The European Journal of Health Economics (2019) 20:107–134
https://doi.org/10.1007/s10198-018-0984-0

ORIGINAL PAPER

Economic burden of stroke: a systematic review on post-stroke care

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Received: 22 September 2017 / Accepted: 3 May 2018 / Published online: 16 June 2018

Abstract

Objectives Stroke is a leading cause for disability and morbidity associated with increased economic burden due to treatment and post-stroke care (PSC). The aim of our study is to provide information on resource consumption for PSC, to identify relevant cost drivers, and to discuss potential information gaps.

Methods A systematic literature review on economic studies reporting PSC-associated data was performed in PubMed/MEDLINE, Scopus/Elsevier and Cochrane databases, Google Scholar and gray literature ranging from January 2000 to August 2016. Results for post-stroke interventions (treatment and care) were systematically extracted and summarized in evidence tables reporting study characteristics and economic outcomes. Economic results were converted to 2015 US Dollars, and the total cost of PSC per patient month (PM) was calculated.

Results We included 42 studies. Overall PSC costs (inpatient/outpatient) were highest in the USA ($4850/PM) and lowest in Australia ($752/PM). Studies assessing only outpatient care reported the highest cost in the United Kingdom ($883/PM), and the lowest in Malaysia ($192/PM). Fifteen different segments of specific services utilization were described, in which rehabilitation and nursing care were identified as the major contributors.

Conclusion The highest PSC costs were observed in the USA, with rehabilitation services being the main cost driver. Due to diversity in reporting, it was not possible to conduct a detailed cost analysis addressing different segments of services. Further approaches should benefit from the advantages of administrative and claims data, focusing on inpatient/outpatient PSC cost and its predictors, assuring appropriate resource allocation.

Keywords Stroke · Cerebrovascular accident · Post-stroke care · Rehabilitation · Economic evaluation · Cost

JEL Classification I19

Abbreviations

TIA	Transient ischemic attacks
WHO	World Health Organization
PPP	Purchasing power parity

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s10198-018-0984-0) contains supplementary material, which is available to authorized users.

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CPI	Consumer Price Index
CHEERS	Consolidated Health Economic Evaluation Reporting Standards
SRF	Skilled nursing facilities
IRF	Inpatient rehabilitation facilities
ESUS	Extended stroke unit services
OSUS	Ordinary stroke unit services
PSC	Post-stroke care
PM	Patient month
GDP	Gross domestic product
AUD	Australian Dollar
CAD	Canadian Dollar
DM	Deutsche Mark
SEK	Swedish Krona
CHF	Swiss Franc
£	UK Pound
$, USD	US Dollar

Introduction

Stroke is one of the leading causes for disability and morbidity in the Western world [1]. According to the World Health Organization (WHO), stroke is the second leading cause of death after heart disease, accounting for almost seven million deaths in 2012 worldwide, which represents 11.1% of total deaths [2, 3]. In Europe, more than one million of new stroke cases occur each year, and currently six million of stroke survivors are estimated to be alive [4]. In 27 European Union (EU) countries, the annual costs for stroke treatment and care are estimated to be 27 billion euros, with 18.5 billion accounting for direct medical costs and 8.5 billion for indirect costs (e.g., loss of productivity). An additional 11.1 billion euros are estimated to account for informal care. In the USA, a total of $65.5 billion was spent on stroke in 2008, with 67% for direct and 33% for indirect costs [5]. The American Heart Association and The American Stroke Association projected for the years 2012 to 2030, that the total direct medical cost for stroke will triple and reach up to $184.1 billion [6].

Depending on the severity of the stroke and its consequences, patients may need constant care for the remaining lifetime. Therefore, the clinical and economic burden of the disease contributes to significant public health relevance. As reported by the National Stroke Association, 40% of all patients acquire moderate to severe impairments and need special care, while 10% require constant care in long-term care facilities [7]. For the years 2001–2005, the average cost for medication and for outpatient stroke rehabilitation services in the first year after discharge were $11,145 per patient with $7318 spent for rehabilitation services and $3376 for medication [3].

Most studies focused on cost of acute care or comparison of two or more rehabilitation programs [8–11], but only a limited number of studies evaluated costs of post-stroke care [12]. Using different types of rehabilitation services or post-stroke care programs offered in the same setting but with different care approaches, the benefits for the patient can be maximized while costs are minimized [13–15]. As the cost of post-stroke care imposes a considerable economic burden on the society, the identification of the major cost drivers in published studies supports an informed policy making process and promotes gaining knowledge on how to guide decisions in the organization of post-stroke care programs. Therefore, our systematic literature review aims to fill the gap by providing information on the costs of post-stroke care, identifying relevant cost drivers and discussing potential information gaps.

Methods

We conducted a systematic review of partial and full economic studies evaluating post-stroke treatment and care. The included studies comprised stroke patients who participated in post-stroke care programs, and the observed outcome was cost of post-stroke care. As our review primarily aims at describing the total cost elicited by post-stroke care, we did not cover any potential comparators to the applied interventions.

Framework

A systematic literature search was performed in Medline (PubMed), Scopus (Elsevier) and Cochrane library databases (data range from January 1, 2000 to August 1, 2016), with the algorithm presented in Online Resource 1. To ensure completeness of the search, we also searched the reference lists of included studies for additional relevant citations. We considered the need to assess gray literature, including searches via Google Scholar, which did not yield any citation beyond the traditional search. We did not apply any language filters in this search. This study is registered in PROSPERO (International prospective register of systematic reviews) under number CRD42016043521.

We included studies that were partial or full economic evaluations. Partial economic evaluation is defined as cost description (reporting only on the cost of a program, without a comparator, e.g., cost of illness, burden of illness) and cost analysis, as a central feature of all economic evaluations, where only the cost of alternatives are evaluated [16]. A full economic evaluation is defined as the comparative analysis of cost and clinical consequences of program alternatives (including cost-effectiveness, cost-minimization, cost-utility and cost-benefit analysis) [16]. All studies not reporting the

costs of post-stroke care were excluded. Systematic reviews, qualitative studies, dissertations, case reports and conference abstracts were not included. Further exclusion criteria were: studies exclusively reporting on diseases other than stroke; enrolling only patients younger than 18 years; focusing only on stroke prevention, on acute stroke or transient ischemic attack (TIA) treatment, or reporting only inpatient post-stroke care costs; studies published in non-Latin languages.

The titles and abstracts screening was performed by two independent assessors (SR, HB), according to the predetermined selection criteria. Full-text articles of selected studies were reviewed and included if they met the inclusion eligibility criteria.

Data extraction and synthesis

Two authors (SR, HB) independently extracted relevant data regarding the following study criteria: first author, publication year, country, currency, study design, index year, number of patients, stroke type, follow-up period and costing perspective ("Appendix 1", Tables 2, 3). Extracted data regarding the cost of post-stroke care program were costs of medical interventions, physiotherapy, occupational and speech therapy, nursing care, primary care visits, readmissions to hospital and emergency care during rehabilitation period, as well as medication, community services, transportation, meals on wheels, assistive devices and other health care related costs. Disagreements were resolved by consensus, and when this was not possible, by a third author (HG). Costs were extracted only for post-stroke care resource utilization. In case of reports on cost of two or more rehabilitation programs, each program was considered separately, as specific for the country where the study was performed.

At first instance, cost figures for post-stroke care were extracted. If acute care was included, this share of costs was subtracted from total costs. The remaining cost share was considered as cost of post-stroke care. To standardize results of included studies, all costs were transformed to 2015 US Dollars using purchasing power parity rates (PPP) [17] and the consumer price index (CPI) [18]. For comparison reasons, we calculated and report the cost of post-stroke care per patient month (PM), as studies reported on different follow-up periods. All calculations were performed by two authors independently (SR, HB). An example of cost calculation is provided in the Online Resource 2.

The mean costs of overall post-stroke care were calculated as the mean costs of all programs and visualized as boxplots. The mean costs of post-stroke care per country were calculated for each country independently, weighted by the number of patients for the respective country and visualized as bar charts ("naïve" analysis).

The Kolmogorov–Smirnov test was performed to check for normality of data, and the unpaired *t* test was used to determine if mean cost of post-stroke care differed between the short (up to 6 months) and long follow-up period (more than 6 months).

Gross domestic product (GDP) per capita for countries included in this review was derived from the World Bank data [19] in 2015 US dollars, and compared to weighted average cost of post-stroke care of each country. Acute stroke care supply and practice patterns of stroke care in each country were extracted or from the included studies or from web sites of state ministries (regarding the availability of stroke units) or from the OECD database (regarding the number of rehabilitation beds) [20]. Duration of acute care (reported in the study as length of stay in stroke unit/acute care) was derived directly from the publications included in this review. We used the Spearman`s rank correlation coefficient (rho) to calculate correlation. A meta-regression was performed based on publications that reported sufficient data to investigate heterogeneity and its reasons across the studies, using study characteristics (stroke type, costing perspective, type of health care funding, data source, presence of stroke units, follow-up period, period of data collection, detailed cost specification and duration of acute hospitalization) and post-stroke care costs. An α level of 0.05 was used to determine statistical significance explaining heterogeneity. All calculations and statistical analyses were performed in the software package STATA (Release 15, 2017. College Station, TX: StataCorp LLC) and SPSS (Version 20.0. Released 2011, Armonk, NY: IBM Corp.).

Assessment of methodological and reporting quality of included publications

The methodological quality of studies was evaluated with a checklist for assessing economic evaluations [21], as this is the most appropriate approach to ensure good quality for economic evaluations.

The Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist [22] was used for evaluating the quality of reporting. A quality score was generated, awarding one point per each item of the checklist if this item has been reported, and zero if not, with maximum of 27 points. Three authors independently (SR, HB, JV) evaluated methodological quality of studies and quality of reporting in the studies, disagreements were resolved through consensus.

Results

Search results and description of studies

The systematic search yielded 1243 references in Medline via PubMed, 1602 in Cochrane databases and 334 in Scopus (Elsevier) database (August 1, 2016). After duplicates

removal, a total of 2683 articles were selected for titles and abstracts screening. In the first step, 2607 papers were excluded: 960 due to publication type, 680 addressed diseases other than stroke, 647 addressed irrelevant intervention, 86 had outcomes other than cost of post-stroke care, 145 focused on acute stroke treatment, 20 studies were published in non-Latin languages and 69 studies evaluated a non-relevant population for the present analysis, that is, patients under 18 years old, caregivers, etc. Thereby, 76 publications were selected for full-text screening, of which 37 were excluded once they reported non-relevant outcome. A list of excluded studies, with the reason for exclusion is available in the Online Resource 3. Furthermore, three studies were selected by manual review of reference lists of all included studies. Finally, our systematic assessment of studies comprised 42 publications, see Fig. 1, flow chart of Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) [23].

Published articles reflect the situation from United Kingdom ($n=7$), Sweden ($n=7$), Australia ($n=6$), Germany ($n=4$), USA ($n=4$), Italy ($n=3$), France ($n=2$), The Netherlands ($n=2$), Cuba ($n=1$), Malaysia ($n=1$), Canada ($n=1$), Denmark ($n=1$) Norway ($n=1$) and Switzerland ($n=1$), while one was multi-centric. All mentioned countries had public health funding, while the Malaysian health system is funded through both public and private sources [24]. Fifteen of the 42 studies reported cost about post-stroke care of ischemic and hemorrhagic stroke patients together, while five addressed only ischemic and two only hemorrhagic. Twenty studies did not provide information on type of stroke (Table 1).

The societal perspective was adopted in 17 out of 42 studies (40%). However, data on indirect costs (productivity losses related to illness or death as described by Luce et al. [25]) were not extracted since they were not part of our analysis. The follow-up period varied between 3 months and 10 years. Most of the included studies applied a follow-up period of 12 months (25 of 42 studies), while 12 adopted a follow-up of up to 6 months, and five studies reported cost on periods up to 10 years (Table 1). We observed a statistically significant difference in cost per patient month for studies that reported on shorter follow-up periods (up to 6 months) compared to longer ones ($p=0.02$). Studies that provided cost for up to 6 months had higher values of cost per patient months than those reporting on 12 or more months of follow-up (mean difference of $968).

The costs in the reviewed publications were mostly obtained through hospital records, insurance administrative data, local or national registers and questionnaires. Detailed report on post-stroke care costs were presented in 40 studies, in form of inpatient and outpatient rehabilitation (including medical interventions, physiotherapy, occupational and speech therapy), nursing care (in nursing homes, specialized rehabilitation facilities or at home), primary care visits (including general physicians, specialist consultations), readmissions to hospital and emergency care during rehabilitation period, and other costs as medication, community services, transportation, meals on wheels, assistive devices and other health care related costs. General rehabilitation costs, without specification of type of care provided, were observed in two studies.

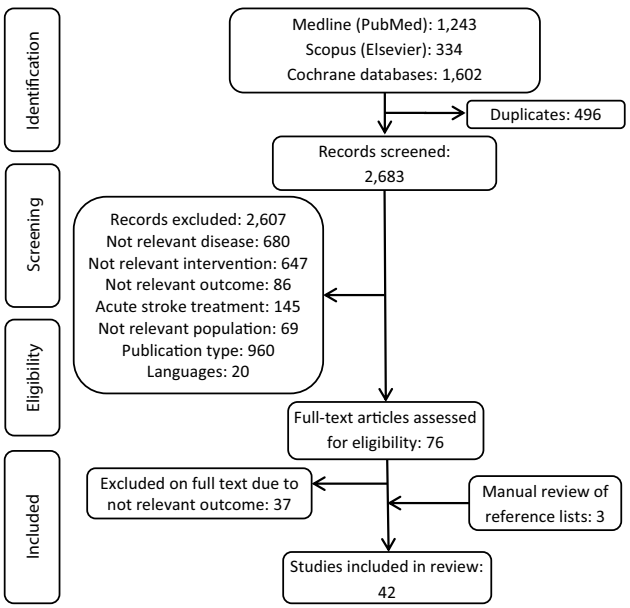

Fig. 1 PRISMA flow chart of studies' identification and selection process

Quality assessment of studies

Methodological quality of studies was evaluated with the Drummond checklist [21], and for applicable criteria 30 studies had more than 17 score points (50% of all questions), including three criteria fulfilled by all and five criteria by more than 40 studies. Within this checklist, 83% of studies achieved yes scores regarding the study design, 85% regarding the data collection and 69% of yes scores in analysis and interpretation of results (Table 5 in Appendix 3 and Online Resource 4).

Reporting quality in studies was assessed with the CHEERS checklist [22]. All studies provided sufficient information on nine items of checklist, while on five items information was not available in more than half of included studies (Table 6 in Appendix 3 and Online Resource 4).

Table 1 Characteristics of the 42 studies included in the systematic review

Study characteristics	No. of studies	References
Countries		
Australia	6	[30, 52, 62–65]
France	2	[53, 66]
Germany	4	[51, 67–69]
Italy	3	[70–72]
The Netherlands	2	[33, 73]
Sweden	7	[27, 43, 49, 50, 74–76]
UK	7	[13–15, 29, 31, 47, 77]
USA	4	[26, 28, 32, 34]
Canada, Cuba, Denmark, Malaysia, Norway and Switzerland (one study from each country)	6	[24, 35, 55, 78–80]
Multi-centric (122 sites in 22 countries)	1	[54]
Stroke type		
Ischemic stroke	5	[32, 51, 55, 66, 67]
Hemorrhagic stroke	2	[54, 69]
Ischemic and hemorrhagic stroke	15	[24, 28–30, 34, 50, 52, 63–65, 68, 71, 72, 74, 75]
Not reported	20	[13–15, 26, 27, 31, 33, 35, 43, 47, 49, 53, 62, 70, 73, 76–80]
Health care system model		
The Beveridge model	7	UK, Sweden, Australia, Italy, Cuba, Denmark and Norway.
The Bismarck model	4	Germany, France, The Netherlands and Switzerland.
The National Health Insurance model	2	USA Medicare and Canada
The Out-of-Pocket model	1	Malaysia
Costing perspective		
Health care	8	[28, 72, 74–78, 80]
Societal	17	[15, 27, 29, 30, 33, 43, 50, 52, 53, 62–66, 69, 71, 73]
Health care and societal	5	[13, 14, 47, 49, 70]
Insurance	7	[26, 32, 34, 35, 51, 54, 67]
Not reported	5	[31, 45, 58, 60, 61]
Data source		
Administrative database	9	[29, 43, 44, 48, 52–55, 57]
Hospital records	13	[21, 25, 31, 34, 38–42, 45, 49, 51, 62]
Questionnaires	7	[22–24, 35, 36, 46, 47]
Hospital records and questionnaires	13	[26–28, 30, 32, 33, 37, 50, 56, 58–61]
Presence of stroke units		
Presence of stroke unit reported in study	21	[28, 31–34, 36–41, 44–46, 48, 50, 52, 56–58, 62]
Stroke unit available in country	19	[21–27, 29, 30, 35, 42, 43, 49, 51, 53–55, 59, 61]
Stroke unit not available	2	[47, 60]
Follow-up period		
Up to 6 months	12	[13, 14, 24, 26, 31, 33, 54, 62, 71, 79, 80]
Up to 12 months	25	[15, 27–30, 32, 34, 35, 43, 47, 55, 63–70, 72–76, 78]
More than 12 months	5	[49–53]
Care setting		
Inpatient and outpatient	31	[13, 26–30, 33, 35, 43, 47, 50–54, 62–68, 70–75, 78–80]
Outpatient	11	[14, 15, 24, 31, 32, 34, 49, 55, 69, 76, 77]
Data collection		
Before year 2000	19	[29, 33, 43, 47, 53, 55, 62, 64–66, 68, 69, 71, 74–78, 80]
After year 2000	23	[13–15, 24, 26–28, 30–32, 34, 35, 49–52, 54, 63, 67, 70, 72, 73, 79]
Detailed cost specification		
Detailed cost	40	
General cost only	2	[26, 79]

Cost of post-stroke care

We observed overall mean cost of post-stroke care, mean and weighted average costs regarding country of care provided (combining all studies reporting on respective country), length of follow-up period, inpatient/outpatient or outpatient-only reporting, and costing of different segments of post-stroke care.

Mean cost per patient month of post-stroke care for all programs ($n=60$) reported in studies with inpatient and outpatient care setting was \$1515 (SD \$1396, median \$1192), and \$820 (SD \$657, median \$556) for programs ($n=17$) in studies reporting only on outpatient care setting (Fig. 2).

The most expensive inpatient/outpatient post-stroke care was reported in the USA, with mean cost of \$4644 per patient month, followed by Denmark (\$3026), The Netherlands (\$2214) and Norway (\$2147). The lowest costs were reported in Italy (\$845), followed by the UK (\$866) and Germany (\$871).

For the studies assessing only outpatient care, the highest costs were observed in the USA, with a mean of \$1236 per patient month, followed by the UK (\$1039). The lowest costs were reported in Malaysia (\$192 per patient month), see Appendix 2, Table 4.

When the costs of post-stroke care were weighted for the number of patients of each program reported across the studies for each country, the USA (\$4850) and Denmark (\$3022) remained on leading positions, followed by Norway (\$2147) and the Netherlands (\$2016). The lowest costs per patient month were reported in Australia (\$752) and Sweden (\$768). For the studies that assessed only outpatient care, the highest costs were observed in the United Kingdom, with a weighted average of \$883 per patient month, followed by the USA (\$773). The lowest costs were reported in Malaysia (\$192 per patient month), see Fig. 3 and Appendix 2, Table 4.

In addition, when the annual GDP per capita was taken into account, USA had the highest costs of post-stroke care per patient year (\$58,200) compared to the GDP per capita (\$55,837) and was followed by Denmark and Norway (Fig. 4). In Australia, Sweden, Switzerland and UK, costs of post-stroke care were only about one quarter of the GDP per capita. There was no information available on GDP per capita for study from Cuba, as well as for multi-centric study considering that this study covers cost data from 22 countries. For inpatient/outpatient studies, a positive correlation between GDP per capita and cost of post-stroke care is observed ($\rho=0.59$, $p=0.045$).

With regard to the acute stroke care supply and practice patterns of stroke care in each country (stroke units, number of rehabilitation beds available, duration of acute care), 14 studies did not report on the presence of stroke units (although stroke units were available in those countries), while in the other 16 studies presence of stroke units is reported for both outpatient and inpatient care setting (see Table 1). In outpatient-only settings, four studies reported on the presence of stroke units, while six studies did not (stroke

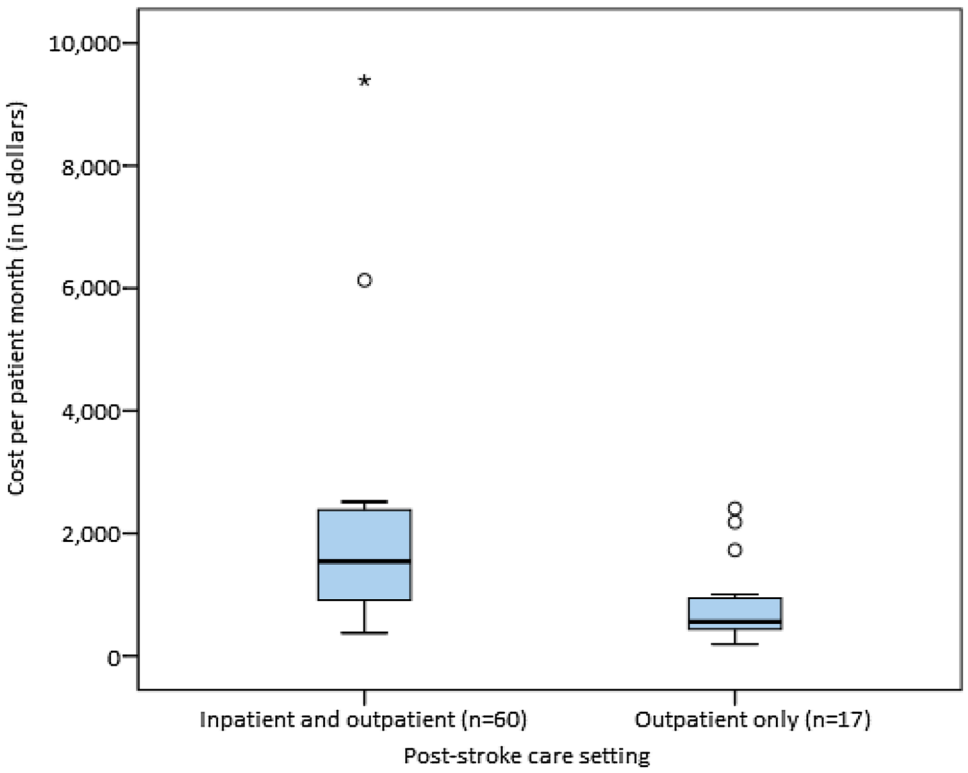

Fig. 2 Mean cost of post-stroke care (per patient month) for all programs reported in studies with inpatient/outpatient and outpatient-only care setting

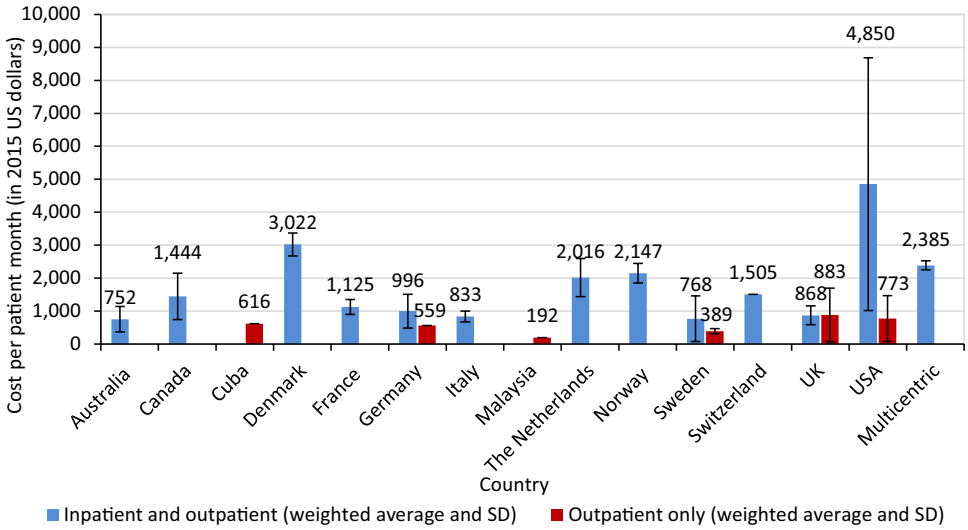

Fig. 3 Weighted average cost of post-stroke care per month stratified by country for inpatient/outpatient and outpatient-only care setting

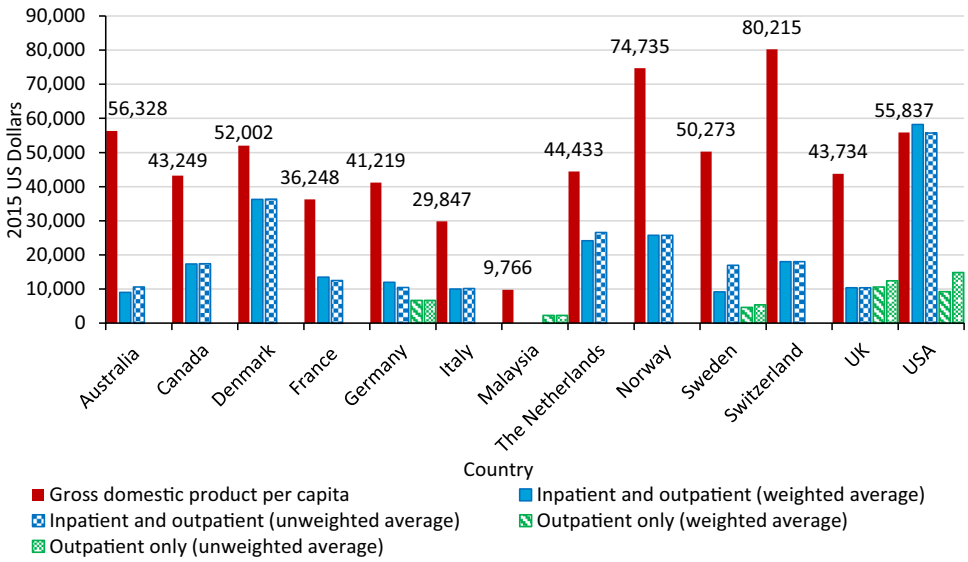

Fig. 4 Mean and weighted average cost of post-stroke care per patient year with gross domestic product per capita (2015 US Dollars)

units were available in those countries). In two publications, there were no stroke units in the hospital (one from UK [14] and one from Malaysia [24]).

Heterogeneity assessment

No statistically significant correlation was identified in the number of rehabilitation beds and cost of post-stroke care for the observed countries ($\rho = 0.071$, $p = 0.811$). Mean duration of acute care was 17.2 (SD 9.7) for inpatient and outpatient studies, and 18.6 (SD 14) days for outpatient-only studies. No statistical significant correlation could be detected regarding the duration of acute care and cost of post-stroke care ($\rho = -0.029$, $p = 0.957$). For the assessment of heterogeneity, part of the studies included in this systematic review could be included in the meta-regression analysis. In total, six studies in the group of inpatient and outpatient studies [13, 26–30], and four studies in the group of outpatient-only studies [14, 15, 31, 32] have been included in the heterogeneity analysis. The remaining studies did not report the parameters needed to derive the variance needed for the meta-regression. In our (limited) meta-regression, none of the assessed characteristics contributed with statistical significance to the explanation of the heterogeneity between studies.

A detailed analysis of the costs of each service segment of post-stroke care was not possible due to heterogeneous reporting in studies. In general, rehabilitation services (including general rehabilitation, home based, inpatient, ward, day clinic, outpatient rehabilitation, nursing homes, aged care facilities and special accommodation) were identified as major contributors to the overall cost of post-stroke

care in the majority of studies, in 26 studies on the first rank, and in 14 studies on the second rank. Within this category, the greatest amount of resources was allocated for rehabilitation and nursing care, which was pointed out by most of the authors. Rehabilitation service was followed by informal care and community services costs (including community and social services, home assistance and assisted living) which were recognized as the most expensive item in six studies, and on the second rank by another six studies. Rehospitalizations and medical interventions, including medications, were next segments of care on the cost-ranking list, being on the first rank in three studies, and on the second rank in eight studies.

Discussion

This systematic assessment of studies included 42 publications from which we have systematically extracted data regarding study characteristics and detailed data on cost of post-stroke care adjusted to 2015 US Dollars. We observed differences in costs of post-stroke care regarding region of care provided, and identified the USA as the country with highest cost of post-stroke care per patient month. We have recognized rehabilitation services as the main cost driver in post-stroke care, and we found significant differences in cost regarding reported diverse follow-up periods between studies. As there was no pattern for resource segments reporting, it was not possible to perform a detailed analysis of different post-stroke care segments.

Cost of post-stroke care is highly related to the stroke severity and length of stay in hospital, resulting with great impact on the level and duration of post-stroke care services utilization [33, 34]. There are several studies, including systematic reviews showing that stroke patients can benefit more from early rehabilitation services, which is also more cost-effective due to a shorter duration of stay in the hospital [8–11, 35].

To our knowledge, this is the first systematic review that addresses the cost specifically related to post-stroke care. It comprises studies conducted in different health care settings, addressing cost of post-stroke care in 14 countries from four different continents. Major strength of this research is that it provides knowledge about the overall expenses regarding post-stroke care setting, comprising also the different segments of services, and the identification of the main cost drivers in a global perspective. This review is reported according to the recommendations of PRISMA checklist, addressing all 27 items [23, 36] (Online Resource 5).

In relation to the current literature regarding the costs of the post-stroke management, most of the published studies have reported mainly on the total cost of stroke treatment or on the cost of acute care only. Demaerschalk et al. [37] reported on economic burden of stroke in the USA, including 28 articles, with main focus on short- and long-term direct costs, indirect and aggregated lifetime costs, limited only on the USA and highlighting that this search did not identify studies dealing with the cost of rehabilitation care. In this study, the most expensive segment of care was acute care, followed by next two main resource segments—nursing home and ambulatory care. In contrast, Ekman [38] and Grieve et al. [39] reported about cost of stroke in Europe. In the first study, direct costs for acute care followed by costs for hospital and home-based rehabilitation were observed as major costing items. Likewise, in the second study, outpatient costs were right after hospitalization costs as the most expensive item.

This systematic review describes the economic burden of stroke, independent of a health care region, with main focus on cost of post-stroke care, designating rehabilitation and nursing care as the major costing items. Like the other authors, we observed that more detailed research is needed in this field to fill the gap regarding accessible information in published studies. There is a need to form a methodologically and clinically supported list of segments of services that should be taken into account when reporting on cost of care. We can confirm the problem recognized by Ekman [38] and Brady et al. [8] regarding the comparability of studies based on different costs.

The highest mean cost per patient month was reported in the USA, which could be due to reports from special rehabilitation facilities described by Beeuwkes-Buntin et al. [26], where home rehabilitation was accounted for an amount of $1589, while the costs of care in inpatient rehabilitation facilities (IRF) and in skilled nursing facilities (SRF) summed up to $9379 and $6124 for a patient per month, respectively. The reason for this discrepancy could be attributed to the described type of patients who use this kind of special care and factors associated with longer stay in IRF and consequential admission to SRF (stroke severity, older age, comorbidities, absence of family caregivers, lower cognitive and functional status) [40, 41]. In Europe, higher cost of post-stroke care per patient month was observed in Denmark ($3022/PM), The Netherlands ($2016/PM) and Norway ($2147/PM) compared to other European countries. The finding could be explained by a lack of representative studies from northern European countries, or by different resource utilization in studies. This should be considered together with the fact that the weighted average cost of post-stroke care in seven studies from Sweden is estimated to be $768/PM (minimum of $548 and maximum of $2517), which is in favor of the previous argument. As reported in literature, the mean hospitalization costs of acute stroke care ranged from $8000 up to $23,000 and more [17, 37, 42], being similar to the burden in our findings, and—together with post-stroke care costs—imposing great economic importance.

The highest cost of post-stroke care were confirmed when compared to GDP per capita and USA was listed in the first place, with a weighted annual average of more than $2000 above GDP per capita. In contrast, the mean annual costs of post-stroke care in Australia were only about one-fifth of the GDP per capita (Fig. 4). Furthermore, we examined the acute stroke care supply and practice patterns of stroke care in each country. Two studies compared stroke care in stroke units and other hospital wards (Claesson et al. [43] and Kalra et al. [29]) and showed that stroke units are more cost-effective than other hospital wards. In two studies reporting on outpatient-only settings, stroke units were not available in the institution [14, 24]. The efficacy of stroke units is proven in many studies and may lead to lower costs of post-stroke care [44–46]. We were not able to confirm this finding in our review, which could be due to the very small number of studies reporting on institutions where stroke units were not existing. The costs of post-stroke care reported for the UK by Humphreys et al. [14] are similar to the costs reported by other authors from the same country (Patel et al. [15]) where stroke units were present.

Regarding the costs from the UK, the study from Kalra et al. [29] reports approximately two times lower post-stroke care costs than other publications [13, 47] for the same country. This difference may be explained by type of stroke patients evaluated in this study (only patients with mild stroke were included, while patients with severe stroke and those with specific neurological features were excluded).

In the available literature, we did not find information on cost differences regarding follow-up periods. We have observed that studies reporting on shorter follow-up (up to six months) exhibited significantly higher cost than those reporting on longer follow-up period ($p < 0.05$). This finding could be expected due to lower costs of care needed by the patients when they become more independent [48]. Furthermore, five studies [49–53] reported on periods longer than 1 year, and four of them described lower costs in subsequent years. In one study, due to prescription of new drugs which were more expensive than those previously used, the costs were higher in fourth year of follow-up [49].

Reporting on costs of each specific service utilization segment was diverse across studies; therefore, detailed analysis of each specific service utilization segment was not possible. Fifteen segments of specific services were observed in the reviewed studies. For example, in the studies from Hayes et al. [28] and Beeuwkes-Buntin et al. [26], only total post-stroke care cost is available, without specifying any costing details. On the other side, Bjorkdahl et al. [27] and Christensen et al. [54] reported on more than ten different costing segments of post-stroke care in their studies. This variety could be attributed to the use of a wide specter of data sources (administrative databases, insurance claims, hospital and care facility records, different kinds of registers, patient questionnaires etc.), as well as a different organization of health systems from country to country.

Our meta-regression did not identify characteristics explaining heterogeneity between studies. However, the number of studies providing the necessary evidence for inclusion into the meta-regression was limited, and therefore, it cannot be ruled out that some of the assessed characteristics do contribute to the observed heterogeneity.

There is a clear need for evaluation of post-stroke care programs, which may be offered in the same settings but with different care approaches. Considering patient education and prevention of complications, this could maximize benefits for patients while minimizing cost for society. A similar kind of evaluation was observed in four studies recognized by the present systematic review, in three studies [13–15] results (in terms of costs and outcomes) were in favor of the intervention, while in one study [31] there was no significant difference between the two groups compared. In those cases, use of health services was compared in the same settings, but with differences in intensity and services provided during the follow-up period. This kind of intervention does not require a structural reorganization of the health care system and could be easily integrated.

This review has several limitations. Publication and retrieval bias may occur while the results of published studies may be different from results of the studies that are not available through the databases included in our search strategy or not published at all. This bias could appear due to small sample size in studies or if the focus on cost of post-stroke care is considered to be interesting in a very limited context (e.g., national interest, health insurance). However, we performed comprehensive search strategies to minimize the retrieval bias, including manual search of the reference lists and searches via Google Scholar. In addition, to gather the most of available studies and minimize potential language bias, no filters regarding languages were applied and only studies published in non-Latin languages were excluded.

It is important to mention that even if the observed outcome (cost of post-stroke care) was the same for all publications, different post-stroke care programs were observed across the studies, including different regions, costing perspectives, monetary units, sample size, reporting on segments of services, type of stroke or level of stroke severity. It was challenging to generalize results reporting from diverse countries worldwide and to compare economical results, due to monetary difficulties (different units, floating exchange rates, purchasing power etc.). From a total number of 42 studies in this review, 40 were reporting from countries classified in the category of high income by the World Bank [42], while two studies reported on data from countries classified in the upper middle income economies (Akhavan Hejazi et al. [24] and Alonso-Freyre et al. [55]).

With the use of CPI, we were able to adjust costs to unique unit system [56], and with PPP we made the costs more comparable, reducing price differences among countries [17, 57]. The lack of data from low, lower middle- and upper middle income economies (as defined by the World Bank) could lead to the overestimation of the costs in this research due to potentially lower cost of care in those categories. The way to overcome this limitation would be stimulation of further health economic research conceivably resulting in more publications from these regions.

Since the number of patients varied across the programs in studies, there was a concern that real average cost of post-stroke care for a single country could be biased. Therefore, we considered the sample size and calculated cost of post-stroke care for each country as mean and as weighted average for number of patients in each program described in studies of respective country. In our review, we could only include the data as published in the included studies, as the underlying raw data were not available. Nevertheless, it could be possible that some segments of costs are less thorough reported or differently categorized (e.g., joint in groups of the specific segments of post-stroke care) in the results of studies that reported costs less detailed. This could lead to potential bias in reporting of costs of post-stroke care segments within the studies, but not necessarily biasing overall costs.

A better picture of health services' utilization could be captured with broader use of secondary data, as these data derive from detailed reimbursement databases and could be assumed to be nearly 100% complete, as enlightened by Swart [58] and Swart et al. [59]. Finally, the results should be viewed with some reserve as reviewed studies provide information on different health care regions, costing perspectives, heterogeneous types of stroke, different numbers of patients, and various forms of care delivered in diverse follow-up periods.

Conclusion

This review comprises cost of post-stroke care in 14 countries highlighting diversity between different health care regions worldwide. We were able to describe in which region the most costly delivery of care prevails, and identified rehabilitation services as the main contributor to the cost of post-stroke care. Due to diversity of reporting in studies, it was not possible to conduct a detailed analysis addressing different segments of services. Therefore, the need of more comprehensive research is evident to close this gap. Future research should focus on the association between the cost of post-stroke care and the supply of acute care, considering the correlation of post-stroke care costs with the availability of stroke units or the number of rehabilitation beds available. We strongly recommend reporting full information on the variance of empirical cost studies to allow for the assessment of uncertainty and the inclusion of the single study results into larger evidence syntheses such as meta-analysis, meta-regression, decision-analytic models, and value-of-information analyses [60, 61]. Future studies could benefit from the advantages of administrative and claims data, focusing on both inpatient and outpatient post-stroke care cost and its predictors, to assure appropriate resources allocation in the future.

Funding This work was supported by the Erasmus-Western Balkans mobility programme (ERAWEB), a project funded by the European Commission. The funding source had no influence on study design, analysis and interpretation of data, in the writing of the manuscript and the decision to submit the manuscript for publication.

Compliance with ethical standards

Ethical Committee This work was approved by the Research Committee for Scientific and Ethical Questions (RCSEQ), University for Health Sciences, Medical Informatics and Technology (UMIT), Hall in Tirol, Austria (Date: April 26, 2016; reference number: 1697).

Conflict of interest The authors declare that they have no conflict of interest.

Appendix 1: Evidence tables

See Tables 2 and 3.

Table 2 Extracted data from observed studies and authors calculations based on observations; for studies with inpatient and outpatient care setting

I Inpatient and outpatient care setting							
Data from observed studies						Authors' calculation based on observations	
Author Year Country (ref. no.)	Comparison groups Costing perspective	Stroke type	Study type Type of economic evaluation Number of patients	Follow-up period	Cost per patient (mean) (Year prices included)	Cost per patient per month (only post-stroke care) USD 2015	Comments Data source Segments included in costs
Abbas et al. (2013) Germany [67]	109 SGB V 111 SGB V Health insurance	Ischemic	Retrospective cohort study 109SGB: 1272 111SGB: 2200	12 months	109SGB: €6658* 111SGB: €7626* (2007)	109SGB: $375 111SGB: $486	Health insurance claims Hospital care, outpatient medical services, medication, specialists therapy and inpatient rehabilitation facilities *Hospital care is included in amount of: 109SGB: €3391; 111SGB: €3385 109 SGB V—geriatric department in hospital 111 SGB V—rehabilitation facilities outside of hospital
Anderson et al. (2000) Australia [62]	Home based Hospital based Societal	–	RCT Cost-minimization analysis Home based: 42 Hospital based: 44	6 months	Home based: AUD8040* Hospital based: AUD10,054* (1997–1998)	Home based: $913 Hospital based: $416	Hospital records and patient questionnaire (for hospital outpatient visit, general practitioner visits etc.) Home help and nursing care, home adaptation, transportation, social worker, physiotherapy, occupational and speech therapy and community services *Hospital care is included in amount of: home based: AUD3142; hospital based: AUD7820
Andersson et al. (2002) Sweden [74]	Home based Hospital based Health care	Ischemic and hemorrhagic	Non-randomized trial Cost of illness Home based: 53 Hospital based: 68	12 months	Home based: SEK194,700 Hospital based: SEK190,500 (1996–1998)	Home based: $2517 Hospital based: $2463	Hospital records Acute care wards after rehabilitation decision, nursing home cost, rehabilitation and home help service cost
Beeuwkes-Buntin et al. (2010) USA [26]	Home IRF SNF Health insurance	–	Observational study – Home: 130,365 IRF: 68,906 SNF: 87,844	4 months	Home: $4941 IRF: $29,160 SNF: $19,039 (2002–2003)	Home: $1591 IRF: $9391 SNF: $6131	Medicare administrative data General rehabilitation cost IRF—inpatient rehabilitation facility SRF—skilled nursing facility

Table 2 (continued)

I Inpatient and outpatient care setting							
Data from observed studies						Authors' calculation based on observations	
Author Year Country (ref. no.)	Comparison groups Costing perspective	Stroke type	Study type Type of economic evaluation Number of patients	Follow-up period	Cost per patient (mean) (Year prices included)	Cost per patient per month (only post-stroke care) USD 2015	Comments Data source Segments included in costs
Bjorkdahl et al. (2007) Sweden [27]	– Societal	–	Longitudinal study Cost of illness 58	12 month	Direct mean cost: €13,802 (2004)	Direct mean cost: $1714	Hospital records Rehabilitation ward, day clinic rehabilitation, home assistance, physician visits, nurse, personal assistant, physiotherapy, occupational therapy, medication, transportation, assistive devices and adaptation
Cadilhac et al. (2009) Australia [63]	– Societal	Ischemic and hemorrhagic	Cost of illness – Ischemic: 27,660 Hemorrhagic : 4291	12 months	Ischemic: AUD24,719* Hemorrhagic: AUD29,220* (2004)	Ischemic: $1194 Hemorrhagic: $1373	Questionnaires and data from NEMESIS study Aged care facilities, medication, physician visits, Investigations, specialist medical care, outpatient rehabilitation, hospitalization for complications, community services, transport, caregiver cost *Pre-admission and acute hospitalization are included in amount of: Ischemic: AUD 9104; hemorrhagic: AUD 11,274
Christensen et al. (2008) 22 countries [54]	– Health insurance	Hemorrhagic	RCT Cost analysis 820	3 months	$6257 (2005–2007)	$2385	Medicare administrative data Home health care assistance, physiotherapy, ergo and speech therapy
Claesson et al. (2000) Sweden [43]	Stroke unit Conventional care Societal	–	RCT Cost-minimization analysis Stroke unit: 166 Conventional: 83	12 months	Stroke unit: SEK170,674* Conventional: SEK191,473* (1996)	Stroke unit: $1377 Conventional: $1541	Hospital records Geriatric ward, post care unit, nursing home, home for the elderly, assisted living, physician visit, other medical visits, prescription drugs, assistive devices and adaptations *Initial hospitalization for index stroke (acute care) is included in amount of: Stroke unit: SEK69,483; Conventional: SEK78,199

Table 2 (continued)

I Inpatient and outpatient care setting							
Data from observed studies						Authors' calculation based on observations	
Author Year Country (ref. no.)	Comparison groups Costing perspective	Stroke type	Study type Type of economic evaluation Number of patients	Follow-up period	Cost per patient (mean) (Year prices included)	Cost per patient per month (only post-stroke care) USD 2015	Comments Data source Segments included in costs
Claesson et al. (2005) Sweden [75]	NCI CI Health care	Ischemic and hemorrhagic	Prospective RCT – NCI: 42 CI: 107	12 months	NCI: SEK73,805* CI: SEK236,425* (1996)	NCI: $548 CI: $1947	Hospital records Patient questionnaire (for hospital outpatient visit, different kinds of support etc.) Geriatric ward, post care unit, nursing home, home for the elderly, assisted living, physician visit, other medical visits, prescription drugs, transportation, assistive devices and adaptations *Acute care included in amount of: NCI (No cognitive impairment): SEK33,566; CI (Cognitive impairment): SEK93,367
Dewey et al. (2001) Australia [64]	– Societal	Ischemic, hemorrhagic and unclassified	Cost of illness – 275	12 months	AUD13,627 (1996–1997)	$1279	Hospital records, nursing homes and hostels records SAH excluded Medication, community rehabilitation centers, inpatient respite care, outpatient rehabilitation, investigations, specialist medical care, community services, emergency department care and transportation

Table 2 (continued)

I Inpatient and outpatient care setting							
Data from observed studies						Authors' calculation based on observations	
Author Year Country (ref. no.)	Comparison groups Costing perspective	Stroke type	Study type Type of economic evaluation Number of patients	Follow-up period	Cost per patient (mean) (Year prices included)	Cost per patient per month (only post-stroke care) USD 2015	Comments Data source Segments included in costs
Dewey et al. (2003) Australia [65]	– Societal	Ischemic, hemorrhagic and unclassified	Cost of illness – IS: 199 ICH: 40 Unclassified: 24 All first ever: 263	12 months	IS: AUD20,033* ICH: AUD21,378* Unclassified: AUD4932* All first ever: AUD18,956* (1997)	IS: $1194 ICH: $948 Unclassified: $391 All first ever: $1045	Hospital records, nursing homes and hostels records SAH excluded Medication, community rehabilitation centers, inpatient respite care, outpatient rehabilitation, investigations, specialist medical care, community services, emergency department care and transportation *Acute care included in amount of: IS: AUD7317; ICH: AUD11,275; Unclassified: AUD762; all first ever: AUD7821
Fattore et al. (2012) Italy [70]	– Health care and societal	–	Observational, prospective, incidence-based, multi-center cost of illness study – 411	12 months	Health care cost: €11,747* (2005–2007)	Health care cost: $854	Hospital records and questionnaire Inpatient days, rehabilitation sessions, inpatient rehabilitation, imaging, physician and specialists visits, medications, nursing home and other cost *Hospital care is included in amount of: €4423
Fjaertoft et al. (2005) Norway [78]	ESUS OSUS Health care	–	RCT Cost-minimization analysis ESUS: 160 OSUS: 160	12 months	ESU: €18,937* OSU: €21,824* (1995–1997)	ESUS: $1938 OSUS: $2356	Hospital records and health service registration cards filled in by patients Inpatient rehabilitation, home-based rehabilitation, hospital readmission, nursing home and assisted living, mobile team *Acute care in stroke unit is included in amount of: ESUS (Extended stroke unit service): €5485; OSUS (ordinary stroke unit service): €5474

Table 2 (continued)

I Inpatient and outpatient care setting							
Data from observed studies						Authors' calculation based on observations	
Author Year Country (ref. no.)	Comparison groups Costing perspective	Stroke type	Study type Type of economic evaluation Number of patients	Follow-up period	Cost per patient (mean) (Year prices included)	Cost per patient per month (only post-stroke care) USD 2015	Comments Data source Segments included in costs
Gerzeli et al. (2005) Italy [71]	– Societal	Ischemic and hemorrhagic	Prospective, incidence-based, observational, multi-center, cost of illness study – 386	6 months	€6111* (1998)	$1003	Italian National Health Services records Admission in acute phase, investigations, specialist visits, inpatients rehabilitation, outpatients and/or at home rehabilitation, nursing care, other hospital admissions, medications and disability aids *Admission in acute phase is included in amount of: €3347
Ghatnekar et al. (2014) Sweden [50]	Stroke care cost in 1997 and 2009 Societal	Hemorrhagic, ischemic and unclassified	Cost of illness study – 9064 1997 cohort: female: 2242; male: 2239 2009 cohort: female: 4514; male: 4550	12 months*	Female: €16,225** Male: €15,983** (1997 cohort) Female: €15,399** Male: €14,861** (2009 cohort)	Cohort 1997: female:$786; male: $754 Cohort 2009: female: $783; male: $629	Swedish national stroke register Index stroke admission, stroke re-admission, rehabilitation and follow-up visits, secondary drug prevention, home assistance and residential housing *Observed period of 12 months. Author reported in study 12, 24 and 36 months **Index stroke admission is included in amount of: 1997 (female: €8935; male: €8986); 2009 (female: €9004; male: €9722)
Gloede et al. (2014) Australia [52]	3–5 years 10 years Ischemic Hemorrhagic Societal	Ischemic and hemorrhagic	Cost of illness study – Ischemic 2004: 25,351 Hemorrhagic 2004: 5356 Ischemic 2010: 27,660 Hemorrhagic 2010: 4291	12 months*	Ischemic 2004: $5438 Ischemic 2010: $5207 Hemorrhagic 2004: $5807 Hemorrhagic 2010: $7607 (2010)	Ischemic 2004: $493 Ischemic 2010: $472 Hemorrhagic 2004: $526 Hemorrhagic 2010: $689	3–5 and 10 years average of annual direct cost Hospital records Aged care facilities, medications, community services, inpatient rehabilitation, other direct medical cost, physician care and hospitalizations for complications *Observed period of 12 months. Author reported on period from 3 to 5 years and 10 years

Table 2 (continued)

I Inpatient and outpatient care setting							
Data from observed studies						Authors' calculation based on observations	
Author Year Country (ref. no.)	Comparison groups Costing perspective	Stroke type	Study type Type of economic evaluation Number of patients	Follow-up period	Cost per patient (mean) (Year prices included)	Cost per patient per month (only post-stroke care) USD 2015	Comments Data source Segments included in costs
Harrington et al. (2010) United Kingdom [13]	Standard care Intervention UK NHS and Social services	-	RCT Cost-consequences analysis Standard care: 124 Intervention: 119	6 months	Standard care: £2994 Intervention: £3741 (2005)	Standard care: $952 Intervention: $1190	Questionnaire, literature, Department of Health tariff and the British National Formulary Primary care, outpatient care inpatient care, community care and medications. Social care cost included use of a day center, social worker time, home care and meals on wheels
Hayes et al. (2008) USA [28]	– Health care	Ischemic and hemorrhagic	Descriptive study – 172	9 months	$9997 (2001–2002)	$1463	Hospital records Inpatient and outpatient rehabilitation cost Follow-up period is from 4th month until 1 year
Kalra et al. (2005) United Kingdom [29]	Stroke unit Stroke team Domiciliary care Societal	Ischemic and hemorrhagic	Prospective single-blind RCT Cost-effectiveness and cost-utility analysis Stroke unit: 152 Stroke team: 152 Domiciliary care: 153	12 months	Stroke unit: £2625 Stroke team: £3575 Domiciliary care: £2984 (1997–1998)	Stroke unit: $493 Stroke team: $672 Domiciliary care: $561	Client Service Receipt Inventory and NHS records Secondary care, community-based care and specialized accommodation *Patients with mild stroke, severe strokes, already admitted to hospitals, and those with specific neurological features were excluded
Kolominsky-Rabas et al. (2006) Germany [51]	– Health insurance	Ischemic	Cost of illness – 1637	12 months*	€18,517** (2004)	$1375	Hospital records and questionnaires Annual component cost, general rehabilitation cost *Observed period of 12 months. Author reported in study on 12 and 24 to 60 months **Includes inpatient care during hospitalization in amount of €6731

Table 2 (continued)

I Inpatient and outpatient care setting							
Data from observed studies						Authors' calculation based on observations	
Author Year Country (ref. no.)	Comparison groups Costing perspective	Stroke type	Study type Type of economic evaluation Number of patients	Follow-up period	Cost per patient (mean) (Year prices included)	Cost per patient per month (only post-stroke care) USD 2015	Comments Data source Segments included in costs
Mahler et al. (2008) Switzerland [35]	– Health insurance	–	Prospective cohort study Cost-benefit analysis 131	12 months	CHF24,873 (2002–2003)	$1505	Insurance records Rehabilitation clinic, nursing home, medication, primary care physician, physiotherapy, outpatient nursing home, outpatient clinic and other cost
Miller et al. (2005) United Kingdom [47]	Early discharge Usual care Health and societal	–	RCT Cost-benefit analysis Early discharge: 185 Usual care: 185	12 months	Early discharge: £8361* Usual care: £10,088* (1999–2000)	Early discharge: $1070 Usual care: $1125	Hospital records Initial inpatient admission, inpatient readmissions, outpatient visits, nursing/residential home stays, physician care, community health services, social services and day hospital Units were calculated based on literature *Initial inpatient admission is included in amount of: early discharge: £2730; usual care: £33,848
Rasmussen et al. (2015) Denmark [79]	Home rehabilitation Standard care –	–	RCT – Home rehabilitation: 31 Standard care: 30	5 months	Home rehabilitation: $12,631 Standard care: $14,854 (2007–2008)	Home rehabilitation: $2781 Standard care: $3270	Hospital records and case report form General rehabilitation cost
Spieler et al. (2003) France [53]	First ever stroke Recurrence Societal	–	Cost of illness – First ever stroke: 346 Recurrence: 89	18 months	First ever stroke: €19,725* Recurrence: €18,560* (1997)	First ever stroke: $975 Recurrence: $859	Hospital records and patient interviews Rehabilitation, nursing home, chronic hospitalizations, ambulatory care, appliances and medications *Initial acute care and acute care during 18 months are included in amount of: first ever stroke: €8138; recurrence: €8348

Table 2 (continued)

I Inpatient and outpatient care setting							
Data from observed studies						Authors' calculation based on observations	
Author Year Country (ref. no.)	Comparison groups Costing perspective	Stroke type	Study type Type of economic evaluation Number of patients	Follow-up period	Cost per patient (mean) (Year prices included)	Cost per patient per month (only post-stroke care) USD 2015	Comments Data source Segments included in costs
Spieler et al. (2004) France [66]	– Societal	Ischemic	Prospective cohort study Cost of illness 435	12 months	Rehabilitation: €17,799* (1997)	Rehabilitation: $1298	Hospital records and questionnaires Acute phase, ambulatory care, orthoses, drugs, convalescent home, rehabilitation, new acute hospitalizations, nursing home and long-term chronic hospitalization *Acute phase is included in amount of: €7512
Tay-Teo et al. (2008) Australia [30]	Early mobilization (VEM) standard care (SC) Societal	Ischemic and hemorrhagic	RCT Cost-effectiveness analysis VEM: 38 SC: 33	12 months	VEM: AUD17,564* SC: AUD29,750* (2004)	VEM: $751 SC: $1606	Hospital records and patient interviews Rehospitalization, inpatient and outpatient rehabilitation, home rehabilitation or therapy, adaptations, community services and respite care *Acute phase hospitalization, VEM implementation, interim care arrangement and emergency attendance are included in specified amount: VEM: AUD7740; SC: AUD8754
Teng et al. (2003) Canada [80]	Home intervention Usual care Health care	–	RCT Cost-benefit analysis Home intervention: 58 Usual care: 56	3 months	Home intervention: CAD7784* Usual care: CAD11,065* (1997–1998)	Home intervention: $954 Usual care: $1952	Hospital records and patient interviews Inpatient rehabilitation, home intervention visits, dietician, occupational, speech and physical therapist, social worker, general physician, ER visits, nursing *Includes acute care in specified amount of: home intervention CAD5448; usual care: CAD6285

Table 2 (continued)

I Inpatient and outpatient care setting							
Data from observed studies						Authors' calculation based on observations	
Author Year Country (ref. no.)	Comparison groups Costing perspective	Stroke type	Study type Type of economic evaluation Number of patients	Follow-up period	Cost per patient (mean) (Year prices included)	Cost per patient per month (only post-stroke care) USD 2015	Comments Data source Segments included in costs
Torbica et al. (2014) Italy [72]	With caregiver Without caregiver health care	Ischemic and hemorrhagic	Observational, prospective, incidence-based, multi-center study Cost of illness 476	12 months	€5825 (2007–2008)	$677	Questionnaires Overall sample rehabilitation cost includes rehabilitation cost, in- and outpatient rehabilitation, hospitalizations, imaging, general physician and specialists visits, medication and nursing home cost
van Eeden et al (2015) Netherlands [73]	– Societal	–	Multi-centre, prospective, bottom-up burden of disease study Cost-utility analysis 395	12 months	health care costs: €18,068* (2011–2013)	$1481	Questionnaires Healthcare costs included costs of general practitioner, specialist, allied health professionals, mental healthcare professionals, rehabilitation treatment, rehabilitation clinic, nursing home, psychiatric clinic and medication. *Includes hospital care in specified amount of: €3,794
van Exel et al. (2003) Netherlands [33]	Delft Nijmegen Haarlem Reference region Societal	–	Observational, non-randomized study – 598 Delft: 151 Haarlem: 111 Nijmegen: 149 Reference regions: 187	6 months	Delft: €13,160 Haarlem: €16,790 Nijmegen: €20,230 Reference regions: €13,810 (1999)	Delft: $2350 Haarlem: $2332 Nijmegen: $3027 Reference regions: $1882	Hospital records and patient interviews Hospital, nursing home, rehabilitation center and at home
Weimar et al. (2002) Germany [68]	Stroke unit Neurology Internal medicine –	Ischemic and hemorrhagic	Prospective cohort study Cost-benefit analysis 5106	12 months	Inpatient: DM3195 Outpatient: DM6700 (1998–1999)	Inpatient: $403 Outpatient: $846 Total: $1249	Hospital records Inpatient general rehabilitation cost and outpatient cost (investigations, medications, nursing, physiotherapy, ergo therapy, speech therapy and primary care physician) Sum of DM6700 was calculated from data provided in Table 5

– Not reported, *AUD* Australian, *CAD* Canadian Dollar, *DM* Deutsche Mark, *SEK* Swedish Krona, *CHF* Swiss Franc, £ UK Pound, $ US Dollar

Table 3 Extracted data from observed studies and authors calculations based on observations; for studies with outpatient-only care setting

Outpatient care setting							
Data from observed studies						Authors' calculation based on observations	
Author Year Country (ref. no.)	Comparison groups Costing perspective	Stroke type	Study type Type of economic evaluation Number of patients	Follow-up period	Cost per patient (mean) (Year prices included)	Cost per patient per month (only post-stroke care) USD 2015	Comments Data source Segments included in costs
Akhavan Hejazi et al. (2015) Malaysia [24]	– –	Ischemic and hemorrhagic	Cross-sectional study – 49	3 months	$547.10 (2010–2011)	$192	Hospital records and questionnaires Home help and nursing care, adaptation, transportation, consultation with a rehabilitation physician, physiotherapy, occupational and speech therapy
Alonso Freyre et al. (2000) Cuba [55]	– –	Ischemic	Prospective cohort study – 52	12 months	$19,764.54* (1999)	$616	Hospital records and primary care cost Outpatient rehabilitation cost, external consultations, home assistance, complications and emergency interventions *Includes hospitalization cost in amount of 14,571.8
Forster et al. (2009) United Kingdom [31]	Structured system Usual care –	–	RCT – Structured system: 132 Usual care: 133	6 months	Structured system: £2963 Usual care: £3159 (2003–2005)	Structured system: $942 Usual care: $1005	Hospital records Hospital readmissions, primary, community, outpatient and social care, care home cost, aids and adaptations
Ghatnekar et al. (2004) Sweden [49]	– Health care and social services	–	Cost of illness study – Male: 2187 Female: 2170	12 months*	Male: SEK22,747 + 8709 Female: SEK21,801 + 8310 (2000)	Male: $395 Female: $378	Risk stroke register Outpatient visits, rehabilitation, medication and readmission cost *Observed period of 12 months. Author reported in study 12, 24, 36 and 48 months
Godwin et al. (2011) USA [34]	– Health insurance	Ischemic and hemorrhagic	Longitudinal interventional study Cost analysis 54	12 months	$17,081 (2001–2005)	$1727	Data on service utilization were obtained through National Institute of Nursing Research, cost via Medicare General rehabilitation cost (outpatient care including medication and service utilization, physical, occupational and speech therapy)

Table 3 (continued)

Outpatient care setting							
Data from observed studies						Authors' calculation based on observations	
Author Year Country (ref. no.)	Comparison groups Costing perspective	Stroke type	Study type Type of economic evaluation Number of patients	Follow-up period	Cost per patient (mean) (Year prices included)	Cost per patient per month (only post-stroke care) USD 2015	Comments Data source Segments included in costs
Humphreys et al. (2015) United Kingdom [14]	Behavior therapy Usual treatment UK NHS and Social services	–	RCT Cost-effectiveness analysis Behavior therapy: 42 Usual treatment: 45	3 months	Behavior therapy: £1093 Usual treatment: £905 (2011)	Behavior therapy: $548 Usual treatment: $454	Questionnaire Physician care, occupational therapist, speech and language therapist, physiotherapist and mental health nurse. NHS—National Health Services
Patel et al. (2004) United Kingdom [15]	Trained caregiver Caregiver no training Societal	–	Single-blind RCT Cost-effectiveness analysis training: 151 No training: 149	12 months	Training: £1953 No training: £2494 (2001–2002)	Training: $341 No training: $436	Hospital records, questionnaires and national statistics Social services, secondary care, other community-based care
Roderick et al. (2001) United Kingdom [77]	Domiciliary care day-hospital-care Health care	–	RCT Cost-effectiveness analysis Domiciliary care: 54 Day-hospital-care: 58	6 months	Domiciliary care: €1170 + 1965 + 3070 Day-hospital-care: €1146 + 2057 + 2428 (1996–1997)	Domiciliary care: $2405 Day-hospital-care: $2183	Medicare Rehabilitation services, occupational therapy, physiotherapy, general physician and district nurse visits, hospital readmissions, hospital outpatient visits, social services (occupational therapy, home care during day or night, meals on wheels)
Simpson et al. (2015) USA [32]	1997 Cohort 2004 cohort Health insurance	Ischemic	Retrospective cohort study Cost analysis Overall: 1849	12 months	Overall: $7127 (2004)	Overall: $745	Medicare hospital records Occupational therapy, physical and speech therapy, general unspecified cost

Table 3 (continued)

Outpatient care setting							
Data from observed studies						Authors' calculation based on observations	
Author Year Country (ref. no.)	Comparison groups Costing perspective	Stroke type	Study type Type of economic evaluation Number of patients	Follow-up period	Cost per patient (mean) (Year prices included)	Cost per patient per month (only post-stroke care) USD 2015	Comments Data source Segments included in costs
von Koch et al. (2001) Sweden [76]	Home rehabilitation Routine rehabilitation Health care	–	RCT Cost-minimization analysis Home rehab.: 41 Routine rehab.: 42	12 months	Home rehab.: SEK40,840 Routine rehab.: SEK33,906 (1993–1996)	Home rehab.: $556 Routine rehab.: $461	National Social insurance and local statistics Recurrent hospitalizations, hospital outpatient (physician and nurse care, physical, occupational and speech therapist), day hospital, home rehabilitation, primary care (physician and nurse care, physical and occupational therapist) and private caregivers (physical and speech therapist, physician)
Weimar et al. (2003) Germany [69]	– Societal	Hemorrhagic	Cost of illness – 578	12 months	€4,598 (1998–1999)	$559	Hospital records and questionnaires Nursing, physiotherapy, ergo therapy, speech therapy and primary care physician

– Not reported, *SEK* Swedish Krona, *£* UK Pound, *$* US Dollar

Appendix 2

See Table 4.

Table 4 Countries oriented mean and weighted average cost of post-stroke care, in USD

Country	Inpatient and outpatient				Outpatient only			
	Weighted average	Mean	Median	SD	Weighted average	Mean	Median	SD
Australia	752	886	913	388	–	–	–	–
	9024	10,632	10,956	–	–	–	–	–
Canada	1444	1453	1453	706	–	–	–	–
	17,328	17,436	17,436	–	–	–	–	–
Cuba	–	–	–	–	616	616	616	–
	–	–	–	–	7392	7392	7392	–
Denmark	3022	3026	3026	346	–	–	–	–
	36,264	36,312	36,312	–	–	–	–	–
France	1125	1044	975	227	–	–	–	–
	13,500	12,528	11,700	–	–	–	–	–
Germany	996	871	868	514	559	559	559	–
	11,952	10,452	10,416	–	6708	6708	6708	–
Italy	833	845	854	163	–	–	–	–
	9996	10,140	10,248	–	–	–	–	–
Malaysia	–	–	–	–	192	192	192	–
	–	–	–	–	2304	2304	2304	–
The Netherlands	2016	2214	2332	579	–	–	–	–
	24,192	26,568	27,984	–	–	–	–	–
Norway	2147	2147	2147	296	–	–	–	–
	25,764	25,764	25,764	–	–	–	–	–
Sweden	768	1416	1377	691	389	448	428	81
	9216	16,992	16,524	–	4668	5376	5136	–
Switzerland	1505	1505	1505	–	–	–	–	–
	18,060	18,060	18,060	–	–	–	–	–
United Kingdom	868	866	952	286	883	1039	745	812
	10,416	10,392	11,424	–	10,596	12,468	8940	–
USA	4850	4644	3861	3838	773	1236	1236	694
	58,200	55,728	46,332	–	9276	14,832	14,832	–
Multi-centric	2385	1193	1193	136	–	–	–	–
	28,620	14,316	14,316	–	–	–	–	–

All costs are reported per patient month in the first row, and per patient year in the second row

SD standard deviation

Appendix 3

See Tables 5 and 6.

Table 5 Assessment of methodological quality of included studies ($N=42$) using the Drummond checklist [17]

No.	Checklist item	Yes	No	Not applicable
Study design				
1	The research question is stated	41	1	
2	The economic importance of the research question is stated	40	2	
3	The viewpoint(s) of the analysis are clearly stated and justified	29	13	
4	The rationale for choosing alternative programmes or interventions compared is stated	22	0	20
5	The alternatives being compared are clearly described	20	2	20
6	The form of economic evaluation used is stated	29	13	
7	The choice of form of economic evaluation is justified in relation to the questions addressed	26	16	
Data collection				
8	The source(s) of effectiveness estimates used are stated	41	1	
9	Details of the design and results of effectiveness study are given (if based on a single study)	41	1	
10	Details of the methods of synthesis or meta-analysis of estimates are given (if based on a synthesis of a number of effectiveness studies)	0	0	42
11	The primary outcome measure(s) for the economic evaluation are clearly stated	42	0	0
12	Methods to value benefits are stated	23	3	16
13	Details of the subjects from whom valuations were obtained were given	23	3	16
14	Productivity changes (if included) are reported separately	5	13	24
15	The relevance of productivity changes to the study question is discussed	5	13	24
16	Quantities of resource use are reported separately from their unit costs	33	9	0
17	Methods for the estimation of quantities and unit costs are described	38	4	0
18	Currency and price data are recorded	42	0	0
19	Details of currency of price adjustments for inflation or currency conversion are given	20	22	0
20	Details of any model used are given	3	0	39
21	The choice of model used and the key parameters on which it is based are justified	3	0	39
Analysis and interpretation of results				
22	Time horizon of costs and benefits is stated	2	2	38
23	The discount rate(s) is stated	6	1	35
24	The choice of discount rate(s) is justified	2	2	38
25	An explanation is given if costs and benefits are not discounted	2	0	40
26	Details of statistical tests and confidence intervals are given for stochastic data	33	6	3
27	The approach to sensitivity analysis is given	14	27	1
28	The choice of variables for sensitivity analysis is justified	13	28	1
29	The ranges over which the variables are varied are justified	12	29	1
30	Relevant alternatives are compared	22	1	19
31	Incremental analysis is reported	7	31	4
32	Major outcomes are presented in a disaggregated as well as aggregated form	41	1	0
33	The answer to the study question is given	41	1	0
34	Conclusions follow from the data reported	42	0	0
35	Conclusions are accompanied by the appropriate caveats	37	5	0

Table 6 Assessment of reporting quality of included studies using the CHEERS checklist [18]

Section	Item	Number of studies reporting ($N=42$)
Title and abstract	Title	36
	Abstract	41
Introduction	Background and objectives	42
Methods	Target population and subgroups	42
	Setting and location	42
	Study perspective	29
	Comparators	28
	Time horizon	2
	Discount rate	7
	Choice of health outcomes	42
	Measurement of effectiveness	41
	Measurement and valuation of preference-based outcomes	42
	Estimating resources and costs	42
	Currency, price date, and conversion	42
	Choice of model	3
	Assumptions	1
	Analytical methods	41
Results	Study parameters	35
	Incremental costs and outcomes	42
	Characterizing uncertainty	26
	Characterizing heterogeneity	25
Discussion	Study findings, limitations, generalizability, and current knowledge	42
Other	Source of funding	37
	Stated conflicts of interest	18

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