

Lifetime Cost of Ischemic Stroke in Germany: Results and National Projections From a Population-Based Stroke Registry

The Erlangen Stroke Project

Peter L. Kolominsky-Rabas, MD, PhD; Peter U. Heuschmann, MD, PhD; Daniela Marschall, MSc; Martin Emmert; Nikoline Baltzer, Bnurs; Bernhard Neundörfer, MD, PhD; Oliver Schöffski, PhD; Karl J. Krobot, MD, PhD; for the CompetenceNet Stroke

Background and Purpose—The number of stroke patients and the healthcare costs of strokes are expected to rise. The objective of this study was to determine the direct costs of first ischemic stroke and to estimate the expected increase in costs in Germany.

Methods—An incidence-based, bottom-up, direct-cost-of-ischemic-stroke study from the third-party payer's perspective was performed, incorporating 10-year survival data and 5-year resource use data from the Erlangen Stroke Registry. Discounted lifetime year 2004 costs per case were obtained and applied to the expected age and sex evolution of the German resident population in the period 2006 to 2025.

Results—The overall cost per first-year survivor of first-ever ischemic stroke was estimated to be 18 517 euros (EUR). Rehabilitation accounted for 37% of this cost, whereas in subsequent years outpatient care was the major cost driver. Discounted lifetime cost per case was 43 129 EUR overall and was higher in men (45 549 EUR) than in women (41 304 EUR). National projections for the period 2006 to 2025 showed 1.5 million and 1.9 million new cases of ischemic stroke in men and women, respectively, at a present value of 51.5 and 57.1 billion EUR, respectively.

Conclusions—The number of stroke patients and the healthcare costs of strokes in Germany will rise continuously until the year 2025. Therefore, stroke prevention and reduction of stroke-related disability should be made priorities in health planning policies. (*Stroke*. 2006;37:1179-1183.)

Key Words: costs and cost analysis ■ cost of illness ■ ischemic stroke ■ resource use ■ stroke

The social and economic consequences of stroke impose a considerable burden on patients, payers, and society in terms of premature death, long-term disability, restricted social functioning, costs of care, lost productivity, and informal caregiver time.¹ In industrialized countries stroke is the third most common cause of death and the major cause of serious long-term disability in adults.² About 1 million first ischemic strokes are estimated to occur each year in the European Union (population 450 million).³

The burden of stroke is expected to rise even further given that the number of elderly people is expected to increase in industrialized countries over the coming decades.⁴ The combination of an aging population, declining stroke case-fatality rates, and limited success in reducing the incidence of stroke has resulted in an increase in the prevalence of stroke survivors.⁵ In England, Wales, Scotland, and The Netherlands, stroke alone accounts for 3% to 4% of the direct costs of healthcare.^{6,7,8,9} Besides the cost

of acute hospitalization, there are direct costs related to rehabilitation, ambulatory medical treatment and long-term care of disabled stroke survivors.

Given the pressures on healthcare funding, it is essential that policymakers acquire a better understanding of the current and future burden associated with stroke. The purpose of the present cost-of-illness (COI) study, therefore, was to estimate life expectancy and costs associated with first ischemic stroke in an unselected population-based cohort of statutorily health-insured (SHI) patients in Germany. To that end, life-years lived and cost in each year poststroke were estimated. The study was undertaken as a component of the Erlangen Stroke Project.

Methods

Study Area and Source Population

All data were collected in the Erlangen Stroke Project (ESPro). The ESPro is a prospective population-based stroke registry based in

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From the Department of Health Economics & Outcomes Research (P.L.K.-R.), Institute for Quality and Efficiency in Health Care (IQWiG), Cologne, Germany; the Unit for Stroke Research & Public Health Medicine (P.L.K.-R., N.B., B.N.) and the Department of Health Management (D.M., M.E., O.S.), Interdisciplinary Center for Public Health Studies, University of Erlangen-Nuremberg, Bavaria, Germany; the Institute of Epidemiology and Social Medicine (P.U.H.), University of Münster, Germany; the Outcomes Research Department (K.J.K.), MSD Sharp & Dohme GmbH, Haar, Germany.

Correspondence to Peter L. Kolominsky-Rabas, MD, PhD, Head of Department, Health Economics & Outcomes Research, Institute for Quality and Efficiency in Health Care (IQWiG), D-51105 Cologne, Germany. E-mail peter.kolominsky-rabas@iqwig.de

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Bavaria, Germany, covering a total study population of 102 000 residents (census 2003) in the Community of Erlangen. The unique feature of the ESPro is its continuing case ascertainment and long-term follow-up, irrespective of age, without any stop since 1994. The study population, clinical definitions, examinations performed, and methods used have been described in detail elsewhere.^{10,11,12,13}

Case Ascertainment

All hospitalized and nonhospitalized patients in the study region with suspected cerebrovascular disease (ie, fatal or nonfatal stroke, transient ischemic attack, or cerebral vein thrombosis) are regularly examined and assessed.

Diagnostic Criteria

Stroke was diagnosed by a study neurologist according to the World Health Organization (WHO) criteria.¹⁴ First-ever-in-a-lifetime strokes were defined as strokes occurring in patients without any prior stroke event.¹⁵

Follow-Up

As demanded in the Helsingborg Declaration, the patients were followed-up at 3 months, 12 months, and then yearly.¹⁶

Study Design

The present study is a disease-specific COI study that focuses on the particularities of first ischemic stroke.¹⁷ An incidence-based, bottom-up approach was used as the study design.¹⁸ The validity of this approach is greater when the sample is unbiased, as in a strictly population-based stroke registry such as ours. All analyses were performed from the perspective of statutory health insurance (SHI), the major source of healthcare funding in Germany, covering nearly 88% of the population in 2003.¹⁹

Resources Included

Direct costs were defined as all the goods, services, and other resources that are consumed during the provision of a healthcare intervention for stroke or its sequelae. Length of stay in hospital was differentiated by department and by level of care. Hospital stays related to the initial stroke event, recurrent strokes, or complications of first or recurrent strokes were included. Following the suggestion of Evers et al, all direct costs were aggregated into 4 main categories¹⁸: inpatient costs, outpatient costs, rehabilitation costs and nursing costs.

Collection of Resource Data

Data were collected by reviewing medical records in hospitals, nursing homes, and general practitioners' offices. In addition, trained research nurses interviewed all patients and their relatives in their homes using structured and standardized questionnaires.

Unit Costs

All costs were calculated in year 2004 euros (EUR) from the perspective of SHI.

Hospitalizations

Costs of hospitalization were calculated on the basis of length of stay and institution-specific daily tariffs. Tariffs were obtained from the health insurance fund and encompassed medical care including drugs and board and lodging (eg, laundry and catering).

Outpatient Services

Costs of outpatient treatment were calculated in accordance with the German uniform value scale (Einheitlicher Bewertungsmaßstab).²⁰ The scale lists all outpatient services reimbursed by SHI. Services are grouped by specialty; in addition, there are 147 basic services (consultations, visits, screening).

Outpatient Prescription Medications

We recorded the number and market price of medications prescribed by office-based physicians. Only outpatient prescriptions were considered because the cost of drugs used during stays in an acute or rehabilitation hospital is covered by the institution's tariffs.

Rehabilitation Services

The costs of inpatient and outpatient rehabilitation were calculated on the basis of the institution's daily tariffs. These tariffs were communicated by the health insurance fund and covered medical care including drugs as well as board and lodging.

Nursing

Costs of stays in nursing homes and retirement homes, home nursing visits, and community services were calculated on the basis of the annual tariffs of German statutory long-term care insurance (Soziale Pflegeversicherung). This provides benefits for domiciliary, semi-inpatient, and inpatient care. The benefits vary by level of care: care category I=considerable need of care; care category II=severe need of care; care category III=extreme need of care.²¹ Institutionalization costs were not considered in patients already institutionalized at the time of first ischemic stroke.

Statistical Analysis

Life Expectancy

Acute and long-term mortality after stroke are driven by different forces. We found that survival within the first year after ischemic stroke was best described using nonparameterized Kaplan-Meier curves, whereas year 2 to 10 survival complied well with a Weibull parameterization. The Weibull parameterization was preferred over the exponential, the Gompertz, the lognormal, the log-logistic, and the generalized γ distributions based on the Akaike information criterion²² and on graphical inspection of the Cox-Snell residuals.²³ The data were consistent with hazards of dying that increased slightly in an exponential fashion in years 2 to 10 poststroke. Stata 7.0 Special Edition²⁴ was used for analyses.

Longitudinal Cost per Stroke

Crude and discounted (3% per annum) estimates of sex-specific and overall longitudinal cost of stroke were calculated. For year 1 after first ischemic stroke we multiplied the area under the 1-year Kaplan-Meier survival curve by the mean total direct cost incurred per first-year survivor. For each subsequent year until death we multiplied the respective area under the Weibull survival projection by an estimate of mean total direct cost incurred during the respective year among those surviving it. As these cost estimates were found to be homogeneous across years 2 to 5 poststroke in both men and women, we collapsed them into a single estimate of mean total direct cost per male and female survivor per year. These 2 estimates were carried forward beyond year 5, where we had no cost data. As opposed to a 1-year-cycle Markov model, our approach thus accounted for the true curvilinear shape of the survival curve in each year poststroke. One-way sensitivity analyses were performed on the 95% confidence limits of life-expectancy poststroke in both sexes and overall.

National Stroke Cost Estimates for 2004

We estimated the financial burden imposed on the German SHI by ischemic strokes in 2004 assuming that the population was stable with respect to age and sex composition and that the age-specific incidence, prognosis, and costs of stroke were constant, in which case undiscounted lifetime costs can be interpreted as yearly (2004) costs. To this end we determined the ESPro incidence of strokes of any kind¹⁰ by sex and linear and squared age and multiplied this rate by the person-time of the population of Germany in 2004. Ischemic strokes in SHI patients accounted for 73% of the cases obtained in this way in both men and women.

National Stroke Cost Projections for 2006 to 2025

In this approach we estimated what resources the SHI would need to have included in its budgeting by the end of 2005 in order to meet the lifetime costs of all first ischemic strokes expected to occur over, for example, the following 10 years. For the purpose of this calculation, future costs were discounted at a rate of 3% per year, the annual change in the age and sex distribution of the population predicted by the Federal Statistical Office was taken into account, and the age- and sex-specific incidence of strokes and the type and unit costs of the resources used were assumed to be constant.²⁵ As in the previous section, estimates were made for each calendar year.

Results

A total of 1637 and 821 patients from the ESPro were available for the survival analyses and the healthcare resource utilization analyses, respectively. A cranial CT or MR scan was performed in 96% of patients. Almost every patient with ischemic stroke (98%) had been admitted to hospital for acute treatment; 55% of patients were female. Mean age at first ischemic stroke was higher in women (76.3 years) than in men (70.6 years). Overall, 52% of patients were in the age group >75 years. During 5 years of follow-up 24% of the cases (95% CI: 18 to 27) had a recurrent stroke. The male and female cohort was projected to decline according to Kaplan-Meier and Weibull as shown in the Figure. Mean undiscounted (discounted) life expectancy after first ischemic stroke was estimated at 8.6 (6.8) years in men, 6.3 (5.3) years in women, and 7.3 (5.9) years overall.

Cost per Survivor per Year

Among first-year survivors mean total direct cost was estimated at 18 517 EUR (Table 1). Rehabilitation accounted for the largest share (37%) of this. In the subsequent 4 years outpatient treatment stood out, accounting for 49% of all expenditure. Mean annual total direct cost per survivor during years 2 to 5 was 5479 EUR (Table 1).

Lifetime Cost

An overview of lifetime cost per stroke in SHI men and women is given in Table 2. First-year cost accounted for about 35% of the present value of the lifetime cost of first ischemic stroke. Mean undiscounted lifetime cost was higher in men (54 552 EUR) than in women (47 596 EUR) because ischemic stroke occurred later in life in women than in men. Overall, the lifetime cost per ischemic stroke in SHI patients was 50 507 EUR undiscounted and 43 129 EUR discounted. True discounted lifetime cost per first ischemic stroke were

TABLE 1. Mean Annual Component Cost of First-Ever-in-a-Lifetime Ischemic Stroke in SHI in Germany (in year 2004 EUR)

	Men	Women	All**
Year 1			
Inpatient	7 002	6 495	6 731
Outpatient	3 250	3 319	3 287
Rehabilitation	6 759	6 876	6 822
Nursing	1 250	2 049	1 678
All	18 262	18 739	18 517
Subsequent years*			
Inpatient	949	782	863
Outpatient	2 407	2 939	2 683
Rehabilitation	672	878	776
Nursing	980	1 321	1 157
All	5 008	5 920	5 479

*Years 2 to 5 after first ischemic stroke.

**Weighted by years spent by males and females.

within about $\pm 10\%$ of the point estimates with 95% confidence considering the precision our study had with regard to life-expectancy as single factor (Table 2).

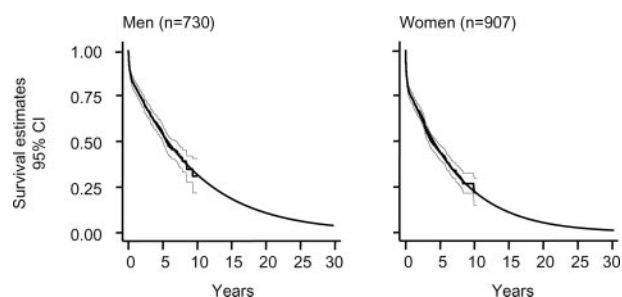
National Estimates

The total financial burden of first ischemic stroke to the SHI in the year 2004 was estimated at 7.1 billion EUR. The largest components were outpatient treatment (40%; 2.8 billion EUR), inpatient treatment (22%; 1.6 billion EUR), rehabilitation (21%; 1.5 billion EUR), and nursing (17%; 1.2 billion EUR). National projections for 2006 to 2025 yielded an expected direct cost at present value of 51.5 billion EUR in men, 57.1 billion in women, and 108.6 billion EUR overall (Table 3). These estimates are for lifetime treatment of newly diagnosed first ischemic strokes (2006 to 2025). They take account of ministerial figures for the expected age and sex evolution of the German resident population over this period and assume age- and sex-specific stroke rates to be constant. Attributable to the higher number of first ischemic strokes in SHI women (1.9 million) than in SHI men (1.5 million), the figures are higher for women than for men.

Discussion

This is the first incidence-based, bottom-up estimate of the overall direct lifetime cost of ischemic stroke based on follow-up 10-year survival and 5-year resource use data derived from a single population-based setting. Our findings detail stroke aftercare and cost in Germany and inform healthcare policies with regard to future fields of action and healthcare priorities.

A strength of the study is that it is designed to collect data on use of healthcare resources for several years after the incident event. It provides data from a large, unselected, community-based cohort of patients with first-ever ischemic stroke who were assessed immediately after the onset of the illness through standardized diagnostic criteria and well-validated and reliable instruments. Another major strength was the high quality of epidemiologic data used for survival projections, which provided us with accurate information on point estimates and precision of long-term survival.



Survival after first ischemic stroke. Erlangen Stroke Project (ESPro) data 1994 to 2003. The irregular lines are Kaplan-Meier survival estimates with pointwise 95% Greenwood confidence bands. The smooth line starts at day 366 and displays the Weibull prediction in men and women.

TABLE 2. Direct Cost of First-Ever-in-a-Lifetime Ischemic Stroke by Time-Horizon in SHI in Germany (in year 2004 EUR)

Horizon	Men		Women		All	
	Undiscounted	Discounted	Undiscounted	Discounted	Undiscounted	Discounted
1 y	15 566	15 566	14 799	14 799	15 140	15 140
5 y	31 405	30 159	30 817	29 582	31 077	29 837
10 y	40 905	37 711	39 097	36 176	39 921	36 873
Lifetime	54 552	45 549	47 596	41 304	50 507	43 129
95% CI#	(46 983; 63 670)	(40 673; 50 951)	(41 685; 54 568)	(37 127; 45 925)	(44 901; 56 940)	(39 312; 47 187)

#One-way sensitivity analyses on the 95% CI of life-expectancy poststroke.

This study does, however, suffer from certain limitations that are commonly present in investigations of this kind. For one thing, our total cost estimates for ischemic stroke in Germany are based on patterns of resource use during the 5 years after a stroke in a population-based cohort of stroke patients living in an urban environment (the city of Erlangen). Patterns of stroke aftercare may differ in rural or remote parts of Germany, and long-term data from these regions would complement our national cost projections.

Also, we did not distinguish outpatient services occasioned by stroke from those occasioned by other pre-existing or new-onset diseases. We may, therefore, have overestimated the costs attributable to ischemic stroke itself because part of the calculated outpatient cost will also arise in an elderly population free of stroke.

The huge worldwide socioeconomic impact of stroke is attributable to the high prevalence and hospitalization rate of this condition and the frequency of long-term sequelae in survivors. Nevertheless, surprisingly few truly incidence-based, bottom-up cost-of-stroke studies have been published in the last 20 years. As highlighted by Payne et al,²⁶ such studies are difficult to compare because of their differences in terms of setting, resources considered, and perspective taken. Among authors that report cost after incident ischemic stroke, 2 authors used data from a hospital-based cohort of patients.^{27,28}

Only few investigators worldwide studied cost in an unbiased population-based setting.^{8,29–33} Persson and Norrving,²⁹ Terent et al³⁰ and Kaste et al³¹ reported direct costs of stroke from community-based registries in Scandinavia. Dewey et al recently reported costs from a societal perspective based on a well-designed population-based study, the North East Melbourne Stroke Incidence Study (NEMESIS).^{32,33}

Stroke rehabilitation costs accounted for 37% of total first-year costs in our study, whereas in Sweden,²⁹ attributable to different admission policies, rehabilitation costs were relatively small (19%) but nursing home costs were relatively high (35%),

particularly in women (53%) compared with men (23%). Acute hospitalization costs were similar in Sweden (39%) and Germany (36%). In our study, first-year costs amounted to ≈35% of the present value of total direct lifetime costs, a figure similar to the 36% reported by Bergman et al for The Netherlands⁸ and somewhat smaller than the 43% reported by Dewey et al for Australia.³³ In the latter study, however, out-of-pocket payments and indirect costs, such as caregiver time and lost productivity, were included and may account for some of the difference.

In our study, the undiscounted lifetime cost of stroke was 15% higher in men than in women, whereas in The Netherlands women had 18% higher costs than men.⁸ These differences may be methodologic in nature. Because long-term, bottom-up incidence-based data collection of resource use in stroke survivors is time- and resource-consuming, most studies confined collection of data on resource use to the first, or occasionally to the first and second, year after stroke.^{30–33} This approach is likely to lead to an overestimate of lifetime cost. Again, because of lack of data, some studies used long-term survival rates from different epidemiologic sources, countries, and time periods to project survival³⁴ without acknowledging the direction and magnitude of bias from potential differences with regard to stroke subtype, patient age, and sex distribution. Because survival is strongly linked to use of healthcare resources, the magnitude of this bias may be substantial, as recently described by Payne et al²⁶ and Evers et al.¹⁸

The number of patients with status poststroke is expected to rise continuously over the next 2 decades as populations age. The increase in absolute incident stroke numbers is estimated at ≈40% and 20% in men and women, respectively.³⁵ Our projections of a present value of 108.6 billion EUR for first-ever ischemic strokes in Germany in the period 2006 to 2025 are based on the projected age and sex evolution of the German population and assume no changes in stroke inci-

TABLE 3. National Direct Ischemic Stroke Cost (in year 2004 EUR) Projections in SHI in Germany

Horizon	Men		Women		All	
	Strokes	Cost* (Billion)	Strokes	Cost* (Billion)	Strokes	Cost* (Billion)
2006–2010	331 000	13.8	425 000	16.1	756 000	29.9
2006–2015	701 000	27.1	880 000	30.9	1 581 000	58.0
2006–2020	1 108 000	39.7	1 367 000	44.6	2 475 000	84.3
2006–2025	1 547 000	51.5	1 883 000	57.1	3 430 000	108.6

*Discounted (3% per annum).

Estimates take account of ministerial figures for the expected evolution of the age and sex composition of the German resident population and assume age- and sex-specific stroke rates to be constant.

dence, mortality, or resource consumption unrelated to age or sex. To the extent that in the future a higher proportion of patients may survive strokes in western countries, we may even have underestimated these costs.^{36,37}

This COI study highlights the social impact of first ischemic stroke in Germany. In addition, we provide cost predictions based on the expected demographic evolution of the country. A proportion of these costs may be preventable by lifestyle changes and primary and secondary prevention programs. This possibility is of paramount importance in terms of public health because progressive aging of the population will otherwise cause an increase in patients with stroke and consequently an increase in healthcare expenditure. By laying a foundation for predicting costs of healthcare and social services, the data from this study can contribute toward the making of informed decisions on allocation of scarce resources while maintaining quality care of stroke patients.

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References

- Caro JJ, Huybrechts KF, Duchesne I; for the Stroke Economic Analysis Group. Management patterns and costs of acute ischemic stroke: an international study. *Stroke*. 2000;31:582–590.
- National Stroke Association. The brain at risk: understanding and preventing stroke. Englewood (CO): National Stroke Association; 1996.
- Hankey GJ, Warlow CP. Treatment and secondary prevention of stroke: evidence, costs, and effects on individuals and populations. *Lancet*. 1999;354:1457–1463.
- Kavanagh S, Knapp M, Patel A. Costs and disability among stroke patients. *J Public Health Med*. 1999;2:385–394.
- Brown RD, Whisnant JP, Sicks RD, O'Fallon WM, Wiebers DO. Stroke incidence, prevalence and survival. Secular trends in Rochester, Minnesota, through 1989. *Stroke*. 1996;27:373–380.
- Office of Health Economics (OHE). *Stroke*. London: Office of Health Economics; 1988.
- Isard PA, Forbes JF. The cost of stroke to the National Health Service in Scotland. *Cerebrovasc Dis*. 1992;5:47–50.
- Bergman L, van der Meulen JHP, Limburg M, Habbema JDF. Costs of medical care after first-ever stroke in The Netherlands. *Stroke*. 1995;26:1830–1836.
- Evers SMAA, Engel GL, Ament AJHA. Cost of stroke in The Netherlands from a societal perspective. *Stroke*. 1997;28:1375–1381.
- Kolominsky-Rabas PL, Sarti C, Heuschmann PU, Graf C, Siemonsen S, Neundoerfer B, Katalinic A, Gassmann KG, Lang E, Ritter von Stockert TH. A prospective community-based study of stroke in Germany: The Erlangen Stroke Project (ESPro). Incidence and case fatality at 1, 3 and 12 months. *Stroke*. 1998;29:2501–2506.
- Kolominsky-Rabas PL, Weber M, Gefeller O, Neundoerfer B, Heuschmann PU. Incidence, recurrence and long-term survival in ischemic stroke subtypes according to the TOAST criteria: a population-based Study. *Stroke*. 2001;32:2735–2740.
- Kolominsky-Rabas PL, Hilz MJ, Neundoerfer B, Heuschmann PU. Impact of urinary incontinence after stroke: results from a prospective population-based stroke register. *Neurology and Urodynamics*. 2003;22:322–327.
- Heuschmann PU, Neureiter D, Gesslein M, Craiovan B, Maass M, Faller G, Beck G, Neundörfer B, Kolominsky-Rabas PL. Helicobacter pylori and Chlamydia pneumoniae infection in ischemic stroke: results from a population-based case-control study. *Stroke*. 2001;32:2253–2258.
- Hatano S. Experience from a multicenter stroke register: a preliminary report. *Bull World Health Organ*. 1976;54:541–553.
- Sudlow CL, Warlow CP. Comparing stroke incidence worldwide: what makes studies comparable? *Stroke*. 1996;27:550–558.
- Adams HP Jr. The importance of the Helsingborg declaration on stroke management in Europe. *J Intern Med*. 1996;240:169–171.
- Drummond MF, O'Brien B, Stoddart GL, Torrance GW. *Methods for the Economic Evaluation of Health Care Programmes*. Oxford, UK: Oxford Medical Publications; 1997.
- Evers SM, Struijs JN, Ament AJ, van Genugten ML, Jager JH, van den Bos GA. International comparison of stroke cost studies. *Stroke*. 2004;35:1209–1215.
- Busse R, Riesberg A. *Health care systems in transition: Germany*. Copenhagen, Denmark: WHO Regional Office for Europe on behalf of the European Observatory of the Health Care Systems and Policies; 2004.
- Kassenärztliche Bundesvereinigung und Spitzenverbände der Gesetzlichen Krankenkassen. Einheitlicher Bewertungsmaßstab (EBM), Deutscher Ärzte-Verlag, Cologne 2004.
- Bundesministerium für Gesundheit und Soziale Sicherung. Bonn, Germany: Available at: http://www.bmg.bund.de/nn_617004/SharedDocs/Download/EN/Long-term-care-insurance.pdf.
- Akaike H. A new look at the statistical model identification. *IEEE Transaction and Automatic Control*. 1974;19:716–723.
- Cox DR, Snell EJ. A general definition of residuals. *Journal of the Royal Statistical Society*. 1968;30:248–275.
- Stata Corporation 2002. Stata Statistical Software: Release 7.0 Special Edition. College Station, TX: Stata Corporation.
- Statistisches Bundesamt (ed). Statistisches Jahrbuch für die Bundesrepublik Deutschland 2003. Wiesbaden, 2004 [published annually].
- Payne KA, Huybrechts KF, Caro JJ, Craig Green TJ, Klittich WS. Long term cost-of-illness in stroke: an international review. *Pharmacoeconomics*. 2002;20:813–825.
- Thorngren M, Westling B. Utilization of health care resources after stroke. A population-based study of 258 hospitalized cases followed during the first year. *Acta Neurol Scand*. 1991;84:303–310.
- Porsdal V, Boysen G. Costs of health care and social services during the first year after ischemic stroke. *Int J Tech Assess Health Care*. 1999;15:573–584.
- Persson U, Silverberg R, Lindgren B, Norrving B, Jadbak G, Johansson B, Puranen BI. Direct costs of stroke for a Swedish population. *Int J Technol Assess Health Care*. 1990;6:125–137.
- Terent A, Marke LA, Asplund K, Norrving B, Jonsson E, Wester PO. Costs of stroke in Sweden. A national perspective. *Stroke*. 1994;25:2363–2369.
- Kaste M, Fogelholm R, Rissanen A. Economic burden of stroke and the evaluation of new therapies. *Public Health*. 1998;112:103–112.
- Dewey HM, Thrift AG, Mihalopoulos C, Carter R, Macdonell RA, McNeil JJ, Donnan GA. Cost of stroke in Australia from a societal perspective: results from the North East Melbourne Stroke Incidence Study (NEMESIS). *Stroke*. 2001;32:2409–2416.
- Dewey HM, Thrift AG, Mihalopoulos C, Carter R, Macdonell RA, McNeil JJ, Donnan GA. Lifetime cost of stroke subtypes in Australia: findings from the North East Melbourne Stroke Incidence Study (NEMESIS). *Stroke*. 2003;34:2502–2507.
- Dennis MS, Burn JP, Sandercock PA, Bamford JM, Wade DT, Warlow CP. Long-term survival after first-ever stroke: the Oxfordshire Community Stroke Project. *Stroke*. 1993;24:796–800.
- Struijs JN, van Genugten ML, Evers SM, Ament AJ, Baan CA, van den Bos GA. Modeling the future burden of stroke in The Netherlands: impact of aging, smoking, and hypertension. *Stroke*. 2005;36:1648–1655.
- Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990–2020: Global Burden of Disease Study. *Lancet*. 1997;349:1498–1504.
- Bonita R, Solomon N, Broad JB. Prevalence of stroke and stroke-related disability: estimates from the Auckland Stroke Studies. *Stroke*. 1997;28:1898–1902.