ABSTRACT

Objectives. The aim of this paper was to critically review the recent literature on psychosocial and behavioural outcome following childhood stroke, to assess whether quality of life is affected and to investigate the factors related to psychosocial outcome.

Methods. Literature searches were conducted and identified 36 relevant papers from the period 1908- 2016.

Results. The systematic review found that many children experience difficulties in a wide range of psychosocial domains. Quality of life can also be significantly reduced. Inconsistent findings regarding the correlates of outcome are likely due to methodological limitations. These issues include small and heterogeneous samples, lack of control groups and measurement difficulties.

Conclusions. This systematic review strongly indicates that childhood stroke can affect a myriad of psychosocial domains and a child's quality of life. Methodological issues, particularly around heterogeneous samples and measures, limit the conclusions that can be drawn regarding the predictors of outcome.

INTRODUCTION

Stroke is an acute, cerebrovascular injury caused by an interruption of blood supply to the brain [1]. Stroke in childhood, defined as stroke between one month to eighteen years of age, has become increasingly recognised as a cause of childhood disability [2, 3]. Reports of incidence rates range from 0.6 to 13 cases per 100.000 [4], with 1.6 to two cases per 100,000 children per year commonly reported [5, 6]. Arterial Ischaemic Stroke (AIS) accounts for approximately half of all strokes in children in contrast to 80-85% of all strokes in adults [7]. AIS occurs due to obstruction of an artery as a result of a clot, causing an interruption to blood flow and leading to infarction. Haemorhagic stroke is the result of bleeding from an arterial rupture. Haemorhagic stroke more commonly leads to diffuse brain injury. Variations in the aetiology of stroke in childhood, in addition to variation in lesion location and volume can lead to a diverse range of physical and cognitive deficits, and secondary functional impairments [8]. Prognostic signs of a poor outcome have been identified as seizures at the onset of stroke and stroke in infancy [9]. These researchers showed that all children who had a pattern of infarction involving the cerebral cortex, subcortical white matter, basal ganglia and posterior limb of the internal capsule had a poor outcome but highlighted that poor outcome was also seen with other patterns of infarction [9]. Common risk factors in childhood stroke include congenital or acquired heart disease, accounting for up to a third of all ischaemic strokes [10], haematological disorders and coagulopathies (e.g. sickle cell anaemia), infection, vasculopathies (e.g. moyamoya syndrome), arterial dissection and rare genetic disorders [2, 11]. In terms of outcome, one of the key differences between stroke in childhood and adulthood is that childhood stroke occurs in a developing brain, potentially changing the trajectory of achieving independence [12].

For the majority of children who experience stroke, lifelong residual neurological, motor and functional impairments persist [12, 13, 3]. Evidence from the wider paediatric literature suggests that children and young people living with disabilities, neurological or chronic health conditions may be at a significantly greater risk for behavioural and emotional adjustment problems and lower quality of life compared to those without disabilities [14, 15]. There has been some emerging evidence into the broader impact of experiencing a stroke on a child's well-being, cognition, communication, behaviour and emotions, indicating that the long-term difficulties are far more wide-ranging than physical and neurological alone [12, 13, 16, 3, 17]. Although potentially the most concerning for children and families, there is a recognised dearth in research around the functional, behavioural and psychosocial outcome following stroke in childhood [12, 18, 3, 8]. Looking specifically at social interaction, participation, cognition and psychological function, Gomes et al [18] concluded that childhood stroke is associated with increased risk of psychosocial impairment.

The multidimensional construct of health-related quality of life (HR-QOL) is recognised as an important outcome indicator of well-being following chronic illness or disability. Health-related QoL (HRQoL) has been described as *"A psychological construct which describes the physical, mental, social, psychological and functional aspects of well-being and function from a patient perspective"* [19]. However, studies exploring the impact on a child's QOL following a stroke have been limited and there has been a call for further research in this area [12, 20, 3].

The aim of this systematic review was to critically examine the recent existing literature on the impact of childhood stroke on functional, educational, behavioural

and psychosocial outcome and quality of life.

The research questions were:

1) Is there evidence of functional disability, behavioural, educational and psychosocial difficulties following childhood stroke?

2) Is there evidence to suggest that quality of life is affected following childhood stroke?

3) What factors can be identified that may be related to psychosocial outcome and QOL following stroke during childhood?

METHOD

Search Methods for Identification of Studies

Information Sources

Relevant articles were sought for inclusion using an a-priori defined search string using EmBase (1980 – October 2016), MEDLINE (1946 – October 2016) and PsychInfo (1908- October 2016).

Search Strategies

A systematic search strategy was designed to maximise sensitivity given the broad-range of outcomes sought for inclusion in the review. The systematic search consisted of intersecting terms related to a) paediatric literature (e.g. "child*", "paediatric*", "adolescent*"), b) stroke (e.g. "stroke*", "cerebrovascular*") and c) psychosocial outcomes (e.g. "health status", "quality of life", "psychosocial*"). Additional search strategies were employed through citation tracking of primary study articles and scaning reference lists from book chapters, commentary articles, reviews, clinical guidelines and opinion pieces.

Criteria for Considering Studies for this Review

Articles were considered for inclusion based on the following criteria:

1) They included an outcome measure of psychosocial functioning and/or quality of life. These included psychological, social, functional, behavioural, emotional and psychiatric outcomes, as well as those relating to quality of life and adaptive behaviour.

2) They included participants who had experienced a stroke between 30 days and 18 years of age.

Articles were excluded if they reported on early focal brain injury with heterogeneous aetiologies that included traumatic brain injury, dysplasia or malformations with stroke as a small subgroup. If childhood stroke participants were amalgamated within an adult sample (as in individuals aged 16-50 years), those papers were also excluded. Articles that exclusively recruited children with congenital or neonatal stroke were excluded. Similarly, articles not published in English in peer-reviewed journals were not sought for inclusion, which incorporated grey-literature and conference proceedings. Finally, case-studies were not included in the review. There were no further restrictions placed on study design.

Data Collection and Analysis

Identification of Studies

Two authors (FOK and DS) independently assessed the titles and abstracts of each study for eligibility for inclusion in the review. Full-text versions were reviewed if

further clarity was required. It was agreed that in instances of discrepancy between the two authors, consensus would be achieved through discussion. Consultation with a third author (TM) was available to assist in determining study eligibility if required.

Data Extraction

For each study eligible for inclusion, the following information was recorded: authors, date of publication, where the study was conducted, setting, study design, demographics of study population, measures used (standardised and unstandardized), the main findings and factors associated with outcome, if any.

RESULTS

The selection process for studies reviwered is presented in Figure 1. Following screening for eligibility a total of 26 records were identified, with 10 further studies identified through reference searching and citation tracking. A total of 36 studies were included in the review.

INSERT FIGURE 1 ABOUT HERE

The studies reviewed were heterogeneous in terms of design and measures used. There was significant within and between subject variation in terms of age range at stroke onset, and at assessment, and stroke type. Thirty studies were cross-sectional and six were prospective in design. Twenty-six studies did not recruit a control group but compared scores to published normative population data. Of the remaining ten that did recruit control participants, these included typically developing children as controls [20, 8, 21]; children with other non-neurological health conditions, such as orthopaedic and chronic asthma controls [22, 23, 24, 25, 26, 21, 8]; and some children

with other neurodevelopmental conditions but without stroke, such as sickle cell disease controls [27] or malformations of cortical development [28]. The participant sample sizes in the studies ranged from fourteen children [28] to 163 children [2]. The age at stroke onset ranged from neonatal to 18 years of age. The age at assessment varied from the infant period to young adulthood. Some of the studies reviewed referred to the same groups of children [22, 23, 24, 25, 17, 29]. Other studies came from the same research groups, research centres or research databases [e.g. Canadian Paediatric Ischemic Stroke Registry, Stroke Outcome Project: 30, 31, 2; Royal Children's Hospital in Melbourne: 32, 33, 28, 21; Swiss Neuropediatric Stroke Registry: 34, 35, 36; Great Ormond Street Hospital in London 37, 16, 17, 30].

Table 1 gives a brief summary of each study, including design, study and participant characteristics, measures, main findings and factors associated with outcome.

INSERT TABLE 1 HERE

Functional and Neurological Disability Outcome

The majority of participants (45%- 85%) in all research groups had residual physical disabilities at follow-up. Many studies considered normal or mild deficits as a "good" outcome. However, the findings from this review indicate that even mild physical and functional deficits can result in recurring experiences of difficulties in adaptive behaviour and keeping up with peers [13, 38, 26] [9, 21]. Following stroke, children and young people were reported to be impaired on adaptive behaviour, indicating ongoing functional concerns in the areas of self-care, play, school and leisure and frequently required more assistance and time with activities of daily living, practical

tasks, mobility, school and social domains [33, 45, 19, 22, 40, 32, 26, 50]. Evidence indicated long-term functional limitations into young adulthood, in terms of financial independence and independent living [47]. A recent study that followed-up young adults who had experienced stroke in childhood, indicated that 65% had ongoing neurological or functional deficits, but most (77%-84%) were independent in driving, relationships and employment [42].

Psychosocial Outcome

Education. Many studies have reported the impact of having a stroke on children's education. In one follow-up study, sixty-four per cent of children were rated as experiencing mild to severe deficits in school activities and performance [40]. Across studies, approximately half the children required extra educational help [13, 41, 16, 17, 29, 35, 36, 39, 43, 45, 46, 47]. In those studies that reported children attending special schools, proportions varied from 19% [16] to 31% [35].

Behaviour and mood. Several studies reported a range of behaviour difficulties following childhood stroke. Overall, it appears that behavioural problems can affect a considerable proportion of children following stroke. The reported range (33%- 59%) depends on the measures and criteria used. Cnossen et al [13] classified behavioural disturbances according to DSM-IV criteria [51]. Just over 50% of their group had behavioural or cognitive symptoms at follow-up. A series of studies specifically assessed behaviour and psychiatric diagnoses in a group of 29 children with stroke [22, 23]. Fifty-nine percent of their sample fulfilled diagnostic criteria for a psychiatric disorder, using two psychiatric rating scales. The most common diagnosis given was ADHD (46%), followed by anxiety disorders (31%), with mood disorders the next most common (21%). Seventeen percent were considered to fulfil "personality change

due to a medical condition". There was frequent comorbidity of externalising and internalising psychiatric traits [23]. Greenham et al [8] also found a significantly proportion (17.6%) of children with stroke with borderline or clinical levels of internalising symptoms (anxiety and depression), compared to typically developing controls. Parents and teachers also identified behavioural difficulties in global everyday behaviours of executive function abilities [29] and indicated moderate rates of impairment in social functions, particularly peer relations, prosocial behaviour and school adjustment [28]. Other behavioural difficulties of note include difficulties with changed routines, fatiguing more quickly, emotional and behavioural regulation difficulties and interpersonal and social problems [35, 36, 29, 34, 48]. At long-term follow-up, thirty percent of one population-based cohort of young adults who experienced stroke in childhood met criteria for depression [41].

Social

Nine studies highlight the risk of a range of social difficulties following childhood stroke, such as poorer social adjustment, participation, difficulties with their peers, or changed friendships [8, 21, 26, 27, 28, 29, 35, 41, 48].

Impact on Parental Well-being

Studies that looked at the impact of childhood stroke on parental health indicated that parental psychosocial well-being can also be affected. Parents rated their own psychosocial well-being in the areas of emotional and social functioning, vitality, and health as lower than standardised norms. The negative impact on time for parental and family activities was also noted [40, 38, 17, 45].

Quality of Life

Seventeen studies attempted to assess quality of life in children with stroke, using both unstandardized and standardized measures [13, 39, 17, 20, 30, 31, 34, 44, 49, 47, 41, 45, 43, 50, 40, 39, 42].Fifteen studies used standardised measures of health-related quality of life (HRQoL) and two used unstandardised measures [41, 34] Twelve report both parent/carer and child rated measures [39, 30, 17, 43, 13, 41, 20, 34, 47, 50, 40, 39]. One study also reported teacher's ratings, along with parent and child [17]. Four report only parent-proxy rated HRQoL measures [31, 32, 45, 49 [32, 33, 22, 34]. One study reports only young person's ratings [42].

In the studies that assessed HRQoL using standardised measures (CHQ, PedsQL, Kidscreen, TAPQOL, KINDL-R, SSQOLS), children frequently rate their own HRQoL across several domains as lower than those of the normative population. Physical functioning, emotional functioning, activity limitations and role limitations were rated as the lowest domains in a number of studies [45, 39, 17, 31, 50, 40]. Two studies found that parent-rated scores of psychosocial functioning were lower than physical health status [50, 30]. Parents rated their children's HRQoL as significantly lower than those of healthy children, across most domains. Children with stroke with moderate and severe disability had a lower HRQoL rating than other children with other chronic health conditions [30].

Positive outcomes

Although negative outcomes were commonly reported in most studies reviewed for the many children with stroke, there were some notable points that indicated positive outcomes were also possible. Goeggell et al [34] reported that the majority (94%) of children reported enjoying life in the week prior to their follow-up appointment and

two-thirds estimated their quality of life as equal or better than their peers. Another study [41] showed that 93% of their group reported feeling 'as happy as other children'. Friefeld et al [31] found that almost one-third of parents rated their children as having 'excellent' QOL. Christerson & Stromberg [40] also reported that children with stroke had significantly higher self-esteem than healthy controls and there were no significant differences in young adults at follow-up compared to normative data on a range of health and well-being items. Sixty-five percent of young adults who experienced stroke in childhood reported QOL within the average range and most were independent in driving, relationships and employment [42].

Factors associated with psychosocial outcome

Age at stroke onset. Several studies investigated whether age at stroke onset had a significant impact on outcome. Studies found that younger age at stroke onset was significantly associated with poorer QoL in the domains of physical functioning and neurological outcome [13], long-term clinical outcomes and independence in daily activities [44, 46], adaptive functioning skills [47], and overall outcome [16]. In contrast, younger age at stroke was associated with better overall well-being and quality of life [20] and better self-rated self-esteem and social participation [21] in other studies. Older age at stroke was associated with more behavioural difficulties in another study [29]. Age at stroke onset was not associated with ADHD traits in children with stroke [24, 23].However, the early onset stroke group had lower CGAS scores when compared to the later onset group. They also had a higher severity and a higher mean number of psychiatric disorders [25].

Neurological factors: Lesion characteristics and seizure history. Several studies investigated whether lesion characteristics such as lesion volume, location or

laterality or other neurological factors, such as the presence or absence of seizures, were associated with outcome. Family psychiatric history and neurological severity both independently predicted 89% of cases with psychiatric diagnoses in children with stroke [22]. Lesion laterality or volume did not differentiate children with stroke with and without psychiatric diagnoses. Neurological severity, seizure history, lesion laterality or volume, were not associated with ADHD traits in children with stroke [23]. Lesion location in the putamen regions showed a statistical trend towards association with ADHD traits. Lower Verbal IQ was also found in the children with stroke with ADHD traits [24]. One study found that use of seizure medication was the strongest predictor of poorer functional outcome [47]. Lesion volume was not associated with social outcome but subcortical stroke and poorer neurological outcome was associated with less social participation [21]. In another study, neurological severity and larger infarcts were found to be associated with impaired social participation [26]. Neurological severity was a predictor of outcome in another study [34]. Right-sided middle cerebral artery lesions were associated with a poor neurological outcome [13]. Lesion location (basal ganglia infarct) or presence of seizures was not associated with neurological outcome in other studies [2]. Lesion size, location and presence of previous risk factors were not found to be associated with residual disability. However, children with large lesion size (>10% of intracranial volume) were more likely to have a moderate or severe level of residual disability [37]. Ganesan et al [37] found that all those with bilateral lesions and small lesions in the basal ganglia were associated with a poor outcome. Seizures and lesion location were not predictive of residual disability in their larger study [16]. Cortical-subcortical infarcts correlated with impaired adaptive behaviour, as compared with all other lesion locations. Another study found that lesion size predicted neurological outcome [44].

Gordon et al [45] found that lesion volume was associated with children's physical health (as measured by CHQ) but not psychological health. Functional status at one year post-stroke, arteriopathy and AIS were all risk factors for poorer functional outcome (mRS) in a follow-up study of young adults [42]. Ischaemic stroke showed a tendency towards poorer outcome on adaptive behaviour than haemorrhagic stroke [47]. In contrast, another study did not find a clear association between stroke type and outcome [25].

Other factors. Other factors investigated for association with outcome included medical factors, sex, time since stroke, age at assessment, socio-economic status, behaviour problems, cognitive functioning, family functioning, and parental education.

Time since stroke, age at assessment, socioeconomic status or child's sex were generally not found to be significantly associated with outcome [13, 22, 24, 23, 36, 16, 45, 30, 47, 30].

A significant influence of family functioning and parent mental health on psychosocial outcome was identified [8]. A strong association between executive components of attention and social function was also identified [28]. Family functioning was found to be the sole predictor of social adjustment [37].

Predictors of HRQoL. Ten studies specifically examined predictors of HRQoL [13, 30, 45, 47, 17, 31, 20, 39, 50].

There were inconsistent findings regarding impact of age of stroke onset on HRQoL. Children with stroke onset under two years of age had significantly lower physical function ratings than those with stroke onset over two years of age [13] Neuner et al. [20] showed that younger age at stroke was associated with better overall well-being and QOL. They also found that neurological severity was a significant

predictor of poorer overall well-being. Neonatal stroke was associated with the best long-term HRQoL compared to perinatal or childhood onset. [44]. However, age at stroke onset was not associated with either lower physical or psychosocial QoL ratings in another study [45].

In terms of disability and neurological severity, children with severe disability (modified Rankin Scale, mRS, of 3) scored lower on both motor and cognitive functions and autonomy than those with no disability (mRS 1). Friefeld et al. [30] found that severity of neurological outcome (measured by Pediatric Stroke Outcome Measure, PSOM) was the most significant predictor for parent-proxy HRQoL, explaining 16% of the variance. Sex and neurological severity was the most significant predictor for child-reported HRQoL, explaining 16% of the variance. Girls rated their HRQoL lower than boys on emotional functioning and overall PedsQL score. Neurological severity outcome (PSOM and mRS) also showed significantly higher HRQoL ratings for those with 'good' outcomes compared to those with 'poor' outcomes [39]. Hurvitz et al. [47] reported that life satisfaction was related to functional outcome. Participants who had lower levels of adaptive functioning (as measured by the VABS) showed trends towards lower life satisfaction. Symptomatic epilepsy, moderate to severe hemiparesis and lower IQ were associated with worse scores on HrQOL measure [50]. Cognitive/behavioural impairment on the PSOM, stroke type (SVT), gender (female), and age (>5 years at testing) were significant predictors of overall QOL [31]. Low Verbal IQ was also a significantly associated with lower QOL. Cognitive/behavioural scores on PSOM had the greatest impact on reduced QOL.

Gordon et al. [45] showed that extent of brain injury was associated with child physical health but not psychological health. Limitations in communication were a

significant predictor for poorer psychological health status (explaining 35% of the variance). Social, emotional and communication difficulties in children with stroke were associated with poorer parental mental health, vitality and social functioning. A significant relationship between a child's HRQoL, parental well-being and family functioning was highlighted [17].

DISCUSSION

A systematic review of the literature identified a total of 36 papers that examined the important clinical areas of psychosocial and behavioural outcomes and quality of life following childhood stroke. The review provided answers to the research questions posed.

1) Is there evidence of functional disability, behavioural, educational and psychosocial difficulties following childhood stroke?

The systematic review indicates that there is evidence of functional disability, behavioural, educational and psychosocial difficulties following childhood stroke. In terms of functional disability, between half to three-quarters of children who have experienced stroke have residual physical difficulties, predominantly hemiparesis, frequently impacting activities of daily living. Several studies reported significant behavioural and emotional difficulties following childhood stroke. Common diagnoses in this group of children included ADHD, particularly inattention subtype, anxiety disorders and mood disorders. Difficulties with emotional and behavioural regulation, interpersonal issues, fatigability, low self-esteem and change in routine were also reported. The impact of childhood stroke on social domains and friendships was also noted in several studies. A consistent finding was that approximately half of

the children with stroke in each group studied need some form of remedial teaching or special education arrangements and approximately one-fifth are in special educational schools. Those who experience stroke in childhood may also be at a higher risk for mood disorders in adulthood [42].

2) Is there evidence to suggest that quality of life is affected following childhood stroke?

Quality of life appears to be significantly affected following childhood stroke compared to normative data from both a healthy population and from a chronically ill sample. Domains relating to school, emotions, physical, social and autonomy are commonly affected.

Of note, although negative outcomes were consistently found, some studies showed that there was also a proportion of children with relatively good outcomes. For example, Friefeld et al [31] found that almost one-third of parents rated their children as having 'excellent' QOL and 93% of children in one study were reported as "feeling as happy as other children" [41]. Christerson & Stromberg [40] also reported that children with stroke had significantly higher self-esteem than healthy controls and there were no significant differences for their young adults at follow-up compared to normative data on a range of health and well-being items. In a follow-up study of young adults who experienced stroke in childhood, 65% of the cohort reported QOL within the normal range and most were independent in driving, relationships and employment [42]. These findings of positive outcomes may relate to what is known as 'Disability Paradox', where those with serious and persistent disabilities report good or excellent quality of life, contrary to other's expectations, [52]. Children with

cerebral palsy have been shown to have QOL similar or better than same-age children in the general population [53]. Further research exploring resilience and factors supporting positive outcomes is warrented. Qualitative approaches to explore children and young people's lived experience of childhood stroke are likely to also provide important insights [54, 55].

3) What factors can be identified that may be related to psychosocial outcome and QOL following stroke during childhood?

Inconsistent findings meant that predictive factors were not clearly identified. Contrasting and non-significant findings were common.

Nevertheless, there are some indications that earlier age of stroke onset may lead to greater vulnerabilities, particularly in functional disabilities. Neurological factors including lesion characteristics and presence of seizures were not consistently found to be associated with outcome. This is likely to be due to small sample sizes and the wide range of outcome variables used. Greater lesion volume appears in some studies to be associated with worse outcome and greater functional disability. However, this is by no means a consistent finding. Some findings suggest that neurological severity may be related in some degree to quality of life [30, 17, 20]. However, again this is not consistently found [13]. Recent studies that have investigated the contribution of environmental factors have supported the influence of parent mental health and family functioning on psychosocial and HRQoL outcome [21, 8, 17] In general, however, inconsistent findings mean that coherent conclusions cannot be established at this point and further research is necessary.

Methodological Limitations and Quality of Studies Reviewed: There is consensus that there has been a dearth of research around psychosocial outcomes following childhood stroke [18, 3]. The last decade has seen a developing interest in a spectrum of outcome factors outside of crude 'good' or 'poor' outcome classifications based on broad measures of neurological severity. This burgeoning research area is vital to inform clinical assessments and interventions. However, significant methodological considerations dominate the reviewed literature, many of them common to research in other rare paediatric populations.

Study Design. The vast majority of studies in this review (thirty of thirty-six) were cross-sectional in design. This design has several advantages, particularly with rare populations, such as childhood stroke. They generally allow for larger sample sizes, are time- effective and inexpensive. However, causality cannot be established conclusively. For example, due to the very nature of the sudden onset of childhood stroke, baseline assessments are not possible for the majority of children. The exceptions to this are children with identified risk factors or syndromes that increase their risk of stroke, such as moyamoya or sickle cell disease. Most studies did not use a control group in their design but compared their data to normative population means, where available. It has been highlighted that there is a significant lack of case controlled design and absence of observational data in looking at psychosocial outcomes following childhood stroke [14]. There is also a need for a qualitative approach to understand the perspectives of children and parents following childhood stroke [3,55]

Several studies reported multiple papers from the same sample of children with stroke [17, 29; 21, 22, 23, 24, 25]. Other studies came from the same research groups, research centres or research databases [e.g. Canadian Paediatric Ischemic Stroke

Registry, Stroke Outcome Project: 30, 31, 2; Royal Children's Hospital in Melbourne: 32, 33, 28, 21; Swiss Neuropediatric Stroke Registry: 34, 35, 36; Great Ormond Street Hospital in London: 16, 17, 29, 37]. Although developing centres of expertise is highly important, there may be some element of bias in reporting from same or similar samples.

Several of the larger outcome studies had a strong neurological focus [16, 2] In studies that adopt a purely medical approach to outcome, children with mild residual physical disabilities are generally grouped in the 'good' outcome category. Such general classifications of neurological severity do not consider subtle cognitive and behavioural and psychosocial difficulties. One study found impaired quality of life in children with both mild to severe disabilities, suggesting that quality of life may be independent of neurological severity [13]. Ratings of children's QOL are likely to also depend on how and when it is measured and whether it includes participation and function or subjective measures of wellbeing. Qualitative research can be helpful in designing better condition-specific HRQoL scales [55, 53].

Heterogeneity. Within-group and between-group variability is likely to have prevented clear conclusions from being established. Studies reviewed included a mix of children with ischaemic, haemorrhagic and SVT stroke; age of stroke onset ranging from the prenatal period up to over 18 years; time since stroke ranged from months to 25 years. Unclear inclusion and exclusion criteria were also problematic in the studies reviewed. For example, not all studies clarified if children with recurrent stroke or medical conditions such as sickle cell disease were included.

Statistical Issues. Small sample sizes were very common in the studies reviewed. Smaller sample sizes can lead to low power and a greater chance of type 2

errors. Descriptive findings were frequentl reported and statistical analyses was limited.

Measurement Issues. As this review highlighted, a wide array of standardized and unstandardized measures was used in the studies reviewed. Many questionnaires regarding psychosocial outcome were completed by parents, excluding the child's own personal experience. In studies that did adopt self-rated questionnaires to assess quality of life, children and young people rated different factors as important compared with what their parents rated. For example, in one study [43], children rated themselves lower in areas of autonomy, relationship with parents and social acceptance. This differed from their parents' ratings of emotional stability and social support. There may also be areas of importance at specific ages. Parents of children aged between 6-15 years rated significantly more problems across all domains than population means [13]. Children aged 8- 15 rated significantly more social problems than the norms, whereas young people 16 years and over rated fine motor and cognitive problems as significantly below the norm. Another study also found that older children specifically rated friend-related and emotional well-being as significantly reduced [20]. This suggests that children of different ages may have different priorities for quality of life and this deserves further investigation.

Clinical Implications. This review highlights the need for psychosocial factors including behaviour, adaptive functioning and quality of life to be carefully assessed as part of routine clinical practice in children who have experienced stroke. Objective, standardised measures should be administered to the child, their parents and to their teachers when possible, in order to ensure multiple perspectives are considered. They are essential to identify vulnerable children and families in need of further support.

These assessments should lead to careful development of tailored interventions for the child and family and guidance for teachers, to maximise learning, independence and quality of life. Adopting a broad framework as proposed by Limond et al. [56] in approaching paediatric neurocognitive interventions may be helpful in developing appropriate interventions for children following stroke. The impact of childhood stroke on parent's psychosocial wellbeing was noted in several studies reviewed [45, 17, 38]. The interrelationship between family functioning, parental mental wellbeing and psychosocial outcome was also shown [8, 22, 17, 40, 45]. Family-based interventions, as developed by Wade and colleagues with children who have experienced traumatic brain injury [57, 58, 59, 60], may also prove helpful in supporting children and families following stroke. Further research could explore the effectiveness of these interventions with children following stroke.

Future Research. The findings from this review and the methodological limitations outlined point to several recommendations in terms of further research.

1) It is essential to include objective, well-validated measures of psychosocial outcome including quality of life, behaviour, mood, adaptive functional disability, preferably from multiple perspectives (child, parent and teacher).

2) Only two of the studies reviewed discussed issues relating to transition to adulthood [47, 42]. Longitudinal studies are needed in order to monitor children with stroke at different transition points, including primary to secondary school and beyond to early adulthood.

3) Larger and more homogeneous sample sizes are clearly needed to increase the power of studies. Given the rarity of childhood stroke, it is likely that collaborative, multicentre studies with large databases are required, such as the International Paediatric Stroke Study. However, as these are not population based, homogeneity is not guaranteed. Other considerations such as joining existing population based cohorts from existing population based registries may also be helpful.

4) In order to begin to fully understand the lived experience of those children, young people and their parents living with the consequences of childhood stroke, a qualitative approach to future research regarding psychosocial outcome would be extremely valuable [54, 55].

5) As the last decade saw an increase in studies investigating outcome, research into efficacy of clinical interventions and support is now needed. This could include interventions found to be effective with other paediatric populations, such as cognitive behaviour therapy for mood difficulties, behavioural interventions and school liaison, as well as family-based [59].

6) The impact of childhood stroke on the family deserves further study. Several studies found that the disabilities associated with childhood stroke had a significant impact on parental health, emotional well-being, social functioning and family functioning [45, 39, 17, 22, 45, 40, 8].

Conclusion

Childhood stroke is a rare but devastating occurrence. Its infrequency has meant that a clear body of knowledge has not yet been established regarding its impact on psychosocial outcome and quality of life. This review indicates that a significant number of children with stroke experience long term difficulties in a wide range of

psychosocial areas. Approximately half the children studied needed additional educational help. Physical and functional disabilities are reported in up to three-quarters of children with stroke. Behaviour difficulties are common. Initial studies strongly indicate that quality of life is significantly impacted for children following stroke. Younger age at stroke onset is associated with poorer outcome in a number of studies, however this finding is not consistent. Inconsistent findings regarding the correlates of outcome are likely to be due to methodological limitations of the studies reviewed. Methodological issues include limited prospective and longitudinal studies, lack of control groups, small sample sizes, measurement issues and heterogeneity of samples. Future research should address these methodological issues and in doing so, answer some of the many remaining questions regarding outcome following childhood stroke. This systematic review strongly indicates that it is vital for children with stroke to be assessed clinically for psychosocial difficulties. Tailored interventions and support can then be developed in order to improve the quality of life of children who have experienced stroke during childhood.

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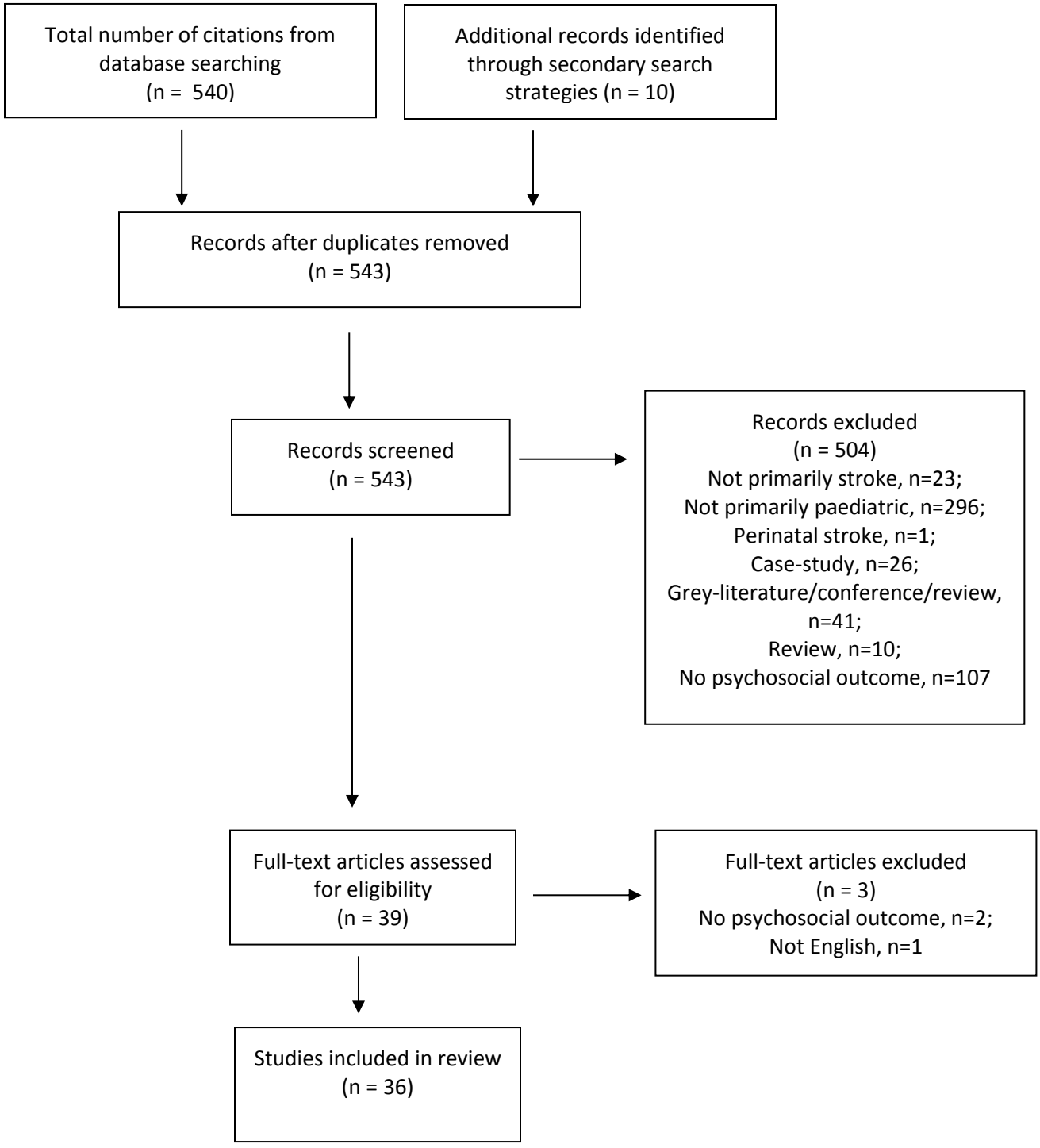

Figure 1: Results of the systematic search and screening of citations

Table 1

Summary of studies reviewed (n=36) investigating psychosocial outcome and quality of life following childhood stroke

Study	Study Design and Source of sample	Sample Size & Types of Stroke	Participant Characteristics Mean (range) (unless otherwise specified)	Psychosocial Measures: [Ratings by child (c), young adult (ya), parent (p), clinician (cl), teacher (t)]	Main Findings	Factors significantly associated with outcome	Factors not significantly associated with outcome
Anderson et al., 2014 [21] (Australia & US)	Cross sectional RCHM Melbourne + NCH Ohio	N= 36 AIS (perinatal n=10) 16 male N=15 Chronic Illness Controls (asthma) N=43 Healthy controls	AgeS = 4.2y (SD 4.3) AgeA = 9.1 y (SD 3.0) TimeS = 5.0 y (SD 3.3)	CBCL(p) FAD (p) GHQ (p) PSOM (cl) FQQ (c) CASP (p) NRI (c) RPQ (c) ABAS-Social (p) Harter-SC (c)	CWS were associated with poorer social participation, parent ratings of social adjustment, self-confidence and for social problems. Perinatal stroke onset led to higher self-esteem and better social interactions.	Subcortical lesions Family functioning Neurological status Age stroke onset	Parental education Lesion volume
Blom et al., 2003 [38] (Netherlands)	Retrospective Cross sectional follow-up Utrecht	N= 31 CWS (haem) 17 male No controls	AgeA = 18.6 y (1.8- 34.1) TimeS = 10.3 y (1.3- 19.9y)	SF36 (ya) CHQ (p & c)	CWS experience low self-esteem, difficulties in family activities, physical functioning, emotional and behavioural problems, lower scores for school participation and peer engagement compared to norms. Parental emotional distress related to child's physical and psychosocial well-being.	-	-
Bulder et al., 2011[39] (Netherlands)	Cross sectional Clinic-based follow-up Utrecht	N= 40 CWS (AIS) 23 male No controls	AgeS (median) = 5.6y (0.3-15.9) AgeA (median) = 9.2 y (1.8-19.8) TimeS (median) = 3.1y (0.6-13.1)	PSOM (cl) mRS (cl) PedsQL (p & c) VAS (p & c)	67% CWS had lasting neurological deficits. 20% attended special schooling. Better HRQoL ratings for those with 'good' outcome.	Neurological severity	-

Christerson et al., 2010 [40] (Sweden)	Population-based cohort Clinic-based follow up Uppsala-Orebro	N= 46 (22 AIS, 20 HS, 4 SVT) No controls	AgeA (median) = 17.5 y (5.5-26.1) TimeS (median) = 4.2y (1.6-8.6)	CHQ (p & c) SF-36 (ya) ICF-CY (p) Unstandardised neurological outcome scale (cl) & School performance scale (cl)	85% CWS had neurological deficit and/or school activity limitations. 64% had difficulties in school activities and participation. Parents indicated that 75% had mild-severe difficulties with learning and 38% unable to perform at least one ADL. Parent- rated HRQoL for physical, social/emotional, social/physical, general health, emotional impact, time impact, family activities significantly lower than norms. Children rated physical and role as lower but no significant differences on 8 of 10 items. They also rated significantly higher self-esteem than normative data. Young adults scores on the SF-36 did not differ from normative data.	-	-
Cnossen et al., 2010 [13] (Netherlands)	Prospective Consecutive admissions 12m f/u and last assessment-RPSR	N= 76 CWS (isch) n= 66 at f/u 31 male No controls	AgeS (Median) = 2y, 5m (0.6-10.5) TimeS= 2y 4m	mRS (cl) TAPQOL(p) TACQOL (p & c) TAAQOL(ya) DSM IV (cl)	Impaired HRQoL across all age groups and levels of residual disability. Approx. 50% had behavioural or cognitive issues and were in special education. Lower mood and anxiety for CWS <6y. More problems in all domains for CWS >6y. CWS 8-15y rated more social problems.	Younger age at stroke onset Lesion location: R MCA associated	Sex
De Schryver et al., 2000 [41] (Netherlands)	Cross sectional follow-up from Utrecht	N= 37 CWS (isch) at b/l n= 27 at f/u No controls	AgeS= 4.6y (3m- 14y) AgeA= 11.6y (- 25y) TimeS = 7.1y (3m- 20y)	Unstandardised Questionnaire- (p & c)	Approx. 1/3 parents reported changes in behaviour at school and fewer friends. Approx. 1/2 participants considered to have developmental stagnation. 93% reported feeling ‘as happy as other children’	-	-

deVeber et al., 2000 [2] (Canada)	Prospective longitudinal Tertiary clinic follow-up HSCT Toronto SOPT	N= 163 CWS (123 isch, 38 SVT) No controls	CWS (isch) AgeS= 4.7 y 73% non- neonatal stroke. CWS (SVT) AgeS = 3.8y 50% non-neonatal	PSOM (cl) Modified Euroqual- (p)	46% CWS (isch) and 18% CWS (SVT) considered to have a 'poor' outcome. 55% reported by parents as needing extra help in activities of daily living.	AIS Associated neurological disorder Need for rehabilitation therapy	Seizures, basal ganglia infarct
Elbers et al., 2014 [42] US/Canada	Population-based follow-up in clinic HSCT Toronto	N= 26 16 females (21 AIS, 5 SVT) No controls	AgeS = 11y 10 m (2- 17y) AgeA = 21y 6 (18- 31y) TimeS= 10 y, 10 m (3-18 y)	mRS (cl) PSOM (cl) Barthel Index (cl) SSQOLS (ya) BDI (ya)	Long-term follow-up into adulthood. 65% showed lasting neurological deficits, 42% mild, 8% moderate, 15% severe. 65% reported quality of life within the normal range. 30% reported mild to severe levels of clinical depression. Most (77%- 84%) were independent in driving, relationships and employment.	AIS Arteriopathy 1 year post-stroke functional status	
Everts et al., 2008 [43] (Switzerland)	Retrospective Cross-sectional in clinic CH Bern & CH Berlin	N=21 CWS (isch) 15 male No controls	AgeS= 7y 3m (1m- 17y 6m) AgeA= 11y 11m (6y 9 m- 21y 2m) TimeS = 4y, 9m (14d- 14y)	Kidscreen QoL (p & c) Connors (p)	Impairments in 5 of 6 domains of Connors Rating Scale. 50% met the criteria for ADHD. Children rated areas of autonomy, parental relationships and social acceptance low. Parents rated emotional stability and social support as low. Approx. half had special educational support.	Larger lesions	Lesion laterality, lesion location, presence of seizures
Friefeld et al., 2004 [30] (Canada)	Prospective Single-centre cohort – CPISRT SOPT Toronto	N= 100 CWS (84 isch, 16 SVT) n= 30 neonatal 56 male No controls	AgeS= 5.8y (non-neonates) AgeA= 8.4y (SD 4.12) TimeS = 4.4 (SD 2.93)	PSOM (cl) PedsQL (p & c)	Approx. half had a 'poor' outcome. CWS and parents rated HRQoL lower on all domains compared to norms. School and emotional functioning rated lowest. Lower HRQoL ratings among CWS with 'poor' outcome on all but physical domains.	Neurological severity, Gender, Sensory-motor outcome, cognitive outcome	SES, age at testing

Friefeld et al., 2011 [31] (Canada)	Prospective longitudinal Tertiary clinic follow-up SOPT Toronto	N= 112 CWS (isch & SVT) n= 34 neonatal stroke 63 males No controls	AgeS= neonates- 18y AgeA= 8y, 1 m (2-18y)	PSOM (cl) CHP-QOL (p)	67% had mild-severe neurological impairment HRQoL: 29% 'excellent'; 52% 'adequate'; 17.8% as 'poor'. Lowest HRQoL rating was for school and play. 1/3 of the group rated low HRQoL in domains of school, leisure and development. Cognitive/ behavioural impairment had the greatest impact on reduced HRQoL.	Cognitive/behavioural impairment, stroke type (SVT), gender (female), AgeA (>5 years), IQ	Neurological severity, SES
Galvin et al., 2010 [32] (Australia)	Cross sectional tertiary outpatient clinic- RCHM Melbourne	N= 26 CWS (isch and haem) 14 male No controls	AgeA = 9.09y (5.13) TimeS = 1.42y (1.42)	COPM (p & c) PEGS (c)	88.5% of CWS reported ongoing functional concerns in the areas of self-care, productivity (play and school) and leisure.	-	-
Galvin et al., 2011 [33] (Australia)	Cross sectional tertiary outpatient clinic- RCHM Melbourne	N=18 CWS (isch) 9 male No controls	AgeS = 7.86y TimeS = 2.81y	PEDI (cl & p)	CWS demonstrated lower functional abilities and required more caregiver assistance than age-expected norms for self-care, mobility and social domains.	-	-
Ganesan et al., 1999 [37] (UK)	Cross sectional Tertiary outpatient clinic GOSH London	N= 38 CWS (isch) No controls	22 male AgeA (median) = 6y (6m – 15y)	Unstandardised Questionnaire (p or cl)	32% had a 'good' outcome, 68% had a 'poor' outcome. Symptomatic stroke (children previous risk factors) had larger lesions than idiopathic stroke.	Large lesion size (>10% of ICV), Bilateral lesions	Lesion size for whole group, lesion location, previous risk factors
Ganesan et al., 2000 [16] (UK)	Cross sectional	N= 90 CWS (isch) No controls	AgeA (median) = 5y (3m-16y)	Unstandardised Questionnaire (p) CBCL (p)	59% had 'good' outcome and 'needed help at home'. 41% of those attending mainstream school needed support.	Younger age at stroke onset	Time since stroke, risk

	Tertiary outpatient clinic GOSH London		TimeS (median) = 3y (3m-13y)		19% attended a special school. CWS had greater difficulties in the areas of withdrawing, social and attention behaviour problems.		factors, seizures, lesion location
Ghotra et al., 2015 [44] (Canada)	Cross sectional from tertiary clinic Alberta	N= 90 n= 31 perinatal n=36 neonatal n=23 childhood (isch) No controls	Perinatal: AgeA = 5y 2m (2y1m- 15y2m) TimeS = 5y 2m (2y1m- 15y,2m) Neonatal: AgeS = 2d (0-21d) AgeA = 5y 2m (2y5m- 15y,1m) TimeS = 5y 2m (2y5m-15y 1m) Childhood: AgeS = 5y 2m (2m- 14y) AgeA = 9y10m (2y2m- 17y 10m) TimeS = 4y 7m (1y-10y 8m)	RRQ (p) PedsQL (p)	Perinatal stroke associated with poorest long-term clinical, global and sensorimotor outcomes and the least independence in ADLs. Neonatal stroke associated with the best long-term HRQoL, with no significant differences from normative scores, except in emotional domain. Perinatal and childhood stroke had similar scores in all HRQoL domains, which were significantly lower than reference norms. HRQoL for childhood stroke was rated as lower than either perinatal or neonatal groups.	Age at stroke onset, Size of stroke	-
Goeggel Simonetti et al., 2015 [34] (Switzerland)	Prospective cohort follow-up from SNPSR (CWS)	N=95 CWS 55 male N= 154 young adults stroke onset 68 male No controls	CWS: AgeA (median) =15y (9.3-19) TimeS (median) = 6.9 y (4.7-9.4) Young Adults: AgeA (median) = 45y (37.4-48.8)	Unstandardised telephone interview (p & c) mRS score (cl) Unstandardised QoL rating scale (p & c)	CWS had increased behavioural disturbances compared to adults. No significant difference in long-term functional outcome or HRQoL between CWS and adults. Young adults more often reported a negative impact of AIS on everyday life. Majority CWS (94%) reported they had enjoyed life in the previous week. 2/3 estimated their HRQoL as equal or better than peers.	Neurological status No acute phase heparin treatment	Age Sex Aetiology

Gomes et al., 2012 [28] (Australia)	Cross sectional Tertiary clinic RCHM Melbourne	N= 14 CWS 8 males N= 14 MCD 6 males	CWS: AgeS = 8.18y (SD 4.3) AgeA = 12.9y (SD 1.87) TimeS= 4.66y (SD 4.4)	FAD (p) TEA-Ch (c) BRIEF (p) SDQ (t) WMSSC (t)	CWS demonstrated moderate levels of impairment in social function areas including peer relations, prosocial behaviour and school adjustment.	Attention and executive function difficulties	-
Gordon et al., 2002 [45] (UK)	Cross sectional GOSH London	N= 17 CWS (isch) 9 males No controls	AgeS (median)= 4y (14m-13y, 6m) AgeA (median)= 8y 5m (5y 2m- 15y 5m) TimeS (median) = 2y 5m (10m- 8y 6m)	CHQ (p) SF36 (p) PSALM (cl) PSOM (cl)	Cognitive functioning and sensorimotor ability greatest area of impairment. CWS significantly lower QoL than normative sample in physical (>2SD below mean) and psychosocial domains. Parental social and psychological functioning was lower than norms. Activity, education and self-care limitations associated with poorer physical QoL.	Communication limitations Emotional skills	Age at time of stroke, laterality, age at assessment
Greenham et al., 2015 [8] (Australia & US)	Retrospective Cross Sectional RCHM Melbourne NCH Ohio	N=36 AIS 16 male N=15 chronic asthma controls N=43 TDC	AIS AgeS = 4.2y (SD 4.3) AgeA=9.1y (SD 3.0) TimeS=5.0y (SD 3.3)	PSOM (cl) CBCL (p) FQQ (c) RPQ (c) CASP (p) GHQ (p) FAD (p)	CWS and chronic illness controls had elevated risk of poorer internalizing (anxiety & depression) mental health and behavioural difficulties and poorer social competence. 17.6 % of the CWS group had clinical or borderline impairment rates for internalizing difficulties. CWS had poorer social participation. CWS or chronic illness did not have severe levels of mental health or social problems.	Presence of chronic illness, parent mental health, family function, child IQ	
Hariman et al, 1991 [27] (US)	Retrospective Cross sectional Tertiary SCD clinic Chicago	N= 14 CWS+SCD 5 male N= 14 SCD controls	CWS+SCD AgeA= 11.6 (SD 4.3) AgeS= 6.1 (1-17)	MAS (cl) Barthel (cl) WISC-R (c) CTP (c)	Social and personal adjustment were significantly affected in CWS. 5/10 scored <25th %ile for social adjustment and 4/10 scored 25th %ile for personal adjustment. Most were independent in ambulation and above the independent living score for ADLs	-	-

Hurvitz et al., 1999 [46] US	Retrospective chart review and follow-up telephone survey Michigan	N= 50 CWS (isch & haem) No controls	AgeS = 8.0 y (7m- 17y,8m) AgeA = 3y 6m (2- 30y) TimeS= 5y, 10m (10-14y,6m)	Chart review (cl) Unstandardized telephone survey (p or c)	76% were independent in all ADLs, 84% were independent in mobility. 40% had speech and language deficits. 50% were in a regular classroom with 20% of those requiring resource hours. 50% were in special education or support services.	Younger age Congenital heart disease Ischaemic aetiology Female	
Hurvitz et al., 2004 [47] (US)	Longitudinal follow-up from Hurvitz et al., 1999 [REF]	N=29 CWS (isch & haem) No controls	AgeS= 7y (8m- 17.7 y) AgeA= 19.3y (9- 36.5y) TimeS = 11.9y (6.6y- 20.8y)	VABS (p) SWLS (p or c)	Adaptive behaviour fell in the moderately low range. Average rating for life satisfaction was in the 'neutral' range. 45% had special education services. 79% of CWS over 16 were driving. 60% were employed. 28% living away from parents. Only 2 were financially independent.	Age at stroke onset Lesion type (Isch) Seizure medication Functional disability (life satisfaction)	Age, laterality, medical history, previous functional status
Lo et al., 2013 [26] (US & Australia)	Retrospective Cross Sectional RCHM Melbourne NCH Ohio	N = 36 AIS (10 perinatal) 16 male N=15 (Asthma controls)	AgeS = 2.6 y (0.0-7.8) AgeA = 8.5 y (6.5- 11.8)	PSOM (cl) ABAS II (p) CBCL (p) CASP (p)	CWS had greater deficits than controls on adaptive functioning overall and specifically with practical functioning, even when cognitive ability and problem behaviours were within normal limits. Severe residual neurological deficits were associated with poorer social adjustment and participation, and adaptive behaviours than controls and low severity stroke.	Neurological severity Problem behaviours IQ Cognitive impairment Lesion volume	Age at stroke onset
Max et al. 2002 [22] (US)	Cross-sectional Tertiary clinic San Diego & Iowa	N= 29 CWS (isch & haem) N = 29 Orthopaedic controls	AgeA= 12.1y (3.9)	K-SADS-PL (p & c) NPRS (p, c & cl) VABS (p) FAD (p)	59% CWS met psychiatric diagnostic criteria, compared with 14% of orthopaedic controls. CWS diagnoses: ADHD = 46%, anxiety disorders = 31%, mood disorders = 21%, personality change = 17%. Mean number of diagnoses in CWS = 2.2. CWS with diagnoses had lower	Family psychiatric history, neurological severity	Age, SES, gender, age at stroke onset, lesion laterality, lesion volume, PIQ, academic function, family function.

					adaptive function, particularly in social areas.		
Max et al., 2002 [24] (US)	Cross-sectional Tertiary clinic San Diego & Iowa	N= 25 CWS 16 males No controls	AgeA = 11.5y	K-SADS-PL (p & c)	60% CWS had ADHD/ADHD traits. With a subgroup (n=13), 7/13 had ADHD/Traits. 6/7 had putamen lesions compared with 2/6 with no putamen lesions with ADHD/Traits.	Lesion location (putamen)	Lesion volume and laterality, age at assessment, age of lesion onset, gender, family history of ADHD
Max et al., 2003 [23] (US)	Cross-sectional Tertiary clinic San Diego & Iowa	As per Max et al. [29 REF]	n= 15 CWS+ADHD AgeA = 11.5 (4.4) n= 13 CWS-ADHD AgeA =12.2 (3.4)	K-SADS-PL (p & c) CBCL (p) VABS (p)	46% CWS developed ADHD after stroke. CWS+ADHD were more impaired than CWS-ADHD on total CBCL, attention and behaviour problems. Over 1/2 CWS+ADHD had comorbid externalizing and/or internalizing psychiatric disorders.	Impaired neurocognition and Inattention-apathy	AgeS, lesion laterality, lesion volume, sex, neurological severity, seizure history, family function, family history of ADHD
Max et al., 2010 [25] (US)	Cross-sectional Tertiary clinic San Diego & Iowa	As per Max et al. [29 REF]	N= 17 EO, EO AgeA = 11.8y (3.6) N = 12 LO LO AgeS= 7.8y LO AgeA = 13.2y (4.2)	K-SADS-PL (p & c) NPRS (p, c & cl) CGAS (cl)	Psychiatric diagnoses were made in 10 of 17 (59%) EO CWS and in 7 of 12 (58%) LO CWS. EO had higher mean number and higher severity of psychiatric disorders.	Age at onset	Lesion aetiology (isch or haem)
Mosch et al., 2005 [48] (US)	Cross sectional comparison	Lesion matched children and adults N= 29 CWS	AgeS= 3.2y (4.4) AgeA = 12.8y (3.8) TimeS = 9.1y (4.6)	Unstandardized Rating of social functioning (cl)	CWS: Mild to moderate impairments in social functioning. No difference between LH and RH groups. Adults: RHL highly associated with social functioning impairments.	-	Lesion laterality for children
Neuner et al., (2011) [20] (Germany)	Cross sectional follow up Münster	N= 133 CWS 73 males N=169 TDC	AgeS (median) = 6.3y (neonate- 17.6 y)	KINDL-R (p & c) PSOM (cl)	HRQoL and overall well-being reduced in CWS. For CWS who had experienced stroke at an older age, scores on emotional well-being and	Age at stroke onset Neurological severity	

					friend-related well-being were also impaired. Parents rated HRQoL lower than child-rated HRQoL.		
O'Keeffe et al., 2012 [17] (UK)	Cross-sectional Tertiary clinic GOSH London	N= 49 CWS (AIS) 30 males No controls	AgeS= 5.08y (4m- 15.6y) AgeA = 11.08y (6-18.4y) TimeS = 6.0 y	PedsQL & Cognitive Functioning Scale (c, p & t) FIM (p) CF-SEI (c) SDQ (c, p & t) GHQ (p)	Child-, parent- and teacher-rated HRQoL was significantly lower than comparative norms across all domains- physical, emotional, social, school and cognitive functioning. 58.3% CWS were on the Special Education Register, with specialized individual education plans. Parents of children with lower HRQoL also rated family functioning and their own well-being as lower.	Neurological severity Lower self-esteem Internalizing and externalizing difficulties Executive Dysfunction Family Functioning	SES Gender Age at stroke
O'Keeffe et al., 2014 [29] (UK)	Cross-sectional Tertiary clinic GOSH London	N= 49 CWS (AIS) 30 males No controls	AgeS= 5.08y (4m- 15.6y) AgeA = 11.08y (6-18.4y) TimeS = 6.0 y	SDQ (c, p & t) BRIEF (c, p & t)	Emotional functioning and overall impact on life were rated by children and parents as areas of difficulty. Children rated increased difficulties with peers. Parents perceived hyperactivity as problematic. Teachers' ratings did not differ from normative data. Parents and teachers identified behavioural difficulties in global everyday behavioural executive function abilities (BRIEF).	Age at stroke onset	
Pavlovic et al., 2006 [36] (Switzerland)	Prospective population-based multi-centre study SNPSR	N= 33 CWS (isch & SVT) No controls	n= 11 neonatal stroke AgeA = 1.8y (1-3,7y) n=22 Childhood stroke AgeS= 8.5y (0.9- 16.3y) AgeA = 10.2 (2.1- 18.2y)	Unstandardized questionnaire (p & c)	43% of school-age children were in special education or receiving additional assistance in mainstream. Low self-esteem, aggression, anxiety, attention difficulties, poor frustration tolerance, affect lability and fatigue reported in 59% of CWS.	Epilepsy	Sex
Simma et al., 2007 [49] (Austria)	Retrospective population-based	N= 20 CWS (isch & haem) at f/u	AgeS (median) = 6 y (0.9- 14) TimeS(median) = 3.7y (0.4-18)	CHQ (p)	Neurological outcome: 55% had no or mild residual disability ('good'). 45% had 'poor' outcome, moderate or	-	-

		No controls			severe disability. QoL: 25% had CHQ Physical or Psychosocial Health Scales as 2 SD below normative mean. 75% were considered to have "good" QoL ratings.		
Smith et al., 2015 [50] (US)	Cross sectional Convenience sample from a tertiary care centre Philadelphia	N= 59 CWS (isch & haem) (21 perinatal) No controls	AgeS (median) = 11y, 6m (6y 5m-13y,5m) AgeA (median) = 10.5y (8.4y-14.5y) TimeS (median) = 3y 11m (1y 8m-8y 7m)	PedsQL& Cerebral Palsy module (p & c)	Child and parent-rated HRQoL was significantly lower than comparative norms. Psychosocial health status scores were lower than physical health status. CWS with hemiparesis, epilepsy and lower IQ had lower scores on HRQoL.	Neurological severity Epilepsy Lower IQ	Stroke mechanism Laterality
Steinlin et al., 2004 [35] (Switzerland)	Retrospective cross sectional tertiary centre Bern	N= 16 CWS (isch) at f/u No controls	AgeS =7.3 y (6m – 16.2)	Unstandardized questionnaire (p & c)	31% required special schooling, 19% had learning difficulties. 50% were in mainstream school. CWS had marked problems with ADLs. 44% showed behaviour problems including increased sensitivity to changes in daily routines, emotional lability, temper tantrums, aggressive outbursts, most pronounced at home. 31% showed a change in sleep, fatigued faster, needed more recreational time and more sleep. CWS had fewer friendships.	Lesion location	-

Note. Abbreviations: ADHD= attention deficit hyperactivity disorder; ADL = Activities of Daily Living; Age_A = mean age at assessment; $Age_{S=}$ mean age at stroke onset; AIS= arterial ischaemic stroke; BDI = Beck Depression Inventory; BL= bilateral lesions; b/l= baseline; BRIEF= Behaviour Rating Inventory of Executive Functioning; CPISRT = Canadian Pediatric Stroke Registry-Toronto Site; CASP = Child and Adolescent Scale of Participation; CBCL = Child Behaviour Checklist; CF-SEI=Culture Free Self Esteem Inventories; CGAS = Children's Global Assessment Scale; CH = Children's Hospital; CHP-QOL= Centre for Health Promotion's Quality of Life Profile; CHQ-Child= Child Health Questionnaire (child rated); CHQ-Parent = Child Health Questionnaire (parent rated); COPM = Canadian Occupational Performance Measure; CTP = California Test of Personality; CWS = children with stroke; DSM-IV= Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; EO= early onset of stroke; FAD = McMaster Family Assessment Device; FIM= Family Impact Module PedsQL; f/u= follow=up; FQQ = Friendship Quality Questionnaire; GOSH = Great Ormond Street Hospital for Children GOSH; haem= haemorrhagic stroke; Harter-SC = Harter Self-perception Profile for Children:

Social Competence; HSCT =Hospital for Sick Children Toronto; ICF-CY= WHO International Classification of Functioning, Disability and Health; ICV= intracranial volume; isch= ischaemic stroke; K-SADS-PL = Kiddie-Sads-Present and Lifetime Version; LO= late onset of stroke; m= months; MAS= Motor Assessment Scale; MCA= middle cerebral artery; MCD= Malformations of Cortical Development NRI = Network of Relationships Inventory; ns= non-significant findings; mRS=modified Rankin Scale; NCH = Nationwide Children's Hospital, Ohio; NPRS = Numeric Pain Rating Scale; PEDI=Pediatric Evaluation of Disability Inventory; PedsQL=Pediatric Quality of Life Inventory; PEGS= Perceived Efficacy and Goal Setting System; PSALM = Pediatric Stroke Activity Limitation Measure; PSOM = Pediatric Stroke Outcome Measure; QoL= quality of life; RCHM = Royal Children's Hospital Melbourne; RPSR= Rotterdam Pediatric Stroke Register
RPQ = Relational Provisions Questionnaire; RRQ = Pediatric Stroke Recurrence and Recovery Questionnaire; S+ADHD= participants with stroke and diagnosis of ADHD/traits; S-ADHD= participants with stroke without diagnosis of ADHD/traits; SCD= sickle cell disease; SDQ=Strengths and Difficulties Questionnaire; SES= socioeconomic status; SF36 =Short Form Health Survey; SNPSR = Swiss Neuropediatric Stroke Registry; SOPT = Stroke Outcome Project Toronto; SSQOLS = Stroke Specific Quality of Life Scale; SVT= sinovenous thrombosis; SWLS = Satisfaction With Life Scale; TAAQOL = TNO/AZL Adult Quality Of Life; TACQOL-PF= TNO-AZL Preschool children Quality of Life – parent form; TACQL-CF= TNO-AZL Preschool children Quality of Life – child form; TAPQOL= TNO-AZL Preschool children Quality of Life; TDC = Typically developing controls; TimeO= mean time since onset of illness; $Time_S$ = mean time since stroke onset; y= years; VABS = Vineland Adaptive Behavior Scale; WMSSC = Walker McConnell Scale for School and Social Competence