Prevalence of cerebral palsy in Uganda: a population-based study

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Summary

Background Few population-based studies of cerebral palsy have been done in low-income and middle-income countries. We aimed to examine cerebral palsy prevalence and subtypes, functional impairments, and presumed time of injury in children in Uganda.

Methods In this population-based study, we used a nested, three-stage, cross-sectional method (Iganga-Mayuge Health and Demographic Surveillance System [HDSS]) to screen for cerebral palsy in children aged 2–17 years in a rural eastern Uganda district. A specialist team confirmed the diagnosis and determined the subtype, motor function (according to the Gross Motor Function Classification System [GMFCS]), and possible time of brain injury for each child. Triangulation and interviews with key village informants were used to identify additional cases of suspected cerebral palsy. We estimated crude and adjusted cerebral palsy prevalence. We did χ² analyses to examine differences between the group screened at stage 1 and the entire population and regression analyses to investigate associations between the number of cases and age, GMFCS level, subtype, and time of injury.

Findings We used data from the March 1, 2015, to June 30, 2015, surveillance round of the Iganga-Mayuge HDSS. 31756 children were screened for cerebral palsy, which was confirmed in 86 (19%) of 442 children who screened positive in the first screening stage. The crude cerebral palsy prevalence was 2·7 (95% CI 2·2–3·3) per 1000 children, and prevalence increased to 2·9 (2·4–3·6) per 1000 children after adjustment for attrition. The prevalence was lower in older (8–17 years) than in younger (<8 years) children. Triangulation added 11 children to the cohort. Spastic unilateral cerebral palsy was the most common subtype (45 [46%] of 97 children) followed by bilateral cerebral palsy (39 [40%] of 97 children). 14 (27%) of 51 children aged 2–7 years had severe cerebral palsy (GMFCS levels 4–5) compared with only five (12%) of 42 children aged 8–17 years. Few children (two [2%] of 97) diagnosed with cerebral palsy were born preterm. Post-neonatal events were the probable cause of cerebral palsy in 24 (25%) of 97 children.

Interpretation Cerebral palsy prevalence was higher in rural Uganda than in high-income countries (HICs), where prevalence is about 1·8–2·3 cases per 1000 children. Children younger than 8 years were more likely to have severe cerebral palsy than older children. Fewer older children than younger children with cerebral palsy suggested a high mortality in severely affected children. The small number of preterm-born children probably resulted from low preterm survival. About five times more children with post-neonatal cerebral palsy in Uganda than in HICs suggested that cerebral malaria and seizures were prevalent risk factors in this population.

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Introduction

Cerebral palsy is a common motor disability in childhood that is often accompanied by sensory and cognitive dysfunctions and other medical conditions. Findings from national cerebral palsy registers and population-based studies in Europe, Australia, and the USA indicate that the cerebral palsy prevalence is about 1·8–2·3 cases per 1000 children.[1–3] A systematic review[4] of 49 studies published between 1996 and 2013 included only one study[5] from a low-income or middle-income country (LMIC), showing the scarcity of epidemiological information from LMICs.

Cerebral palsy has been suggested to be more prevalent in LMICs than in high-income countries (HICs),[6–10] although a study[11] in China reported a slightly lower cerebral palsy prevalence than in HICs. This increased prevalence could be due to risk factors affecting fetal and postnatal brain development (eg, preterm birth, obstetric complications, birth asphyxia, neonatal jaundice, cerebral infections, and convulsions),[12] although these factors are life-threatening in LMICs[13] and thus might actually decrease the incidence of cerebral palsy. In our 2015 study[14] of a clinical cohort of Ugandan children with cerebral palsy, we showed that few children were older than 5 years and few children had been born preterm, which might reflect high mortality in preterm infants and reduced survival in children with cerebral palsy. Preterm-born children comprise about 40% of the children with cerebral palsy in HICs.[1–3] These conflicting findings suggest differences in causes and mortality between Uganda and HICs.

Research in context

Evidence before this study
Knowledge of the prevalence, causes, and mortality of cerebral palsy in low-income settings is scarce. We searched PubMed from inception to Nov 30, 2016, using the search terms "cerebral palsy" AND "epidemiology" OR "prevalence" OR "frequency" OR "surveillance" OR "screening" OR "low income" OR "resource poor". We only included English-language studies. We included studies from the reference lists of systematic reviews identified in the database search. We found few population-based studies of the epidemiology of cerebral palsy in low-income and middle-income countries (LMICs), whereas registries and population-based studies from high-income countries (HIC) were numerous. The studies from LMICs were heterogeneous in the populations assessed and the methods and classification systems used, making comparisons difficult.

Added value of this study
To our knowledge, this population-based study of cerebral palsy is the largest to be done in sub-Saharan Africa. We found that cerebral palsy was more common in Uganda than in HICs. We observed a high mortality during the first 6–8 years of life, particularly among the most severely affected (Gross Motor

Function Classification System level 4–5). Compared with HICs, fewer children with cerebral palsy were born preterm (probably because of the high mortality of preterm babies in LMICs) and a higher proportion of children developed cerebral palsy after the first postnatal month (probably because of cerebral malaria, which is endemic in the area).

Implications of all the available evidence
This study will contribute to a more accurate estimate of the number of children in the world living with cerebral palsy. This information will be important to increase public awareness and to develop national health programmes and international initiatives for children with neurodevelopmental disorders. The suggestion of a high mortality among younger children with severe forms of cerebral palsy requires confirmation in longitudinal studies and, if confirmed, calls for improvements in general care in promoting better nutrition and preventing infections. The high proportion of children with post-neonatal cerebral palsy suggests that prevention of the causative agents (eg, malaria with febrile seizures) might be effective. The low number of preterm-born children with cerebral palsy suggests the importance of protecting the brain in new programmes to increase the survival of preterm-born infants.

A workshop on cerebral palsy in 2015,[15] which had representatives from 22 African countries, emphasised the dearth of population-based studies from LMICs, with most existing reports being from hospital clinics. We collected basic epidemiological information about cerebral palsy in rural Uganda using a Health and Demographic Surveillance System (HDSS), which does annual surveys of the population in a defined geographical area. Using a three-stage, cross-sectional screening method, we aimed to determine the prevalence of cerebral palsy in children in Uganda and assess subtypes, extent of gross motor impairment, and presumed time of brain injury.

Methods

Study design
We did a population-based, cross-sectional study of data from the Iganga-Mayuge HDSS site, which is located in eastern Uganda and comprises 65 villages. The population predominantly consists of rural subsistence farmers, but 20% of the population resides in the semi-urban locality of Iganga. Active surveillance of the region has been done annually since 2005 by trained fieldworkers who collect vital demographic data (eg, pregnancies, births, deaths, and migration). The data used for this study were from the March 1, 2015, to June 30, 2015, surveillance round, which included 15 964 households and 85 562 individuals, 41 319 of whom were aged 2–17 years.

The study was approved by the Higher Degrees Research and Ethics Committee of the School of Public

Health, College of Health Sciences, Makerere University and the Uganda National Council for Science and Technology (reference HS 1734). All caregivers gave written informed consent and assent was obtained from participants older than 8 years.

Participants and procedures
We used a three-stage screening process[16] to identify children aged 2–17 years with cerebral palsy. In the first stage, Ugandan fieldworkers fluent in the local language, Lusoga, and English asked heads of households two screening questions (appendix) during a routine door-to-door survey organised by the HDSS. The questions focused on movement and posture and were derived from the Ten Question screen for childhood disability.[17] The questions had been adapted to the cultural context and terminology during a qualitative preparatory study (unpublished) involving caregivers, health workers, community leaders, and traditional healers.

During the second stage of screening, a mobile team of specially trained fieldworkers visited all households with a positive response to either question. The fieldworkers followed a protocol that included questions for the household head and assessments of mobility and fine motor control derived from Surveillance of Cerebral Palsy in Europe (SCPE) guidelines[18,19] and that had been adapted to the cultural context (appendix). All children with suspected motor impairment or other clinical signs of cerebral palsy were referred to the third stage of screening.

See **Online** for appendix

During the third screening stage, children were assessed at the Iganga Referral Hospital, Uganda, by a specialist cerebral palsy team (clinician, physiotherapist or occupational therapist with experience in cerebral palsy, and study nurse) trained to do the examinations and interviews. The international definition and classification system for cerebral palsy was used to diagnose children,[20] and the diagnosis was confirmed with the SCPE flow scheme.[19] Children diagnosed with cerebral palsy were assigned to clinical subtypes: spastic bilateral, spastic unilateral, dyskinetic, ataxic, or not classified. The Ugandan and Swedish team members discussed and confirmed all cases via the internet using video clips of each child. Children with cerebral palsy underwent standard neurological and medical examinations, and the caregiver was interviewed to obtain information about the pregnancy, birth history, medical problems, development, and sociodemographic factors. Information about gestational age at birth and occurrence of harmful events during or after birth was collected. The event that possibly resulted in cerebral palsy was categorised as preterm birth (<37 gestational weeks) or a post-neonatal incident (event occurring >1 month after birth); the remaining children were considered neonatal full-term cases.[21] Children with symptoms of cerebral palsy were excluded if the event occurred more than 24 months after birth (those children were diagnosed with an acquired brain injury).[21] Data from children with positive responses in the first stage but who were negative in the subsequent stages were used to analyse the conditions causing false-positive responses.

About 2 weeks after diagnosis, a team of expert physiotherapists and occupational therapists confirmed the diagnosis and assessed the extent of motor impairment using the Gross Motor Function Classification System (GMFCS).[22] To address the entire spectrum of presenting symptoms and to investigate the causes, the children underwent standard clinical examination of medical comorbidities, gross motor function (with the Gross Motor Function Measure), fine motor function (with the Manual Ability Classification System), communicative ability (with the Communication Function Classification System), and disability (with the Ugandan version of the Pediatric Evaluation Disability Inventory), and blood samples were collected for biochemical, microbiological, and genetic analyses. Extended interviews were done with caregivers to obtain information about pregnancy, birth, postnatal period, subsequent psychomotor development, illnesses, nutrition, and participation in societal activities (eg, schooling). Analyses of these data will be presented in subsequent reports.

Key informants (ie, members of village health teams or community workers with good knowledge of the village population) were asked by fieldworkers to identify children with similar conditions to neighbourhood children who had previously been diagnosed with cerebral palsy. The fieldworkers verified that the child was part of the HDSS, then visited the household to interview the household head and examine the child (stage 2). Children with suspected cerebral palsy were referred to the specialist cerebral palsy team at the Iganga Referral Hospital (stage 3).

Statistical analyses

We double-entered and verified all data using Visual FoxPro version 9.0. Stata software (version 13) and R software (glm function and MASS package) were used for all statistical analyses. We estimated cerebral palsy prevalence with 95% CIs by dividing the number of cases identified from screening by the total number of children screened at stage one. We used multiple imputation to reduce bias from between-stage attrition.[23] The specificity of the three-stage screen was calculated as the number of true negatives divided by the sum of the number of true negatives and the number of false positives. The χ^2 test was used to investigate differences between the group
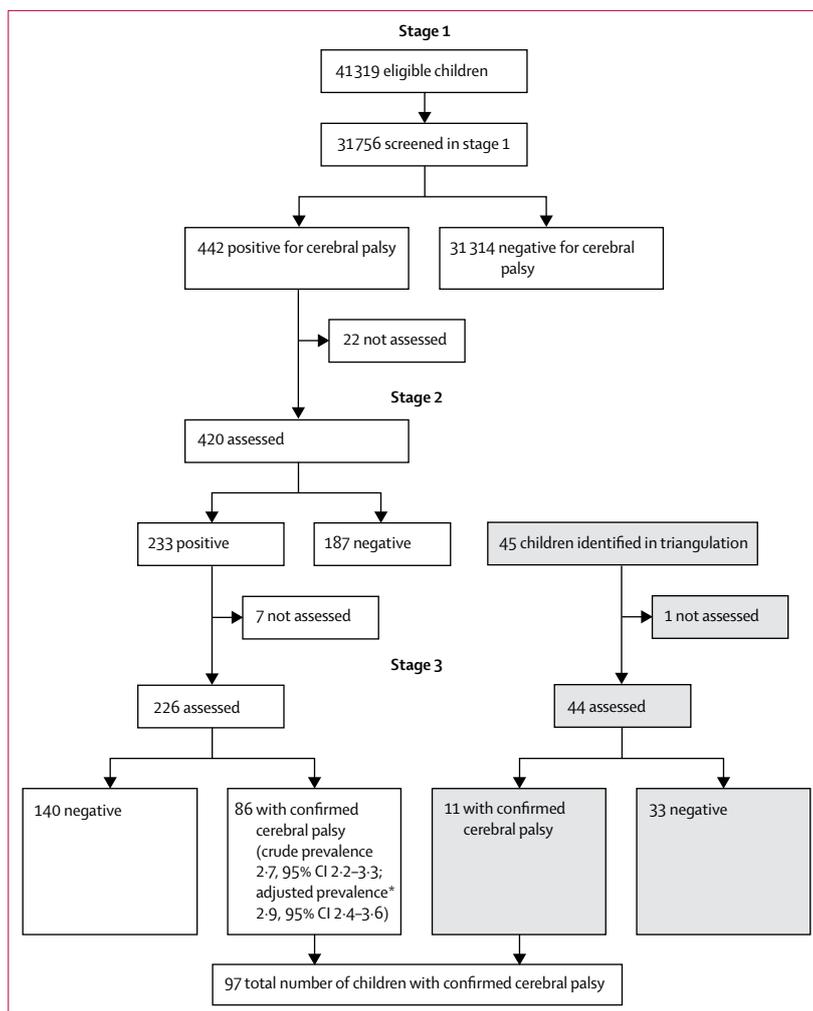

Figure 1: Flow diagram
*Prevalence was adjusted for attrition.

	Stage 2 (n=187)	Stage 3 (n=140)	Triangulation (n=33)	All (n=360)
Motor or musculoskeletal	25 (13%)	63 (45%)	16 (48%)	104 (29%)
Intellectual disability	42 (22%)	49 (35%)	3 (9%)	94 (26%)
Epilepsy	35 (19%)	38 (27%)	4 (12%)	77 (21%)
Speech and language impairment	36 (19%)	20 (14%)	1 (3%)	57 (16%)
Hearing impairment	35 (19%)	9 (6%)	0 (0%)	44 (12%)
Other medical conditions	33 (18%)	9 (6%)	0 (0%)	42 (12%)
Behavioural disorder	3 (2%)	14 (10%)	1 (3%)	18 (5%)
Visual impairment	8 (4%)	5 (4%)	2 (6%)	15 (4%)
Syndromes*	0 (0%)	9 (6%)	3 (9%)	12 (3%)
Post-injection or sciatic nerve injury	2 (1%)	6 (4%)	2 (6%)	10 (3%)
Myelomeningocele or hydrocephalus	1 (1%)	4 (3%)	1 (3%)	6 (2%)
Microcephalus	0 (0%)	4 (3%)	1 (3%)	5 (1%)
Acquired brain injury	0 (0%)	2 (1%)	2 (6%)	4 (1%)
Unclear or no impairment detected	7 (4%)	4 (3%)	2 (6%)	13 (4%)
Combination of two or more categories	33 (18%)	41 (29%)	3 (9%)	77 (21%)
Combination of three or more categories	4 (2%)	23 (16%)	1 (3%)	28 (8%)

Data are n (%). False-positive children were not diagnosed with cerebral palsy but had a positive response to either of the two screening questions. The mobile and specialist cerebral palsy teams were instructed to categorise why children had screened positive at the previous stage but negative at the present stage. Several children had problems in more than one domain. *Included Down's syndrome (n=7), Turner's syndrome (n=1), congenital rubella syndrome (n=1), and unclear genetic syndromes (n=3).

Table 1: Functional impairments and other clinical signs in 360 children identified as false positive at different stages of screening
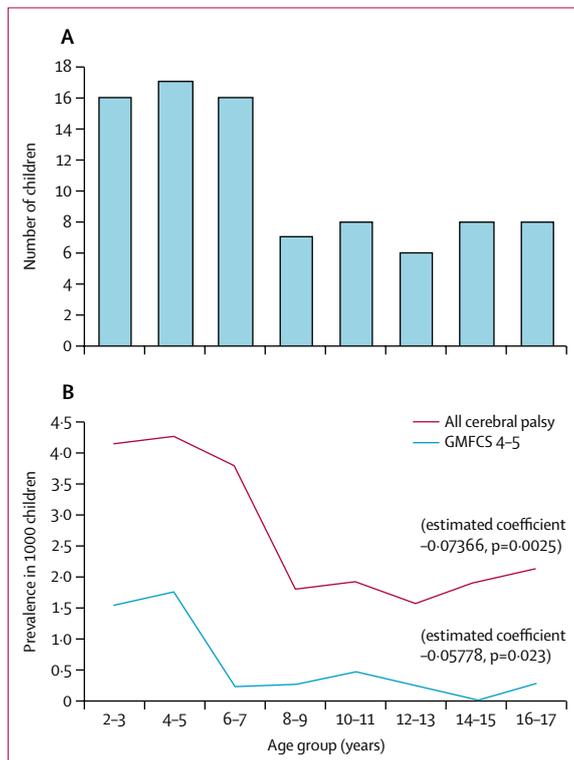

Figure 2: **Number of children diagnosed with cerebral palsy in the three-stage screen (A) and estimated crude prevalence (B), by age group**
GMFCS=Gross Motor Function Classification System.

screened at stage 1 and the entire population of the HDSS. We used generalised linear models to study the association between the number of observed cases and age, GMFCS level, type of cerebral palsy, and time of injury. The effect of age on number of children with cerebral palsy was analysed with Poisson regression. All other analyses were done with negative binomial regression with the log link function because of overdispersion in the data. Overdispersion was tested with a likelihood ratio test for overdispersion in count data in the R package pscl. A p value of less than $0\cdot05$ was considered to indicate a significant result.

Role of the funding source
The funders had no role in the study design, data collection, data analysis, data interpretation, or manuscript preparation. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results
In the first screening stage, 31756 of 41319 eligible children were screened by fieldworkers (figure 1). No age or sex differences were seen between the screened sample and the entire population of the HDSS. Positive responses to one or both questions were given for 442 children. During the second stage, the mobile team assessed 420 of 442 children (21 children were not available during any of three visits and one was deceased), 233 of whom were positive for cerebral palsy. Only 226 children were examined during the third screening stage because seven caregivers declined to visit the hospital. A cerebral palsy diagnosis was confirmed in 86 children, giving an estimated crude prevalence of $2\cdot7$ (95% CI $2\cdot2–3\cdot3$) per 1000 children. After adjustment for attrition, the prevalence increased to $2\cdot9$ ($2\cdot4–3\cdot6$) per 1000 children.

The triangulation process identified 45 children with suspected cerebral palsy, 44 of whom were examined by the specialist cerebral palsy team (one declined). 11 of the 44 children were diagnosed with cerebral palsy. Of these children, ten were missed by the initial screening because heads of households gave negative responses to both screening questions and one was missed because fieldworkers had not correctly completed the protocol. In total, cerebral palsy was confirmed in 97 children, 59 of whom were boys.

86 of the 442 children identified as potentially positive in the first stage were confirmed to have cerebral palsy, giving a specificity of 99%. Almost all children without cerebral palsy who had a positive response during screening (ie, false-positive children) had other forms of developmental disability or medical conditions (table 1).

Fewer older children (8–17 years) than younger children (<8 years) in the three-stage-screening population had cerebral palsy (figure 2A) and, thus, older children had a lower crude prevalence than younger children (figure 2B and table 2). The effect of age on number of cases was

	2–17 years	2–3 years	4–5 years	6–7 years	8–9 years	10–11 years	12–13 years	14–15 years	16–17 years
Three-stage screen									
Children with cerebral palsy	86/31 756	16/3849	17/3975	16/4192	7/3882	8/4123	6/3833	8/4156	8/3746
Crude prevalence	2·7	4·2	4·3	3·8	1·8	1·9	1·6	1·9	2·1
Three-stage screen plus triangulation									
Subtype of cerebral palsy									
Bilateral	39/97 (40%)	8/17 (47%)	9/18 (50%)	4/18 (22%)	4/9 (44%)	4/9 (44%)	4/9 (44%)	1/8 (13%)	5/9 (56%)
Unilateral	45/97 (46%)	6/17 (35%)	6/18 (33%)	11/18 (61%)	4/9 (44%)	5/9 (56%)	4/9 (44%)	6/8 (75%)	3/9 (33%)
Dyskinetic	9/97 (9%)	2/17 (12%)	3/18 (17%)	2/18 (11%)	0/9 (0%)	0/9 (0%)	1/9 (11%)	1/8 (13%)	0/9 (0%)
Ataxic	2/97 (2%)	1/17 (6%)	0/18 (0%)	0/18 (0%)	1/9 (11%)	0/9 (0%)	0/9 (0%)	0/8 (0%)	0/9 (0%)
Not classified	2/97 (2%)	0/17 (0%)	0/18 (0%)	1/18 (6%)	0/9 (0%)	0/9 (0%)	0/9 (0%)	0/8 (0%)	1/9 (11%)
GMFCS level									
1–2	56/93 (60%)	8/16 (50%)	5/17 (29%)	13/18 (72%)	6/8 (75%)	5/9 (56%)	7/9 (78%)	6/7 (86%)	6/9 (67%)
3	18/93 (19%)	2/16 (13%)	5/17 (29%)	4/18 (22%)	1/8 (13%)	2/9 (22%)	1/9 (11%)	1/7 (14%)	2/9 (22%)
4–5	19/93 (20%)	6/16 (38%)	7/17 (41%)	1/18 (6%)	1/8 (13%)	2/9 (22%)	1/9 (11%)	0/7 (0%)	1/9 (11%)
Not assessed*	4	1	1	0	1	0	0	1	0

Data are n/N, n/N (%), or prevalence per 1000 children. GMFCS=Gross Motor Function Classification System. *Four children were not functionally assessed (three were deceased and one migrated).

Table 2: Effect of age on cerebral palsy subtype and GMFCS level

significant (estimated coefficient –0·07366, p=0·0025); the expected number of cases decreased with age with a multiplicative factor of 0·93. We used a negative binomial regression model to examine whether the decrease in number of cases with age depended on GMFCS level (figure 2B). The interaction was significant (estimated coefficient –0·05778, p=0·023); the effect of age on number of cases was associated with GMFCS level. The effect of age was only significant for severe cerebral palsy (GMFCS levels 4–5; –0·2136, p=0·008), thus the lower number of older children with cerebral palsy was driven by a reduction in the number of children with higher GMFCS levels.

The dyskinetic subtype was more common in children aged 2–7 years than in children aged 8–17 years (seven [13%] of 53 children *vs* two [5%] of 44 children). Conversely, the proportion of children with unilateral cerebral palsy was lower in the younger subgroup than in the older subgroup (23 [43%] of 53 children *vs* 22 [50%] of 44 children; table 3). The sample identified by triangulation differed from the screening sample in severity of motor impairment (no child identified by triangulation had GMFCS levels 4–5; figure 3) and subtype (a higher proportion of children identified by triangulation had unilateral cerebral palsy; table 3). However, the absence of statistical interactions was probably due to the small sample size.

Two (2%) of 97 children were born preterm, and cerebral palsy in 24 (25%) of 97 children was thought to be due to a post-neonatal event (table 3). Typically, children with post-neonatal cerebral palsy had a normal perinatal history, but suddenly became ill with fever and convulsions followed by chronic motor impairments. Time of brain injury was significant (estimated coefficient

	2–17 years	2–7 years	8–17 years	Screening	Triangulation	Post-neonatal cerebral palsy
Subtype of cerebral palsy						
Unilateral	45/97 (46%)	23/53 (43%)	22/44 (50%)	37/86 (43%)	8/11 (73%)	14/24 (59%)
Bilateral	39/97 (40%)	21/53 (40%)	18/44 (41%)	37/86 (43%)	2/11 (18%)	7/24 (29%)
Dyskinetic	9/97 (9%)	7/53 (13%)	2/44 (5%)	9/86 (11%)	0/11 (0%)	2/24 (8%)
Ataxic	2/97 (2%)	1/53 (2%)	1/44 (2%)	1/86 (1%)	1/11 (9%)	0/24 (0%)
Not-classified	2/97 (2%)	1/53 (2%)	1/44 (2%)	2/86 (2%)	0/11 (0%)	1/24 (4%)
GMFCS level*						
1	49/93 (53%)	23/51 (45%)	26/42 (62%)	42/82 (51%)	7/11 (64%)	17/24 (71%)
2	7/93 (8%)	3/51 (6%)	4/42 (9%)	4/82 (5%)	3/11 (27%)	1/24 (4%)
3	18/93 (19%)	11/51 (21%)	7/42 (17%)	17/82 (21%)	1/11 (9%)	3/24 (13%)
4	6/93 (6%)	4/51 (8%)	2/42 (5%)	6/82 (7%)	0/11 (0%)	2/24 (8%)
5	13/93 (14%)	10/51 (20%)	3/42 (7%)	13/82 (16%)	0/11 (0%)	1/24 (4%)

Data are n/N (%). GMFCS=Gross Motor Function Classification System. *Four children identified in the three-stage screening process were not functionally assessed (three were deceased and one migrated).

Table 3: Proportion of children with cerebral palsy subtypes and GMFCS levels by age group, screening group, and time of brain injury

1·6726, p=0·0085) for children with a high GMFCS level (ie, few children with a high GMFCS level were post-neonatal cases; figure 3), even after accounting for the effect of age. Of the 360 false-positive children, four had a cerebral palsy phenotype but were diagnosed with an acquired brain injury because the event occurred after the second birthday.

Discussion

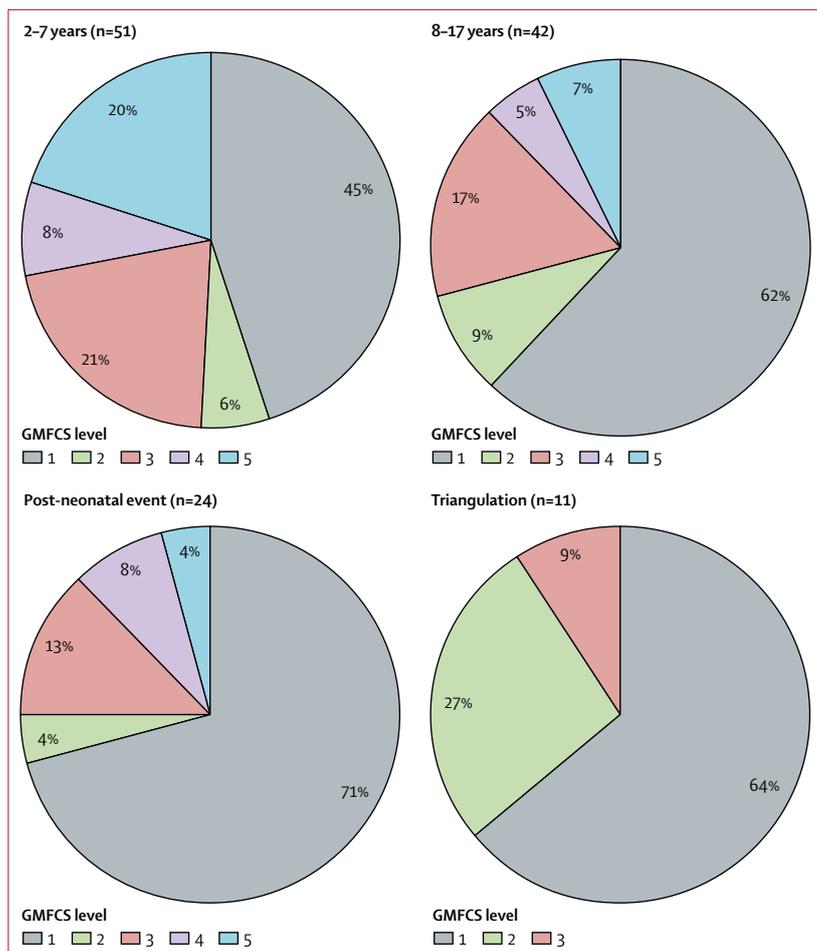This study is the first to provide population-based information about children with cerebral palsy in

2–7 years (n=51)

8–17 years (n=42)

Post-neonatal event (n=24)

Triangulation (n=11)

Figure 3: Proportion of children with GMFCS levels 1–5 by cerebral palsy subcohort
GMFCS=Gross Motor Function Classification System.

with cerebral palsy or poor awareness of the interviewed heads of households. Children who were identified as false negative in triangulation had mild forms of unilateral cerebral palsy, which suggested a contribution of un-awareness of the household heads. With inclusion of the 11 children identified by triangulation, the crude prevalence would increase to 3·1 per 1000 children. Even the unadjusted prevalence of the screened cases (n=86) was higher than the prevalence in HICs, particularly for young children (<8 years), supporting our hypothesis that the prevalence of cerebral palsy in young children is higher in sub-Saharan Africa than in HICs.

The significant decrease in the number of children with cerebral palsy with increasing age, the corresponding reduction in crude prevalence, and the fewer children with severe cerebral palsy (GMFCS levels 4–5) at older than younger ages suggested a high mortality among children with cerebral palsy, particularly among those most severely affected. Our previous study[14] of a clinical cohort of children with cerebral palsy from Mulago Hospital in Uganda showed that help was sought for only a few children older than 5 years and that more than 50% of the children were malnourished.[24] Malnutrition makes children with severe types of cerebral palsy susceptible to infection. Three children in this cohort died before functional assessment, and the audit results suggested infection as the cause of deaths. Studies[25–27] of high-income populations have shown a reduced life expectancy in children with cerebral palsy, particularly in children with severe motor and eating impairments, and a decreased prevalence with age has been observed in China and India.[9,11] A longitudinal follow-up study should be done to obtain an accurate estimate for mortality. Nevertheless, the decline in prevalence is an important finding and suggests a high risk of preventable death in this population.

The high prevalence of cerebral palsy, particularly in children aged 2–7 years, indicates a higher prevalence of risk factors of cerebral palsy in Uganda than in HICs. In this study, the injury that possibly caused cerebral palsy occurred more than 28 days after birth in 25% of children, compared with only 5–6% of children in HICs.[1,21] Four children had symptoms of cerebral palsy but were excluded and diagnosed with an acquired brain injury because the incident occurred more than 2 years after birth.[21] Frequently, caregivers reported normal perinatal development until a sudden episode of fever and seizures, followed by impaired motor function. Malaria is endemic in Uganda, and epileptic seizure is a complication of cerebral malaria.[28] However, we cannot rule out other brain infections, such as bacterial meningitis. The combination of a cerebral infection, high fever, and untreated seizures probably increased the risk of unrepairable brain injuries, leading to cerebral palsy (or acquired brain injury). Most children had unilateral cerebral palsy with GFMCS levels 1–2, suggesting a focal injury with mild motor impairments.

sub-Saharan Africa. We used a three-stage screening method[16] and triangulation to identify children with cerebral palsy, and estimated the crude cerebral palsy prevalence for children aged 2–17 years to be 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. This prevalence was higher than the prevalence previously reported for HICs based on livebirths (1·8–2·3[1–4]) and was consistent with some previous estimates from several populations in LMICs,[7–10] although not with estimates from a study in China.[11] The difference in prevalence between Uganda and HICs might be even larger because we could not adjust for false-negative responses because no estimate of sensitivity is available for the three-stage screening process for cerebral palsy. In the triangulation process, we identified 11 children with cerebral palsy who had been missed at the first stage, which would suggest a high sensitivity. However, there might still be children with cerebral palsy symptoms who were not identified in the screening or the triangulation. False-negative responses might have been related to the stigma associated

Only 2% of the children in our cohort were born preterm, whereas preterm-born children make up more than 40% of all cases in HICs.[1–3] Preterm birth is the leading cause of child death in LMICs because of insufficient maternal and neonatal care.[29,30] International initiatives are addressing stillbirth and preterm death to increase neonate survival,[31] which will probably increase the number of preterm children with cerebral palsy; this pattern occurred in North India during 2000–09.[32] The prevalence of preterm-born children with cerebral palsy in Europe and Australia is decreasing,[1,2] suggesting that high-quality perinatal care can reduce the number of children with cerebral palsy. Ongoing initiatives to reduce stillbirth and increase preterm survival in Uganda[33] should also focus on prevention of brain injuries that cause cerebral palsy and other neurodevelopmental disabilities, such as hypoxic-ischaemic encephalopathy, which is a major cause of severe types of cerebral palsy. Compared with HICs, the proportion of preterm-born children was low (2% vs 40%) and the proportion of post-neonatal cases was high (25% vs 5–6%) in our cohort. This difference indicates different risk factors, necessitating comprehensive investigation to develop effective prevention strategies.

The screening questions had a high specificity (99%). Among the 360 children who were false positive, most had some form of functional impairment or clinical sign; only 13 had no visible clinical signs. Because development of screening questions that distinguish various neuro-developmental disabilities is challenging, the specificity was optimal for this type of study design. The most frequent clinical signs were other motor and musculo-skeletal problems, including ten children with foot drop after gluteal intramuscular injections of quinine.[34] Intellectual disability, speech and language problems, hearing and vision impairments, behavioural problems, seizures, and other medical problems were common in the study population.

We used a population-based, three-stage screening method to compensate for the absence of registers in Uganda, which would have been required to obtain accurate and precise data on the epidemiology of cerebral palsy. A strength of this method, which requires the infrastructure of an HDSS through which the population is annually monitored, is the access to information about all households and children living in the area, making it possible to reach all children by interviewing the household head. This method permitted us to do the largest and most comprehensive population-based study of cerebral palsy in sub-Saharan Africa, including more than 30 000 children. We used two screening questions that had been validated for use in low-resource settings[17] and adjusted to suit the local language and culture in a previous qualitative study (unpublished). We used trained, community-based interviewers for stage one of the survey. Their work was closely supervised and the data instantly entered. Experienced clinicians (child neurologists, physiotherapists, and occupational therapists) used the contemporary international system, which is also used by the leading cerebral palsy registers in Europe, Australia, and the USA, to diagnose cerebral palsy, define subtypes, and assess severity of motor impairments. This approach enabled comparison with other studies, dissimilar to most other studies in LMICs, which have used other classification systems.

Limitations of our study included the uncertainty introduced by attrition in the three-stage process and the sensitivity of the screening questions. We used multiple imputations to adjust for attrition, which was reasonably low in our study population.[23] Adjusting for sensitivity was more challenging than adjusting for attrition because we had no measure of sensitivity for the three-stage screening process. However, only 11 children with cerebral palsy who had not been identified by screening were identified in the triangulation, which suggested that our method had a high sensitivity. The sensitivity estimate derived from a similar three-stage screening method for detection of convulsive epilepsy was low,[16] suggesting that the true prevalence of cerebral palsy is higher than reported.

Another limitation was the difficulty in diagnosis of cerebral palsy in young children. Most cerebral palsy registers include children aged 5 years or older because the cerebral palsy subtype and motor impairment level might change over time. Clinicians aim for an early diagnosis (<1 year) to initiate early interventions.[35] We chose 2 years as the study entry age; therefore, the data for the cohort of children aged 2–4 years might be less precise than that of the older cohorts. Additionally, mild cases of cerebral palsy might be missing from the study population.

We found that the timing of the brain injury causing cerebral palsy was different between our population and HICs. However, this analysis was based on information from caregivers, which could have been affected by recall bias, poor knowledge of developmental milestones in young children, or problems understanding and responding accurately to the questions.

The well established HDSS provided the opportunity to do the largest population-based survey of cerebral palsy in sub-Saharan Africa. The results showed that cerebral palsy prevalence was higher in Uganda than in HICs, especially in children younger than 8 years. A decline in prevalence with age seemed to be caused by high mortality among children with severe forms of cerebral palsy. This mortality resulted in differences between younger (<8 years) and older (8–17 years) children, with the older children having milder forms of motor impairments. The study also showed that the causes of cerebral palsy in Uganda differed greatly from the causes in HICs. Few children were born preterm, and a large proportion experienced a post-neonatal event, leading to cerebral palsy. These findings can be used to assess the burden of cerebral palsy in Uganda and inform national health policies.

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