

A Systematic Literature Review on the economic burden of families and health care systems affected by pediatric stroke

Abstract

The main objective of this literature review was to identify existing studies on costs associated with pediatric stroke, that are incurred by affected families and health care systems.

The database of Pubmed was searched to conduct the review. Key words of the search string included: stroke, children and costs. This resulted in 454 relevant articles of which 393 were excluded due to irrelevance of the titles, abstracts and unavailability of the full text paper. The remaining 61 studies were examined by full text review and assessed with the following inclusion criteria: (a) population: children between one month and 20 years; (b) exposure: patients diagnosed with stroke as primary diagnoses; (c) outcome: costs for health care system or families must be examined; (d) study design: no article was excluded explicitly based on the study design. 50 reports were excluded for not meeting the inclusion criteria and one article was excluded for being a systematic literature review on costs of pediatric stroke care for health care systems in the United States from the year 2014. All six studies included by Ellis et al. are comprised in this review. Due to methodological heterogeneity, meta-analysis was precluded in an a priori decision. Instead, we performed a narrative synthesis of empirical evidence.

The search outcome included ten studies of whom nine reports were based on the USA and Canada and one article was restricted to Taiwan. No study could be retrieved that geographically focuses on European countries, which strengthens the need for further investigation of costs associated with pediatric stroke. Nine studies report on the gender ratio of patients affected by stroke and conclude that more boys than girls suffer a stroke. A median age of 9-10 years at stroke onset is identified by four articles. The economic burden for families within the first year after the initial stroke is examined by only one study. It was found that out-of-pocket costs were highest for the first quarter after the initial stroke and gradually declined for the remaining nine months. Lost income, transportation and uncompensated health care yielded in the highest cost items in the first three months. Lost wages declined after the first quarter and transportation costs continued to be a significant expense in the entire year. No reports could be identified on costs for home adaptions, special care or education related to pediatric stroke. Most studies focus on short term hospital care costs, only one evaluates a time horizon of five years post stroke. In general, hemorrhagic stroke is considered to be more expensive than ischemic stroke.

Introduction

Even though pediatric stroke is a rare event, it is an increasingly acknowledged cause of morbidity and mortality in children (Chiang & Cheng, 2018; Mackay et al., 2011; Numis & Fox, 2014). Childhood stroke is defined as a cerebrovascular event emerging between the age of 1 month and 18 years (Ferriero et al., 2019; Lynch et al., 2002) and typically differentiated between hemorrhagic and ischemic subtypes (Moharir & deVeber, 2014).

Hemorrhagic stroke occurs due to bleeding of a ruptured cerebral artery or as a result of bleeding into the area of an arterial ischemic stroke (AIS) (Tsze & Valente, 2011). This stroke type includes intracerebral hemorrhage (ICH) as well as subarachnoid hemorrhage (SAH) (Jordan et al., 2009; Pappachan & Kirkham, 2008; Tsze & Valente, 2011) and accounts for approximately half of all childhood strokes compared to <20% adult strokes that are hemorrhagic (Bamford et al., 1990; Broderick et al., 1993; Fullerton et al., 2003). Causes for ischemic stroke are arterial occlusion, but may also be venous occlusion of cerebral veins or sinuses (Tsze & Valente, 2011). Ischemic stroke commonly includes arterial ischemic stroke (AIS), cerebral sinovenous thrombosis (CSVT) and cortical vein thrombosis (Ferriero et al., 2019; Pappachan & Kirkham, 2008).

Estimates of hemorrhagic stroke incidence in children range from 1.1 – 5.11 per 100 000 and for pediatric ischemic stroke incidence rates rank between 1.1-7.91 per 100 000 (Agrawal et al., 2009; Barnes et al., 2004; Chiang & Cheng, 2018; Fullerton et al., 2003; Giroud et al., 1995; Lehman et al., 2018; Mallick et al., 2014; Steinlin et al., 2005; Zahuranec et al., 2005). Ranges are due to differences in definition of stroke and age range, geographical area and methods to detect cases. Stroke incidence also varies by sex and age. Boys are generally more at risk than girls due to yet unknown causes as well as infants and children younger than 5 years of age and adolescents ≥ 12 years (Chiang & Cheng, 2018; Gerstl et al., 2018; Meyer et al., 2017; Steinlin et al., 2005).

It is estimated that cerebrovascular diseases in children under the age of 15 years in Germany have amounted to about 24 million Euros only in 2020, though data on cost of care for pediatric stroke is limited (Destatis, 2023; Gardner et al., 2010; Hamilton et al., 2015; Plumb et al., 2015). Burden of economic costs are borne by health care systems and affected families and can be differentiated between direct and indirect health care costs (Jo, 2014). Those costs can be distinguished between short-term costs incurring acute costs after the initial stroke up to one year after stroke occurrence and long-term costs that amount after the first year up to 20 years after stroke onset. Direct medical costs for health care systems include expenses for diagnosis, treatment, care and rehabilitation through inpatient and outpatient services (Hodgson & Meiners, 1982) and indirect costs for health care systems concern reimbursement of costs for families, social services and other (Bettio & Plantenga, 2004). Families have to pay for unreimbursed direct medical and home care costs and costs of rehabilitation (Cha, 2018) as well as indirect non-medical costs. This entails lost wages by parents, income loss of affected families, travel and transportation costs, as well as expenses for home remodelling (Akobundu et al., 2006; Batista et al., 2021; Ekman, 2004; Luengo-Fernandez et al., 2009; Plumb et al., 2015)

The objective of this review is to investigate existing literature on costs in terms of pediatric stroke and to identify knowledge gaps related to the economic burden on the health care system, society and families of stroke in childhood.

Methods

To conduct this systematic literature review the database PubMed was searched. Relevant keywords were identified through screening of literature about pediatric stroke and economic burden. The used search string included following terms: stroke, children (child(ren), pediatric) and costs (cost(s), (so-cio)economic, financial, income, expense, burden). The results were limited to the age of children between birth and 18 years old. The search was conducted on March 18th, 2024, and yielded in 454 results.

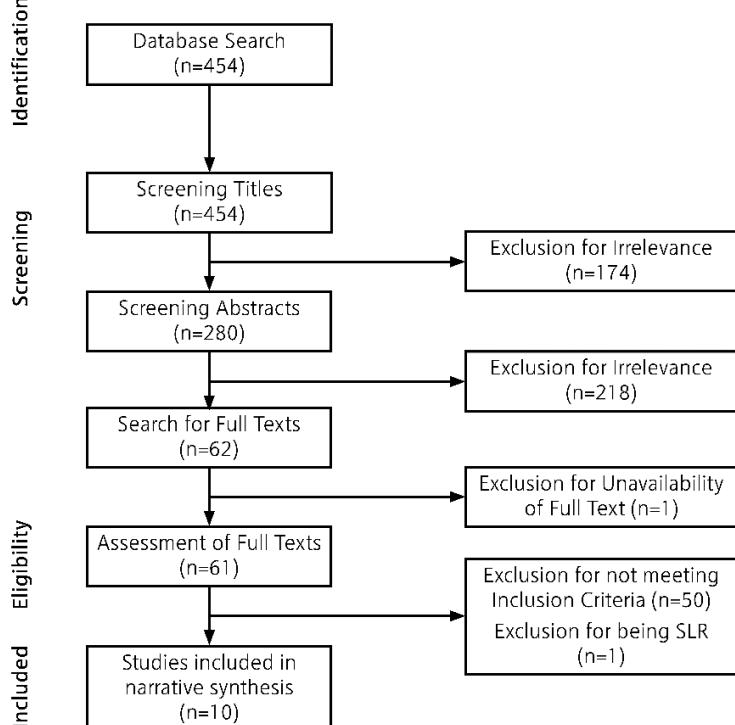
Based on the research objective 174 articles were excluded after review of the title and 218 articles according to the review of the abstract. One study was excluded due to access restrictions.

For the remaining 61 articles a full-text review was performed, and the studies were included based on the following criteria:

- 1) Population: Children, who were older than 28 days (1 month) and younger than 20 years old, were included.
- 2) Exposure: Patients diagnosed with stroke as primary diagnoses were included.
- 3) Outcome: Costs for health care system or families must be examined. This includes direct medical and indirect costs.
- 4) Study Design: No article was excluded explicitly based on the study design.

Based on the characterization of medical costs, we identified three different topics covered by the studies: a) cost for the health care system, b) cost for families and c) cost and outcome. Short-term costs are defined as costs arising until one year after the onset of the stroke. Long-term costs describe costs occurring after the first year up to 20 years after the initial stroke. Due to methodological heterogeneity meta-analysis was precluded in an a priori decision. Instead, we performed a narrative synthesis of empirical evidence.

Figure 1: Study selection process



Search String: (stroke[MeSH Terms]) AND (child* OR pediatric) AND (cost* OR *economic OR financial OR income OR expense OR burden) Filters: Child: birth-18 years

Search outcome

The search outcome resulted in eleven studies that focused on cost of care for pediatric stroke. One of them included a systematic literature review on costs of pediatric stroke care for health care systems in the United States by Ellis et al. from the year 2014, which analyzed six papers restricting to US patients and reported in English. As a systematic literature review, the paper by Ellis et al. (2014) was excluded but can be seen as a connection point and will be extended and enhanced by our Systematic Literature Review. Nine studies were based in the USA and Canada, while one was restricted to Taiwan. As none of these studies cover any European countries, this demonstrates the need for further investigation of the economic burden resulting from pediatric stroke for EU-countries. Short-term costs for direct medical expenses borne by health care systems are studied in nine articles and one article also includes direct long-term medical costs for health care systems. Only one paper focuses on direct and indirect costs for affected families within the first year after the stroke. Relations between costs for treatment of pediatric stroke and the outcome in the context of impairment are discussed in four papers (see Table 6 in the Supplementary Material).

Results

Cost for health care systems

Seven studies reported on direct medical costs for the **first hospitalization** after the pediatric stroke (Table 1). Janjua et al. (2007) report mean total costs of \$39 400 for all pediatric stroke patients and compare costs for patients who received or did not receive thrombolysis treatment. While 98.4% of patients (n=2 858) did not receive thrombolysis treatment and endured mean costs of around \$38 700, 46 children received thrombolysis treatment, which resulted in mean hospitalization costs of \$81 800 (Janjua et al., 2007). In comparison, similar total median costs for patients without complications of \$42 900 (n=114) are presented. Median total costs for patients with complications amounted to \$161 000 (n=93) (Michelson et al., 2019). Mean charges for hemorrhagic stroke (SAH & ICH) and ischemic stroke are compared and it is concluded that hemorrhagic stroke causes higher costs than ischemic stroke (Engle & Ellis, 2012; Gardner et al., 2010; Perkins et al., 2009). Similar results are provided for hemorrhagic and ischemic stroke by median hospital cost (Gardner et al., 2010; Turney et al., 2011). Furthermore, it is indicated that between the year 2000 and 2006 hospitalization costs for all types of stroke increased (Engle & Ellis, 2012). For ischemic stroke was a range of mean total costs between \$15 003 at minimum (Perkins et al., 2009) and \$81 800 at maximum (Janjua et al., 2007) and median total cost between \$16 954 (Turney et al., 2011) and \$21 317 (Gardner et al., 2010) reported. Mean total costs ranged between \$24 117 for intracerebral hemorrhagic stroke (ICH) (Perkins et al., 2009) and \$139,970 for subarachnoid hemorrhagic stroke (SAH) (Engle & Ellis, 2012). A minimum of \$24,843 (Turney et al., 2011) and a maximum of \$34 256 (Gardner et al., 2010) median hospitalization cost were measured for hemorrhagic stroke. In total mean hospitalization charges were reported between \$20 927 (Perkins et al., 2009) and \$81 869 (Gardner et al., 2010) and median charges between \$19 548 (Turney et al., 2011) and \$161 000 (Michelson et al., 2019). Chen et al. (2008) differentiates between two age groups (>10 and 10-19) and shows that within both groups hemorrhagic stroke is more expensive than ischemic stroke. In comparison to the studies conducted in the Anglo-American region, this study, focused on Taiwan, discloses hospitalization cost at a significantly lower cost level (Chen et al., 2008).

Table 1: Direct health care costs for first hospitalization of initial stroke

Study, year	Time period	Age	Total cost	Cost for Hemorrhagic Stroke		Cost for Ischemic Stroke	Comment
				SAH	ICH		
Janjua et al., 2007	2000-2003	1-17 years				\$39 400 • With thrombolysis: \$81 800 • Without thrombolysis: \$38 700	Mean cost
Perkins et al., 2009	2003	3 months - 20 years	\$20 927	\$31 653	\$24 117	\$15 003	Mean cost
Engle & Ellis, 2012	2000, 2003, 2006	0 - 17 years		2000: \$65 027 2003: \$97 985 2006: \$139 970	2000: \$47 622 2003: \$64 000 2006: \$86 680	2000: \$26 056 2003: \$40 815 2006: \$56 349	Mean cost
Gardner et al., 2010	1996-2003	1 month - 19 years	\$81 869 \$26 557	\$90 693 \$34 256		\$70 717 \$21 317	Mean cost Median cost
Turney et al., 2011	2003-2009	5 - 14 years	\$19 548	\$24 843		\$16 954	Median cost

Michelson et al., 2019	01/2013-09/2015 (MD), 01/2011-09/2013 (NY)*	< 18 years				• With complications: \$161 000 • Without complications: \$42 900	Median cost
Chen et al., 2008	1997-2003	1 month – <10 years	\$3 963 \$2 181 (1)	\$5 531 \$3 090	\$5 255 \$3 283	\$2 403 \$1 018 (2)	Mean cost Median cost
		10 – 19 years	\$3 324 \$1 739 (1)	\$4 120 \$1 860	\$5 125 \$2 570	\$1 451 \$990 (2)	Mean cost Median cost

¹ Total Costs were calculated based on weighted mean and weighted median costs for all stroke subtypes excl. OIH to ensure comparability with other studies.

² Cost for Ischemic Stroke calculated based on the weighted mean and weighted median of stroke subtypes: IS (433, 434), TIA (435) and other (436, 437).

Six articles reported hospitalization costs for longer periods of time e.g. the first month or year after stroke onset (Table 2). Lo et al.(2008) reported a median total cost of \$36 132 for the first year after stroke diagnosis. They also compared hemorrhagic stroke with ischemic stroke and concluded that the former is more expensive with a median cost of \$67 860 while the latter costs around \$31 678 (Lo et al., 2008). Similar median total costs with \$39 451 for all discharges in the study period are published by Turney et al. (2011). In comparison, substantially higher median total costs for the first year after the initial stroke are presented by another study with \$66 847 (Hamilton et al., 2015). A further study reports median charges per patient for all hospitalization encounters within 30 days of the diagnosis visit of \$51 500 for patients without any complications. Patients with complications have significantly higher median hospitalization costs with \$223 600 (Michelson et al., 2019). This study represents the most recent data with cost charges between 2013-2015 what may partly explain the comparably high costs. Gardner et al. (2010) are the only researchers that report higher mean chronic cost for the first year post stroke excluding admission costs for the initial hospitalization of ischemic stroke (\$42,404) than for hemorrhagic stroke (\$37 353). Median and mean total cost for first and recurrent hospitalization during the study period were also reported by Chen et al. (2008) for Taiwan. Median costs range between \$2 105 for children 10 – 19 years of age and \$2 706 for children older than one month and below ten years. Mean costs range between \$3 967 for children 10 – 19 years old and \$4 768 for children older than one month and below ten years (Chen et al., 2008).

Table 2: Hospital care cost for recurrent hospitalization after stroke onset

Study, year	Time period	Age	Total cost	Total cost for Hemorrhagic Stroke	Total cost for Ischemic Stroke	Comment
Lo et al., 2008 *	2001-2004	3 months – 19 years	\$36 132	\$67 860	\$31 678	Median cost for 1 st year post stroke
Gardner et al., 2010	1996-2003	1 month – 19 years		\$37 353	\$42 404	Mean chronic costs excluding acute admission costs for 1 st year post stroke
Turney et al., 2011	2003-2009	5 – 14 years	\$39 451			Median costs for all discharges (in the study period)
Hamilton et al., 2015 *	2005-2010	1 month – 18 years	\$66 847			Median costs for 1 st year post stroke
Michelson et al., 2019	01/2013-09/2015 (MD),	< 18 years	• With complications: \$223 600			Median charges per patient for all hospitalization encounters

	01/2011-09/2013 (NY)*		• Without complications: \$51 500			within 30 days of diagnosis visit
Chen et al., 2008	1997-2003	1 month - <10 years	\$4 768 \$2 706 ⁽¹⁾	\$5 968 \$3 613 ⁽²⁾	\$3 421 \$1 688 ⁽³⁾	Weighted average of mean and median cost of first and recurrent hospitalization (during the study period)
		10 – 19 years	\$3 967 \$2 105 ⁽¹⁾	\$5 488 \$2 691 ⁽²⁾	\$1 984 \$1 341 ⁽³⁾	

¹ Total Costs were calculated based on weighted mean and weighted median costs for all stroke subtypes excl. OIH to ensure comparability with other studies.

² Cost for Hemorrhagic Stroke calculated based on the weighted mean and weighted median of stroke subtypes: SAH (430) and ICH (431).

³ Cost for Ischemic Stroke calculated based on the weighted mean and weighted median of stroke subtypes: IS (433, 434), TIA (435) and other (436, 437).

* Study based on a low sample size (n < 100 patients).

Pediatric stroke patients typically receive care at different sites of medical care (Felling et al., 2023; Sporns et al., 2022). Two studies aim to differentiate the cost for pediatric stroke patients at **different locations of patient care** (Table 3). Lo et al. calculated inpatient, outpatient and emergency cost for all discharges of 39 patients in the study period 2001-2004. Inpatient cost was more than twice as high for hemorrhagic stroke (\$49 948) than for ischemic stroke (\$21 666). Similar trends can be identified for emergency cost with median costs of \$1 923 for hemorrhagic stroke and \$966 for ischemic stroke. At about the same level of around \$3 000 for both stroke types ranged outpatient costs. This leads to the result that the total costs of hemorrhagic stroke (\$67 860) are distinctly higher than ischemic stroke (\$31 678) (Lo et al., 2008). Median inpatient and outpatient costs for the first year after the arterial ischemic stroke are determined by Hamilton et al. (2015) where inpatient costs amount to \$64 515 and outpatient cost totaled up to \$1 652 for 69 pediatric patients.

Table 3: Hospital costs differentiated by medical site

Study, year	Stroke type	Inpatient cost	Outpatient cost	Emergency cost	Total cost	Comment
Lo et al., 2008 *	HS	\$49 948 (\$14 241-\$480 965)	\$3 002 (\$1 267-\$48 221)	\$1 923 (\$622-\$8 200)	\$67 860 (\$20 479-\$486 515)	Median costs for all discharges (in the study period) (min-max)
	IS	\$21 666 (\$1 891-\$176 802)	\$3 005 (\$223-\$39 942)	\$966 (\$34-\$28 312)	\$31 678 (\$3 070-\$202 862)	
Hamilton et al., 2015 *	AIS	\$64 515 (\$9 333-\$958 009)	\$1 652 (\$0-\$22 546)	-	\$66 847 (\$10 294-\$958 009)	Median costs for 1 st year post stroke (min-max)

Notes: * Study based on a low sample size (n < 100 patients).

Turney et al. focus on **contributors of hospital costs** and differentiate between the categories nursing, imaging, laboratory, pharmacy, clinical services and supply for 1667 patients identified through the Pediatric Health Information System (PHIS) between 2003-2009. The results show that there are significant cost differences between hemorrhagic and ischemic stroke in the categories of nursing, pharmacy and supplies. In general, hemorrhagic stroke contributes to higher health care costs. Charges for imaging, laboratory and clinical services remain at a similar level (Turney et al., 2011).

Care received at the intensive care unit (39%) and general medical ward (19%) accounted for most nursing costs. Most patients were treated at the emergency department with median costs of \$197 and in the intensive care unit with median costs of \$2834.

For imaging studies brain MRI, brain CT and MRI head and neck arteriography scans were the three most frequently ordered examinations. About 72% of pediatric patients received brain MRI studies, which accounts for a median cost of about \$1 174 per study. Brain CT studies were ordered for 70% of children with a median cost of \$706 per study and MRI head and neck arteriography were performed on 60% of patients, which costs around \$908 per examination (Turney et al., 2011).

The variable **Length of Stay (LOS)** describes how many days patients spent in hospital care. Seven studies provide information in this regard (Table 4). For hemorrhagic stroke a median LOS between 7-8.5 days and a mean hospital stay of 12 days is reported (Gardner et al., 2010; Lo et al., 2008). Two studies compare LOS between subarachnoid hemorrhagic stroke (SAH) and intracerebral hemorrhagic stroke (ICH) and conclude that the former results on average in longer hospital stays (11.2-14.2 days) than the latter (9.6-11.0 days) (Engle & Ellis, 2012; Perkins et al., 2009). A median of 5-7.6 days in hospital is reported by five out of seven data details. For patients receiving thrombolysis (15.3 days) treatment and for patients with complications (19 days) higher median LOS are indicated (Janjua et al., 2007; Michelson et al., 2019). On average a hospital stay after ischemic stroke lasts between 6.6-7.2 days (Engle & Ellis, 2012; Perkins et al., 2009), only one study reports a longer mean LOS of 16 days (Gardner et al., 2010).

Table 4: Length of Stay (LOS) in hospital

Study, year	LOS results	Hemorrhagic Stroke		Ischemic Stroke	Comment
		Total	SAH	ICH	
Janjua et al., 2007				7.6 days \pm 12.1 <ul style="list-style-type: none">Receiving thrombolysis: 15.3 days \pm 12.4Not receiving thrombolysis: 7.4 days \pm 12.1	Median LOS \pm SD
Michelson et al., 2019				<ul style="list-style-type: none">With complications: 19 days (IQR: 12-33)Without complications: 5 days (IQR: 3-9)	Median LOS
Lo et al., 2008 *		8.5 days		5 days	Median LOS
Turney et al., 2011	5 days 10 days				Median LOS Mean LOS
Gardner et al., 2010		7 days (IQR: 2-16) 12 days		6 days (IQR 2-17) 16 days	Median LOS Mean LOS
Perkins et al., 2009	8.3 days	11.2 days	9.6 days	6.6 days	Mean LOS
Engle & Ellis, 2012		2000: 11.5 days 2003: 13.2 days 2006: 14.2 days	2000: 10.4 days 2003: 11.0 days 2006: 10.9 days	2000: 6.9 days 2003: 7.2 days 2006: 6.9 days	Mean LOS
Note: Chen et al. (2018) report an average LOS among age groups and stroke subtypes for patients with no recurrent admission of approximately 11-13 days. * Study based on a low sample size (n < 100 patients).					

Gardner et al. (2010) are the only researchers investigating **long-term costs for health care systems**. They focus on chronic costs that include all inpatient and outpatient costs that occurred after the first hospitalization for the first five years after stroke onset. The highest mean chronic costs were recorded one year after the initial hospitalization and subsequently declined in the following years. It is suggested that most of the long-term medical costs are due to a subgroup of patients with severe cases of stroke and continuously high treatment costs. Five-year-total chronic costs adjusted amount to \$66 760 (median) and \$10 835 (mean) for ischemic stroke and to \$58 874 (median) and \$20 656 (mean) for hemorrhagic stroke (Gardner et al., 2010).

The synthesis of the studies indicates that most researchers focus on short-term direct medical costs for the health care system. This includes acute stroke admission costs, expenses for recurrent hospitalizations, breakdown of locations where costs have been incurred, contributors to hospital cost and length of hospital stay (LOS) (Chen et al., 2008; Engle & Ellis, 2012; Gardner et al., 2010; Hamilton et al., 2015; Janjua et al., 2007; Lo et al., 2008; Michelson et al., 2019; Perkins et al., 2009; Turney et al., 2011). Only one study addresses long-term direct medical costs borne by the health care system (Gardner et al., 2010). There is no data on care level payments or other indirect health care system costs like reimbursement for families or social services.

Costs for families

Although many studies have concluded that pediatric stroke bears a tremendous financial burden for families (Chiang & Cheng, 2018; Meyer et al., 2017; Numis & Fox, 2014), only one study is concerned with **direct and indirect medical costs for families** resulting from the 1st year post stroke (Table 5). 22 families from the USA and Canada participated in the study and reported cost information in 3-month-intervals based on a standard questionnaire. Direct medical costs are reported in the categories health care, home care and nonprescribed treatment and indirect medical costs are noted for lost income, transportation and lodging costs. Overall, out-of-pocket costs were the highest for the first quarter after the initial stroke and gradually declined for the remaining nine months. Lost income, transportation and uncompensated health care yielded in the highest cost items in the first three months. Lost wages declined after the first quarter and transportation costs continued to be a significant expense in the entire year. In total a median expense of \$4 354 had to be covered by families affected by pediatric stroke (mean: \$6 619) (Plumb et al., 2015).

Table 5: Out-of-pocket costs for families, source: own presentation after Plumb et al. 2015 *

	Lost income	Transportation	Health care	Home care	Lodging	Nonprescribed treatment	Total
Quarter 1	\$2 398; \$474 (\$0-20 480)	\$462; \$250 (\$0-1 704)	\$642; \$16 (\$0-5 100)	\$125; \$0 (\$0-2500)	\$349; \$0 (\$0-3 687)	\$22; \$0 (\$0-250)	\$3 997; \$2 297 (\$0-22 100)
Quarter 2	\$726; \$0 (\$0-5 149)	\$160; \$115 (\$0-630)	\$172; \$0 (\$0-1 250)	\$83; \$0 (\$0-1 250)	\$26; \$0 (\$0-250)	\$83; \$0 (\$0-1 250)	\$1 251; \$509 (\$0-7 369)
Quarter 3	\$75; \$0 (\$0-625)	\$122; \$89 (\$0-307)	\$287; \$115 (\$0-1 250)	\$0; \$0 (\$0-0)	\$14; \$0 (\$0-200)	\$34; \$0 (\$0-250)	\$534; \$456 (\$0-1 557)
Quarter 4	\$434; \$10 (\$0-6 293)	\$425; \$250 (\$0-4 080)	\$518; \$0 (\$0-5 940)	\$69; \$0 (\$0-1 250)	\$64; \$0 (\$0-1 152)	\$28; \$0 (\$0-250)	\$1 538; \$436 (\$0-10 373)
Total	\$3 395; \$883 (\$0-20 732)	\$1 018; \$647 (\$0-4 768)	\$1 390; \$250 (\$0-8 560)	\$250; \$0 (\$0-3 750)	\$431; \$0 (\$0-4 839)	\$135; \$0 (\$0-1 250)	\$6 619; \$4 354 (\$0-28 666)
... Mean, median (range)							
* Study based on a low sample size (n < 100 patients).							

Overall, there is very little data on the economic burden for families affected by pediatric stroke. One study illustrates direct and indirect costs that affected families encounter within the first year after the incident (Plumb et al., 2015). No studies are available on long-term financial costs for families, which concern e.g. costs for long-term care and rehabilitation, forgone income of parents and children, special education or necessary home adaptations.

Costs & Outcomes

The relationship between costs of stroke care and clinical outcomes are assessed by Lo et al. (2008) for families of 19 patients who were discharged at the Nationwide Children's Hospital of Columbus, Ohio between 2001-2004. The Children's Hospital's cost accounting system was used to identify costs for the initial stroke and for the year after the incident. Stroke outcome data was obtained through telephone

interviews with caregivers after 2-5 years of stroke onset. A modified version of the Pediatric Stroke Outcome Measure (PSOM) was applied for the evaluation of neurological impairments and for the assessment of functional outcomes the PedsQL was used. Cost of care positively correlated with the infarct ratio (ratio of cerebral infarct volume to the brain volume) for the assessed subjects ($r = 0.60$, $p = 0.01$). The analysis suggested that greater costs for stroke care correlated with worse neurological impairment measured by the PSOM ($r = 0.62$, $p < 0.01$) and it was determined that higher costs correlated with a poorer level of social ($r = -0.79$, $p < 0.01$) and physical function ($r = -0.42$, $p = 0.08$) identified by PedsQL (Lo et al., 2008).

Another group of pediatric stroke researchers (Hamilton et al 2015) calculated inpatient and outpatient charges for stroke care for the first year after the stroke incident using the same cost accounting system as Lo et al (2008). They studied over 40 families affected by pediatric stroke diagnosed between 2005-2010 at least 1 year after the incident via telephone interviews. To measure neurological deficits and quality of life the Pediatric Recurrence and Recovery Questionnaire (PRRQ) and the Pediatric Quality of Life Inventory were used. Families reported mild neurological impairment for most children (median PRRQ = 0.5; range: 0-11, $n = 46$) and a median total quality of life score of 79 (range = 37-100, $n = 41$). Hamilton et al. (2015) observed correlations between higher total costs and lower neurological functions (coefficient = 0.494, $p < 0.001$). Higher cost moderately correlated with poorer total quality of life mostly due to poorer social quality of life. These findings confirm similar results from Lo et al. (2008). Severity of the initial stroke measured with the Pediatric NIH Stroke Scale showed no correlations with cost (coefficient = 0.032, $n=42$) (Hamilton et al., 2015).

5-year total direct costs were measured by Gardner et al.(2010). This includes the sum of acute hospitalization cost as well as all inpatient and outpatient cost that arose after the initial admission estimated for the first five years after the incident. For children with neurological impairments at discharge ($n = 67$: mean \$71,434; median \$25,551; IQR \$5,807-\$89,239) the cost was higher than compared to those with inconspicuous neurological examination results at discharge ($n = 60$: mean \$52,604; median \$10,579; IQR \$2,444 -\$36,023; $p = 0.03$) (Gardner et al., 2010).

Plumb et al. (2015) focused on out-of-pocket expenses paid by 22 families for the 1st year post stroke and concluded that total indirect costs did not correlate with age of stroke onset, initial stroke severity assessed by the Pediatric NIH Stroke scale, or severity of neurological deficits after one year measured by the Pediatric Stroke Outcome Measure (PSOM). The missing correlation implies that families from different income groups might face similar out-of-pocket costs concerning neurological diseases developed by their children requiring chronic care and rehabilitation (Plumb et al., 2015).

Summary and conclusions

Overall, ten studies were identified that focus on stroke in childhood years. Pediatric stroke is mainly studied in Northern Amerika, only one study was detected beyond this geographical region in Taiwan. No studies were available that were geographically limited to Europe. Most studies reported direct medical costs for health care systems within the first year after the pediatric stroke incident. Higher initial hospital stay costs incurred for hemorrhagic stroke than for ischemic stroke. Median total costs for the initial hospitalization lay between \$24,843 and \$34 256 for hemorrhagic stroke and between \$16 954 and \$21 317 for ischemic stroke in Northern America (Gardner et al., 2010; Turney et al., 2011). For Taiwan costs levels were significantly lower (Chen et al., 2008). This finding correlates with the length of hospital stay (LOS), where studies concluded that for hemorrhagic stroke more days were spent hospitalized than ischemic stroke. In general, the median LOS lasted 5-15.3 days (Janjua et al., 2007; Turney et al., 2011). Similar results can be observed by the differentiation of the categories nursing, pharmacy and supplies that contribute to hospital cost, where hemorrhagic stroke was more expensive than ischemic stroke. Charges for imaging, laboratory and clinical services remained at a comparable level. Most nursing costs were recorded for charges in the intensive care unit (39%) and general medical ward (19%). The majority of patients received imaging procedures using brain MRI (72%) and brain CT (70%) (Turney et al., 2011). Only one study is concerned with long-term costs for health care systems. Gardner et al. present data

for the first 5 years after stroke onset and conclude that the highest costs arise within the 1st year post stroke and decline in the following years subsequently. It is suggested that long-term medical charges result from a subgroup of severe pediatric stroke cases, which receive treatments with continuously high costs (Gardner et al., 2010). While most studies report on costs for health care systems, data on direct or indirect financial impacts for families due to pediatric stroke remains mostly unavailable. Only one study identified out-of-pocket costs for the first year after the acute stroke with median expenses of \$4 354 per family (Plumb et al., 2015).

Some studies attempted to assess correlations between costs and neurological outcome. Two researcher groups concluded that higher costs for stroke care correlated with greater neurological deficits and determined that correlations between greater total costs and poorer total quality of life due to limited social and physical functions after at least one year of stroke onset (Hamilton et al., 2015; Lo et al., 2008). It was also observed that patients with neurological deficits at discharge had higher costs than compared to those with normal neurological functions at discharge (Gardner et al., 2010). For out-of-pocket costs covered by parents a lack of correlation was determined between costs of care and age of stroke onset, initial stroke severity and neurological impairments after one year, which implies that families from different financial groups face a similar economic burden (Plumb et al., 2015).

There are some limitations to this systematic literature review. This includes that the sample size of many studies was small and heterogeneous and that the ICD-9 coding method might have varied in different hospital settings, which could lead to missed cases. Another restriction might be that search strategies underestimate the true stroke cost due to a skew towards less complicated cases. As most studies date back to the 1990s and 2010s and the latest cost data concerns the year 2015 it is likely that the inflation rate has increased since then and therefore present an underestimate of stroke care costs.

Evidence on the financial burden of pediatric stroke shows that there is a lack of information regarding short-term and long-term indirect costs for health care systems including care level payments or other social services. In addition, very little data is available for short-term costs for families affected by pediatric stroke. Further research investigating long-term costs in terms of post-stroke care and rehabilitation as well as indirect costs like foregone income for parents, special education, home adaptations or loss of income for affected children is needed.

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Supplementary Material

Table 6: Overview of research studies focusing on financial burden of pediatric stroke

Study, year	Sample size and database	Stroke subtypes with ICD-9-CM coding	Age cohort	Time period	Country	Comment	Method
Janjua et al., 2007	2904 patients from the Nationwide Inpatient Sample	IS: 433, 434, 436, 437.0, 437.1, 437.4, 437.5, 437.7, 437.8, 437.9	1 – 17 years	2000-2003	USA	Costs were adjusted for inflation to 2005 USD.	Comparative cost analysis
Chen et al., 2008	1979 patients from the National Health Insurance	SAH: 430 ICH: 431 OIH: 432 IS: 433, 434 TIA: 435 others: 436, 437	1 month – <10 years 10 – 19 years	1997-2003	Taiwan	Costs were expressed in USD (1 USD ≈ 33 TWD).	Comparative cost analysis
Lo et al., 2008 *	39 patients from one children's Hospital's cost accounting system	HS, IS (ICD – 9 coding: 430-438, 348 & screening of radiology reports and actual brain scans)	3 months – 19 years	2001-2004	USA		Comparative cost analysis
Perkins et al., 2009	1070 actual discharges which equals 2224 patients after statistical weighting from the Kids' Inpatient Database	SAH: 430 ICH: 431 IS: 433.xx, 434.xx, 436.xx, 437.4-437.6	3 months – 20 years	2003	USA	Costs are reported in 2003 USD.	Comparative cost analysis

Gardner et al., 2010	185 patients from the Kaiser Pediatric Stroke Study (KPSS)	HS, IS Based on documented clinical presentation and CT & MRI scans	1 month – 19 years	1996-2003	USA	Costs were adjusted for inflation to 2003 USD.	Comparative cost analysis
Turney et al., 2011	1667 patients in the Pediatric Health Information System (PHIS)	HS: 430, 431 IS: 433.xx, 434.xx, 964	5 – 14 years	2003-2009	USA,	Costs were adjusted to 2009 USD.	Comparative cost analysis
Engle & Ellis., 2012	6857 patients from the Kid's Inpatient Database	SAH: 430 ICH: 431 IS: 433-437	0 – 17 years	2000, 2003, 2006	USA		Descriptive cost analysis
Hamilton et al., 2015 *	69 patients from 1 tertiary care pediatric hospital + Nationwide Children's Hospital cost accounting system	AIS: 433.xx, 434.xx, 436, 997.02, 437.4, 437.5, 437.6 CSVT: 325	1 month – 18 years	2005-2010	USA	Costs were adjusted to 2010 USD.	Comparative cost analysis
Plumb et al., 2015 *	22 patients from four tertiary care centers	IS	1.9 – 17.9 years	2008-2009	USA, Canada	Canadian dollars were converted to US dollars using the average exchange rates in 2008 through 2010.	Comparative cost analysis
Michelson et al., 2019	226 patients from the Healthcare Cost and Utilization Project Statewide Databases of Maryland and New York	Stroke: 433.x1, 434.x1, 437.1 AND hospitalized or died	0 – 18 years	01/2013-09/2015 (Maryland), 01/11-09/13 (New York) * excluding data from Oct-Dec	USA		Descriptive cost analysis

* Study based on a low sample size (n < 100 patients).

Abbreviations:

AIS	Arterial ischemic stroke
CSVT	Sinovenous thrombosis
HS	Hemorrhagic stroke
ICH	Intracerebral hemorrhagic stroke

IS	Ischemic stroke
OIH	Other intracranial hemorrhagic stroke
others	Other cerebrovascular disease
SAH	Subarachnoid hemorrhagic stroke
TIA	Transient cerebral ischemia

Table 7: Overview of categories of reported financial burden

Study, year	Short-term cost for families			Long-term cost for families		Short-term cost for healthcare system							Long term cost for healthcare system		Cost & Outcome	
	direct medical		indirect medical	direct medical	indirect medical	direct medical					indirect medical	direct medical	indirect medical	direct medical	indirect medical	
	Hospital/physician cost	Rehabilitation	Travel time, babysitter cost, ...			1 st hospitalization	Recurrent/overall hospitalization (up to 1y)	Sources of hospital cost	Contributors of hospital cost	LOS		Hospital/physician cost				
Janjua et al., 2007						x				x						
Chen et al., 2008						x	x									
Lo et al., 2008 *							x	x		x						x
Perkins et al., 2009						x				x						
Gardner et al., 2010						x	x			x		x				x
Turney et al., 2011						x	x		x	x						
Engle & Ellis, 2012						x				x						
Hamilton et al., 2015 *	x	x	x				x	x								x
Plumb et al., 2015 *	x	x	x													x
Michelson et al., 2019						x	x			x						
* Study based on a low sample size (n < 100 patients).																