HHS Public Access

Author manuscript

J Stroke Cerebrovasc Dis. Author manuscript; available in PMC 2015 August 01.

Published in final edited form as:

J Stroke Cerebrovasc Dis. 2014 August ; 23(7): 1753–1763. doi:10.1016/j.jstrokecerebrovasdis.2014.02.017.

A literature review of indirect costs associated with stroke

Heesoo Joo, PhD, **Mary G. George, MD, MSPH**, **Jing Fang, MD**, and **Guijing Wang, PhD**

Division for Heart Disease and Stroke Prevention, US Centers for Disease Control and Prevention (CDC), 4770 Buford Hwy NE, Mailstop F-72, Atlanta, GA 30341

Keywords

stroke; ischemic stroke; hemorrhage; economic burden; indirect cost; productivity loss; cost of informal care

1. Introduction

Stroke, a leading cause of death and long-term disability, is a public health problem worldwide. Globally, there are an estimated 15 million strokes, leading to nearly 5 million deaths and another 5 million cases of permanent disability per year.[1] Because of the increasing size of the elderly population and increasing prevalence of major risk factors such as hypertension and obesity, stroke is predicted to continuously increase.[2] Moreover, the mortality rates of stroke have kept increasing in some countries in recent decades.[2] Although the US and some European countries experienced decreasing stroke mortality rates in the same period,[2-4] the decreasing stroke mortality rate and the increasing size of the elderly population increase the long-term disability among stroke survivors.[5]

Many studies have found high direct costs associated with stroke, including costs for inpatient stays, outpatient visits, rehabilitation, medications, and nursing home, etc. For example, total annual direct costs were estimated at $22.8 billion in 2009 for the US[6] and €26.6 billion in 2010 for the EU plus Iceland, Norway, and Switzerland.[7] Far fewer studies have considered the indirect costs of stroke, including productivity loss due to morbidity and mortality, and costs of informal caregiving usually provided by unpaid family members, although the indirect costs has been claimed to be large.[8]

To better understand the total economic burden of stroke, especially the indirect costs of stroke consisting of productivity loss and informal caregiving costs, we examined peer-reviewed publications of the past two decades, including an analysis of the indirect cost. The information we present here will be useful to decision makers in public health, and researchers for developing strategies for stroke prevention, treatment, and rehabilitation.

Corresponding author: Heesoo Joo, PhD, Health Economist, Division for Heart Disease and Stroke Prevention, US Centers for Disease Control and Prevention (CDC), 4770 Buford Hwy NE, Mailstop F-72, Atlanta, GA 30341, hjoo@cdc.gov, Tel: +1-770-488-7093, Fax: +1-770-488-8334.

2. Methods

We performed a comprehensive literature search of peer-reviewed journal articles published in English between January 1990 and September 2012 by using the databases PubMed, MEDLINE, and EconLit. We augmented the search by using Google Scholar and checking the references of the articles we obtained. Keywords for the search included *stroke, cerebrovascular disease, subarachnoid hemorrhage, intracerebral hemorrhage, cost-of-illness, productivity loss, indirect cost, economic burden, and informal caregiving*. We investigated two main categories of indirect cost, productivity loss and informal care cost. Productivity loss consisted of loss due to premature death (mortality cost) and the cost of disability because of the reduced productivity of stroke survivors (morbidity cost).[9] The cost of informal caregiving is the value of time spent by family members or other caregivers that is not considered to be part of the care given by formal health care providers.[10] A cost for care provided by formal health care providers such as a home health aide is considered to be a direct cost. Because the proportion of total cost that was represented by indirect cost is a useful indicator measuring the importance of indirect costs estimation, we included cost-of-illness (COI) studies with sufficient analyses of the indirect cost. COI studies estimate the value of all resources spent or foregone, including health care cost and productivity loss, due to stroke.

Figure 1 shows the algorithm used for selecting studies for this review. The initial review of titles and abstracts excluded studies that: (a) were not about stroke, (b) assessed the burden of stroke using nonmonetary terms, such as hours of caregiving or emotional distress, or (c) were only about direct medical costs. In addition, we excluded review articles, editorials, and commentaries. We completed full-text review of all articles that passed the initial review and finalized the set of original research articles for this study by further excluding studies that: (a) were focused on cost-effectiveness; (b) used an unspecified indirect cost for stroke within broad disease categories, such as cardiovascular disease or brain disorders; (c) were about direct costs only, such as studies that included the cost of informal caregiving as a part of direct cost and did not specify indirect costs at all; and (d) were not original studies. We included articles on cardiovascular diseases and brain disorders if the indirect costs of stroke were estimated separately.

We investigated three types of study designs. First, we investigated whether a study is a prevalence based or an incidence based study. A prevalence-based study examines the costs incurred during a given time period regardless of the date of stroke onset, while an incidence-based study estimates costs of new onset of stroke within a specific period of time for defined lengths of follow-up (lifetime, one year, or six months).[11]

Next, for estimating the productivity loss, there are two approaches: the human capital approach (HCA), which estimates forgone earnings due to stroke as the productivity loss,[12, 13] and the friction approach (FA), which assumes a friction cost, a cost associated with the replacement of workers including productivity losses due to substitution of workers or the training costs of new employees, as the productivity loss.

Last, for estimating the cost of informal caregiving, we found two methods: the opportunity cost (OC) approach and the replacement approach (RA). The cost of informal caregiving under the OC approach is estimated by using the value of each activity that informal caregivers forego in order to provide informal care.[10, 14] In contrast, the RA, also known as the proxy good method, assumes that an informal caregiver substitutes for a paid caregiver who would have provided the same type of caregiving services.[10, 14]

To compare indirect costs of different countries in different study period, we derived 2012 US dollar value by using consumer price indices of study countries in the years of costs and in 2012 from the World Bank and purchasing power parity (PPP) exchange rate in 2012 from the Organisation for Economic Co-operation and Development (OECD).[15]

3. Results

In all, 31 original articles were selected for our review. Six of them solely investigated the indirect cost, [10, 14, 16-19] and the remaining 25 were COI studies, which included both the direct and indirect costs(Table 1) [7, 9, 20-42]. Among the six studies focusing on indirect costs, four investigated the costs of informal caregiving, one studied mortality cost, and one studied morbidity cost. None of them examined both the productivity loss and the cost of informal caregiving.

As shown in Table 2, which summarized the data sources used to estimate the indirect costs, the US studies relied on national-level survey data, such as Census data or the National Health and Nutrition Examination Survey (NHANES), or area-specific surveillance data for the estimation of incidence or prevalence rates of stroke. To estimate the productivity loss or costs of informal caregiving, government data or national-level survey data were used. Non-US studies used various data sources, such as hospital and local area data and national surveys.

Table 3 presents methods and results of the COI studies, 12 prevalence-based studies and 13 studies based on incidence, while Table 4 summarized studies dealing with indirect costs only.

The “study design” column in Tables 3 and 4 included the methods used for estimating the productivity loss and the cost of informal care. From the HCA and the FA methods estimating the productivity loss, the HCA, which was used by 22 of the 25 studies in Table 3 and two of the six studies in Table 4, was the more common approach. Two studies from Australia used the FA only for estimating productivity loss.[40, 41] In addition, two studies used both the FA and the HCA (in these instances for sensitivity analyses).[38, 39] Among 13 COI studies including the cost of informal care in Table 3 and four studies of informal care that did so in Table 4, seven studies used the OC approach only, six studies used the RA only, and four studies used both approaches.

Eight COI studies (Table 3), all based on incidence, provided a per-patient indirect costs. Five of them used one year as the follow-up period, one used six months, and the other two used lifetime. In 2012 US dollars (shown in parentheses in the table) the lowest per-patient indirect cost among one-year follow-up studies was $2,960 in a German study, which did

not include informal caregiving cost,[25] while for lifetime follow-up the costs were $22,243 per male and $11,765 per female in a Swedish study, which did not include informal caregiving cost, [34] and $54,067 per patient, including informal caregiving cost, in a study from Spain[32]. Informal caregiving cost in the study from Spain was around 80% of the total indirect cost.[32] The study from Spain focused on intracerebral hemorrhage,[32] while the Swedish study used all type of stroke[34].

The proportion of total cost that was represented by indirect cost for COI studies ranged from a low of 3% for ischemic stroke in a study from Australia[40] to a high of 71%in two studies, one from Spain[31] and the other from the US in which this figure was for subarachnoid hemorrhage only[22] (Table 3). The median and mean proportions of total cost represented by indirect cost were 32% and 33%, respectively (not shown in table).

Among the six studies that were confined to indirect cost (Table 4), three provided a per-patient estimate of the annual cost of informal caregiving. These costs ranged from a low of $904–$1,453 in a study from Thailand[19] to a high of $16,687-$23,451 in a study from the Netherlands[14] (all figures in 2012 US dollars). The annual morbidity cost in Sweden (in 2012 US dollars) was estimated to be $14,963 per patient in 2006.

4. Discussion

4.1. Indirect cost of stroke around the world

In this review, six of the 31 studies were from the US (Table 1). Of these six, two focused solely on indirect costs; the other four were COI studies. Of the two that focused entirely on indirect costs, one was a national-level study that examined informal caregiving for elderly stroke patients[17]; this report estimated the annual cost of such care (in 2012 US dollars) to be$8.4 billion in 1993. The other study, which was limited to the state of California,[16] estimated the annual cost of lost productivity associated with stroke mortality in that state to be US$1.8 billion in 1991.

Of the four US studies of COI, two used prevalence approach, and the other two used incidence approach. In one of the prevalence-based studies, Brown and colleagues estimated that the indirect cost of ischemic stroke (in 2012 US dollars) was $1,384 billion and indirect costs would account for 53% of the total costs of ischemic stroke for the period of 2005-2050.[21] Brown and coworkers suggested that indirect costs will continue to increase, especially among African Americans and Hispanics, because of increasing salaries among those two groups.[21] More recently, Heidenreich and coworkers, also a prevalence-based study, predicted that annual indirect cost (in 2012 US dollars) will increase from $27 billion in 2010 to $47 billion in 2030.[20] However, the proportion of total cost made up of indirect cost was predicted to decrease from 47% to 32% over the 20-year period because of rapidly increasing direct medical costs.[20]

In the more recent of the two incidence-based studies in the US, Taylor and associates found that indirect costs accounted for 58% of the total cost of first-ever stroke, including subarachnoid hemorrhage, intracerebral hemorrhage, and ischemic stroke.[9] The authors estimated the lifetime indirect costs of the combination of these three major types of stroke

to be $41.5 billion (in 2012 US dollars) in 1990.[9] Another incidence-based study compared the lifetime costs of unruptured intracranial aneurysms and aneurysmal subarachnoid hemorrhage.[22] One-year productivity losses due to unruptured intracranial aneurysms were estimated to be $507 million; the comparable figure for aneurysmal subarachnoid hemorrhage was $2,033 million (in 2012 US dollars).[22] The estimated proportions of total cost made up of indirect cost were 59% for unruptured intracranial aneurysms and 71% for aneurysmal subarachnoid hemorrhage.[22]

In the four US COI studies overall, therefore, the proportion of total cost represented by indirect cost ranged from 32% to 71%, confirming that the burden of indirect cost in stroke patients, as expected, was quite considerable.

Among the 31 studies reviewed, 19 were from European countries, four from Oceania, and one each from Canada and Thailand. Among the 19 European studies, the proportion of total cost represented by indirect cost varied considerably. Large wage variations within Europe may affect the variation of the proportion of total cost represented by indirect cost as well as the variation of indirect cost level. Even within one country, the variation in this parameter could be considerable. The proportion of total cost represented by indirect cost ranged from 14% to 25% in Sweden.[33-36] Studies in Australia and New Zealand revealed a lower proportion of indirect cost as a percentage of total cost comparing to other studies (3–10% in Australia, 6–9% in New Zealand).[40-42] Because the study from Thailand was not a COI study, indirect cost as a percentage of total cost was not available. Notably, the annual per-patient cost (in 2012 US dollars) in the Thai study ($904 to 1,453) was much lower than the estimate from a national study in the US ($4,823 to 11,301).[17, 19] This big difference can be partly explained by the much lower wages in Thailand.

4.2. Factors affecting the estimation of indirect costs

In this report, several major factors affected the estimation of indirect cost. First, the levels of indirect cost depended on the cost categories included in the studies. For 11 of the 25 COI studies, either one or two of the three categories in Table 1 (mortality, morbidity, and informal caregiving) had to be marked as “No” in the table either because the study did not include that category or did not clearly delineated it. Because the total indirect costs in COI studies were treated as the sum of the three indirect cost categories, the size of indirect cost depended on the indirect cost categories that were included in the studies.

The cost of informal caregiving was the most common missing component in estimating the indirect costs. Among the 11 COI studies that were missing at least one of the three categories of indirect cost, nine did not include the cost of informal care. Another concern was that some studies did not report the cost of informal care separately even though those studies included that cost. This problem can be explained in part by the absence of a consensus whether or not informal caregiving cost is an established category of indirect cost. In the present review, when a study treated the cost of informal care as a part of direct nonmedical cost, sometimes it did not report the cost of informal care separately. For those studies, the cost of informal care could not be included as a part of indirect cost but was included as a part of direct cost for calculating the proportions under the last column head in Table 3. For instance, Cadilhac and coworkers[40], Gustavsson and associates[7], Pugliatti and

colleagues[28], and Scott and Scott[42] included the cost of informal care as a part of direct cost, and thus in Table 3 the figure only productivity loss was left as the indirect cost and used in calculating the proportion of total costs represented by indirect costs.

Another concern was that although mortality and morbidity costs were included in almost every COI study in Table 1, the subcategories of morbidity and mortality cost were not fully addressed in all the studies. In addition to the cost of informal caregiving, the productivity loss in nonmarket production, such as in housekeeping or volunteer work, and the morbidity cost of decreased market production because of sick leave were the most common missing components in deriving the indirect cost.

Beyond the categories of indirect cost, the criteria for including direct costs affected the proportion of total stroke-related costs represented by indirect costs. For example, the cost of staying in a nursing home, which should be treated as a part of direct cost, has been found to constitute a significant proportion of the total cost of stroke (18–19%)[8] but it was often missed in the COI studies we reviewed. Those studies, which did not include the cost of nursing homes, underestimated the direct cost and leading to an overestimation (Table 3) of the proportion of total cost represented by indirect cost.

Estimating the indirect cost depended on study designs. The choice of the length of follow-up and whether prevalence or incidence was used influenced the levels of indirect cost. The direct medical cost was incurred primarily within one year of stroke onset, while indirect costs might be amassed over the course of many years. Thus, when the incidence-based method was used, the proportion of total costs represented by indirect costs was higher when lifetime follow-up was used than when one year follow-up was used. The proportion of total stroke cost represented by indirect costs when a prevalence-based approach was used lies between those two approaches.

Another issue to consider was that the methods chosen to estimate the productivity loss greatly affected the estimation of indirect cost. In 2001, Dewey and coworkers (2001) found that the estimation of productivity loss to mortality using the FA was only about 10% of the estimated cost using the HCA.[41] In Table 3, the proportion of total cost represented by indirect cost was 3% (ischemic stroke) or 5% (intracerebral hemorrhage) and 10%, respectively, in two studies from Australia [40, 41] using the FA, while indirect cost was between 6% [42] and 71% [22, 31] of total cost for studies using the HCA. Also, the choice between the opportunity cost approach (OC in the present paper) and the replacement approach (RA) was known to considerably affecting the levels of indirect cost.[14]

In addition to cost categories and study design, characteristics of the stroke patients, such as the type of stroke and the patient's age, and country-specific factors, such as the structure of the health care system and income level, affected the level of indirect cost. Although we adjusted the indirect cost to 2012 US dollars, the year that costs were incurred also affected the level of indirect cost, as mortality and long-term disability rates after the incidence of stroke changed over time, as they were highly related to technological advances in stroke treatment and the population profile.

4.3. Potential research areas

Although the literature treated the estimation of indirect cost with various methods, study designs, stroke types, and study settings, some potential research areas remained in studies of indirect cost of stroke. First, there was an underestimation of the indirect cost if nonmarket productivity loss was not considered. As was stated above, nonmarket productivity loss was not included in current studies of indirect cost. In addition, estimation of the indirect cost was limited to those younger than 65 years because nonmarket productivity loss was not treated as a part of the indirect cost of stroke. We found relevant information about the nonmarket productivity loss was lacking, and this shortcoming lead to an underestimation of the indirect cost.

In general, the quality of data used for estimating the cost of informal care was poor. Information about types of activities forgone because of caregiving using the opportunity cost approach or types of informal caregiving activities for the replacement cost approach was not available at the national level. Some special surveys designed for informal care studies included more detailed information about the types of activities provided by a caregiver or the types of activities foregone due to caregiving [14, 19], but such studies are scarce.

Another concern with the data quality of informal care was the lack of information to verify the informal care costs of stroke patients that were not due to stroke but instead were due to other health conditions. Because most stroke patients were elderly, it was possible that the patients would use informal caregiving services even without stroke. However, data that provided the reasons for using informal care were not available. Only one study compared the use of informal care during “pre-stroke” and “post-stroke” periods as a way to resolve this issue.[35] As an alternative, Hickenbottom and coworkers used regression analysis to control for comorbidities, which might increase the use of informal caregiving among stroke patients.[17]

Finally, research on the indirect cost of stroke in developing countries was lacking. Among the 31 studies reviewed, only one study was about a developing country, Thailand. Because some components of indirect cost, such as informal caregiving cost, were more important in developing countries where were often lacking formal care facilities or nursing home services for stroke survivors, studies on informal caregiving in developing countries should have public health significance in improving the quality of life for stroke patients.

5. Conclusions

This study found that the indirect costs of stroke varied from 3% to 71% of the total cost of that event. The level of the indirect cost depended on the length of study periods, methods, study design, types of stroke, and cost components. Regardless, the level of indirect cost was considerable, and in the present review the median proportion of indirect cost was 32% of the total cost of stroke. The indirect cost will increase even further with the aging population and improving survival rate of stroke patients. To better quantify the economic burden of stroke, developing proper methods to study indirect costs, and establishing relevant data sources for those studies are in critical need. More-refined studies will facilitate the

development of interventions for stroke prevention to reduce the health and economic burden associated with stroke.

Acknowledgments

The findings and conclusions of this article are those of the authors and do not necessarily represent the official position of the U.S. Centers for Disease Control and Prevention (CDC).

References

1. World Health Organization. The world health report 2002. Midwifery. 2003; 19:72–73. [PubMed: 12691085]
2. Redon J, Olsen MH, Cooper RS, Zurriaga O, Martinez-Beneito MA, Laurent S, et al. Stroke mortality and trends from 1990 to 2006 in 39 countries from europe and central asia: Implications for control of high blood pressure. European Heart Journal. 2011; 32:1424–1431. [PubMed: 21487117]
3. Gillum RF, Kwagyan J, Obisesan TO. Ethnic and geographic variation in stroke mortality trends. Stroke. 2011; 42:3294–3296. [PubMed: 21940976]
4. Kunst AE, Amiri M, Janssen F. The decline in stroke mortality: Exploration of future trends in 7 western european countries. Stroke. 2011; 42:2126–2130. [PubMed: 21700943]
5. Chiu L, Shyu WC, Chen TR. A cost-effectiveness analysis of home care and community-based nursing homes for stroke patients and their families. Journal of Advanced Nursing. 1997; 26:872–878. [PubMed: 9372390]
6. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Borden WB, et al. Heart disease and stroke statistics--2013 update: A report from the american heart association. Circulation. 2013; 127:e6–e245. [PubMed: 23239837]
7. Gustavsson A, Svensson M, Jacobi F, Allgulander C, Alonso J, Beghi E, et al. Cost of disorders of the brain in europe 2010. European neuropsychopharmacologyy. 2011; 21:718–779.
8. Demaerschalk BM, Hwang HM, Leung G. Us cost burden of ischemic stroke: A systematic literature review. The American Journal of Managed Care. 2010; 16:525–533. [PubMed: 20645668]
9. Taylor TN, Davis PH, Torner JC, Holmes J, Meyer JW, Jacobson MF. Lifetime cost of stroke in the United States. Stroke. 1996; 27:1459–1466. [PubMed: 8784113]
10. Dewey HM, Thrift AG, Mihalopoulos C, Carter R, Macdonell RA, McNeil JJ, et al. Informal care for stroke survivors: Results from the north east melbourne stroke incidence study (NEMESIS). Stroke. 2002; 33:1028–1033. [PubMed: 11935056]
11. Ekman M. Economic evidence in stroke: A review. The European Journal of Health Economics. 2004; 5(Suppl 1):S74–83. [PubMed: 15754078]
12. Kang HY, Lim SJ, Suh HS, Liew D. Estimating the lifetime economic burden of stroke according to the age of onset in south korea: A cost of illness study. BMC Public Health. 2011; 11:646. [PubMed: 21838919]
13. Zheng H, Ehrlich F, Amin J. Productivity loss resulting from coronary heart disease in australia. Applied Health Economics and Health Policy. 2010; 8:179–189. [PubMed: 20408602]
14. van den Berg B, Brouwer W, van Exel J, Koopmanschap M, van den Bos GA, Rutten F. Economic valuation of informal care: Lessons from the application of the opportunity costs and proxy good methods. Social Science & Medicine (1982). 2006; 62:835–845. [PubMed: 16137814]
15. Grieve R, Hutton J, Bhalla A, Rastenyte D, Ryglewicz D, Sarti C, et al. A comparison of the costs and survival of hospital-admitted stroke patients across europe. Stroke. 2001; 32:1684–1691. [PubMed: 11441220]
16. Fox P, Gazzaniga J, Karter A, Max W. The economic costs of cardiovascular disease mortality in california, 1991: Implications for public health policy. Journal of Public Health Policy. 1996; 17:442–459. [PubMed: 9009539]

17. Hickenbottom SL, Fendrick AM, Kutcher JS, Kabeto MU, Katz SJ, Langa KM. A national study of the quantity and cost of informal caregiving for the elderly with stroke. Neurology. 2002; 58:1754–1759. [PubMed: 12084872]
18. Lindgren P, Glader EL, Jonsson B. Utility loss and indirect costs after stroke in sweden. European Journal of Cardiovascular Prevention and Rehabilitation. 2008; 15:230–233. [PubMed: 18391653]
19. Riewpaiboon A, Riewpaiboon W, Ponsoongnern K, Van den Berg B. Economic valuation of informal care in asia: A case study of care for disabled stroke survivors in thailand. Social Science & Medicine (1982). 2009; 69:648–653. [PubMed: 19573969]
20. Heidenreich PA, Trogdon JG, Khavjou OA, Butler J, Dracup K, Ezekowitz MD, et al. Forecasting the future of cardiovascular disease in the united states: A policy statement from the american heart association. Circulation. 2011; 123:933–944. [PubMed: 21262990]
21. Brown DL, Boden-Albala B, Langa KM, Lisabeth LD, Fair M, Smith MA, et al. Projected costs of ischemic stroke in the united states. Neurology. 2006; 67:1390–1395. [PubMed: 16914694]
22. Wiebers DO, Torner JC, Meissner I. Impact of unruptured intracranial aneurysms on public health in the united states. Stroke. 1992; 23:1416–1419. [PubMed: 1412577]
23. Chan BBH. Cost of stroke in ontario, 1994/95. Canadian Medical Association Journal. 1998; 159:S2–S8.
24. Dodel R, Winter Y, Ringel F, Spottke A, Gharevi N, Muller I, et al. Cost of illness in subarachnoid hemorrhage: A German longitudinal study. Stroke. 2010; 41:2918–2923. [PubMed: 21071720]
25. Rossnagel K, Nolte CH, Muller-Nordhorn J, Jungehulsing GJ, Selim D, Bruggenjurgen B, et al. Medical resource use and costs of health care after acute stroke in Germany. European Journal of Neurology. 2005; 12:862–868. [PubMed: 16241975]
26. Weimar, C.; Weber, C.; Wagner, M.; Busse, O.; Haberl, RL.; Lauterbach, KW., et al. Cerebrovascular diseases. Vol. 15. Basel, Switzerland: 2003. Management patterns and health care use after intracerebral hemorrhage. A cost-of-illness study from a societal perspective in Germany; p. 29-36.
27. Smith S, Horgan F, Sexton E, Cowman S, Hickey A, Kelly P, et al. The cost of stroke and transient ischaemic attack in Ireland: A prevalence-based estimate. Age and Ageing. 2012; 41:332–338. [PubMed: 22134905]
28. Pugliatti M, Sobocki P, Beghi E, Pini S, Cassano GB, Altamura AC, et al. Cost of disorders of the brain in Italy. Neurological Sciences. 2008; 29:99–107. [PubMed: 18483707]
29. Gerzeli S, Tarricone R, Zolo P, Colangelo I, Busca MR, Gandolfo C. The economic burden of stroke in Italy. The eclipse study: Economic longitudinal incidence-based project for stroke evaluation. Neurological Sciences. 2005; 26:72–80. [PubMed: 15995823]
30. Evers SM, Engel GL, Ament AJ. Cost of stroke in the Netherlands from a societal perspective. Stroke. 1997; 28:1375–1381. [PubMed: 9227686]
31. Lopez-Bastida J, Oliva Moreno J, Worbes Cerezo M, Perestelo Perez L, Serrano-Aguilar P, Monton-Alvarez F. Social and economic costs and health-related quality of life in stroke survivors in the Canary islands, Spain. BMC health services research. 2012; 12:315. [PubMed: 22970797]
32. Navarrete-Navarro P, Hart WM, Lopez-Bastida J, Christensen MC. The societal costs of intracerebral hemorrhage in Spain. European Journal of Neurology. 2007; 14:556–562. [PubMed: 17437616]
33. Persson J, Ferraz-Nunes J, Karlberg I. Economic burden of stroke in a large county in Sweden. BMC health services research. 2012; 12:341. [PubMed: 23013284]
34. Ghatnekar O, Persson U, Glader EL, Terent A. Cost of stroke in Sweden: An incidence estimate. International Journal of Technology Assessment in Health Care. 2004; 20:375–380. [PubMed: 15446769]
35. Zethraeus N, Molin T, Henriksson P, Jonsson B. Costs of coronary heart disease and stroke: The case of Sweden. Journal of Internal Medicine. 1999; 246:151–159. [PubMed: 10447784]
36. Terent A, Marke L, Asplund K, Norrving B, Jonsson E, Wester P. Costs of stroke in Sweden: A national paerspective. Stroke. 1994; 25:2363–2369. [PubMed: 7974574]
37. Saka O, McGuire A, Wolfe C. Cost of stroke in the United Kingdom. Age and Ageing. 2009; 38:27–32. [PubMed: 19141506]

38. Luengo-Fernandez R, Leal J, Gray A, Petersen S, Rayner M. Cost of cardiovascular diseases in the United Kingdom. Heart (British Cardiac Society). 2006; 92:1384–1389. [PubMed: 16702172]

39. Leal J, Luengo-Fernandez R, Gray A, Petersen S, Rayner M. Economic burden of cardiovascular diseases in the enlarged European Union. European Heart Journal. 2006; 27:1610–1619. [PubMed: 16495286]

40. Cadilhac DA, Carter R, Thrift AG, Dewey HM. Estimating the long-term costs of ischemic and hemorrhagic stroke for australia: New evidence derived from the North East Melbourne Stroke Incidence Study (NEMESIS). Stroke. 2009; 40:915–921. [PubMed: 19182091]

41. Dewey HM, Thrift AG, Mihalopoulos C, Carter R, Macdonell RA, McNeil JJ, et al. Cost of stroke in australia from a societal perspective: Results from the North East Melbourne Stroke Incidence Study (NEMESIS). Stroke. 2001; 32:2409–2416. [PubMed: 11588334]

42. Scott WG, Scott H. Ischaemic stroke in New Zealand: An economic study. The New Zealand Medical Journal. 1994; 107:443–446. [PubMed: 7970352]

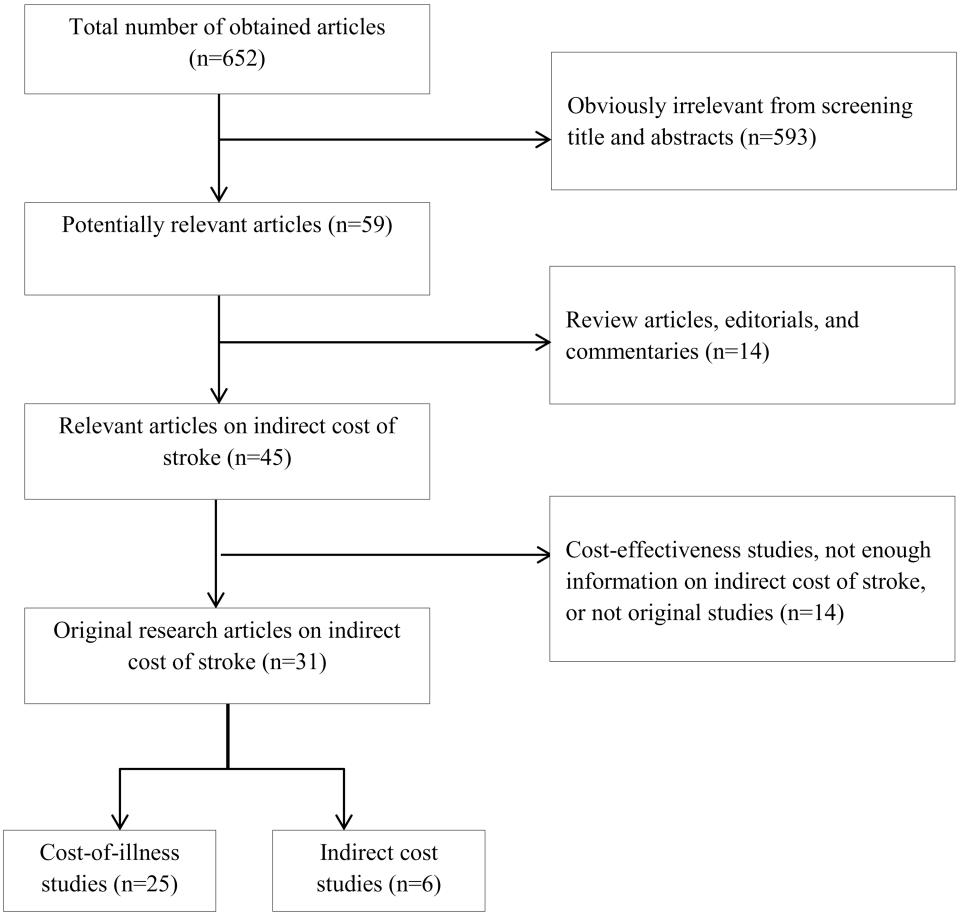

Figure 1. Diagram for selection of studies on the indirect cost of stroke, 1990-2012

Table 1

Type of indirect costs of stroke investigated in the literature, 1990-2012

Study type	Country	First author/Year of publication	Type of indirect costs included		
			Mortality	Morbidity	Informal caregiving
Cost-of-illness	US	Heidenreich [20], 2011	Yes	Yes	No
	US	Brown [21], 2006	Yes	Yes	Yes
	US	Taylor [9], 1996	Yes	Yes	No
	US	Wiebers [22], 1992	Yes	Yes	Yes
	Canada	Chan [23], 1998	Yes	Yes	No
	Germany	Dodel [24], 2010	Yes	Yes	Yes
	Germany	Rossnagel [25], 2005	No	Yes	No
	Germany	Weimar [26], 2003	No	Yes	No
	Ireland	Smith [27], 2012	Yes	Yes	Yes
	Italy	Pugliatti [28], 2008	Yes	Yes	Yes
	Italy	Gerzeli [29], 2005	Yes	Yes	Yes
	Netherlands	Evers [30], 1997	Yes	Yes	No
	Spain	Lopez-Bastida [31], 2012	No	Yes	Yes
	Spain	Navarrete-Navarro [32], 2007	Yes	Yes	Yes
	Sweden	Persson [33], 2012	Yes	Yes	Yes
	Sweden	Ghatnekar [34], 2004	Yes	Yes	No
	Sweden	Zethraeus [35], 1999	No	Yes	No
	Sweden	Terént [36], 1994	Yes	Yes	No
	UK	Saka [37], 2009	Yes	Yes	Yes
	UK	Luengo-Fernández [38], 2006	Yes	Yes	Yes
	EU*	Gustavsson [7], 2011	Yes	Yes	Yes
	EU	Leal [39], 2006	Yes	Yes	Yes
	Australia	Cadilhac [40], 2009	Yes	Yes	Yes
	Australia	Dewey [41], 2001	Yes	Yes	Yes

Study type	Country	First author/Year of publication	Type of indirect costs included		
			Mortality	Morbidity	Informal caregiving
	New Zealand	Scott [42], 1994	No	Yes	Yes
Indirect cost	US	Hickenbottom, 2002	No	No	Yes
	US	Fox [16], 1996	Yes	No	No
	Sweden	Lindgren [18], 2008	No	Yes	No
	Netherlands	van den Berg [14], 2006	No	No	Yes
	Australia	Dewey [10], 2002	No	No	Yes
	Thailand	Riewpaiboon [19], 2009	No	No	Yes

Notes: Cost-of-illness (COI) studies included both direct and indirect cost analyses. Indirect cost studies include analysis of indirect costs only. EU: European Union; UK: United Kingdom; US: United States.

*European Union plus Iceland, Norway, and Switzerland

Table 2
Data sources used in the literature of indirect costs of stroke, 1990-2012

Country/References	Prevalence/incidence	Productivity loss and informal care cost
US[9, 16, 17, 20-22]	• 2000 US Census • NOMASS: Northern Manhattan Stroke Study • BASIC: Brain Attack Surveillance in Corpus Christi • NHANES: National Health and Nutrition Examination Survey • National Hospital Discharge Survey	• AHEAD: The Asset and Health Dynamics • BLS: Bureau of Labor Statistics • NMES: National Medical Expenditure Survey • MEPS: Medical Expenditure Panel Survey • CMS: Centers for Medicare & Medicaid Services • Current Population Survey • National Vital Statistics • California State Department of Health Services (Health Demographics)
Canada[23]	• National vital statistics data • 1990 OHS (Ontario Health Survey)	• Statistics Canada Survey Data
Germany[24-26]	• Hospital data (Department of Neurosurgery and Neuroradiology at the University of Bonn) • German Stroke Data Bank • German version of the National Institutes of Health Stroke Scale	• Hospital-based health economic questionnaires (Department of Neurosurgery and Neuroradiology at the University of Bonn) • Federal Statistics • German Stroke Data Bank
Ireland[27]	• NDPSS: North Dublin Population Stroke Study	• National Employment Survey 2007–2009 • Census of Population • SHARE: The Survey of Health, Ageing and Retirement in Europe • INASC: Irish National Audit of Stroke Care
Italy[28, 29]	• EcLIPSE: Economic Longitudinal Incidence-based Project for Stroke Evaluation Study	• EcLIPSE
Netherlands[14, 30]	• EDISS: Evaluation of Dutch Integrated Stroke Service Experiments	• Mortality registration data • Chronicle of social insurance • EDISS
Spain [31, 32]	• Hospital data from 28 hospitals in Andalusia and five hospitals in Canary Islands	• 2004 Wage Structure Survey of the Spanish National Statistics Institute • Hospital-based stroke survivor questionnaires from five hospitals in the Canary Islands
Sweden[18, 33-36]	• Local and national clinical registers • Hospital data from the department of medicine at Sodertalje Hospital	• Social insurance authority • The Stroke Register • Socialforsakringsstatistik 1973–1991 • Den ersatta sjukfranvarons diagnoser 1983 (vol. 8) • Local insurance office in Sodertalje

Country/References	Prevalence/incidence	Productivity loss and informal care cost
UK[37, 38]	• WHOSIS: World Health Organization Statistical Information System • ONS: Office of National Statistics • SLSR: South London Stroke Register	• Department for Work and Pensions • The General Household Survey
Australia [10, 40, 41]	• NEMESIS: North East Melbourne Stroke Incidence Study	• MORUCOS: Model of Resource Utilization, Costs, and Outcomes for Stroke • NEMESIS
New Zealand[42]	• New Zealand hospital admission data	• Information Network for Official Statistics (INFOS): Online computerized official statistics for New Zealand
Thailand[19]	• Hospital data from Sirindhorn National Medical Rehabilitation Center (SNMRC) and Buriam Hospital	• Hospital-based survey data from SNMRC and Buriam Hospital

Notes: When a data source is previous literature, we did not include it as a data source in this table. UK: United Kingdom; US: United States.

Table 3

Methods and results of cost-of-illness studies for stroke patients, 1990-2012

Prevalence-based studies

First author/ year of publication/country	Patients		Study design[b]	Year of cost (Study period)	Annual indirect cost in millions		Proportion of total cost represented by indirect cost, %[d] (Study period)
	Stroke type[a]	Age range			Local currency (Study period)	2012 USD[c] (Study period)	
Heindenreich, 2011, US[20]	All types (as a part of CVD)	All	HCA	2008 (2010∼2030)	25,600 (2010) [e] 44,400 (2030) [e]	27,299 (2010) [e] 47,347 (2030) [e]	47 (2010) 32 (2030)
Brown, 2006, US[21]	IS	45∼64	HCA, RA	2005 (2005∼2050)	1,177,000[f] (2005∼2050)	1,383,736[f] (2005∼2050)	53 (2005∼2050)
Chan, 1998, Canada (Ontario)[23]	All types (CI, ICH, SAH, TIA)	Under 75	HCA	1994∼95	328[e]	381 [e]	38
Smith, 2012, Ireland[27]	All types and TIA	All	HCA, OC	2007	143∼248 [g]	176∼305 [g]	29–31
Gustavsson, 2011, European countries[7]	All types (as a part of brain disorders)	Unclear	Unclear	2010	4,932[g, h]	N/A[j]	8
Saka, 2009, UK[37]	All types	Under 65	HCA, RA	2005	3,754	6,784	42
Pugliatti, 2008, Italy[28]	All types (as a part of brain disorders)	Unclear	HCA, RA	2004	792 [g, h]	1,189 [g, h]	23
Leal, 2006, EU[39]	All types (as a part of CVD)	All	HCA/FA, OC	2003	13,285 [g]	19,508 [g]	39
Luengo-Fernandez, 2006, UK[38]	All types (as a part of CVD)	All	HCA/FA, OC	2004	3,328 (HCA) 2,770 (FA)	6,137 (HCA) 5,108 (FA)	39 (HCA) 35 (FA)
Evers, 1997, Netherlands[30]	All types	18∼64	HCA	1993	566[e]	1,012[e]	22
Terént, 1994, Sweden[36]	All types	Under 65	HCA	1991 (1983)	2,430 [e]	379 [e]	24
Scott, 1994, New Zealand[42]	IS	15–64 (n=912)	HCA, OC/RA	1992	6∼14 [h]	7∼14 [h]	6∼9

Incidence-based studies

First author/ year of publication/ country	Patients		Study design[b]	Year of cost (Study period)	Annual indirect cost in millions		Per patient indirect cost, local currency (2012 USD)[c]	Proportion of total cost represented by indirect cost,%[d]
	Stroke type[a]	Age (sample size) [i]			Local currency	2012 USD[c]		
Wiebers, 1992, US[22]	Unruptured intracranial aneurysms, aneurysmal SAH	All (n=10,300/17,250)	lifetime, HCA	Unclear (1979,1984,1989)	309.8 (unruptured aneurysm), 1,242.5 (SAH)	507 (unruptured aneurysm), 2033 (SAH)[k]	N/A	59 (unruptured aneurysm), 71 (SAH)
Taylor, 1996, US[9]	First SAH, ICH,IS	All (n=N/A)	lifetime, HCA	1990	23,600[e]	41,470 [e]	N/A	58
Navarrete-Navarro, 2007, Spain[32]	First ICH survivors	All (n=425)	lifetime, HCA, RA	2004	N/A	N/A	31,108[g] (54,067)	67

Ghatnekar, 2004, Sweden[34]	First all type	Under 65 (n=4357)	lifetime, HCA	2000 (first 6 months in 1997)	N/A	N/A	163,694 (male)[e] 86,586 (female) [e] (22,243/11,765)	25 (male) 14 (female)
Lopez-Bastida, 2012, Spain[31]	All type	Under 65 (n=94)	1 year, HCA, OC	2004	N/A	N/A	12,449 [g] (21,637)	71
Persson, 2012, Sweden (VästraGötaland county)[33]	First ICH, CI, stroke	All (n=3074)	1 year, HCA, OC	2008	97	11	N/A	15
Dodel, 2010, Germany[24]	SAH	Under 65 (n=101)	1 year, HCA, RA	2009 (2004∼2005)	N/A	N/A	17,350 [g] (22,850)	45
Rossnagel, 2005, Germany[25]	All types and TIA	18∼64 (n=383)	1 year, HCA	2002	N/A	N/A	2,014[e, g] (2,960)	18
Weimar, 2003, Germany[26]	ICH	All (n=266)	1 year, HCA	Unclear (Jan. 1998 ∼ Oct. 1999)	N/A	N/A	5,537 [e, g, k] (8,053)	55
Zethraeus, 1999, Sweden[35]	All types (as a part of CVD)	Under 64 (n=12)	1 year, HCA	1994 (1993∼1995)	N/A	N/A	71,731[e] (10,229)	N/A
Gerzeli, 2005, Italy[29]	First IS and hemorrhage	Over 18 (n=449)	6 months, HCA, OC/RA	1998	N/A	N/A	5,026 [g] (8,691)	43
Cadilhac,2009, Australia[40]	First IS and ICH	Unclear (n=4291/27660)	lifetime, FA	2004	12.8 (ICH)[h] 46.5 (IS) [h]	10 (ICH)[h] 38 (IS) [h]	N/A	5 (ICH) 3 (IS)
Dewey, 2001, Australia[41]	First CI, ICH, and unclassified stroke	Under 65 (n=165)	1 year, FA, OC	1997 (May 1996 ∼April 1997)	56	56	N/A	10

Notes:

[a] CVD (cardiovascular disease, includes hypertension, coronary heart disease, heart failure, stroke, and all other cardiovascular disease); ICH (intracerebral hemorrhagic stroke); IS (ischemic stroke); SAH (subarachnoid hemorrhage); TIA (transient ischemic attack); CI (cerebral infarction); N/A (not available).

[b] Estimation approaches for productivity loss: HCA (the human capital approach), and FA (the friction cost approach). Estimation approaches for the time cost of informal caregiving: OC (the opportunity cost approach), and RA (the replacement approach).

[c] Indirect cost in 2012 USD is estimated by using consumer price indices of study countries in the years of cost and in 2012 from the World Bank (http://data.worldbank.org/indicator/FP.CPI.TOTL) and purchasing power parity (PPP) exchange rate in 2012 from OECD website (http://stats.oecd.org/Index.aspx?datasetcode=SNA_TABLE4).

[d] The proportion of total cost represented by indirect cost = (indirect cost/total cost) × 100. Total cost includes both direct and indirect cost.

[e] Cost of informal caregiving is not included in indirect cost. Also, the total cost does not include the cost of informal caregiving.

[f] Costs are accumulated costs during study periods.

[g] Euro is used as a local currency.

[h] The cost of informal caregiving is included in direct cost and is not separable from that cost. In the calculation of the proportion of total cost represented by indirect cost, the cost of informal caregiving is included in the total cost but not in indirect cost.

[i] When the sample size of the indirect cost is different from the total sample size, the sample size for indirect cost is shown.

[j] Because indirect cost of each country was not provided, we cannot estimate indirect cost in 2012 ISD.

[k] We assume that the year of cost is the publication year.

Table 4

Methods and results of indirect cost studies for stroke patients, 1990- 2012

First author/ year of publication/ country	Patients		Study design[c]	Year of cost (Study period)	Type of indirect cost	Annual indirect cost in millions		Annual per-patient indirect cost	
	Stroke type[a]	Age (Sample size)[b]				Local currency[c]	2012 USD[c, d]	Local currency[c]	2012 USD[c, d]
Fox,1996, US (California)[16]	Cerebrovascular disease (as a part of CVD)	All (n=15,222)	Incidence (1 year), HCA	1991 (1989–1991)	Mortality	1,082	1,824	71,081	119,829
Hickenbottom, 2002, US[17]	All types	Over 70 (n=7,443)	Prevalence, RA	1999	Informal care	6,100	8,408	3,500–8,200	4,824–11,302
Dewey, 2002, Australia[10]	First CI, ICH, and unclassified	N/A (n=340)	Incidence (lifetime), OC/RA	1997	Informal care	332 (OC) 171 (RC)	329 (OC) 170 (RC)	N/A	N/A
van den Berg, 2006, Netherlands[14]	All types	All (n=218)	Incidence (6 months), OC/RA	2001	Informal care	N/A	N/A	17,482 (OC)[e] 12,440 (RA)[e]	23,451 (OC)[e] 16,687 (RA)[e]
Lindgren, 2008, Sweden[18]	IS	18–76 (n=275)	Incidence (1 year), HCA	2006	Morbidity	N/A	N/A	120,000	14,963
Riewpaiboon 2009, Thailand[19]	All types	All (n=149)	Prevalence, OC	2006 (2001–2005)	Informal care	N/A	N/A	42,336–68,052	904–1,453

Notes:

[a] CVD (cardiovascular disease, includes hypertension, coronary heart disease, heart failure, stroke, and all other cardiovascular disease); ICH (intracerebral hemorrhagic stroke); IS (ischemic stroke); SAH (subarachnoid hemorrhage); TIA (transient ischemic attack); CI (cerebral infarction); N/A (not available).

[b] When the sample size of the indirect cost is different from the total sample size, the sample size for indirect cost is shown.

[c] Estimation approaches for productivity loss: HCA (the human capital approach).Estimation approaches for the time cost of informal caregiving: OC (the opportunity cost approach), and RA (the replacement approach).

[d] Indirect cost in 2012 USD is estimated by using consumer price indices of study countries in the years of cost and in 2012 from the World Bank (http://data.worldbank.org/indicator/FP.CPI.TOTL) and purchasing power parity (PPP) exchange rate in 2012 from OECD website (http://stats.oecd.org/Index.aspx?datasetcode=SNA_TABLE4). For Thailand, we use a PPP conversion factor from the World Bank and an exchange rate in 2012 from the webpage of the Federal Reserve Bank of St. Louis, Economic Research, at the following link:http://research.stlouisfed.org/fred2/release?rid=186&soid=1&t=g5a&at=g5a&ob=pv&od=desc.

[e] Euro is used as a local currency.