1305 deaths per 100 000 person-years, p =0.009) and risk of death was almost 7 times higher with GMFCS IV-V versus I-III (HR 6.8; p = 0.007) (67). The latter two findings were consistent with those reported by the study in Nigeria, which found an increased risk

of death with impaired growth (OR 5.76, 95% CI 1.31-25.27, p=0.018) and GMFCS IV-V (OR 1.30, 95% CI 1.11-1.54, p=0.015) (47).

Referral for therapeutic services, use of assistive devices and school attendance

Six studies commented on the use of assistive devices, referral for therapeutic services or school attendance among children with CP (23,36,42,49,50,55), with varying rates of referrals and access to assistive devices between countries, and discrepancies reported between those children seen in the community compared to hospital clinics.

A cross-sectional study in Uganda reported that more children at the hospital clinics were referred for physical therapy compared to children seen at outreach clinics (50% versus 24%), although a similar proportion of children received assistive devices (34% versus 37%) (42). Although a much higher proportion of children at outreach clinics were referred for a surgical opinion, only children seen at the hospital clinics had documented surgical interventions (42). A cross-sectional study in Nigeria reported that almost all children (94%) received physiotherapy, 41% drugs for spasticity, 35% anti-seizure medication, 6% mobility assistive devices, 5% visual aids, 1% orthoses and 1% speech; however, there was no reported use of cochlear implants, orthopaedic surgery, occupational therapy, psychotherapy, alternative communication devices, nasogastric tube/gastrostomy feeding, intrathecal baclofen or selective dorsal rhizotomy (23). Similarly, another community-based cross-sectional study in Uganda found that none of the children with vision or hearing impairment or communication difficulties had any assistive devices, e.g. a hearing aid (55).

Where referrals were made, long-term compliance with therapy was reported as poor. Even when children were referred to physiotherapy, a cross-sectional study in Nigeria showed poor long-term attendance, with 59% attending ≤ 5 sessions and only 7.5% attending ≥ 25 sessions (49).

In a community-based study in Uganda, only 30% of children aged 6–17 years with CP attended school and school attendance decreased with increasing GMFCS and CFCS levels

and with associated impairments and seizures (55). Similarly, in a cross-sectional study in Benin, attendance at school was significantly associated with older age, better functional outcome (GMFCS I-II and MACS I-II), and absence of communication disorders ($p<0.05$ for all) (50).

Barriers to accessing healthcare

Children with CP struggle to access appropriate healthcare due to a number of caregiver and economic factors (47,55,68). Badaru *et al* found that the major source of funding for treatment of children with CP was the parents themselves (94.3%), followed by financial help from relatives (2.8%) despite 80.2% of caregivers earning incomes that were below the minimum wage in a cross-sectional study in Kano, Nigeria (68). The same study reported that the average monthly cost of outpatient management of children with CP in Kano city was ₦14 295.38 ($46.87) with an average monthly direct cost of outpatient medical care of ₦7741.89 ($25.38), which was higher than the direct cost of outpatient stroke management in the same environment (68). In another prospective cohort study in Nigeria, reasons given for defaulting treatment included financial constraints (50.0%), parents being discouraged (26.5%) and the hospital being too far from home (17.6%) (47), which was echoed by a community-based study in Uganda (55). The Nigerian study found that the absence of epilepsy (OR 3.95, 95% CI 1.25-12.46, p=0.014), GMFCS IV-V (OR=3.25, 95% CI 1.094-9.68, p=0.03) and lower level of maternal education (OR 0.07, 95% CI 0.01-0.58, p=0.002) were significant risk factors for defaulting treatment (47).

Therapeutic interventions

Most intervention studies looked at therapies or surgeries to improve functional mobility as the primary outcome (69–76), but generally included very small numbers in each arm of the study, with several studies using cross-over methods. More than one study reported that

children with greater functional mobility at baseline and younger age at time of intervention had better outcomes (72,73).

Non-surgical interventions such as orthotics (69), strapping and muscle strengthening exercise regimens (70,73,76) were shown to be effective in improving multiple gait parameters, especially when combined (69), rather than one therapy showing superiority over another in terms of outcomes (70) in studies in Nigeria, Egypt, South Africa and Zimbabwe. A small study of the effect of an aquatic-based intervention programme in South Africa reported a post-intervention increase in average score on the 66-item Gross Motor Function Measure (GMFM-66) of 4.25 points compared to the control group ($z = -2.803$, $p = 0.005$) (71). Similarly, a study in Zimbabwe reported that children who received community-based rehabilitation services improved 2.49 points more on the GMFM-66 than children receiving hospital-based services (~6% difference, $p=0.002$), although both groups showed improvement in GMFM-66 scores ($p=0.047$) (73). Children who were less severely disabled showed 1.96 points more improvement ($p=0.005$); by contrast, for each month increase in age, GMFM-66 scores dropped by 0.02 points ($p=0.03$) (73). Children in a South African study looking at the effect of muscle-strengthening exercises on gait parameters also reported better self-perceived body image compared to the control group ($p=0.01$) even though there was no difference in functional competence ($p=0.9$) (76).

Surgical interventions evaluated by studies included botulinum toxin injection (74) and musculotendinous release procedures (72), with the majority of children experiencing good outcomes. A randomised control trial evaluating botulinum toxin injection followed by physiotherapy against physiotherapy alone, found a decrease in spasticity in the botulinum group measured by the Modified Ashworth Scale (1.93 ± 0.27 versus 0.89 ± 0.59, $p<0.001$), as well as electromyogram ($p<0.001$) (74). The botulinum group also showed improvement in overall gait pattern as measured by the Physician Rating Scale (7.6 ± 2.12 versus 11.73 ± 2.24, $p<0.001$) as well as individual parameters (during foot strike, hind foot position during foot strike, hind foot position during gait, degree of crouch and speed of gait; $p\leq0.012$ for all) (74). A study in Egypt reported that 22% of children had excellent outcomes and 54% good outcomes with no adverse sequelae or direct complication of the surgery after 2 years of

follow-up post musculotendinous release (72). However, children with a better functional baseline (e.g. able to walk and had spastic diplegia) had significantly better results compared to children with more severe or chronic limb involvement (72). A retrospective cohort study in South Africa followed up 30 adults with spastic diplegic CP who underwent an interval surgery approach when aged 2-12 years with GMFCS I-II and found that all the adults were still ambulant with 40% improved, 50% unchanged, 10% showing deterioration (75).

Only one study looked at the effect of a nutritional and feeding education programme on the child's oromotor feeding skills and functional feeding skills, caregiver feeding skills and caregiver-child interaction (77). In this study in Tanzania, participants received 6 sessions of group/individual nutrition education including positioning during feeding, and occupational therapy for oral motor and functional skills (food consistency, specific feeding techniques, and appropriate utensils for feeding). They were also provided with free sets of plastic cups, spoons, and plates to use at home. Although there was improved feeding positioning (aOR = 5.3, 95% CI 2.00– 13.96, $p < 0.001$); better feeding speed (aOR = 5.2, 95% CI 1.99–13.44, $p < 0.001$); increased child involvement (aOR = 3.5, 95% CI 1.42–8.44, $p <0.01$), less caregiver stress during feeding (aOR = 2.5, 95% CI 1.04–6.13, $p <0 .05$) and improved child mood (aOR = 3.1, 95% CI 1.33–7.47, $p = 0.01$), there was no statistically significant differences in observed oral motor feeding skills (aOR = 1.7, 95% CI 0.72–3.91, $p = 0.235$) and functional feeding skills (aOR = 2.3, 95% CI 0.86–6.06, $p = 0.098$) (77).

Qualitative studies

The four qualitative studies included in this review were all drawn from the same 15 adolescents with CP attending a special needs school in Cape Town, South Africa (78–81). The themes revolved around their perceptions of CP (80), inclusion and participation in sport (79,81), and factors for consideration in designing school sports programmes for children with CP (78). Given the small number of participants, there were often contradictory or inconsistent responses for each theme. Participants' knowledge of CP ranged from a relatively accurate understanding of it being a primary neuromuscular

condition to being unable to articulate how it is caused (80), but there was a general sense that these adolescents felt that non-disabled individuals were 'normal' and used as the reference for their own experiences (80). The studies also raised an interesting point that, while post-apartheid South Africa has struggled to ensure inclusion of all students in school activities, children with CP who share their learning environment with other children who do not struggle from the same motor impairment can feel paradoxically excluded in sports programmes (81). Overall, there was a strong desire for school sports programmes to better meet the needs of these adolescents with CP (78,79,81).

Discussion

Summary of findings and comparison with high-income countries

Since the review by Donald *et* al in 2014, several new studies on the prevalence of and burden of disease from CP in Africa have been published, which offers important new information. The prevalence of CP among African children ranged from 0.8 to 10 per 1000 children with most of included seven studies reporting a prevalence of approximately 1-3 per 1000 children. Although this reported range is comparable to estimates of CP prevalence among developed countries (3–5,82–85), the true prevalence in Africa is likely to be higher given the limited number of community-based studies and the relatively higher burden of disease reported by African studies (86,87). The use of the key informant method or the "Ten Questions'' Questionnaire to identify cases in the community may only detect children with moderate-severe neurological impairment (88) but not necessarily more subtle impairment, resulting in undercounting of the true number of children with CP. Furthermore, it is not yet possible to comment on the trends in prevalence of CP in Africa, whereas there has been a documented decrease in the overall prevalence of CP in Europe and North America over two decades (10,83–85). More community-based studies on CP using validated screening tools and trained field workers, as well as the establishment of national CP registers would provide better estimates of the true prevalence and trends of CP in Africa. Although children and adolescents with CP reportedly make more use of healthcare services than the general population globally, there appears to be a higher burden of disease from CP in Africa, even in terms of hospital admissions and emergency presentations (86,87,89).

Among African children, risk factors for CP were most commonly identified in the perinatal period compared to the antenatal or postnatal periods, although up to a quarter of children with CP did not have an identifiable risk factor. In many cases, CP may be attributable to multiple insults in the perinatal period (e.g. low birth weight with risk of intraventricular haemorrhage and kernicterus) and even with comprehensive medical records and extensive investigation, it may not be possible to separate the effect of one insult from another when

determining the aetiology of CP (90). Many potentially preventable risk factors for CP such as birth asphyxia, neonatal infections and kernicterus also reflect the reduced availability of diagnostic and therapeutic services for these conditions in African countries. A similar risk factor profile is found among children with CP in India (91) and Nepal (92). Studies in this review did not report consistent findings on the association of various risk factors with presence of CP or functional outcomes, which may be due to the differences in sample size, settings and risk factors examined. Prematurity and low birth weight were not found to be as significant as risk factors for CP among children in Africa despite being major risk factors in developed countries (3,5,10,82,93). This may be due to survival bias, as many African countries lack capacity to provide specialised neonatal services to extremely premature and low birth weight infants.

The variability in the clinical subtypes of CP reported by studies is partly attributable to the evolving classification system over the review period. Spasticity was reported as the commonest clinical subtype by the majority of studies, likely reflecting the severity of impairment as well as the type of initial insult in these children which was most often global in nature, although clinical subtype varied by aetiology and age. This is consistent with reports on clinical subtypes in other developing (91,92) and developed countries (85,94), but the trends in developed countries indicate changes in topographical distribution among birth weight categories over time (82,94). No similar information on trends in Africa was found for this review, but it is uncertain whether sufficient data exists even from medical records to document such changes given concerns about under-reporting of CP in Africa and the lack of national CP registers as a repository for such information.

The range of co-morbidities reported across studies included seizure disorders, visual and/or hearing impairment, communication disorders, feeding difficulties, intellectual disability, and orthopaedic complications as with children with CP in the global North (82,84,94–97). More severely impaired children tended to have multiple co-morbidities (94,96–98), with approximately a third of children having $\geq$2 co-morbidities which mirrors some reports from developed countries (95). There appears to be a larger proportion of African children with

CP affected by seizure disorders, intellectual disability, sleep disorders and visual impairment than that seen in Canadian (99), British (93), Australian (97) and European populations (84,94–96), which is likely related to the greater degree of impairment also seen in African populations. Malnutrition as a common co-morbidity among African children with CP, with growth affected across multiple parameters and greater risk of growth failure with more severe impairment and feeding difficulties, is consistent with findings from North America and Europe (98,100,101); however, the proportion of children with confirmed malnutrition is higher in African populations. A similar risk profile and burden of malnutrition amongst children with CP is seen in other LMICs (102); however, concerns around possible food insecurity secondary to financial insecurity as well as natural disasters and political instability are additional risk factors for malnutrition among African children with CP (103).

Despite the use of different assessment tools, studies of African children with CP showed consistently that younger children were more severely affected than older children, hospital-based populations had a larger proportion of severely impaired children than community-based populations and functional domains showed concordance with regards to degree of impairment. The difference with age is possibly due to survival bias, with less impaired children more likely to survive to an older age compared to younger more severely affected children, who are also more likely to suffer from multiple co-morbidities. Similarly, children who require hospital-based care are more likely to have complex needs requiring specialist intervention compared to children who can be predominantly managed in the community. There were no consistent findings around the association of aetiology with functional outcome. These findings among African children with CP are in stark contrast to studies in the global North, where the majority of children with CP showed relatively less functional impairment irrespective of topography or clinical subtype (84,85,93–96). This difference may again be due to better and more comprehensive medical and rehabilitation services through all vulnerable periods antenatally to postnatally in HICs.

Only three studies in Africa commented on imaging of hospital-based populations and found a large proportion of children had abnormal findings, which varied from single to multiple lesions. The yield of imaging was likely to be higher in these groups because they have also been shown to have more severe functional impairments, as was seen in imaging studies in other parts of the world (98,104–106). The benefit of imaging in terms of diagnosis of CP has been illustrated in the global North, especially where there is no clear history of events that may predispose to CP e.g. birth asphyxia or prematurity (1,104,106). The utility of imaging in terms of management has not been examined in any of the included studies. In order to justify the cost of imaging, particularly where it is a scarce resource, more information is needed on the association of imaging findings with clinical subtypes and functional impairment, as well as with long-term outcomes in Africa. It would be difficult to rationalise use of imaging in children with CP if it does not impact on management strategies, but only serves to elucidate possible aetiology, especially where there is a clear history of events that predispose to CP e.g. birth asphyxia.

African children with CP face excess mortality, especially in the under-5 age group, predominantly from infections or the sequelae thereof. Although there was no association with age, there were significant associations found with malnutrition and severity of impairment. These findings are consistent with mortality data from Australia (107) and Sweden (108), although children with CP in those countries had a much higher survival probability than African children even in the most impaired or malnourished categories. Better documentation around mortality rates and cause of death for children with CP is needed in Africa, to enable allocation of resources to services that have greatest impact on morbidity and mortality.

This review found varying rates of referrals and access to assistive devices among African countries. Where referrals were made, long-term compliance with therapy was poor. There were discrepancies reported between those children seen in the community compared to hospital clinics, with the latter having better access to rehabilitation and surgical services. Significant financial barriers exist to children with CP accessing proper care in Africa,

including high out-of-pocket expenditure and the large proportion of caregivers who are unemployed. These difficulties are likely compounded by geographical barriers as physical access to services is limited in under-resourced settings due to fewer rehabilitation centres or hospitals per capita. For this reason, those children already able to access hospital-based care may be better placed to access a greater range of specialist services, apart from their increased medical complexity which make them more likely to require specialist intervention. Similar concerns around unmet healthcare needs, inadequate access to rehabilitation services and financial constraints were reported in studies of children with CP in Bangladesh (109) and even North America (110), although South Korean children appeared less financially vulnerable as there is a substantial government subsidy with only a small co-payment by the caregiver for services (111). Overall, it appears that African children with CP struggle with the same barriers to accessing appropriate and comprehensive ongoing medical and rehabilitation services as other LMICs (112).

In Uganda, only a third of eligible African children with CP are placed at a school and in Benin and Uganda, school attendance is strongly associated with better function and fewer impairments. Overall, there was very little information published about formal education for children with CP which may be due to many of these children being hidden away due to stigma or else the paucity of schools equipped to deal with children with disabilities.

In this review, there were consistent reports of improvement in various functional domains from both surgical and non-surgical interventions, with children with a better baseline function and younger age at time of intervention showing greater benefit than their older, more impaired peers. However, the included studies often had a small total study population (with even smaller numbers per arm), measured functional outcome by different assessment tools and had a limited duration of follow up. Two systematic reviews of non-surgical interventions aimed at improving functional mobility in children with CP found similar outcomes in other regions but also raised concerns about the quality of the studies on the subject (113,114). Nonetheless, African children with CP seemed to derive the same benefit as seen in Swedish (115), French (116) and North American children (117)

undergoing the same interventions. Larger, more robust trials that evaluate both the clinical efficacy and cost-effectiveness of different surgical and non-surgical interventions over a longer period in the African context are required.

A 2020 review by Abdel Malek *et al* concluded that the majority of research on CP in Africa still has a biomedical focus looking at deficits rather than functioning and fails to consider the ICF as a guiding framework (29). Similarly, the four qualitative studies in this review illustrated briefly the impact of CP on the lived experiences of children and adolescents in Africa, but none of the other included studies explicitly addressed the impact of personal or environmental factors on African children with CP. Included studies also focused on motor impairment as the primary measure of function and almost all intervention studies targeted this end point. Quality of life issues were neglected in the final body of research represented in this review. As such, this review supports the need to use the ICF to guide future research around service development and targets for intervention for CP in Africa (118).

Reasons for variability in results and among studies

There was a large amount of heterogeneity among the 58 included studies, which were drawn from 11 countries and four regions across Africa. The majority of quantitative studies were tertiary hospital-based, cross-sectional in design and involved a review of medical records with or without direct assessment of the child. All four qualitative studies – despite being of good quality - came from a single group of urban South African adolescents and the review did not include information on the lived experiences of children with CP in other African countries. The majority of studies were also assessed as being of medium quality with various concerns around methodology and analysis: most authors adopted a pragmatic approach, using a combination of medical records, direct assessment, interviews and high-yield settings e.g. neurology clinics. Selection bias, survival bias, antecedent-consequent bias, lack of a comparison group and lack of adjustment for confounders were concerns for a large number of the studies included in this review (Appendix B). There was

variation in the tools used to assess outcomes of interest, possibly as the investigators chose tools in which they were already trained. Of the various themes examined, 15-19 studies contributed to the results on prevalence, aetiology, co-morbidities or clinical subtypes versus three studies on mortality, imaging or barriers to accessing healthcare, and only eight intervention studies met inclusion criteria. Consequently, the detail, range of results and quality of information reported on each theme is affected by what is available in published literature. However, community-based studies of good quality provided different estimates of the outcomes of interest, indicating a different profile of patients seen compared to hospital clinics. This suggests that the true profile of children with CP in Africa lies somewhere between the picture painted by hospital versus community-based studies.

In addition, there are different risk profiles among countries due to geography, health system infrastructure etc. For example, malaria is endemic in some African countries and epidemic in others, and therefore plays a larger role in the morbidity and mortality of CP in some regions. Some countries provide a more comprehensive range of government-funded health services whereas others require caregivers to carry cost of care by themselves, which in turn will affect access and compliance. South Africa, Uganda and Nigeria each provided ≥10 studies and together contributed 41 of the 58 studies included in this review, skewing the results towards the findings in these three specific countries and not accurately representing what may be found elsewhere. Africa itself is such a diverse continent that it may make more sense to examine CP within regions rather than across Africa as a whole, which may in turn yield greater consistency in reports of these various outcomes.

Strengths and limitations of the review

There has been a surge of studies on CP among African children over the last eight years since the prior review by Donald *et al* (30). This updated review covers two decades of published literature on CP among children in Africa over a range of themes from aetiology through to intervention. It provides information on 11 countries across four regions, although it is dominated by three countries who have produced the vast majority of

research on the topic over this period. Where English language translations where available, literature published in another primary language was also included; only seven articles published primarily in another language were excluded because no full text English translation was available. The three databases selected were reputed to have the largest selection of indexed journals covering African content, and the search strategies employed were deliberately designed to cast as wide a net as possible in finding content related to CP in Africa. An exhaustive attempt was made to find any article deemed eligible after the primary review, including contacting international institutions to obtain hard copies as needed. Although the primary survey was conducted by one individual, the secondary and tertiary surveys were conducted by three individuals and a consensus was reached over the final 58 included studies. All studies were subjected to a quality assessment based on internationally validated quality assessment tools prior to inclusion in the review and concerns around methodology and data analyses were meticulously documented in Appendices B and C. As such, this review provides a comprehensive overview of many important themes related to CP in Africa, while highlighting both the strengths and limitations of the research conducted in this field over the last two decades.

The review does not include literature from those journals not indexed in the three databases listed nor does it include grey literature e.g. conference abstracts. The authors are aware of a number of publications by colleagues with extensive experience in this field that have been omitted as a result, but in order to perform a systematic review, a clearly defined and reproducible search strategy had to be employed. Similarly, literature published in a primary language other than English, especially French literature from francophone regions of Africa, may not be indexed in the databases used for this review and so good quality studies on this topic may have been omitted on the basis of language. A larger team of reviewers would also have added weight to the review in order to reduce the chance of selection bias in the primary survey, but given this work is being submitted for a Masters in Medicine degree, the primary author was required to perform the bulk of the work independently. Any review is also limited by the quality of studies included, and although there were many inconsistencies and methodological concerns around these

studies, overall, the included studies were of adequate quality to comment on the subject of CP in African children.

What this review adds

This updated review on CP in African children provides:

1. New estimates of the prevalence of CP in Africa, which appear to approximate HICs, but with significant concerns around case-finding and under-counting, thereby highlighting the need for more community-based population studies and national CP registers to investigate the true prevalence. There is also good evidence of a higher burden of disease from CP among African children compared to the global North.

2. Updated information on risk factors for CP in Africa (many of which are modifiable), thereby providing targets for interventions from both antenatal, perinatal and postnatal medical services. This also helps identify high risk groups that require careful follow-up throughout childhood to facilitate early diagnosis and intervention.

3. More information on the clinical subtypes and burden of co-morbidities faced by African children with CP, motivating for multidisciplinary care in services for children with CP and incentivising for screening for these co-morbidities in a systematic manner throughout childhood. Similarly, the suboptimal referral pathways and poor compliance with outpatient care for children with CP reported in this review highlight key vulnerabilities for caregivers and children with CP, especially financial barriers. These vulnerabilities need to be considered across multiple sectors when structuring services and in provision of government subsidies for children with chronic conditions.

4. Stronger evidence for malnutrition as a specific concern for African children with CP, particularly as a major risk factor for mortality. Increased effort must be made to

address the high burden of feeding difficulties and macro- and micronutrient deficiencies as well as provide caregiver training on optimal feeding techniques and culturally-appropriate diets for children with CP.

5. Key questions around utility of imaging and feasibility of various interventions for African children with CP. More quantitative studies of high-quality are required to assess internationally validated diagnostic and treatment modalities that are cost-effective, clinically efficacious and culturally-acceptable, and how they can best be adapted to suit the needs of the local population and health system. As a starting point, qualitative studies that take into account the lived experiences of African children with CP and their caregivers may provide insight into where the gaps are.

6. Further weight to the argument that the ICF does not play a central role in discourse on CP in Africa and that there needs to be a paradigm shift in future research to address the quality-of-life issues faced by African children with CP.

7. A critical assessment of the breadth and quality of published literature on CP among African children over the last two decades, showcasing the recent surge in good quality studies, particular community-based, on the topic. Simultaneously, this review provides a basis for further research on important themes. In particular, larger, community-based observational and intervention studies are required and more African countries need to be encouraged and capacitated to conduct research on CP. One possible solution is collaboration between centres within African regions, so that academic resources can be shared and comparisons between ethnically and culturally similar populations can be drawn.

Conclusion

"Cerebral palsy" refers to a heterogenous group of conditions arising from a static, non-progressive insult to the developing foetal or infant brain, with the primary pathology being motor dysfunction. The majority of our knowledge on CP comes from studies in North American and European populations, which makes translating this information into African contexts difficult and flawed, given the unique challenges on the continent. A previous review in 2014 of CP among African children highlighted several important research gaps to be addressed in subsequent studies. Since that review, there has been a surge in studies on CP in Africa, warranting an updated systematic review on African children with CP.

From 1452 articles sourced from the three databases reputed to have the largest indexed content from Africa, 58 articles made the final selection for inclusion following three rounds of scrutiny against strict inclusion and exclusion criteria and a final adjudication process. All 58 articles underwent a quality assessment and data extraction process before being synthesised into the final reporting of results. Although the studies were dominated by three countries, were predominantly quantitative and cross-sectional in design and did not employ consistent methodology or robust statistical analyses, they were of sufficient quality to allow a comprehensive overview of multiple themes connected to African children with CP.

The major findings in this review include the large range in prevalence reported among community-based studies, with the majority of studies reporting a prevalence that approximated the global North, despite a seemingly higher burden of disease in Africa. However, given serious concerns around the limited number of studies and the methods of case identification, the true prevalence of CP in Africa is still uncertain. Spasticity was the most common clinical subtype, likely reflecting the global and severe nature of initial insult sustained by these children, predominantly in the perinatal period. The major co-morbidities among African children with CP (sensory impairment, seizure disorders, intellectual disability and malnutrition) mirror those found in HIC but a larger proportion of

African children with CP are more severely affected. Children with CP in Africa face excess mortality, especially in the under-5 age group, with malnutrition being a major modifiable risk factor. Imaging studies found abnormalities in a high proportion of African children with CP and intervention studies showed that these children derived benefit from both surgical and non-surgical therapies even within short periods of follow-up. While findings from imaging and intervention studies mirror those seen from studies in high-income countries, there is limited information on the utility of imaging and treatment modalities for African children with CP. The ICF remains an under-utilised tool in research on CP in Africa.

This review adds new information on prevalence, aetiology, co-morbidities and mortality among African children with CP, providing targets for improved services and interventions from the antenatal period throughout childhood. It also provides insights on the experiences of children with CP and their caregivers, especially the barriers they face to accessing optimal care. The true prevalence of CP in Africa remains uncertain, and more research is needed to accurately report trends on CP among African children. Larger, more robust studies evaluating diagnostic and treatment modalities suitable more suited to the African context are also needed, but current evidence suggests that African children with CP are as likely to benefit from these interventions when able to access them.

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Appendices

Appendix A: Online database search strategies

PubMed search strategy

MESH terms - PubMed

1. "Pediatrics"[Mesh]
2. "Disabled Children"[Mesh]
3. "Cerebral Palsy"[Mesh]
4. "Neurodevelopmental Disorders"[Mesh]
5. "Developing Countries"[Mesh]
6. "Africa"[Mesh]

Search terms – PubMed

1. Child*
2. Developmental delay
3. Low and middle income countries
4. Neurodisability
5. Neurological impairment
6. Developmental disability

PubMed search string:

("cerebral palsy"[Title/Abstract] OR "Neurodevelopmental Disorders"[MeSH Terms] OR "developmental delay"[Title/Abstract] OR "neurodisability"[Title/Abstract] OR "neurological impairment"[Title/Abstract] OR "developmental disability"[Title/Abstract]) AND ("Africa"[MeSH Terms] OR "developing countries"[Title/Abstract] OR ("Low"[Title/Abstract] AND "middle income countries"[Title/Abstract])) AND (2000:2020[pdat])

Total results 1165 on 28 February 2021

SCOPUS search strategy

SCOPUS search string

(TITLE-ABS ("cerebral palsy" OR "Neurodevelopmental Disorders" OR "developmental delay*" OR neurodisabilit* OR "neurological impairment" OR "developmental disabilit*") AND PUBYEAR > 1999) AND (TITLE-ABS (africa OR "developing countr*" OR "Low - middle income countr*") AND PUBYEAR > 1999) AND (EXCLUDE (PUBYEAR , 2021))

Total results on 16 June 2021

385

Total results after restriction to articles and English only

285

Results after duplicates with PubMed removed

139

Web of Science search strategy

Web of Science search string

(TS=("cerebral palsy" OR "Neurodevelopmental Disorders" OR "developmental delay*" OR neurodisabilit* OR "neurological impairment" OR "developmental disabilit*")) AND TS=(africa OR "developing countr*" OR "Low - middle income countr*")

Index date range 1/1/2000 to 30/6/2020

Total results on 8 July 2021

443

Total results after restriction to English only and book chapters and letters excluded

431

Results after duplicates with PubMed and SCOPUS removed (also book chapter)

148

Appendix B: Quality assessment of quantitative studies included in systematic review

First author	Year of publication	Design (quality)	Ascertainment of exposure (quality)	Ascertainment of outcome (quality)	Control for confounding (quality)	Final quality assessment
Abas	2017	Cross-sectional (medium)	Pre-existing diagnosis of CP from medical records (medium)	Direct assessment via GMFCS and neurological examination (high)	Controlled for single confounder in binary logistic regression model (medium)	Medium
Abd El-Kafy	2014	Randomised controlled trial (high)	Pre-existing diagnosis of CP from medical records (medium)	Direct assessment of gait (high)	Blinded randomised allocation to treatment groups but no explicit adjustment for confounding in analyses. Minimal loss to follow-up (high-medium)	High-medium
Abdullahi	2013	Case-control (medium)	Pre-existing diagnosis of CP based on specific criteria including brain imaging (high-medium)	Caregiver questionnaires (low)	Adjustment for confounders in multivariate analyses and 2 controls matched per case based on time and place of birth (high)	Medium
Adamu	2018	Cross-sectional, case-control (medium)	Pre-existing diagnosis of CP based on specific criteria with further clarification of likely aetiology from history and medical records (high-medium)	Direct standardised measurement of anthropometry (high)	Controls matched for age and sex. No significant difference in baseline characteristics between cases and controls. No explicit adjustment for confounders in analyses (medium)	Medium
Adepoju	2017	Intervention study with sequential assignment of participants to intervention arms (high-medium)	Diagnosis of CP made by paediatric neurologist prior to study and baseline function of participants directly assessed by study team using GMFCS (high-medium)	Direct measurement of balance and functional mobility by physiotherapist blinded to intervention (high-medium)	Participants systematically signed to alternating intervention groups with no significant differences between intervention arms but no explicit control for confounders in analyses (medium)	High-medium

First author	Year of publication	Design (quality)	Ascertainment of exposure (quality)	Ascertainment of outcome (quality)	Control for confounding (quality)	Final quality assessment
Alves	2018	Cross-sectional (medium)	Pre-existing diagnosis of CP based on medical records (medium)	All data taken from clinic logbook entered by orthopaedic medical officer or community health worker (low-medium)	Descriptive statistics only – no adjustment for confounders (low)	Low-medium - Accuracy of data indeterminate given review of medical records only with no direct assessment of patients, descriptive statistics with no 95% CI provided for CP results
Andrews	2020	Cross-sectional (medium)	Direct assessment and diagnosis of CP by trained study team (high)	Direct assessment of baseline function using GMFCS; impairment assessed by questionnaires administered to caregivers and physical examination by medical officer and assessment by physical therapist (high)	Multivariate linear regression models used in analysis to control for confounding (high)	High-medium
Badaru	2019	Cross-sectional with purposive sampling (medium)	Pre-existing diagnosis of CP based on medical records (medium)	Questionnaires administered to caregivers - all outcomes self-reported (low)	Descriptive statistics only – no adjustment for confounders (low)	Low-medium - Concerns about data quality based on method of outcome measurement and adjustment for confounding

First author	Year of publication	Design (quality)	Ascertainment of exposure (quality)	Ascertainment of outcome (quality)	Control for confounding (quality)	Final quality assessment
Ballington	2018	Intervention study with cross-over design but total number of study participants =10 (medium)	Pre-existing diagnosis of CP diagnosed by medical practitioner (medium)	Direct assessment of functional mobility by study team, unblinded (high-medium)	Cross-over design so each participant serves as his own control but very small participant number at outset and some participants did not complete intervention. No explicit adjustment for confounders in analyses (low-medium)	Low-medium - Concerns about data quality based on low number of participants and lack of adjustment for confounding
Ballot	2012	Prospective observational study (medium-high)	Very low birth weight infants born within specific period, who survived to discharge with defined exclusion criteria that would affect follow up (medium)	Developmental assessment was done using BSID III, by one of two neurodevelopmentally trained physiotherapists blinded to details of patient's birth and hospital admission. No explicit criteria for diagnosis of CP given (medium).	Multivariate linear regression models used in analysis to control for confounding (high)	Medium-high
Ballot	2020	Prospective observational study (medium-high)	Neonatal hypoxic ischaemic encephalopathy was diagnosed in neonates with evidence of encephalopathy and perinatal asphyxia (medium)	Infants were seen at a dedicated follow-up clinic every 3 months. Neurodevelopmental assessments were performed by either an appropriately trained physiotherapist or a paediatrician, using the Bayley Scales of Infant Development version III. CP was defined as a permanent, non-progressive disorder in the development of movement and posture, which in this study was attributed to neonatal NHIE (medium-high)	Controls were matched by gestational age and age at assessment. No further adjustment for confounders made Small total number of children diagnosed with CP – cautious interpretation of subgroup analyses (medium)	Medium-high

First author	Year of publication	Design (quality)	Ascertainment of exposure (quality)	Ascertainment of outcome (quality)	Control for confounding (quality)	Final quality assessment
Barratt	2010	Cross-sectional study (medium) – systematic sampling of medical records at a clinic (every 15th file reviewed)	Pre-existing diagnosis of CP based on medical records (medium)	Report from medical records of "feeding difficulties" or referral for feeding assessment. No clear criteria for "feeding difficulties" (low-medium)	Data tabulated in a nominal fashion and analysed using descriptive statistics. No explicit adjustment for confounding (low)	Low-medium - Concerns about data quality based on method of outcome measurement and adjustment for confounding
Bazaraa	2012	Cross-sectional study (medium)	Pre-existing diagnosis of CP from medical records (medium)	Review of medical records for all data collected (medium)	Data were tabulated and analysed using frequency and percentage. Nominal data were compared using Chi-squared tests. $P < 0.05$ was considered significant. No explicit adjustment for confounders (low-medium)	Low-medium
Bearden	2016	Cross-sectional study (medium)	Pre-existing diagnosis of CP but verified again by direct examination and review of medical records and imaging of study paediatric neurologist. Explicit diagnostic criteria. (high)	Direct examination of child, specialised testing (e.g. audiometry), reviews of medical records by study team and questionnaires administered to caregivers (high-medium)	No adjustment for confounding in study design but results of analyses presented by sub-group and then stratified prior to significance test being applied (medium)	Medium-high
Belonwu	2009	Cross-sectional (medium)	Pre-existing diagnosis of CP from medical records (medium)	Review of medical records for all data collected (medium)	Examined differences by sex but no other explicit adjustment for confounders (medium)	Medium

First author	Year of publication	Design (quality)	Ascertainment of exposure (quality)	Ascertainment of outcome (quality)	Control for confounding (quality)	Final quality assessment
Bischof	2012	Cross-sectional study with convenience sampling (medium)	Parent questionnaire for antenatal, birth and neonatal history but no medical records. Activity limitation determined by functional mobility scale. Beery developmental test for visuo-motor integration used (low-high depending on parameter)	Diagnosis of spastic diplegia confirmed by complete and comprehensive clinical examination, focusing on the nature and distribution of the spasticity in population of children known with CP (medium-high)	Statistical analyses included descriptive statistics, means testing, simple correlations, and frequency analysis with significance values set at $p<0.05$ but no adjustment for confounders (low-medium)	Medium
Bishay	2008	Intervention study – no control/comparison group. Effectively prospective cohort study (medium)	Pre-existing diagnosis of CP from medical records (medium)	Detailed assessment of functional outcome reported at >2years post-intervention but not stated if collected from medical records or by direct assessment (medium)	Mentions significant impact of age on results but no other explicit adjustment for confounders. Some results reported by sub-groups (low-medium)	Medium - Concerns about data quality: no comparison group, unclear methodology or role of study team in assessment or intervention, and descriptive analyses used.
Christianson	2002	Cross-sectional study (medium)	Initial community-based screening via validated questionnaire and then diagnosis of intellectual disability made via history, physical examination and use of formal testing of vision, audiometry and neurodevelopment using standardised tools (high)	Cases examined by neurodevelopmental paediatricians to diagnose underlying neurodevelopmental disorder - CP not primary disorder being evaluated. No case definitions provided. (medium-high)	Descriptive statistics only with no adjustment made for confounders or tests of statistical significance (low)	Medium

First author	Year of publication	Design (quality)	Ascertainment of exposure (quality)	Ascertainment of outcome (quality)	Control for confounding (quality)	Final quality assessment
Couper	2002	Cross-sectional study (medium)	Initial community-based screening via validated questionnaire and then diagnosis of neurodevelopmental disorder was made via history and assessment by trained rehabilitation team (medium-high)	Standard definitions of severity provided for overall disability. No case definitions provided for primary diagnosis e.g. difference between motor disability and CP or perceptual disability and blindness. Large overlap in reported diagnostic categories (Low-medium)	Descriptive statistics only with no adjustment made for confounders or tests of statistical significance (low)	Medium - Concern about data quality – difficult to interpret results given large overlap in diagnostic categories and lack of clarity around how final prevalence results are reported.
Dambi	2014	Intervention study – convenience sampling and geographical allocation to intervention (medium)	Pre-existing diagnosis of CP from medical records (medium)	Direct assessment of functional mobility by study team and self-administered questionnaires (validated and translated to local language) to caregivers (medium)	Multivariate regression analyses used and confounders acknowledged and accounted for (high)	Medium
Duggan	2010	Cross-sectional study (medium)	Possible cases were self-selected from the community following advertisement of the study – all children with seizures or movements disorders invited by public announcement (low)	Diagnosis of seizure disorder and subtype was made by interview of caregiver. Co-morbid neurological conditions were assessed by direct examination of 600/618 possible cases by the study team and 18/600 had existing diagnoses (medium)	Statistical analyses included descriptive statistics, with confidence intervals and tests for statistical significance but no adjustment for confounders (medium)	Medium

First author	Year of publication	Design (quality)	Ascertainment of exposure (quality)	Ascertainment of outcome (quality)	Control for confounding (quality)	Final quality assessment
Duke	2019	Cross-sectional (medium)	Possible cases identified by key informant method and then diagnosis made by paediatric neurologist (high)	Caregiver report of measurements (antenatal/postnatal) using study data collection form and history documented by medical practitioner during diagnostic procedure (medium)	Acknowledges potential confounders but no explicit adjustment for confounders in later analyses despite detecting significant differences in initial analyses e.g. age and residence statistically significant differences (medium)	Medium
El-Etribi	2004	Randomised controlled trial (high)	Pre-existing diagnosis of CP from medical records (medium)	Direct assessment of functional outcome by examination and EMG but not blinded (high-medium)	Restricting and randomisation in study design to account for confounders and no significant differences in age and IQ but no further adjustment for confounders in analyses (high-medium)	High-medium
El-Tallawy	2011	Cross-sectional (medium)	Possible cases identified by community-based screening and then diagnosis made by paediatric neurologist (high)	Clinical examination, brain imaging, EEG, and caregiver interviews by study team (high)	Analyses stratified by residence and sex to account for those confounders but no explicit adjustment in analyses (medium)	High-medium
Frank-Briggs	2011	Cross-sectional (medium)	Majority of data collected from medical records including pre-existing diagnoses and results of special investigations (medium)	Cases of diagnostic uncertainty referred for further evaluation by other services. Specialist investigations also ordered for cases of diagnostic uncertainty (medium)	Descriptive statistics only with no adjustment made for confounders or tests of statistical significance (low)	Medium

First author	Year of publication	Design (quality)	Ascertainment of exposure (quality)	Ascertainment of outcome (quality)	Control for confounding (quality)	Final quality assessment
Hassell	2018	Cross-sectional (medium)	Possible cases identified from hospital settings then examined by study team to confirm diagnosis of CP (high)	Caregiver interviews by study team (low-medium)	No explicit methodology for analyses given. Only descriptive statistics provided (low)	Low-medium - Concerns about data quality based on ascertainment of outcome and lack of explicit methodology for statistical analyses
Johnson	2017	Nested case-control study (medium)	Pre-existing diagnosis of CP from parent study - Diagnosis of CP verified by direct examination and review of medical records and imaging of study paediatric neurologist (high)	Caregiver interviews, chart review of inpatient and outpatient records, and physical examinations by study team (high-medium)	Controls not matched to cases but confounding addressed through multivariate logistic regression (high)	High-medium
Kakooza-Mwesige	2015 (April)	Cross-sectional (medium)	Possible cases identified from hospital clinic then examined by study team to confirm diagnosis of CP (high)	Direct assessment via clinical examination, review of medical records, blood tests, audiometry and extended caregiver interviews (high-medium)	Analyses stratified by sub-groups but no explicit adjustment in analyses (medium)	High-medium
Kakooza-Mwesige	2015 (June)	Cross-sectional (medium)	Possible cases identified from hospital clinic then examined by study team to confirm diagnosis of CP (high)	Direct assessment via clinical examination, anthropometry, blood tests, and extended caregiver interviews (high-medium)	Outliers excluded from analyses and multivariate logistic regression used (high)	High-medium

First author	Year of publication	Design (quality)	Ascertainment of exposure (quality)	Ascertainment of outcome (quality)	Control for confounding (quality)	Final quality assessment
Kakooza-Mwesige	2016	Cross-sectional (medium)	Sub-group of children already diagnosed with CP by study team in original study who accepted invitation for CT scan – in original study, possible cases identified from hospital clinic then examined by study team to confirm diagnosis of CP (high)	Contrasted CT brain scans performed for the purpose of the study reviewed by radiologists (high)	Radiologists blinded as to underlying diagnosis and results all stratified by sub-groups. Differences in cohorts (scanned versus unscanned) acknowledged but not accounted for in analyses (high-medium)	High-medium
Kakooza-Mwesige	2017	Cross-sectional (medium)	Three-stage screening process with final diagnosis of CP made by study team (high)	Direct assessment via clinical examination, blood tests and functional/developmental assessment, and extended caregiver interviews (high-medium)	Analyses stratified, binomial regression models used and effect of attrition addressed (high)	High-medium
Lagunju	2007 (January)	Cross-sectional (medium)	Participants diagnosed with CP based on clinical examination but no specific criteria given, and epilepsy with EEG during recruitment into study (high-medium)	Outcomes were ascertained by combination of caregiver report, and medical records etc (low-medium)	No explicit methodology given around statistical analyses or adjustment for confounding (low)	Low-medium - Concerns about data quality – lack of explicit methodology around ascertainment of outcomes and statistical analyses
Lagunju	2007 (March)	Cross-sectional (medium)	Possible cases referred to paediatric neurology clinic were examined at enrolment to confirm diagnosis of CP. Detailed history also taken from caregiver. (high)	Initial eye examination done by paediatric neurologist and all participants with abnormalities then assessed by ophthalmologist (high)	Results stratified by CP subtype but no additional adjustment for confounders in analyses (low-medium)	Medium

First author	Year of publication	Design (quality)	Ascertainment of exposure (quality)	Ascertainment of outcome (quality)	Control for confounding (quality)	Final quality assessment
Lagunju	2009 (January)	Cross-sectional (medium)	Possible cases referred to paediatric neurology clinic were examined at enrolment to confirm diagnosis of neurological disorder. Detailed history also taken from caregiver. EEG done for children with history of seizures (high)	Not applicable – prevalence study	Descriptive statistics only with no adjustment for confounders or test of significance (low)	Medium
Lagunju	2009 (May)	Prospective cohort study (high)	Possible cases referred to paediatric neurology clinic were examined at enrolment to confirm diagnosis of CP. Detailed history also taken from caregiver. EEG done for children with history of seizures (high)	Direct assessment and information collected by study team on outcomes at 1 year post-enrolment (high-medium)	Large loss to follow up and no adjustment for loss to follow up or confounders in analyses (low)	Medium
Langerak	2020	Retrospective cohort study (medium-high)	Eligible participants recruited from database of special needs school with pre-existing diagnosis of spastic diplegic CP. Inclusion criteria for cases clearly defined but eligibility determined by review of records and questionnaires (medium)	Outcome directly measured by means of gait analysis with multiple trials by each participant and 3 best attempts selected for analysis (high)	Descriptive statistics with tests of significance performed and presented with normative data for same age group. No explicit adjustment for confounders (medium)	Medium

First author	Year of publication	Design (quality)	Ascertainment of exposure (quality)	Ascertainment of outcome (quality)	Control for confounding (quality)	Final quality assessment
Levira	2019	Cross-sectional (medium)	Baseline census data used to establish sociodemographic information. Verbal autopsy interviews conducted by trained personnel using standardised WHO questionnaires (medium)	Verbal autopsy reports reviewed by two independent physicians who verbally resolved any discrepancies in coding. ICD-10 system used for coding (medium)	Explicit methodology for weighting of data according to population census data (medium)	Medium
Mahlaba	2020	Cross-sectional (medium)	Newly diagnosed cases of CP at a hospital clinic – diagnosis obtained from medical records (medium)	Outcomes obtained from review of medical records (medium)	Results stratified by sub-group but no additional adjustment for confounders in analyses (low-medium)	Medium
Mlinda	2017	Randomised controlled trial (high)	Pre-existing diagnosis of CP by paediatrician using specified criteria obtained from medical records (high-medium)	Outcomes obtained by direct observation as well as caregiver interview by study team (high-medium)	All identified potential confounders included in multivariate regression analyses (high)	High-medium
Monokwane	2017	Case-control (medium)	Same cohort from study by Bearden et al (2016) - Pre-existing diagnosis of CP but verified again by direct examination and review of medical records and imaging of study paediatric neurologist. Explicit diagnostic criteria. (high)	Direct examination of child, reviews of medical records by study team and questionnaires administered to caregivers (high-medium)	Age-matched controls recruited from similar hospital settings. Potential confounders adjusted for in multivariate conditional logistic regression analyses (high)	High-medium
Munyumu	2018	Cross-sectional (medium)	Pre-existing diagnosis of CP obtained from hospital clinic records (medium)	Direct examination of participants and questionnaires administered to caregivers by study team (high-medium)	Results stratified by sub-group and potential confounders entered into multivariate logistic regression model (high)	High-medium

First author	Year of publication	Design (quality)	Ascertainment of exposure (quality)	Ascertainment of outcome (quality)	Control for confounding (quality)	Final quality assessment
Naik	2018	Case-control (medium)	Pre-existing diagnosis of spastic diplegic CP versus spastic diplegia secondary to HIV obtained from medical records (medium)	Direct examination of participants, review of medical records and questionnaires administered to caregivers by study team (high-medium)	Cases and controls not matched with differences between groups not accounted for in analyses. Results stratified by sub-group (low-medium)	Medium - Need to interpret results with caution as small numbers included in certain sub-group analyses
Namaganda	2020	Prospective cohort study (high)	Same cohort from study by Kakooza-Mwesige *et al* (2017) - Three-stage screening process with final diagnosis of CP made by study team. Review of medical records including the results of the baseline assessments conducted by the original study team (high-medium)	Outcomes obtained via verbal autopsy and census data and cause of death assigned by medical officers based on information obtained (medium)	Cox proportional hazards regression models used to evaluate the effect of different variables on mortality outcomes (high)	High-medium
Nwaneri	2013	Case-control study (medium)	Pre-existing diagnosis of neurological disorders including CP from hospital clinic records. Controls sourced from schools in same district using multi-staged sampling technique. Clear inclusion and exclusion criteria (medium)	Stool samples collected same-day from both cases and controls, examined by single designated microbiologist. Graded using standardised WHO guidelines (high)	Explicit sampling method, age and sex-matched controls, Multivariate logistic regression analyses used with explicit adjustment for potential confounders (high)	Medium-high
Ogoke	2017	Cross-sectional (medium)	Pre-existing diagnosis of CP from hospital clinic records (medium)	Direct examination of participants, review of medical records and caregiver interviews (high-medium)	Descriptive statistics only with no adjustment for confounders or test of significance (low)	Medium - Need to interpret results with caution

First author	Year of publication	Design (quality)	Ascertainment of exposure (quality)	Ascertainment of outcome (quality)	Control for confounding (quality)	Final quality assessment
Ogunlesi	2007	Cross-sectional study (medium)	Demographic factors and diagnosis of bilirubin encephalopathy from hospital records (medium)	Diagnosis of CP from review of medical records at outpatient follow-up but very large loss to follow up i.e. 80% of participants (low-medium)	Data analysed using odds ratios and Chi-squared test for statistical significance. Only descriptive statistics used for analyses for CP (low-medium)	Low-Medium - Difficult to interpret results given only 20% of patient cohort seen at follow up where diagnosis was made, and all data derived from medical records
Okenwa	2019	Cross-sectional (medium)	Pre-existing diagnosis of CP from hospital clinic records (medium)	Review of medical records to determine treatment modalities and attendance (medium)	Descriptive statistics only with no adjustment for confounders or test of significance (low)	Medium
Okike	2013	Cross-sectional (medium)	Pre-existing diagnosis of CP from hospital clinic records (medium)	Review of medical records and caregiver report. Seizure disorders confirmed with EEG (medium)	Results stratified by sub-group; only descriptive analyses used but tests of significance applied (low-medium)	Medium
Polack	2018	Cross-sectional (medium)	Pre-existing diagnosis of CP by developmental paediatrician or physiotherapist. Possible participants identified through databases of community rehabilitation programmes, community members and hospital clinics (medium)	Direct measurement of anthropometry and structured questionnaires and interviews of caregivers by study team (high-medium)	Multivariate logistic regression analyses used with explicit adjustment for potential confounders (high)	High-medium
Sogbossi	2019	Cross-sectional (medium)	Pre-existing diagnosis of CP based on medical records and registers from community rehabilitation centre (medium)	Basic assessment of vision otherwise all parameters obtained by caregiver report or from medical records (medium)	Descriptive analyses with no adjustment for confounders but tests of statistical significance applied. Looked at differences in results when certain subgroups were excluded (medium)	Medium

First author	Year of publication	Design (quality)	Ascertainment of exposure (quality)	Ascertainment of outcome (quality)	Control for confounding (quality)	Final quality assessment
Tartaryn	2017	Cross-sectional (medium)	Possible cases identified by key informant method and then diagnosis made by study team – criteria for diagnosis of CP not specified (high-medium)	Direct assessment by study team including physical examination and caregiver interview. CP only one of the conditions listed as a cause for the various types of disability – criteria for diagnosis of CP not specified (medium)	Only descriptive analyses used for reporting on CP (low)	Medium - CP not the main outcome or exposure examined. No clear case definition for CP.
Tomoum	2009	Case-control study (medium)	Pre-existing diagnosis of CP based on hospital clinic records (medium)	Direct functional assessment and anthropometric measurement, history taken from caregivers by study team and blood samples taken (high-medium)	Controls matched by age and sex. Tests of significance applied but not explicit adjustment for confounders in analyses (high-medium)	Medium
Unger	2005	Randomised controlled trial (high)	Pre-existing diagnosis of CP based on school records (medium)	Direct measurement of outcome via 3D gait analysis and self-administered questionnaires by participants (high-medium)	Systematic randomisation, evaluation of differences in baseline characteristics between intervention groups and results stratified by sub-group. However, very small numbers in intervention versus control groups ?sufficient power to detect differences (Medium)	Medium
Wammanda	2007	Cross-sectional study (medium)	Pre-existing diagnosis of CP from hospital clinic records (medium)	All demographic and treatment data were collected via review of medical records (medium)	Only descriptive analyses used for reporting on CP (low)	Medium

Appendix C: Quality assessment of qualitative studies included in systematic review

First author	Bantjes	Bantjes	Bantjes	Conchar
Year	2015	2015	2015	2016
Title	Developing Programmes to Promote Participation in Sport among Adolescents with Disabilities: Perceptions Expressed by a Group of South African Adolescents with Cerebral Palsy	When they call me cripple: a group of South African adolescents with cerebral palsy attending a special needs school talk about being disabled	"There is soccer but we have to watch": the embodied consequences of rhetorics of inclusion for South African children with cerebral palsy	Barriers and facilitators to participation in physical activity: The experiences of a group of South African adolescents with cerebral palsy
Clear statement of the aims of the research?	Yes	Yes	Yes	Yes
Is a qualitative methodology appropriate?	Yes	Yes	Yes	Yes
Was the research design appropriate to address the aims of the research?	Yes	Yes	Yes	Yes
Was the recruitment strategy appropriate to the aims of the research?	Yes	Yes	Yes	Yes
Was the data collected in a way that addressed the research issue?	Yes	Yes	Yes	Yes
Has the relationship between researcher and participants been adequately considered?	No	No	No	No
Have ethical issues been taken into consideration?	Yes	Yes	Yes	Yes
Was the data analysis sufficiently rigorous?	Yes	Yes	Yes	Yes
Is there a clear statement of findings?	Yes	Yes	Yes	Yes
How valuable is the research?	Provides input into development of school sports programmes for children with CP	Provides insight into the views around disability and experience of being disabled amongst South African adolescents	Provides comment on the experiences of South African adolescents with CP around inclusion in sport when schools are diverse	Provides insight on the factors that South African adolescents with CP perceive to influence their participation in sport and exercise
Final score (x/10)	9	9	9	9

Appendix D: Data extraction tables for 54 quantitative studies included in systematic review

Primary author (Publication date)	Journal	Study title (Country)	Study design	Study population	Component evaluated	Summary measure (with confidence intervals)	Study quality and risk of bias
Abas (2017)	Macedonian Journal of Clinical Sciences	Clinical Spectrum of Cerebral Palsy and Associated Disability in South Egypt: A Local Survey Study (Egypt)	Cross-sectional	200 documented CP cases aged 3 months to 18 years recruited from physiotherapy and rehabilitation centres in area.	Prevalence of CP; clinical subtypes; Co-morbidities	Overall CP prevalence of 1 per 1000 live births. Proportion of subtype spastic (72.5%), dyskinetic (16%), ataxic (7%), and hypotonic (4.5%) Cases with hemiplegic type fall mostly level I -III on GMFCS scale, while cases with quadriplegia level III - V ($p<0.001$) Each grade higher on GMFCS associated with 2.5 and 1.5-fold increased risk for cognitive impairment and epilepsy, respectively ($p=0.01$)	Medium -significant risk of selection bias. Only cases receiving physiotherapy identified so may underestimate true prevalence and skew severity and subtype characteristics. Also risk of survival bias
Abd El-Kafy (2014)	Clinical Rehabilitation	The clinical impact of orthotic correction of lower limb rotational deformities in children with cerebral palsy: a randomized controlled trial (Egypt)	Randomised controlled trial	57 children of both sexes, aged 6 to 8 years, known with spastic diplegic CP recruited from hospital clinic	Mobility: Gait speed, cadence, stride length, and hip and knee flexion angles in the mid-stance phase pre-and post-treatment using three-dimensional motion analysis system (prereflex system)	No statistically significant ($p<0.05$) differences among the three groups pre-treatment in all measured variables; Statistically significant differences post-treatment, in all parameters, were greater in group C (intervention as per Group B and solid ground reaction ankle foot orthoses in both lower limbs) than that in both groups A (traditional/control intervention) and B (traditional/control plus TheraTogs™ orthotic undergarment and strapping system for both lower extremities). Statistical significance was not achieved between Groups A and B for all parameters	High-medium – minimal loss to follow up. Risk of survival and selection bias as participants derived from hospital rather than community and not necessarily representative of community. Risk of performance/detection bias as trial not blinded.

Primary author (Publication date)	**Journal**	**Study title (Country)**	**Study design**	**Study population**	**Component evaluated**	**Summary measure (with confidence intervals)**	**Study quality and risk of bias**
Abdullahi (2013)	BMC Research notes	Intra-partum fever and cerebral palsy in Khartoum, Sudan (Sudan)	Case-control study	111 cases with pre-existing diagnosis of CP based on specific criteria including brain imaging recruited from hospital clinic; 222 controls recruited from hospital matched for time and place of birth	Risk factors for CP: sociodemographic indicators, maternal age, parity, antepartum haemorrhage, intra-partum fever, mode of delivery, gestational age, birth weight, and admission to the nursery	1. Sociodemographic factors in cases versus controls • History of neonatal death 16 [14.4%] vs. 9 [4.1%], P = 0.001 • Previous newborns with CP 7 [6.3%] vs. 1 • [0.5], P = 0.002 • Fever during delivery of the index • baby 22 [19.8%] vs. 4 [1.8%], P < 0.001 • Breech presentation 15 [13.5%] vs 14 [6.3%] P = 0.03 • Poor sucking 53 [47.7%] vs 6 [2.7%], P < 0.001 • Admission to the neonatal care unit • 23 [20.7%] vs 7 [3.2%], P < 0.001 2. Univariate analysis: • Previous baby with cerebral Palsy OR (14.9 1.8—122.4) p=0.012 • Previous neonatal death OR 4.0 (1.7—9.3) p= 0.001 • Fever during labour OR 31.5 (4.5—40.2) p <0.001 • Breech presentation OR 2.3 (1.1—5.0) p= 0.031 • Admission to the neonatal unit OR 8.(0 3.3—19.4) p<0.001 • Poor sucking OR 32.9 (13.5—80.3) p<0.001 3. Multivariate analysis: • Previous neonatal death OR 5.4 (1.8—16.2) p=0.003 • Fever during labour OR 8.4 (2.3—30.5) p=0.001 • Poor sucking OR 30.5 (10.0—93.1) p<0.001	Medium – recall bias as certain factors based only on history from mother; risk of selection bias as CP cases and controls derived from hospital rather than community and not necessarily representative of community. Risk of survival bias

Primary author (Publication date)	Journal	Study title (Country)	Study design	Study population	Component evaluated	Summary measure (with confidence intervals)	Study quality and risk of bias
Adamu (2018)	Nigerian Postgraduate Medical Journal	Nutritional Status in Cerebral Palsy: A Cross-Sectional Comparative Survey of Children in Kano, Nigeria (Nigeria)	Case-control study	150 children aged 2-12 years with CP recruited from hospital neurology clinic matched for age and sex, with 150 children without CP as controls recruited from Paediatric Outpatient Department with acute illnesses	Anthropometry: Height, weight, BMI, height-for-age, weight-for-age, weight-for-height by direct measurement	The overall prevalence of malnutrition in CP cases was 86% (Of these, 79.3% had under-nutrition, while remaining 6.7% had over-nutrition) versus 55.3% among the controls (45.3% were under-nourished, while 10% had over-nutrition; $\chi 2$: 34.027. $P < 0.0001$) 31.1% of CP group had severe wasting compared to 1.9% in control group ($\chi 2$: 32.887, $P < 0.0001$).	Medium – risk of selection and survival bias as CP cases and controls derived from hospital rather than community and not necessarily representative of community. Also excluded children with contractures due to difficulty in measuring height, which would contain most severely affected cases in terms of GMFCS score
Adepoju (2017)	Ethiopian Journal of Health Sciences	Comparative Efficacy of Progressive Resistance Exercise and Biomechanical Ankle Platform System on Functional Indices of Children with Cerebral Palsy (Nigeria)	Intervention study with sequential assignment of participants to intervention arms: Group 1- Strengthening exercise group Group 2: Biomechanical ankle platform system group	28 children aged 4 - 12 years with hemiplegic or diplegic CP consecutively recruited from outpatient paediatric neurology clinic of tertiary health facility and special children centres	Baseline function via GMFCS score; Berg Balance Scale (BBS) to assess balance; Modified Ashworth scale (MAS) to assess muscle spasticity; Modified 'timed up to go' test (TUG) as a measure of functional mobility.	No significant difference ($p > 0.05$) between intervention groups at baseline. BBS scores and walking speed of participants in the BAPS group improved significantly ($p < 0.05$) from baseline to the end of the intervention, but no significant difference between intervention groups in terms of BBS score or walking speed from baseline to end of intervention	High-medium – risk of selection and survival bias as participants derived from hospital rather than community and not necessarily representative of community. Risk of performance/detection bias as trial not blinded.
Alves (2018)	International Orthopaedics	Pediatric Musculoskeletal Disease in Kumi District, Uganda: A Cross-sectional Survey (Uganda)	Cross-sectional	All children aged ≤18 yrs seen for first visit at hospital musculoskeletal clinic or Kumi District outreach clinic for disabling impairments between January 2013 and December 2015	Burden of disease; referral for therapy	7% of all patients presenting to these clinics over the time period had diagnosis of CP 8% of outreach visits were for cerebral palsy, only 4% of clinic visits were for cerebral palsy Children with CP were seen at a median age of 4 years in outreach vs 2.75years in hospital clinic Outreach patients: 16% referred to surgeon; 37% assistive device; 24% physical therapy; 1% further testing; 23% other Hospital patients: 5% surgery; 34% assistive device; 50% physical therapy; 3% further testing; 7% other	Low-medium – concern about accuracy of data given data sources and no direct assessment of patients; descriptive statistics with no 95% CI provided for CP results; risk of survival bias Category of "other" for interventions not defined

Primary author (Publication date)	Journal	Study title (Country)	Study design	Study population	Component evaluated	Summary measure (with confidence intervals)	Study quality and risk of bias
Andrews (2020)	Developmental Medicine and Child Neurology	Impairments, functional limitations, and access to services and education for children with cerebral palsy in Uganda: a population-based study (Uganda)	Cross-sectional	97 children with CP (42 females, 55 males; age range 2–17y) were identified in a three-stage population-based screening with subsequent medical examinations and functional assessments to confirm diagnosis	Functional outcome as measured by Gross Motor Function Classification System (GMFCS), Manual Ability Classification System (MACS), and Communication Function Classification System (CFCS); co-morbidities; referral for therapy; barriers to healthcare	36% children aged 2 to 5 years had severe mobility impairment (GMFCS levels IV–V) versus 10% children aged 6 to 17 years (p=0.002). 48% of children aged 2 to 5 years had severe hand function impairments (MACS levels IV–V) versus 10% children aged 6 to 17 years (p=0.01). The difference in proportion between age groups was significant (GMFCS levels IV–V p=0.002 and MACS levels IV–V p=0.01). Proportionally more severe motor impairments in the Ugandan sample compared to Swedish cohort for the younger age group in GMFCS levels (p<0.001), but not in MACS (p=0.29). For the older age group, there were less severe impairments in the Ugandan cohort differences in both GMFCS levels (p<0_001) and MACS levels (p=0.006). Verbal ability from the PEDI social skills age group of 6-17 years showed 37% non-verbal, 5% single words, 10% two-word sentences, 2% four- to five-word sentences, and 47% tell simple story. Prevalence of intellectual disability 45% in younger age group versus 58% in older age group. 41% prevalence of ID in those with GMFCS levels I–II vs 89% of those with GMFCS levels IV–V. Overall prevalence of seizures 68% with epilepsy treatment gap of 61%. Overall, 32% had no associated impairments, 37% had one associated impairment, and 31% had two or more associated impairments. Mobility skills increased with age for both Swedish and Ugandan cohorts for GMFCS I-II and MACS I, but only for Swedish cohort for GMFCS III-V and MACS II-V (p<0.001 for difference between cohorts). None of the children with vision or hearing impairment or communication difficulties had any assistive devices, e.g. hearing aid 30% of children (aged 6–17y) with CP attended school. School attendance decreased with increasing GMFCS and CFCS levels and with associated impairments and seizures 80% of caregivers wanted their children to improve in gross motor activities or using hands. Of these, 31% had searched for help during the previous year at the various sites. Themes identified for not seeking care: lack of money; lack of knowledge; lost hope; thinking motor difficulties were not the major problem and would go away with time; their main concern were convulsions	High-medium – comparative international cohorts were not matched for age or sex. Risk of recall and survival bias.

Primary author (Publication date)	**Journal**	**Study title (Country)**	**Study design**	**Study population**	**Component evaluated**	**Summary measure (with confidence intervals)**	**Study quality and risk of bias**
Badaru (2019)	Value in Health Regional Issues	Analysis of Direct Monthly Cost of Outpatient Hospital-Based Care for Children With Cerebral Palsy in Kano, Nigeria (Nigeria)	Cross-sectional with purposive sampling	106 children with CP aged 1-11 years and their caregiver who presented at the outpatient physiotherapy departments of 4 hospitals in Kano, Nigeria from June 10, 2016 to October 14, 2016. children who were being treated on humanitarian grounds (not paying for any treatment) were excluded	*Barriers to healthcare* Caregiver-related variables: occupational status, level of educational attainment, level of monthly income, and marital status Economic variables: monthly cost of outpatient medical care and monthly cost of out-of-pocket expenses. Direct cost of outpatient care = cost of outpatient medical care + monthly cost of out-of-pocket expenses	44.3% of the caregivers were unemployed, 21.7% never attended school, and 80.2% earned incomes that were below the minimum wage Major source of funding for treatment of children with CP was the parents themselves (94.3%), followed by financial help from relatives (2.8%) Average monthly cost of physiotherapy was ₦503.77 ($1.65) ± ₦220.79 ($0.72). Average monthly cost of drugs was ₦2110.79 ($6.92) ± ₦ 1550.54 ($5.08) Average monthly cost of radiological investigations was 3771.46 ($12.37) ± 5135.32 ($16.84) Average monthly cost of hiring a nanny was ₦3326.09 ($10.91) ± ₦1173.66 ($3.85) Average monthly cost incurred on transportation was ₦1861.49 ($6.10) ± ₦1435.06 ($4.71) Average monthly cost of outpatient management of children with CP in Kano city was ₦14 295.38 ($46.87) Average monthly direct cost of outpatient medical care for children with CP of ₦7741.89 ($25.38) in this study was higher than the direct cost of outpatient stroke management in the same environment	Low-medium - Concerns about data quality based on method of outcome measurement (self-report/recall from caregivers), use of descriptive statistics only and lack of adjustment for confounding. Risk of recall bias.
Ballington (2018)	African Journal of Disability	The carry-over effect of an aquatic-based intervention in children with cerebral palsy (South Africa)	Intervention study with cross-over design	10 children aged 8–12 years with CP (GMFCS I-II only) – n=5 for both intervention and control groups. After washout period of 1 month, participants allocated to alternative group	Intervention: 16 sessions over 8 weeks of 10-point programme of the Halliwick Concept (included water adjustment skills, longitudinal rotations, sagittal rotations and swimming skills) Outcome: changes in scoring in Gross Motor Function Measure (GMFM-66)	Intervention group's post-intervention score increased more (z = -2.803, p = 0.005) than the control group's score, with increase in average score on the 66-item GMFM-66 of 4.25 points	Low-medium - Concerns about data quality based on low number of participants and lack of adjustment for confounding. Risk of selection bias. Risk of performance/detection bias as trial not blinded.

Primary author (Publication date)	Journal	Study title (Country)	Study design	Study population	Component evaluated	Summary measure (with confidence intervals)	Study quality and risk of bias
Ballot (2012)	BMC Paediatrics	Developmental outcome of very low birth weight infants in a developing country (South Africa)	Prospective observational study	106 of 178 eligible VLBW infants born between 2006/06/01 and 2007/02/28 treated at the CMJAH neonatal unit who survived to discharge and were able to attend at least one Bayley Scales of Infant and Toddler Development (third edition) (BSID 111) assessment	Risk factor; Prevalence of CP in high-risk group	Prevalence of cerebral palsy was 3.7% in participants.	Medium-high – however, main outcome of interest was not cerebral palsy but rather the range of deficits across developmental domains and associations with risk factors in birth history. Risk of survival bias.
Ballot (2020)	South African Medical Journal	A prospective observational study of developmental outcomes in survivors of neonatal hypoxic ischaemic encephalopathy in South Africa (South Africa)	Prospective observational study	Cases: 84 infants who had survived neonatal hypoxic ischaemic encephalopathy, with an assigned NHIE grade, discharged from the hospital's neonatal unit between June 2013 and December 2016 and had at least one BSID 111 assessment Controls: 64 full-term infants born at same hospital and not admitted at birth	Prevalence of CP in high-risk group; aetiology/risk factors	Prevalence of CP 15.5% amongst NHIE group versus 0% control group (p<0.001). 92% of infants with CP were classified as delayed on the BSID-III motor subscale, and 8% as at risk. 62% of infants with CP had global delay (classified as delay in the cognitive, motor and language domains), versus 0% in control group, and 15% of infants with CP were also blind. The grade of NHIE was not significantly associated with the incidence of CP. 7.1% of infants with NHIE grade 1 had CP, compared with 16.1% infants with NHIE grade 2 and 21.4% infants with NHIE grade 3 (p=0.566, $\chi 2$ analysis). No significant association between use therapeutic hypothermia and diagnosis of CP (p=0.11)	Medium-high - Controls were matched by gestational age and age at assessment. No further adjustment for confounders made. Small total number of children diagnosed with CP – cautious interpretation of subgroup analyses. Risk of survival bias given study population drawn from hospital population. Cerebral palsy case definition clearly defined.
Barratt (2010)	South African Journal of Child Health	Recorded incidence and management of dysphagia in an outpatient paediatric neurodevelopmental clinic (South Africa)	Cross-sectional study– systematic sampling of medical records at a clinic (every 15th file reviewed)	1 472 patients aged 0 - 14 years attending the paediatric neurodevelopmental clinic at a tertiary hospital between June 2008 and April 2009	Burden of disease; burden of reported feeding difficulties; referral for feeding assessment	Proportion of children with CP amongst patients attending the clinic was 19% 35% of children with CP were referred for feeding assessments for reported feeding difficulties 75% of children receiving non-oral feeds had CP	Low-medium - Concerns about data quality based on method of outcome measurement and use of only descriptive statistics, small sample size, risk of survival and selection bias and lack of adjustment for confounding

Primary author (Publication date)	Journal	Study title (Country)	Study design	Study population	Component evaluated	Summary measure (with confidence intervals)	Study quality and risk of bias
Bazaraa (2012)	Pediatric Emergency Care	Profile of Patients Visiting the Pediatric Emergency Service in an Egyptian University Hospital (Egypt)	Cross-sectional study	Children presenting to the paediatric ED of Cairo University Mounira Children Hospital from November 2008 to October 2009	Burden of disease among children attending emergency services	Proportion of children with CP among children with an existing diagnosis presenting to ED was 13.3%	Low-medium - Data were tabulated and analysed using frequency and percentage. No explicit adjustment for confounders. Unclear how subgroup analyses total number of children derived. Survival bias possible. Selection bias due to average of 3639 visits per month but records complete for average 1441 visits per month
Bearden (2016)	Pediatric Neurology	Pediatric Cerebral Palsy in Botswana: Etiology, Outcomes, and Comorbidities (Botswana)	Cross-sectional study	68 children aged 2-18 years known with CP enrolled from inpatient and outpatient settings at a tertiary referral center in Gaborone, Botswana, from 2013 to 2014	Aetiology of CP; CP subtype; functional outcome; co-morbidities	Aetiology: 18% intrapartum hypoxic events, 15% prematurity, 15% postnatal infections, 10% focal ischemic stroke 10% prenatal infections, 3% kernicterus, 3% congenital brain malformations and 26% unknown cause. CP subtype: 82% spastic CP (46% spastic quadriplegia, 24% spastic hemiplegia, 4% spastic diplegia, and 9% mixed spastic/dyskinetic); 7% hypotonic cerebral palsy, 6% dyskinetic cerebral palsy, 3% ataxic cerebral palsy, and 3% other Functional outcome: 41% were GMFCS V and 16% GMFCS IV. Cerebral performance score was highly correlated with GMFCS score (Spearman correlation coefficient = 0.59, $P < 0.001$) as was overall performance score (Spearman correlation coefficient = 0.83, $P < 0.001$). Outcomes on GMFCS, cerebral performance score, and overall performance score did not vary by aetiology ($P \geq 0.5$, small numbers for subgroup analyses) Outcomes also did not vary by inpatient versus outpatient status ($P = 0.7$) Co-morbidities: 82% cognitive impairment (95% CI = 73%–91%), 76% epilepsy (95% CI = 62%–88%), 46% visual impairment (95% CI = 33%–58%), 43% malnutrition, 16% hearing impairment, 26% contractures, and 28% other orthopaedic complications. Cognitive impairment, visual impairment and malnutrition significantly associated with GMFCS score ($p<0.05$). Co-morbidities did not vary by aetiology or by inpatient status ($p>0.05$)	Medium-high - No adjustment for confounding in study design but results of analyses presented by sub-group and then stratified prior to significance test being applied. Selection bias from recruiting from a tertiary centre where more severe cases are seen. Survival bias possible

Primary author (Publication date)	Journal	Study title (Country)	Study design	Study population	Component evaluated	Summary measure (with confidence intervals)	Study quality and risk of bias
Belonwu (2009)	Nigerian Journal of Medicine	Cerebral palsy in Kano, Nigeria -A review (Nigeria)	Cross-sectional	356 children who attended the paediatric neurology clinic January 1998 – December 2005	Burden of disease; aetiology; CP subtype; co-morbidities	42.4% of all cases had a diagnosis of CP. Causes of CP: birth asphyxia 45.7%; unknown 13.2%; neonatal jaundice 12.6%; seizures 11.9%; meningitis 7.3%; prematurity/low birth weight 3.3%; encephalitis 2.6%; genetic disorder 1.3%; trauma 1.3%; craniosynostosis 0.6% CP subtype: spastic 41.7%; 21.9%; 6.6% dyskinetic; mixed 29.8%; ataxic 0% Co-morbidities: speech impairment 15.2%; mental retardation 13.2%; auditory impairment 11.9%; seizure disorders 11%; microcephaly 7.3%; visual impairment 6%; behavioural disorders 4%; strabismus 11.3%; nystagmus 1.3%	Medium – risk of survival bias as well as antecedent-consequence bias, especially when seizures were listed as both aetiology and co-morbidity
Bischof (2012)	South African Medical Journal	Aspects of birth history and outcome in diplegics attending specialised educational facilities (South Africa)	Cross-sectional	40 children aged 7-19 years attending 4 special needs schools in Johannesburg, South Africa with confirmed diagnosis of spastic diplegic CP	Risk factors; functional outcomes as measured by functional mobility scale (FMS), visual motor integration z-score (VMI-z) and visual perception z-score (VIS-z)	No significant correlations between BW or GA and outcomes Chronological age significantly correlated with VIS-z (r=0.36 p=0.02), implying that there were improvements as the participants grew older Male sex and FMS were significantly correlated (r=0.34, p=0.03), particularly for those who could walk independently	Medium- risk of selection bias (school-only cohort), recall bias (history from parents, not records) and survival bias. Use of only descriptive statistics with no adjustment for confounders.

Primary author (Publication date)	Journal	Study title (Country)	Study design	Study population	Component evaluated	Summary measure (with confidence intervals)	Study quality and risk of bias
Bishay (2008)	Annals of The Royal College of Surgeons of England	Short-term results of musculotendinous release for paralytic hip subluxation in children with spastic cerebral palsy (Egypt)	Intervention study – no control/ comparison group. Effectively prospective cohort study (medium)	50 children aged 3-5 years with spastic CP who underwent bilateral open adductor longus, proximal gracilis, and proximal rectus femoris myotomy, and iliopsoas lengthening, in Giza, Egypt, between September 2003- September 2004, for spastic hip subluxation. Results reported in September 2006 after at least 2 years of follow-up.	Containment of femoral head in acetabulum and/or migration; complications of procedure and adverse sequelae	Overall, 22% classified as excellent with full containment of the femoral head into the acetabulum and with no migration; 54% classified as good with < 20% migration and 24% classified as fair with 20–25% migration No child with > 25% migration, abduction contracture or wide-based gait that required treatment at follow-up. No complications (such as wound infections and femoral neurovascular injuries) or other acute problems related to the surgery were recorded Children with higher pre-operative migration percentage had a less favourable final outcome. Children with a better functional baseline (e.g. able to walk and had spastic diplegia) had significantly better results	Medium - concerns about data quality: no comparison group, unclear methodology or role of study team in assessment or intervention, and only descriptive analyses performed (No tests of statistical significance or adjustment for confounders). Selection bias – narrow age range of participants. Risk of performance/detection bias as trial not blinded.
Christianson (2002)	Journal of Intellectual Disability Research	Children with intellectual disability in rural South Africa: prevalence and associated disability (South Africa)	Cross-sectional study with two-phase design: phase one = screening; phase two = formal assessment	6692 children aged 2-9 years in eight selected villages in the Mhala district, Northern Province, South Africa, screened for disability with the Ten Question Questionnaire. 722 children were selected for formal assessment following a positive screening result	Community-based prevalence of CP; co-morbidity with ID	Overall community-based prevalence of CP 3 per 1000 children (using 6692 as total population in study area) Of children with ID, 8.4% also had CP. 25.6% of children with severe ID had CP versus 4.6% of children with mild ID (no test of statistical significance applied)	Medium- Descriptive statistics only with no adjustment made for confounders or tests of statistical significance. Possible selection bias based on consistency and accuracy of screening tool. CP not primary outcome of interest

Primary author (Publication date)	Journal	Study title (Country)	Study design	Study population	Component evaluated	Summary measure (with confidence intervals)	Study quality and risk of bias
Couper (2002)	South African Medical Journal	Prevalence of childhood disability in rural KwaZulu-Natal (South Africa)	Cross-sectional study with two-phase design: phase one = screening; phase two = formal assessment	2036 children under 10 years of age living in Manguzi Health Subdistrict, KwaZulu-Natal, South Africa, screened for disability using Ten Question Questionnaire adapted with the addition of six developmental questions to include the under-2 age group. 158 children underwent formal assessment following a positive screening result	Prevalence of CP	Prevalence of CP was 10 per 1000	Medium- Descriptive statistics only with no adjustment made for confounders or tests of statistical significance. Possible selection bias based on consistency and accuracy of screening tool. CP not primary outcome of interest.
Dambi (2014)	BMC Paediatrics	The impact of hospital-based and community based models of cerebral palsy rehabilitation: a quasi-experimental study (Zimbabwe)	Intervention study – convenience sampling and geographical allocation to intervention	46 children aged 0.5-12 years with known diagnosis of CP; 20 children receiving community-based rehabilitation services (OR group) and 26 children receiving hospital-based services (IB group). Allocation dependent on geographical location i.e. not randomly assigned.	Change in gross motor function over time measured by GMFCS and GMFM-66 at baseline and 3-month follow-up	Children in OR group improved 2.49 points more on the GMFM-66 than children receiving IB services (~6% difference, p=0.002), but both groups showed improvement in GMFM-66 scores (p=0.047) Children who were less severely disabled showed 1.96 points more improvement (p=0.005) For each month increase in age, GMFM-66 scores dropped by 0.02 points (p=0.03)	Medium - Multivariate regression analyses used and confounders acknowledged and accounted for. However, significant difference in mean age of children between groups indicating selection bias. Also significant difference in amount of therapy time between groups. Risk of performance/detection bias as trial not blinded.
Duggan (2010)	African Health Sciences	Epilepsy in rural Ugandan children: seizure pattern, age of onset and associated findings (Uganda)	Cross-sectional study	440 children ≤18 years of age from Rukungiri District, Uganda, self-identified from community advertising of study as having possible seizure disorder that was subsequently confirmed by study author from 18 August to 10 September 1997 Total 193 126 children aged <15 years in study area based on census data	Co-morbidity of CP with epilepsy	Of children with epilepsy, 6.4% also had CP. Among children with CP, 64.3% had complex partial seizures and 10.7% had generalised tonic clonic seizures. Non-athetoid CP was significantly more common in children with complex partial seizures versus other seizure types (17.8% compared with 2.1%, p<0.01).	Medium - Statistical analyses included descriptive statistics, with confidence intervals and tests for statistical significance but no adjustment for confounders. CP not primary outcome of interest. Selection bias given participants had to self-identify as having a likely seizure disorder prior to formal assessment.

Primary author (Publication date)	Journal	Study title (Country)	Study design	Study population	Component evaluated	Summary measure (with confidence intervals)	Study quality and risk of bias
Duke (2019)	Archives of Disease in Childhood	Clinical features and aetiology of cerebral palsy in children from Cross River State, Nigeria (Nigeria)	Cross-sectional study (community-based)	1024 children aged 4-15 years identified initially using key informant method and Ten Question Questionnaire in Cross River State, Nigeria between December 2017 and July 2018. 388 children confirmed to have CP from history and clinical assessment by a paediatric neurologist.	Prevalence of CP; CP subtype; aetiology; functional outcome as measured by GMFCS and MACS	Prevalence of CP 2.3/1000 (0.23%) children (95% CI 2.0 to 2.5/1000). Gross Motor Function Classification System: level 1 18.1%; II 40.2%; III 13.9%; IV 13.9%; V 13.9% Manual Ability Classification Scale: 77.3% level 1–3; 22.7% level 4–5. CP subtypes 70% spastic (60% bilateral and 40% unilateral); 9.8% ataxic; 4.6% dystonic; 7.5% choreoathetoid and 8.3% unclassifiable Postneonatal risk factors identified in 36.1% of children: 72.1% malaria with seizures; 15% malaria with coma; 8.6% meningitis; 1.4% tuberculosis; 2.2% sickle cell disease; 0.7% HIV Prenatal/perinatal risk factors identified in 63.9% of children: 47.6% birth asphyxia; 3.3% clinical congenital rubella syndrome; 23.8% hyperbilirubinaemia	Medium – selection bias despite being community-based as relied on key informant method and self-selection to recruit patients. Acknowledges potential confounders but no explicit adjustment for confounders in later analyses despite detecting significant differences in initial analyses e.g. age and residence statistically significant differences. Risk of survival bias as only children >4 years recruited
El-Etribi (2004)	International Journal of Rehabilitation Research	The effect of botulinum toxin type-A injection on spasticity, range of motion and gait patterns in children with spastic diplegic cerebral palsy: an Egyptian study (Egypt)	Randomised control trial	40 children aged 2-6 years with spastic diplegic CP who showed mobile equinus deformity and had no fixed contractures or associated orthopaedic problems, recruited between March 2001 and March 2003, and randomly allocated to either intervention or control group. Group 1: 20 children received botulinum toxin type-A injection followed by physiotherapy rehabilitation program. Group 2: 20 children received physiotherapy rehabilitation program only.	Spasticity (Modified Ashworth Scale and electromyogram); range of motion (goniometry) and gait patterns (Physician Rating Scale) after 3 months	Group 1 had decrease in spasticity measured by MAS before and after treatment (1.93±0.27 versus 0.89±0.59, $p<0.001$), as well as EMG ($p<0.001$). No significant difference in spasticity seen in Group 2 ($p>0.05$) Group 1 showed improvement in overall gait pattern as measured by PRS (7.6±2.12 versus 11.73±2.24, $p<0.001$) as well as individual parameters (during foot strike, hind foot position during foot strike, hind foot position during gait, degree of crouch and speed of gait; $p\leq0.012$ for all) Group 2 did not show any significant change in gait pattern overall or within specific parameters. Both groups showed statistically significant improvement in passive ankle ROM with intervention ($0<0.05$ for all)	High-medium – Risk of performance/detection bias as trial not blinded. Short period of follow-up. Unclear whether study population drawn from hospital or community -> risk of selection bias.

Primary author (Publication date)	Journal	Study title (Country)	Study design	Study population	Component evaluated	Summary measure (with confidence intervals)	Study quality and risk of bias
El-Tallawy (2011)	Brain and Development	Epidemiology of cerebral palsy in Al-Kharga District -New Valley (Egypt) (Egypt)	Cross-sectional study	25,540 children ≤18 years of age born 1990-2007 in Al-Kharga District, Egypt screened by door-to-door visits in community and possible cases reviewed at hospital by paedatric neurologists including medical exam, imaging and EEG	Prevalence of CP; CP subtype; aetiology; co-morbidities; imaging findings	Community-based prevalence of CP of 2.04 per 1000 (0.2%) children (95% CI 1.48–2.59/1000 children) CP subtype: 65.4% spastic; 26.9% mixed; 3.8% ataxic; 3.8% dyskinetic Aetiology: 90.4% had prenatal complications which required admission to intensive care units. 34.6% cyanosis /apnoea at birth; 17.3% preterm; 15.4% hyperbilirubinaemia and kernickterus; 11.5% “below average birth weight”; 11.5% “difficult prolonged labors” Co-morbidities: 51.9% of children with CP had epilepsy; 70.3% had ID ≤67 (Stanford Binet scale) Imaging: 32.7% of children with CP showed abnormal finding as brain atrophic changes, white matter changes, corpus callosum agenesis etc	High-medium - Analyses stratified by residence and sex to account for those confounders but no explicit adjustment in analyses. Minimal risk of selection bias assuming screening tool valid.
Frank-Briggs (2011)	International Journal of Biomedical Science	Pattern of Paediatric Neurological Disorders in Port Harcourt, Nigeria (Nigeria)	Cross-sectional study	35 473 children seen in the Paediatric Neurology unit of the University of Port-Harcourt Teaching Hospital, Nigeria from January 2004 to December 2009 – inpatients and outpatients	Burden of disease; CP subtype	Proportion of children with CP 15.4% among children attending neurology service. CP subtype: spastic quadriplegia 5.4%; choreoathetoid 4.4%; spastic hemiplegia 2.0%; spastic diplegic 0.9%; mixed 2.7%	Medium - Descriptive statistics only with no adjustment made for confounders or tests of statistical significance; risk of selection and survival bias as hospital-based population specifically from neurology unit

Primary author (Publication date)	Journal	Study title (Country)	Study design	Study population	Component evaluated	Summary measure (with confidence intervals)	Study quality and risk of bias
Hassell (2018)	The Lancet	Contribution of perinatal conditions to cerebral palsy in Uganda (Uganda)	Cross-sectional study	130 children aged <18 years seen at Mulago National Referral Hospital, Uganda over 8-week period in 2013. Participants referred to study with concern of CP by healthcare professionals working in outpatient clinics and wards of hospital	CP subtype; aetiology; subtype by aetiology	CP subtype: spastic quadriplegia 77.7%; spastic hemiplegia 11.5%; dyskinetic 10.8% Aetiology: 6% premature birth <37 weeks; 76% term neonatal illness (intrapartum-related encephalopathy, with or without infection; neonatal sepsis, with no evidence of encephalopathy; neonatal jaundice; other neonatal illness); 11% post neonatal event (CNS infection; other); 7% unknown Subtype by aetiology: 100% of children born <37 weeks had spastic quadriplegia; Of children with intrapartum-related encephalopathy, 88% had spastic quadriplegia, 7% spastic hemiplegia and 5% dyskinetic subtype; Of children with neonatal sepsis, 93% had spastic quadriplegia and 7% spastic hemiplegia; Of children with CNS infection, 75% has spastic quadriplegia, 17% spastic hemiplegia and 8% dyskinetic subtype	Low-medium - No explicit methodology for analyses given and only descriptive statistics provided. Risk of selection bias and survival bias as drawn from hospital population. Small study population means subgroup analyses need to be interpreted with caution
Johnson (2017)	Pediatric Neurology	Risk Factors for Malnutrition Among Children With Cerebral Palsy in Botswana (Botswana)	Nested case-control study	61 children with CP aged 2-15years receiving care at Princess Marina Hospital in Gaborone, Botswana, from 2013 to 2015 with complete nutrition data available (drawn from same study population as Bearden et al)	Risk factors for malnutrition among children with CP	Univariate analyses: Non-ambulatory OR 13.8 (95% CI 3.8-50.1, p <0.001); Socioeconomic risk index (composite of low income, absence of running water in the home, absence of electricity in the home, low maternal education) OR 1.6 (95% CI 1.0-2.5, p=0.03); Food insecurity OR 14 (95% CI 1.2-156.6, p= 0.03); Maternal HIV OR 3.5 (95% CI 1.1-11.5, p=0.03) Multivariate analyses: adjusted OR for GMFCS 3.8 (95% CI 1.5-9.6, p=0.006); adjusted OR for SERI 2.1 (95% CI 1.0-4.1, p=0.04)	High-medium - Controls not matched to cases with significant differences in baseline characteristics. Risk of selection bias as only children with complete data included and survival bias as drawn from hospital population. Confounding addressed through multivariate logistic regression but socioeconomic factors only reach statistical significance once all were combined into single composite score

Primary author (Publication date)	Journal	Study title (Country)	Study design	Study population	Component evaluated	Summary measure (with confidence intervals)	Study quality and risk of bias
Kakooza-Mwesige (2015)	BMC Research Notes	Cerebral palsy in children in Kampala, Uganda: Clinical subtypes, motor function and co-morbidities (Uganda)	Cross-sectional study	135 children aged 2-12 years with CP recruited from CP clinic at Mulago Hospital, Uganda, from September 2009 to August 2010: Screening was done in two steps by a specially trained physiotherapist using validated screening tools. Possible participants then examined by a medical doctor and paediatric neurologist to confirm diagnosis and inclusion criteria	Aetiology; CP subtype; co-morbidities; functional impairment	Aetiology: Preterm birth (<37wks GA) 13.3%; prenatal complications 27.2%; neonatal complications 20.6%; post neonatal complications 18.4% CP subtype: Spastic quadriplegia 45.9%; spastic hemiplegia 23.7%; dyskinetic 12.6%; ataxic 9.6%; unclassifiable 8.1% Co-morbidities: Epilepsy 45.2%; speech and language disorders 37.0%; visual impairments 29.6%; hearing impairments 15.6%; anxiety/depression 19.3%; ADHD 34.1%; learning disability 75.6%; ASD 23.7% Gross motor functional impairment: mild 25.2%; moderate 43.7%; severe 31.1% Fine motor functional impairment: mild 37.8%; moderate 24.4%; severe 37.8% Significant difference in distribution of co-morbidity scores between the CP clinical types (χ^2 (4) = 21.51, p<0.001), gross motor function levels (χ^2 (2) = 14.98, p=0.001) and fine motor function levels (χ^2 (2) = 25.60, p<0.001)	High-medium – analyses stratified by sub-group but no multivariate analyses reported. Tests of statistical significance between groups applied. Risk of selection bias and survival bias as population drawn from tertiary hospital-based CP clinic
Kakooza-Mwesige (2015)	Acta Pa ediatrica	Malnutrition is common in Ugandan children with cerebral palsy, particularly those over the age of five and those who had neonatal complications (Uganda)	Cross-sectional study	135 children aged 2-12 years with CP recruited from CP clinic at Mulago Hospital, Uganda, from September 2009 to August 2010 (same study population as Kakooze-Mwesige et al 2015)	Anthropometry: underweight for age; stunted (low height for age), wasted (low weight for height); thinness (low BMI for age); malnutrition (z-score <-2 for any indicator)	Underweight for age 42% (95% CI 33–51%); Stunting 38% (95% CI 30–46%) Significant associations with being malnourished: presence of cognitive impairment aOR 4.5 (95% CI 1.6-12.5, p=0.004); age ≥5 years aOR = 3.4 (95% CI 1.2-9.7, p=0.02); feeding difficulties in the perinatal period aOR = 3.2 (95% CI 1.3-7.9, p=0.008) Significant associations with being UWFA: presence of cognitive impairment aOR 4.9 (95% CI 1.5-15.8, p=0.008); age ≥5 years aOR = 6.0 (95% CI 1.9-19.0, p=0.002); infection in the perinatal period aOR = 3.6 (95% CI 1.2-10.3, p=0.017); microcephaly aOR = 2.9 (95% CI 1.1-7.4, p=0.024) Significant association between low BMI-for-age and being unable to feed self aOR = 5.2 (95% CI 1.9-14.0, p=0.001) No significant association between duration of breastfeeding and any indicators of malnutrition	High-medium - Outliers excluded from analyses and multivariate logistic regression used. Risk of selection bias and survival bias as original study population drawn from tertiary hospital-based CP clinic

Primary author (Publication date)	Journal	Study title (Country)	Study design	Study population	Component evaluated	Summary measure (with confidence intervals)	Study quality and risk of bias
Kakooza-Mwesige (2016)	Acta Paediatrica	Grey matter brain injuries are common in Ugandan children with cerebral palsy suggesting a perinatal aetiology in full-term infants (Uganda)	Cross-sectional study	78 children with CP aged 2-12 year recruited from CP clinic at Mulago Hospital, Uganda, from September 2009 to August 2010 (same study population as Kakooze-Mwesige et al 2015	Imaging - pre- and post-contrast CT scans reviewed by blinded radiologists	CT abnormalities detected in 69% of the sample: 53% single abnormality and 17% combination of primary grey and white matter abnormalities. 31% had no abnormalities on CT Only one postnatal factor significant in bivariate analyses: children admitted to hospital following birth were three times more likely to have primary grey matter injury than any of the other neuroimaging patterns OR 2.8 (95% CI 1.1–7.1, p = 0.026)	High-medium - Radiologists blinded as to underlying diagnosis and results all stratified by sub-groups. Differences in cohorts (scanned versus unscanned) acknowledged but not accounted for in analyses. Risk of selection bias and survival bias as original study population drawn from tertiary hospital-based CP clinic
Kakooza-Mwesige (2017)	Lancet Global Health	Prevalence of cerebral palsy in Uganda: a population-based Study (Uganda)	Cross-sectional study (community-based)	31 756 children screened for cerebral palsy from the March 1, 2015, to June 30, 2015 in Iganga-Mayuge District, Uganda. Community screening done in two stages, first using selected questions from Ten Question Questionnaire and then review by fieldworkers with adapted validated screening tool if screened positive in first stage. Possible participants referred to Iganga Hospital for formal assessment by specialist CP team 97 children finally confirmed to have CP	Prevalence of CP; CP subtype; functional impairment (GMFCS)	Community-based crude prevalence of 2·7 (95% CI 2·2–3·3) per 1000 children. After adjustment for attrition, the prevalence increased to 2·9 (2·4–3·6) per 1000 children GMFCS level: I 53%; II 8%; III 19%; IV 6%; V 14% The expected number of cases decreased with age which was significantly associated with GMFCS level (estimated coefficient –0·05778, p=0·023). The effect of age was only significant for GMFCS levels 4–5 (estimated coefficient –0·2136, p=0·008) i.e. the lower number of older children with CP was driven by a reduction in the number of children with higher GMFCS levels. Time of brain injury was significant (estimated coefficient 1·6726, p=0·0085) for children with a high GMFCS level i.e. few children with a high GMFCS level were post-neonatal cases CP subtype: spastic hemiplegia 46%; spastic quadriplegia 40%; dyskinetic 9%; ataxic 2%; unclassified 2%. Dyskinetic subtype more common in children aged 2–7 years than in children aged 8–17 years (13% versus 5%); spastic hemiplegia lower in the younger subgroup than older subgroup (43% versus 50%) – no p-value	High-medium - Analyses stratified, binomial regression models used and effect of attrition addressed. Minimal risk of selection bias assuming screening tool valid. Risk of survival bias evident when results displayed by age group

Primary author (Publication date)	Journal	Study title (Country)	Study design	Study population	Component evaluated	Summary measure (with confidence intervals)	Study quality and risk of bias
Lagunju (2007)	Developmental Medicine and Child Neurology	Epilepsy in Nigerian children with cerebral palsy (Nigeria)	Cross-sectional study	130 children aged ≤13 years with existing diagnosis of CP seen at the Paediatric Neurology Clinic, University College Hospital, Ibadan, Nigeria over a period of 15 months	Aetiology; CP subtype; epilepsy as a co-morbidity	Aetiology: birth asphyxia 45.4%; severe neonatal jaundice 26.2%; intracranial infections 10.7%; other causes including prematurity, intrauterine infections, craniosynostosis, and trauma (13.1%); unknown 4.6%; post-neonatal intracranial infections 9.2% CP subtype: spastic 80.0%; mixed 9.2%; dyskinetic 7.7%; hypotonic 3.1% Prevalence of epilepsy 38.5%. Seizure subtype: generalised tonic–clonic seizures 58.0%; partial seizures 18.0%; infantile spasms 14.0%. Timing: Neonatal seizures 40%; first seizure in their first year of life 74%. Increased risk of epilepsy significantly associated with history of neonatal seizures (p=0.001) and presence of spastic hemiplegia (p=0.013)	Low-medium - lack of explicit information around methodology and statistical analyses. No adjustment for confounding and inconsistent use of tests of statistical significance. Risk of selection bias and survival bias as population drawn from tertiary hospital-based CP clinic
Lagunju (2007)	African Journal of Medicine and Medical Sciences	Ocular abnormalities in children with cerebral palsy (Nigeria)	Cross-sectional study	149 children aged ≤13 years with existing diagnosis of CP seen at the Paediatric Neurology Clinic, University College Hospital, Ibadan, Nigeria over a period of 18 months	Aetiology; CP subtype; ocular abnormalities as a co-morbidity	Aetiology: severe birth asphyxia 49.7%; severe neonatal jaundice 26.8%; post-infectious brain damage 10.7%; prematurity 3.4%; craniosynostosis 1.3%; intrauterine infections 2.0%; metabolic disorders 1.3%; unknown 4.0% CP subtype: spastic 82.6%; dyskinetic 8.1%; mixed 6.7% and hypotonic 2.7% Prevalence of ocular abnormalities 28.2% Visual impairment type: 61.9% total blindness; 31.0% partially blind and 7.1% normal vision Cause of visual impairment: optic atrophy 50.0%; strabismus 50.0%; cortical visual impairment 47.7% Larger proportion of children with spastic quadriplegia had associated visual impairment when compared to other CP subtypes (39.5% versus 17.8%; χ^2=6.18, p=0.01)	Medium - Results stratified by CP subtype but no additional adjustment for confounders in analyses. Tests of statistical significance not consistently applied/reported. Risk of selection bias and survival bias as population drawn from tertiary hospital-based CP clinic

Primary author (Publication date)	Journal	Study title (Country)	Study design	Study population	Component evaluated	Summary measure (with confidence intervals)	Study quality and risk of bias
Lagunju (2009)	West African Journal of Medicine	An Analysis of Disorders seen at the Paediatric Neurology Clinic, University College Hospital, Ibadan, Nigeria (Nigeria)	Cross-sectional study	644 children aged ≤14 years presenting at the paediatric neurology clinic of the University College Hospital, Ibadan, Nigeria from May 2004 to December 2005	Burden of disease; aetiology; CP co-morbidities	Proportion of children with CP 36.0% among all cases Aetiology among new cases: severe birth asphyxia 45.2%; severe neonatal jaundice 26.2%; post-infectious brain damage 10.7% Co-morbidities for both old and new cases: epilepsy 30.9-34.8%; mental retardation 44.4-48.5%; hearing impairment 24.4%; visual impairment 25.2%	Medium - Descriptive statistics only with no adjustment for confounders or test of significance. Risk of selection bias and survival bias as population drawn from tertiary hospital-based CP clinic
Lagunju (2009)	Journal of Pediatric Neurology	The child with cerebral palsy in a developing country – diagnosis and beyond (Nigeria)	Prospective cohort study, with cross-sectional analyses as well	82 children aged <11 years with a new diagnosis of CP seen at University College Hospital, Ibadan, Nigeria over 6-month period	Cross-sectional: Aetiology; CP subtype; co-morbidities; functional outcome measured by GMFCS; Prospective: risk factors for mortality; risk factors and reasons for defaulting treatment; change in function as measured by GMFCS	Aetiology: severe perinatal asphyxia (39.0%); bilirubin encephalopathy 24.4%; postinfectious brain damage 18.3%; prematurity 7.3%; intrauterine infections 6.1%; congenital brain malformation 2.4%. Prenatal 7.3%; perinatal 46.3%; neonatal 24.4% and post neonatal 18.3% CP subtype: spastic 79.3%; mixed 8.5%; dyskinetic 7.3%; ataxic 4.9% Co-morbidities: epilepsy 45.1%; growth impairment 35.4%; hearing impairment 29.3%; speech disorders in 23.2%; visual impairment in 20.7%; cognitive impairment in 75% of children aged >6 years. GMFCS level: I 12.2%; II 7.3%; III 9.8%; IV-V 70.7% Mortality: mean age at death 18.3 ±(SD =6.5) months; place of death at home in 100%; increased risk of death with impaired growth (OR 5.76, 95% CI 1.31-25.27, p=0.018) and GMFCS IV-V (OR 1.30, 95% CI 1.11-1.54, p=0.015) Risk factors for defaulting treatment: Absence of epilepsy OR 3.95 (95% CI 1.25-12.46, p=0.014); GMFCS IV-V OR=3.25 (95% CI 1.094-9.68, p=0.03); lower level of maternal education OR 0.07 (95% CI 0.01-0.58, p=0.002) Reasons for defaulting treatment: financial constraints 50.0%; parents discouraged 26.5%; child relocated to another caregiver 26.5%; hospital too far from home 17.6%; birth of another baby 8.8% Change in function over 1 year: inverse relationship between severity of CP and improvement in motor function OR 10.5 (95% CI 2.91-37.95, p<0.001)	Medium - Large loss to follow up and no adjustment for loss to follow up or confounders in analyses. High risk of survival and selection bias given hospital-based population. Short follow-up period.

Primary author (Publication date)	Journal	Study title (Country)	Study design	Study population	Component evaluated	Summary measure (with confidence intervals)	Study quality and risk of bias
Langerak (2020)	Indian Journal of Orthopaedics	Gait Pattern of Adults with Cerebral Palsy and Spastic Diplegia More Than 15 Years after Being Treated with an Interval Surgery Approach: Implications for Low-Resource Settings (South Africa)	Retrospective cohort study	30 adults with spastic diplegic CP who underwent an interval surgery approach when aged 2-12 years with GMFCS I-III, recruited from the database of special needs school in Cape Town, currently living within 100km of Cape Town; compared with normative data of typically developing adults	Gait parameters and gait deviation index in adulthood following ISA in childhood	All adults still ambulant: GMFCS level I (50%), II (37%), or III (13%). 40% improved, 50% were unchanged, 10% had deteriorated. Statistically significant differences ($p<0.05$) between adults with CP and normative data seen: increased anterior pelvic tilt throughout gait cycle, decreased peak hip extension and associated decreased hip flexion/extension ROM, reduced peak knee flexion and extension resulting in a decreased knee flexion ROM and a more dorsiflexed pattern for the ankle with reduced peak plantar and increased dorsal flexion throughout gait cycle, reduced hip adduction/abduction ROM and an increased hip internal rotation throughout the gait cycle. Mean GDI score in the adults with CP of 68.2 ± 14.0 versus 100.0 ± 10.0 for the TD adults.	Medium - Descriptive statistics with tests of significance presented using normative data for same age group. No explicit adjustment for confounders. Risk of selection bias as study population drawn only from single school.
Levira (2019)	Global Health Action	Mortality of neurological disorders in Tanzania: analysis of baseline data from sample vital registration with verbal autopsy (SAVVY) (Tanzania)	Cross-sectional study	Verbal autopsy interview of 6645 deaths among total of 650,864 residents across 23 districts, 1397 census enumeration areas and 154,603 households in the year prior to the baseline survey in 2011-2014	Cause-specific mortality fraction attributable to CP in children aged ≤20	CP accounted for 11.1% of neurological disorder deaths among children < 5 years and 18.2% among children aged 5–19. Mortality of CP in children aged ≤5 years was estimated with a CSMF of 0.40% (95% CI: 0.10–0.70)	Medium – risk of recall bias, missing data and misclassification of data using verbal autopsy method

Primary author (Publication date)	Journal	Study title (Country)	Study design	Study population	Component evaluated	Summary measure (with confidence intervals)	Study quality and risk of bias
Mahlaba (2020)	South African Journal of Child Health	A descriptive study of children with cerebral palsy at Chris Hani Baragwanath Academic Hospital (South Africa)	Cross-sectional study	145 children with CP aged ≤18 years seen for the first time at the CP clinic at Chris Hani Baragwanath Academic Hospital, South Africa in 2012	Aetiology/risk factors; CP subtype; co-morbidities; imaging and functional outcome as measured by GMFCS	Aetiology/risk factors: *Antenatal:* neonatal cerebral malformations 4.1%; congenital infections (congenital CMV, HIV) 5.5%; major and minor birth defects 4.1% *Perinatal:* neonatal encephalopathy 48.2%; maternal pre-eclampsia 3.4%; antepartum haemorrhage 2.0%; prolonged/obstructive labour 2.7%; meconium aspiration 8.2%; cord around the neck 3.4% *Neonatal:* intraventricular haemorrhage 2.0%; jaundice 5.5%; respiratory distress syndrome 6.8%; chronic lung disease 4.1%; infections (meningitis and sepsis) 13.7%; necrotising enterocolitis 2% CP subtype: spastic diplegia 17%; spastic hemiplegia 13%; spastic quadriplegia 5%; dyskinetic 9%; hypotonic 14%; ataxic 2%; mixed 39% Imaging: periventricular white matter lesions (periventricular leukomalacia etc) 54%; brain maldevelopments (lissencephaly, schizencephaly etc) 6.8%; normal 12.5% Co-morbidities: focal seizures 7%; generalised tonic clonic 29%; other seizure type 7%; intellectual disability 35%; feeding difficulties 35%; language delay 34%; undernutrition 30%; orthopaedic complications 28%; pneumonia (aspiration/recurrent etc) 17%; visual impairment 10%; GIT complications 7%; hearing impairment 7% GMFCS level: I 6.2%; II 16.5%; III 36.5%; IV 26.8%; V 13.7% Type of CP (p=0.008), intellectual impairment (p=0.027) and orthopaedic complications (p=0.003) correlated with a higher GMCSF level	Medium - Results stratified by sub-group but no additional adjustment for confounders in analyses. Risk of selection bias as study population drawn from tertiary hospital clinic. Risk of antecedent-consequence bias as several risk factors listed are also independently associated with other risk factors for CP e.g prematurity and necrotising enterocolitis or respiratory distress syndrome

Primary author (Publication date)	Journal	Study title (Country)	Study design	Study population	Component evaluated	Summary measure (with confidence intervals)	Study quality and risk of bias
Mlinda (2018)	Child: Care, Health and Development	The effect of a practical nutrition education programme on feeding skills of caregivers of children with cerebral palsy at Muhimbili National Hospital, in Tanzania (Tanzania)	Randomised control trial	110 (63 intervention and 47 control) children aged ≤5 years with moderate-to-severe CP attending CP clinic at Muhimbili National Hospital, Dar es Salaam, Tanzania, between July 2013 and May 2015 Intervention: ≥6 sessions of group/individual nutrition education including positioning during feeding, and occupational therapy for oral motor and functional skills (food consistency, specific feeding techniques, and appropriate utensils for feeding). Free sets of plastic cups, spoons, and plates provided Control: routine care at CP clinic including general health education and nutritional assessment	Child's oromotor feeding skills and functional feeding skills; caregiver feeding skills; Caregiver-child interaction	Child's feeding skills: No statistically significant differences in observed oral motor feeding skills (AOR = 1.7, 95% CI 0.72–3.91, p = 0.235) and functional feeding skills (AOR = 2.3, 95% CI 0.86–6.06, p = 0.098) Caregiver feeding skills: improved feeding positioning (AOR = 5.3, 95% CI 2.00– 13.96, p < 0.001); better feeding speed (AOR = 5.2, 95% CI 1.99–13.44, p < 0.001); increased child involvement (AOR = 3.5, 95% CI 1.42–8.44, p <0.01) Caregiver-child interaction: Less caregiver stress during feeding (AOR = 2.5, 95% CI 1.04–6.13, p <0 .05) and improved child mood (AOR = 3.1, 95% CI 1.33–7.47, p = 0.01)	High-medium - All identified potential confounders included in multivariate regression analyses. Risk of selection bias as study population drawn from tertiary hospital clinic. Risk of performance/detection bias as trial not blinded.
Monokwane (2017)	Pediatric Neurology	Risk Factors for Cerebral Palsy in Children in Botswana (Botswana)	Case-control study	56 children with CP aged 2-18 years and 56 age-matched healthy controls enrolled from inpatient and outpatient settings from 2013 to 2014 at a referral centre in Gaborone, Botswana (Same study population as Bearden et al, 2016)	Aetiology/risk factors; CP subtype	Aetiology: Significant associations found with birth complications (aOR 11.8, 95% CI 2.2-63.5, p= 0.004); postnatal infection (aOR 80.2, 95%CI 2.3-2782.4, p= 0.015); maternal HIV (aOR 13.2, 95%CI 1.0-171.6, p= 0.05) Gestational age ≤32 weeks not significantly associated with CP (aOR 13.1, 95% CI 0.8-198.1, p= 0.06) CP subtype: spastic quadriplegia 41%; spastic hemiplegia 23%; hypotonia 9%; dyskinetic 9%; mixed spastic-dyskinetic 9%; spastic diplegia 4%	High-medium - Age-matched controls recruited from similar hospital settings. Potential confounders adjusted for in multivariate conditional logistic regression analyses. Risk of selection and survival bias as study population drawn from tertiary hospital.

Primary author (Publication date)	Journal	Study title (Country)	Study design	Study population	Component evaluated	Summary measure (with confidence intervals)	Study quality and risk of bias
Munyumu (2018)	BMC Pediatrics	Prevalence and factors associated with sleep disorders among children with cerebral palsy in Uganda; a cross-sectional study (Uganda)	Cross-sectional study	135 children with CP aged 2-12 years recruited from the paediatric neurology clinic at Mulago Hospital, Kampala, Uganda, from June to December 2015	Burden of disease from sleep disorders as measured by Sleep Disorders Scale in children; associations between CP subtype/co-morbidities/subtype/function (GMFCS and MACS) and sleep disorders	Proportion of children with CP with sleep disorders 32 % (95% CI 24.0-39.7) Statistically significant associations found between sleep disorders and: bilateral spastic cerebral palsy aOR 11.193 (95% CI 2.1 – 59.0, p=0.004); GMFCS V aOR 13.182 (95%CI 3.7 – 47.0, p = < 0.001); GMFCS IV aOR 12.921 (95%CI 2.0– 82.3, p = 0.007); MACS V aOR 11.162 (95% CI 2.2 – 56.4, p = 0.004); epilepsy aOR 3.865 (95% CI 1.4 – 10.9, p = 0.011)	High-medium - Results stratified by sub-group and potential confounders entered into multivariate logistic regression model. Risk of selection and survival bias as study population drawn from tertiary hospital.
Naik (2018)	Vulnerable Children and Youth Studies	A comparison of the clinical presentation of with HIV infected (HIVE) to uninfected (CP) children with spastic diplegia in South Africa (South Africa)	Case-control study	64 children with spastic diplegia (GMFCS I to IV) aged 4 to 16 years recruited from the physiotherapy, orthopaedic and neurological departments of four institutions in Johannesburg, South Africa from December 2014 to October 2015: 33 HIV-infected children versus 31 HIV-uninfected children	Baseline function assessed using the Gross Motor Function Measure 66 (GMFM-66), Functional Mobility Scale (FMS), Modified Ashworth Scale (MAS) for tone, and a hand-held dynamometer for strength	No significant difference between the HIVE infected and CP groups for GMFCS level (p = 0.2) FMS scores showed no significant differences at 5 m (p = 0.18), 50 m (p = 0.14) and 500 m (p = 0.08) between cases and controls or between ambulant and non-ambulant groups. No significant difference in tone or muscle strength between cases and controls (p>0.05) Non-significant trend for HIVE ambulant participants to be weaker with milder tone from proximal to distal. Non-significant trend for non-ambulant HIV-infected participants to be stronger mild rather than severe tone from proximal to distal compared to CP group	Medium - Cases and controls not matched with differences between groups not accounted for in analyses. Results stratified by sub-group but small number of participants within certain subgroups. Risk of survival bias as only children >4 years included and risk of selection bias as population not drawn from community.

Primary author (Publication date)	Journal	Study title (Country)	Study design	Study population	Component evaluated	Summary measure (with confidence intervals)	Study quality and risk of bias
Namaganda (2020)	PLOS ONE	Excessive premature mortality among children with cerebral palsy in rural Uganda: A longitudinal, population-based study (Uganda)	Prospective cohort study	97 children with CP aged 2–17 years enrolled in initial study in 2015 and followed to 2019. Compared with 41 319 age-matched children from the general population in the Iganga-Mayuge Health and Demographic Surveillance System, Uganda (Same study population as Kakooza-Mwesige et al, 2017)	Mortality overall and by motor impairment (GMFCS), impairments/seizure disorder and nutritional status; cause of death by verbal autopsy	Mortality rate ratio of CP cohort 29.0 (95% CI 17.1–49.1; p<0.0001), with general population as reference. Standardized mortality rate 3455 per 100 000 person years for the CP cohort, with a standardized MRR of 25.3. Survival probability not significantly different between age groups (log-rank, p = 0.28) or sexes (log-rank, p = 0.15) or with associated impairments/seizures (log-rank, p = 0.213) in children with CP MR was higher in children with GFMCS IV-V (8718 deaths per 100 000 person years) than GMFCS I-II (1305 deaths per 100 000 person years; log-rank, p = 0.009) Risk of death almost 7 times higher with GMFCS IV-V versus I-III (HR 6.8; p = 0.007) Survival probability was significantly lower in children with severe malnutrition (log-rank, p = 0.037), and risk of death was almost 4 times higher in children with severe malnutrition (HR, 3.7; p = 0.052) Immediate cause of death in children with CP: anaemia (secondary to malaria)/malnutrition 40%; malaria 33%; pneumonia 17%; meningitis 13%	High-medium - Cox proportional hazards regression models used to evaluate the effect of different variables on mortality outcomes. CP cases compared to age-matched control population from same area. Small number of verbal autopsies for COD analyses – need to be interpreted with caution

Primary author (Publication date)	Journal	Study title (Country)	Study design	Study population	Component evaluated	Summary measure (with confidence intervals)	Study quality and risk of bias
Nwaneri (2013)	World Journal of Pediatrics	Intestinal helminthiasis in children with chronic neurological disorders in Benin City, Nigeria: intensity and behavioral risk factors (Nigeria)	Case-control study	155 children aged 2-17 years with chronic neurological disorders seen at the child neurology clinic at University of Benin Child Teaching Hospital and 155 age and sex matched controls from nursery and primary schools in Benin City, Nigeria from November 2008 to April 2009	Burden of disease from intestinal helminthiasis; associated behaviours	Intestinal helminthiasis confirmed in 32.2% of children with CP Behaviours more commonly found in children with CP infected with helminths versus uninfected children with CP: nail-biting, finger-sucking and encopresis. Nail-biting and encopresis significantly associated with increased prevalence of intestinal helminthiasis ($p \leq 0.03$)	Medium-high - Explicit sampling method, age and sex-matched controls, Multivariate logistic regression analyses used with explicit adjustment for potential confounders. CP not the primary exposure group of interest so results need to be interpreted with caution.
Ogoke (2017)	Pan African Medical Journal	Severity of motor dysfunction in children with cerebral palsy seen in Enugu, Nigeria (Nigeria)	Cross-sectional study	100 children with CP aged 9 months to 8 years attending two paediatric neurology clinics at teaching hospitals in Enugu, Nigeria recruited from April 2010 and October 2010	Motor function as measured by GMFCS; use of assistive devices and interventions	GMFCS: I-II 47%; III 7%; IV-V 46% Interventions: physiotherapy 94%; drugs for spasticity 41%; anti-seizure medication 35%; use of mobility assistive devices 6%; visual aids 5%; orthoses 1%; speech therapy 1% No use of cochlear implant, orthopaedic surgery; occupational therapy; psychotherapy; alternative communication devices; NG tube/gastrostomy feeding, intrathecal baclofen, selective dorsal rhizotomy	Medium - Descriptive statistics only with no adjustment for confounders or test of significance. Risk of selection bias as study population drawn from tertiary hospital
Ogunlesi (2007)	Nigerian Journal of Medicine	The Incidence and Outcome of Bilirubin Encephalopathy in Nigeria: a bi-centre study (Nigeria)	Cross-sectional study	115 babies admitted between age 2-15 days with bilirubin encephalopathy admitted to the Special Care Baby Units of two tertiary hospitals in South-Western Nigeria between January 2001 and December 2005	Risk factor; prevalence of CP in high-risk group	Proportion of children with CP 86.4% among survivors of bilirubin encephalopathy	Low-medium - Difficult to interpret results given only 20% of patient cohort seen at follow up where diagnosis was made, and all data derived from medical records, and only descriptive statistics used

Primary author (Publication date)	Journal	Study title (Country)	Study design	Study population	Component evaluated	Summary measure (with confidence intervals)	Study quality and risk of bias
Okenwa (2019)	African Health Sciences	A review of clinical presentation and physiotherapy management of cerebral palsy patients in Esut teaching hospital, Enugu, Nigeria (Nigeria)	Cross-sectional study	146 children with CP aged 5 months to 9 years recruited from the physiotherapy out-patient clinic of ESUT Teaching Hospital Enugu, Nigeria, between June 2009 and May 2015	CP subtype; aetiology; utilisation of physiotherapy services	CP subtype: spastic 78.1%; mixed 12.3%; dyskinetic 4.1%; hypotonia 3.4%; ataxic 2.1%. Topographic distribution: quadriplegic 20.2%; hemiplegic 28.0%; diplegic 40.4%; unknown 11.4% Aetiology: birth asphyxia 38.4%; febrile convulsions 26.7%; neonatal jaundice 25.3%; meningitis 6.2%; prematurity 3.4% Utilisation of physiotherapy services: 59.0% ≤5 physiotherapy sessions; 13.6% 6 – 10 sessions; 8.2% 11-15 sessions; 9.0% 16-20 sessions; 2.7% 21–25 sessions; 7.5% ≥25 sessions	Medium - Descriptive statistics only with no adjustment for confounders or test of significance. Risk of selection bias as study population drawn from tertiary hospital
Okike (2013)	Journal of Community Health	Cerebral Palsy Among Children Seen in the Neurology Clinic of Federal Medical Centre (FMC), Asaba (Nigeria)	Cross-sectional study	27 children seen in the neurology unit of Federal Medical Centre (FMC), Asaba, Delta State of Nigeria from June 2009 to June 2011	Burden of disease; CP subtype; aetiology; co-morbidities	Proportion of children with CP 45% among children attending hospital neurology clinic CP subtype: hemiplegia 44.4%; quadriplegia 29.6%; diplegia 7.4%; mixed 14.8%; dyskinetic 3.7% Aetiology: birth asphyxia 70.4%; neonatal jaundice 22.2%; CNS infection 3.7%; unknown 3.7% No significant association between CP subtype and mode of delivery (p=0.175) or presence of antenatal care (p=0.14) Co-morbidities: mental retardation 18.5%; seizure 18.5%; blindness 3.7%; mental retardation and seizures 14.8%; speech defect 3.7%; none 40.7% Co-morbidities commoner in children with spastic hemiplegia and quadriplegia (p = 0.024)	Medium - Results stratified by sub-group, but small number of participants within certain subgroups. Only descriptive analyses used but tests of significance applied. Risk of selection bias as study population drawn from tertiary hospital

Primary author (Publication date)	Journal	Study title (Country)	Study design	Study population	Component evaluated	Summary measure (with confidence intervals)	Study quality and risk of bias
Polack (2018)	Developmental Medicine and Child Neurology	Children with cerebral palsy in Ghana: malnutrition, feeding challenges, and caregiver quality of life (Ghana)	Cross-sectional study	76 children with CP aged 18 months –12 years from four regions of Ghana recruited from 1) databases of local community-based rehabilitation programmes (n=46), 2) key informants (n=8), and 3) physiotherapy records from Agogo Presbyterian Hospital (n=22).	Feeding difficulties; malnutrition as measured by weight for age, height for age and BMI	More than half the caregivers reported their child experienced feeding problems at least 'sometimes' in all eight domains. 75% reported their child 'always' needed help with feeding. Two-thirds of caregivers reported 'always' worrying about their child's feeding and 50% reported 'always' worrying their child was not eating enough. Weight for age (all ages): Normal (WAZ≥–2) 37% (95% CI 25.8–49.5); underweight (≥–3 to <2) 23% (95% CI 14.2–35.1); severely underweight (<–3) 40% (CI 28.5–52.6) Height for age (all ages): Normal (HAZ≥–2) 41% (95% CI 29.8–52.9); stunted (≥–3 to <2) 25% (95% CI 16.4–37.0); severely stunted (<–3) 34% (95% CI 23.6–45.8) Weight for height (aged <5years): Normal (WHZ≥–2) 42% (95% CI 28.3–56.4); wasted (≥–3 to <2) 33% (95% CI 21.1–48.2); severely wasted (<–3) 25% (95% CI 14.5–39.6) Mid-upper arm circumference (aged < 5 years): Normal (≥125mm) 80% (95% CI 66.4–88.9); wasted (115–124mm) 19% (95% CI 10.1–31.2); severely wasted (<115mm) 1% (95% CI 0–13) Risk of being underweight was only significantly associated with severe feeding difficulties (i.e. in the highest feeding score tertile): OR 10.7, 95% CI 2.3–49.6, p=0.002 in multivariable regression analyses	High-medium - Multivariate logistic regression analyses used with explicit adjustment for potential confounders. Risk of recall bias as some outcomes measured by parental report; risk of selection bias as sample not necessarily representative of community

Primary author (Publication date)	Journal	Study title (Country)	Study design	Study population	Component evaluated	Summary measure (with confidence intervals)	Study quality and risk of bias
Sogbossi (2019)	Journal of Child Neurology	A Cross-sectional Study of the Clinical Profile of Children With Cerebral Palsy in Benin, a West African Low-Income Country (Benin)	Cross-sectional study	114 children aged 2-17 years recruited from 5 community-based rehabilitation centres and 2 rehabilitation departments of teaching hospitals in the south (Cotonou) and the north (Parakou) of Benin	Aetiology/risk factors; CP subtype; functional outcome as measured by GMFCS and MACS; co-morbidities; attendance at school	Aetiology/risk factors: Malaria in pregnancy 14.9%; infection in pregnancy 8.8%; abnormal bleeding in pregnancy 3.5%; Preterm birth <37 weeks 7%; complications during delivery 52.6%; not crying at birth 53.5%; admitted into NICU 46.5%; postneonatal seizures 4.4%; postneonatal cerebral malaria 6.1%; postneonatal jaundice 1.8%; head trauma 0.9% CP subtype: Bilateral spastic 67.5%, including 47.4% quadriplegia, 20.2% diplegia and 19.3% unilateral; dyskinetic 4.4%; ataxic 1.8%; unclassified 7% 54% GMFCS IV-V and 45% MACS IV-V Only risk factor significantly associated with GMFCS level was complications during delivery (χ2(df) 9.3 (4), p= 0.05) No association between age and GMFCS until children grouped as “independent walkers” (GMFCS I-II) versus “non-walkers” (GMFCS III-V), χ2(df) 12.27 (3), p= 0.01, where proportion of severely affected children decreased with increasing age Co-morbidities: seizures 15.8%; communication disorders 51.7%; cognitive impairment 77.2% Presence of seizures significantly associated with CP subtype, GMFCS level and age (p<0.05 for all) Presence of communication disorder significantly associated with CP subtype and GMFCS level (p<0.05 for both) but not age Cognitive impairment not associated with age, subtype or GMFCS (p>0.05) Attendance at school significantly associated with older age, better functional outcome (GMFCS I-II and MACS I-II), and absence of communication disorder (p<0.05 for all)	Medium – risk of selection bias as sample not necessarily representative of community. Risk of recall bias as large amount of data collected by caregiver interview. Risk of antecedent-consequent bias for aetiology/risk factors. Risk of survival bias as illustrated in difference in results for age and functional outcome when exposure groups reclassified into larger numbers per group

Primary author (Publication date)	**Journal**	**Study title (Country)**	**Study design**	**Study population**	**Component evaluated**	**Summary measure (with confidence intervals)**	**Study quality and risk of bias**
Tataryn (2017)	BMC Pediatrics	Childhood disability in Malawi: a population based assessment using the key informant method (Malawi)	Cross-sectional study	Key informant method identified estimated 15000 children aged <18 years for referral to 33 screening camps in Thyolo and Ntcheu Districts, Malawi from April to November, 2013; 15 000 children identified by KI method, 7220 children attended screening and 2788 children screened positive for a disability/epilepsy	Prevalence of CP; co-morbidities	Proportion of children with CP 26% (number = 282) among 1094 children with moderate/severe physical impairment – overall prevalence of 0.8 per 1000 children assuming 338 235 children living in area covered by the study 15% of children with intellectual disability had CP; just under a third of children with multiple impairments had CP	Medium – CP not main outcome of interest and no explicit case definition. Risk of selection and survival bias using key informant method; sample not necessarily representative of community. Descriptive statistics used with no tests of significance for CP results.

Primary author (Publication date)	Journal	Study title (Country)	Study design	Study population	Component evaluated	Summary measure (with confidence intervals)	Study quality and risk of bias
Tomoum (2010)	Clinical Nutrition	Anthropometry and body composition analysis in children with cerebral palsy (Egypt)	Case-control study	Cases: 40 children with CP aged 2-8 years attending the Paediatric Neurology Outpatient Clinic, Children's hospital, Ain Shams University, Cairo, Egypt from April to October 2007 Controls: 40 age- and sex-matched controls who were apparently healthy siblings of children attending the Outpatients Paediatric Clinic, Faculty of Medicine, Ain Shams University for minor illness	Anthropometry (heigh, weight, BMI, head circumference); body composition; biochemical parameters for malnutrition (full blood count; serum total proteins, serum albumin, serum ferritin and serum leptin)	Weight for age: 14.3% of boys and 15.8% of girls WFA <10th centile; 38.1% of boys and 47.4% of girls WFA <50th centile Height for age: 4.8% of boys and 5.3% of girls HFA <10th centile; 47.7% of boys and 78.9% of girls HFA <50th centile Compared to controls, HFA, WFA, head circumference, triceps skin fold and waist circumference were significantly lower in case ($p<0.04$). BMI, hip circumference, waist-to-hip circumferences ratio, MAC, and subscapular skin fold thickness not statistically different. Compared to controls, statistically significant reduction in total body water (TBW), fat mass, fat free mass, fat percentage and BMR in cases ($p<0.01$) Compared to controls, statistically significant lower values in haemoglobin concentration, serum ferritin, and serum albumin in cases ($p<0.01$) but serum protein and leptin levels were not significantly different. Leptin levels significantly correlated to weight, subscapular skin fold thickness and triceps skin fold thickness in controls ($r =0.382$, 0.399 and 0.302, respectively, $p <0.05$) and cases ($r=0.207$, 0.366 and 0.514, respectively, $p < 0.05$). Leptin levels were correlated to fat percentage only in cases ($r =0.495$, $p <0.01$) Cases with GMFCS III-V had lower subscapular, triceps skin fold thicknesses, fat percentage and serum ferritin levels, versus cases with GMFCS I-II ($p<0.001$, 0.035, 0.028 and 0.037, respectively). Cases with oromotor dysfunction had significantly lower subscapular and triceps skin fold thicknesses versus those cases without oromotor dysfunction ($p< 0.01$)	Medium - Controls matched by age and sex. Tests of significance applied but not explicit adjustment for other confounders in analyses. Risk of selection bias as cases drawn from hospital clinic.

Primary author (Publication date)	Journal	Study title (Country)	Study design	Study population	Component evaluated	Summary measure (with confidence intervals)	Study quality and risk of bias
Unger (2006)	Clinical Rehabilitation	Strength training in adolescent learners with cerebral palsy: a randomized controlled trial (South Africa)	Randomised control trial	31 adolescents independently ambulant aged 13-18 years with spastic CP (15 diplegic and 16 hemiplegic) recruited from a special needs school in Cape Town, South Africa – 20 in intervention group and 10 in control group Intervention: 8-12 exercises, including 5-min warm-up on a stationary bicycle as part of a strength training programme 1-3 times per week for 8 weeks Control: no additional therapy	3-dimensional gait analysis and self-perception (questionnaire)	More upright posture, represented by the sum of all changes that occurred at ankle, knee and hip angles noted between both groups: the mean for the experimental group decreased from pre to post intervention (i.e. improvement in crouch gait), whereas it increased for the control group ($p<0.05$). No significant change for stride length, velocity or cadence. Better self-perceived body image reported by intervention versus control group ($p=0.01$) but no difference for functional competence ($p=0.9$)	Medium – risk of selection bias as sample drawn only from one school. Small numbers in intervention and control arms raise concern about power of study.
Wammanda (2007)	Annals of African Medicine	Pattern of Neurological Disorder Presenting At a Paediatric Neurology Clinic in Nigeria (Nigeria)	Cross-sectional study	114 children aged ≤15 years seen as a new patient at paediatric neurology clinic of Ahmadu Bello University Teaching Hospital, Zaria, Nigeria from January 2002 to December 2003	Burden of disease; CP subtype; co-morbidities	Proportion of children with CP 55.3% among children attending hospital neurology clinic CP subtype: spastic quadriplegia 20.6%; spastic diplegia 20.6%; atonic 19.1%; spastic hemiplegia 12.7%; mixed 4.8%; unknown 22.2% Co-morbidities: speech impairment 22.2%; defaulted follow-up 58.7%	Medium - Only descriptive analyses used for reporting on CP and CP not primary outcome of interest. Risk of selection and survival bias as sample drawn from hospital clinic.