Economic Evaluation in Stroke Research
A Systematic Review
Silvia M.A.A. Evers, MSc; André J.H.A. Ament, PhD; Gerhard Blauuw, PhD

Background and Purpose—The purpose of this review is to provide insight into the quality of economic evaluation in the field of cerebrovascular diseases (CVD) on the basis of a systematic analysis.

Methods—A literature search was performed using several sources. Trial-based full economic evaluation studies, were included in this review. The quality of the studies was independently assessed by 2 reviewers using a checklist.

Results—Twenty-three articles were found to comply with our inclusion and exclusion criteria. Only a few studies mentioned the perspective of the study, and in these cases it was always the societal perspective. The majority of the studies were cost-minimization and cost-effectiveness analyses based on cohort studies. All studies included healthcare costs, and in some instances patient and family costs were considered. Costs were usually measured by tariffs. Clinical end points and mortality were used to measure effects. Cost and effect measurements were based on hospital records.

Conclusions—Only a few full economic evaluations have been undertaken in the domain of CVD. In most of the studies, the technical execution and methodology were limited. (Stroke. 2000;31:1046-1053.)

Key Words: stroke • economics • review

Since the editorial by Feigenson,1 the rising cost of cerebrovascular diseases (CVD) has become an issue of paramount importance. However, one can question whether this increased interest signals a corresponding improvement in quality. The present study scrutinizes economic evaluation studies in the field of CVD, through application of methodological criteria. For this analysis, a previously developed and applied checklist2,3 was used.

No complete systematic review of the quality of trial-based economic evaluation studies in the field of CVD has been performed in the literature, although some efforts have been made to illustrate the state of economic evaluation in the field of CVD. We would like to draw some attention to the review of Holloway et al4 regarding cost-effectiveness studies of stroke. The current systematic review differs from this study on a number of issues. Holloway and colleagues selected only studies in which the health effects were measured in quality-adjusted life-years and left out studies regarding preventive strategies. Finally, the studies in the Holloway review used overall modeling (96%) as the principle research method.4,5 In contrast to Holloway et al,4,5 the objectives of this study were (1) to systematically obtain and review all published, trial-based, full economic evaluation studies in the field of stroke and (2) to gain insight into the methodological quality of both the epidemiological and the economic study design. This review focuses on trial-based studies rather than on studies based on modeling, for 2 reasons. First, a model is a simplified version of reality that is used to describe the essential elements of a real situation. One of the major limitations of modeling is the interdependence of the validity of the input data. That is why trial-based data generally provide the most unbiased and precise data on outcomes. The second, and more practical, reason is that the checklist used in this review is not suitable for scoring the quality of economic evaluation studies based on modeling. Because of these selection criteria, there is no overlap with the study of Holloway et al.

The purpose of this article is to provide insight into the status and the quality of economic evaluation studies performed through 1998 in the field of CVD. To start, a brief outline of the basic designs of economic evaluation studies will be given. After that, the methods of this review will be explained. The first result section discusses the main results of the studies involved. The subsequent sections outline the epidemiological quality of the studies, and, finally, the quality of the economic evaluation designs will be discussed.

Economic Evaluation Designs
This systematic review concentrates on full economic evaluation studies. A full economic evaluation study must compare 2 or more program alternatives, examining both the costs and the consequences.6 Broadly, there are 4 types of full economic evaluation, which differ in the way that the consequences are measured, eg, cost-minimization analysis.

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From the Department of Health Organization Policy and Economics, Maastricht University (S.M.A.A.E., A.J.H.A.A.), and the Department of Neurosurgery, University Hospital Maastricht (S.M.A.A.E., G.B.), Maastricht, the Netherlands.
Correspondence to Silvia Evers, Maastricht University, Dept. Health Organization Policy and Economics, PO Box 616, 6200 MD Maastricht, Netherlands. E-mail S.Evers@BEOZ.unimaas.nl
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(CMA), cost-effectiveness analysis (CEA), cost-benefit analysis (CBA), and cost-utility analysis (CUA). A CMA examines alternative health care programs, which are equally effective, so that only the costs need to be compared further. The evaluation is then essentially a search for the “least-cost” alternative. In a CEA, the outcome can be assessed in a variety of ways, such as life-years gained, cases prevented, decreased length of hospital stay, or pain-free days. One of the major limitations of the cost-effectiveness analysis is that the outcomes of the various studies are measured in a different way, so that comparison between the various studies is hampered. A CUA, however, does express health improvement in 1 uniform measure, the quality-adjusted life-year (QALY). In the CUA, the outcome is the number of life-years saved adjusted for the quality of these saved life-years with use of utilities (1 corresponds to optimal health and 0 to death). Finally, a CBA expresses the outcomes of the study in monetary terms. Costs and benefits are then measured in the same unit, and one can see immediately whether the benefits outweigh the costs.

Methods

Literature Selection

An extensive search of the literature from 1966 until 1998 was performed with MEDLINE, EMBASE, and other databases (Cochrane, OHE-HEED, NHS, and overview issue of Health Economics’). Finally, additional information was found by screening relevant journals, citation tracking, and calling for articles to a discussion MAILBASE list on health economic evaluation.8 Included were published (several articles and 1 report), trial-based, full economic evaluation studies in the field of CVD. Exclusion criteria were editorials, letters, non-English articles, and reviews. To guarantee a certain level of scientific quality, the intention of this review was to select only economic evaluation studies, with use of these very strict criteria.

Methodological Quality of the Study

The selected studies were evaluated with a checklist applied in other studies.3–5 The checklist consists of 3 parts: a general part, an epidemiological part, and an economic part. For details regarding the checklist, we refer to a report that includes the checklist and explains the definition and criteria used.6 The quality of the studies was independently assessed by 2 reviewers (A.A. and S.E.) using this checklist. Disagreement between the reviewers was resolved in a consensus meeting.

Results

Study Selection

Initially 137 articles were regarded as possibly relevant for this review. A large number of these studies had to be excluded due to the fact that they were based on modeling, lack of a control group, or the absence of a cost analysis. After screening the abstract, or if necessary the whole article, only 23 articles were found to comply with the study criteria.

General Characteristics

Most of the studies included were Anglo-American (17 USA, 3 UK) and were published during the last decade (70%). Considering the importance of the perspective of an evaluation study,10 it was remarkable that only 2 studies explicitly mentioned the perspective used.11,12 Both studies were performed from the societal perspective, ie, all costs and effects were included regardless of who incurred the costs and who obtained the effects.

In the absence of a statement regarding the perspective, it was likely that the external source financing the study might give some indication of this. Ten studies were financed by external grants, the majority (6) by public funding12–17; 2 studies received funds from pharmaceutical companies18,19 and another 2 from hospital-related funding organizations.20,21

Main Results of the Studies

The studies reviewed evaluated a wide range of interventions. Unfortunately, in most cases, no comprehensive description was given of the interventions in the control group. Therefore, we could not judge whether the control intervention was the most relevant for the policy questions being addressed. Two studies compared 3 interventions16,22; another study compared 418 and another20 compared 6 interventions. To provide an overview of these studies, we grouped the interventions into 6 categories: diagnosis, therapy, rehabilitation, management teams, protocol, and location of care (Table 1).

Diagnosis

CVD diagnoses form the basis for rational management. Three relatively old studies16,20,23 evaluated the cost-effectiveness of the CT scan versus other neuroradiologic armamentaria (such as bedside examinations, cerebrospinal fluid analysis, radionuclide brain scans). Although not always statistically tested, these studies overall came out in favor of CT scanning. Angiography prior to carotid endarterectomy was studied by Garrard et al,24 who showed that nonroutine use of angiography does not increase the operative risk or length of stay but does significantly lowers costs.

Therapy

In recent years the nihilistic view of the treatment of CVD, which was mainly due to the belief that brain death was irreversible, has changed into a more active management of CVD, especially in the acute phase. Nevertheless, only 5 studies11,12,15,18,25 in our review try to prove the cost-effectiveness of CVD treatment. The study by Jordan et al11 compared endovascular therapy (embolization) in combination with surgery versus surgical excision in patients with an arteriovenous malformation. Surprisingly, the study concluded that endovascular therapy in combination with surgery in patients with an arteriovenous malformation resulted in significant economic benefits, although these results were not statistically tested.11 Another study examined emergency thrombolysis (intra-arterial urokinase) as a treatment strategy in patients with thromboembolic intracerebral events compared with standard care. This small study revealed no significant cost difference between the 2 groups, with a statistically significant positive change in the National Institutes of Health Score in the experimental groups of at least 5 points.29 Kelley et al19 evaluated prospectively the costs of kinetic therapy, ie, a bed that provides continuous slow rotation over 124° in the horizontal plane, versus standard medical care (routine hospital bed). Kinetic therapy aims at a reduced incidence of infection, which improves the pulmonary toilet, and the prevention of urinary stasis. No significant difference was found in any of the outcome measures.
<table>
<thead>
<tr>
<th>Author</th>
<th>Intervention</th>
<th>Reference Treatment</th>
<th>Author’s Main Results</th>
<th>Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diagnosis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bahr23</td>
<td>CT scan</td>
<td>No CT control versus CT (after introduction and 1 year after)</td>
<td>Decreased hospital costs (NS), decreased invasive procedure (S)</td>
<td>Both tested</td>
</tr>
<tr>
<td>Britton20</td>
<td>CT scan</td>
<td>Bedside examination, routine laboratory tests, bedside examination, cerebrospinal analysis, radionuclide brain scan</td>
<td>Most cost-effective strategy is to perform CT scan as sole investigation (NT)</td>
<td>Neither tested</td>
</tr>
<tr>
<td>Larson16</td>
<td>CT scan</td>
<td>No CT control</td>
<td>Increased specific diagnosis (S), decreased lumbar punctures (S), decreased radionuclide brain scan (S)</td>
<td>Both tested</td>
</tr>
<tr>
<td>Garrard24</td>
<td>Nonroutine angiography</td>
<td>Routine angiography</td>
<td>No increased operative risk (NT), no increased length of stay (NT), decrease costs (S)</td>
<td>Costs tested</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glick18,38</td>
<td>Tirilazad mesylate in 3 different doses</td>
<td>Placebo control</td>
<td>Increased survival (S), increased costs (S), no effects for ?</td>
<td>Both tested</td>
</tr>
<tr>
<td>Jordan11</td>
<td>Embolization with surgery</td>
<td>Surgery alone</td>
<td>Decreased costs (NT), decreased morbidity (NT), decreased cost per QALY (NT)</td>
<td>Neither tested</td>
</tr>
<tr>
<td>Kelley15</td>
<td>Kinetic therapy with a rotational hospital bed</td>
<td>Routine hospital bed</td>
<td>Kinetic therapy is cost-effective (NS)</td>
<td>Both tested</td>
</tr>
<tr>
<td>Lanzieri25</td>
<td>Emergency thrombolysis (intra-arterial urokinase)</td>
<td>Standard medical care</td>
<td>Improvement in clinical status (S) without additional costs</td>
<td>Both tested</td>
</tr>
<tr>
<td>Murphy12</td>
<td>Piracetam</td>
<td>Placebo</td>
<td>No difference in outcome (NS) without additional costs</td>
<td>Both tested</td>
</tr>
<tr>
<td><strong>Rehabilitation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Byford26,39,40</td>
<td>Short-term intensive community support</td>
<td>Usual rehabilitation</td>
<td>Increased outcome (NT), decreased cost (NT)</td>
<td>Neither tested</td>
</tr>
<tr>
<td>Gladman14,41</td>
<td>Domiciliary rehabilitation</td>
<td>Hospital-based rehabilitation</td>
<td>No difference (NS) in effect but increased costs (S) due to domiciliary services</td>
<td>Both tested</td>
</tr>
<tr>
<td>Keith29</td>
<td>Subacute rehabilitation (less intense)</td>
<td>Acute rehabilitation (comprehensive inpatient)</td>
<td>Decreased costs (S), decreased length of stay (S), decreased functional outcome (NS)</td>
<td>Both tested</td>
</tr>
<tr>
<td>Young17,42–44</td>
<td>Home physiotherapy</td>
<td>Day hospital</td>
<td>Decreased costs (S), no significant difference in outcome</td>
<td>Both tested</td>
</tr>
<tr>
<td><strong>Teams</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Falconer13</td>
<td>Coordinated comprehensive team care</td>
<td>Usual team care</td>
<td>No significant difference in costs and outcomes</td>
<td>Both tested</td>
</tr>
<tr>
<td>Webb19</td>
<td>Multidisciplinary stroke team</td>
<td>Usual care</td>
<td>Decreased length of stay (S), decreased urinary tract infections (S)</td>
<td>Effects tested</td>
</tr>
<tr>
<td><strong>Protocol</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Back31</td>
<td>Critical, selective clinical pathway</td>
<td>Usual care</td>
<td>Decreased costs (S), no difference in mortality and complications (NS)</td>
<td>Both tested</td>
</tr>
<tr>
<td>Bowen22</td>
<td>Stroke protocol (critical care path)</td>
<td>Usual care (historic control group and concurrent control group)</td>
<td>Decreased costs (S), no difference in outcomes (NS)</td>
<td>Both tested</td>
</tr>
<tr>
<td>Calligaro21</td>
<td>Stroke protocol (same day admission, early discharge)</td>
<td>Usual care</td>
<td>Decreased costs (NT), decreased length of stay (S), no difference in outcome (NS)</td>
<td>Effects tested</td>
</tr>
<tr>
<td>Kraiss30</td>
<td>Protocol (duplex, scanning, regional anesthesia, selective admission to ICU)</td>
<td>Conventional carotid endarterectomy</td>
<td>Decreased costs (S) without differences in outcome</td>
<td>Both tested</td>
</tr>
</tbody>
</table>
Nevertheless, the authors conclude that the results suggest that kinetic therapy can be cost-effective.

Finally, 2 studies looked at drug treatment. Glick et al. examined tirilazad mesylate therapy in male patients with subarachnoid hemorrhage and showed a significant increase in survival, with corresponding increase in the cost of care in men but no difference in survival for women. In the study by Murphy et al., the economic impact of neuroprotective treatment (piracetam versus placebo) of acute ischemic CVD was investigated. No significant differences in the effects were found, but the study in fact showed a slight difference in costs in favor of piracetam.

Rehabilitation
Rehabilitation of a victim of CVD was mostly designed to help the individual overcome disability resulting from brain damage and to enable the patient to function despite the disability that remains after the spontaneous recovery from brain damage has ceased. Six studies – looked at rehabilitation, sometimes in combination with another care location. In general, the studies illustrated that rehabilitation was more efficient than other interventions.

Management Teams
To accomplish continuity of care and accessibility, some institutions implement stroke management teams. These teams usually consist of a number of professionals who work together in accordance with a coordinated plan. The study by Webb et al. showed that such a stroke management team may reduce the length of stay and morbidity in hospitalized CVD patients. Team care on admission to a large, academic, inpatient rehabilitation hospital was studied by Falconer et al. Adults who had had a recent CVD were randomly assigned to receive rehabilitation services from a team trained in Clinical Path Method (coordinated, comprehensive team care provided by persons who integrate their observations, expertise, and decisions) or from usual care. Results showed that the Clinical Path Method did not contain costs or improve outcomes of inpatient CVD rehabilitation.

Protocol
Based on experience and scientific findings, it may be optimal to develop protocols for the short-term and long-term care of CVD patients. A pilot study by Kraiss et al. looked at patients who had carotid endarterectomy performed according to an alternative protocol (duplex scanning only, operation under regional or “awake” anesthesia, and admission to the ICU only in cases of a proven need for services unique to the ICU) versus patients undergoing conventional carotid endarterectomy (angiography, general anesthesia, routine ICU admission) during the same period. The study suggested that carotid endarterectomy can be safely performed according to the alternative protocol with a significant reduction of hospital charges. Patients with carotid endarterectomy were also the subject of a study which investigated a critical and selective treatment that included avoidance of cerebral arteriography, preferential use of regional anesthesia, selective use of the ICU, and early hospital discharge. The rates of mortality and complications did not vary between the 2 groups, but the implementation of this pathway resulted in a significant reduction in the hospital cost. A project by Calligaro et al. also studied a clinical pathway with same-day admission and early hospital discharge for patients undergoing major vascular surgery that resulted in costs savings with no increase in morbidity or mortality rates. In another study there were significant savings in hospitalization costs for patients with acute CVD after the introduction of an alternative treatment protocol. These savings were almost entirely related to decreased length of stay. There were no differences in outcome measures such as death or discharge disposition. Medical complications were similar in both groups.

Location of Care
In recent years there has been a tendency to provide more patient-oriented care, inducing a trend from specialized care to general care, from inpatient to outpatient care and from outpatient care to home care. Green and McNamara compared the results and costs of carotid endarterectomy performed by a single surgeon over a 1-year period working at both a university hospital and a community hospital. There were no differences in the complication rates and mortality, but the costs in the university hospital were significantly higher. In another study comparing CVD patients with and without home care, Bryant et al. showed that during their 9-month follow-up period, CVD patients who received home care had, in total, a shorter hospital stay, fewer readmissions, and fewer deaths, while overall costs were greatly reduced. Results were not statistically tested.

Epidemiological Quality of the Studies
In this review it was assumed that epidemiological aspects are as important as economic aspects, because only economic

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**TABLE 1. Continued**

<table>
<thead>
<tr>
<th>Location of care</th>
<th>Intervention</th>
<th>Reference Treatment</th>
<th>Author’s Main Results</th>
<th>Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bryant23</td>
<td>Home care</td>
<td>No home care</td>
<td>Decreased costs, decreased length of stay, decreased readmissions, continuity of care, patient more self-sufficient (NT)</td>
<td>Neither tested</td>
</tr>
<tr>
<td>Feigenson27</td>
<td>Community hospital</td>
<td>Academic hospital</td>
<td>No difference in outcome (NS), decreased cost (S)</td>
<td>Both tested</td>
</tr>
<tr>
<td>Green12</td>
<td>Community hospital</td>
<td>Academic hospital</td>
<td>No difference in outcome (NS), decreased cost (S)</td>
<td>Both tested</td>
</tr>
<tr>
<td>Hui28,34</td>
<td>Day hospital</td>
<td>Usual care</td>
<td>Increased functional outcome (S), reduced outpatient visits (S), no difference in costs (NS)</td>
<td>Both tested</td>
</tr>
</tbody>
</table>

For results, S indicates significant; NS, not significant; and NT, not tested. For statistical analysis, both tested indicates that both costs and effects are tested statistically; neither tested, neither costs nor effects are tested statistically.
evaluation studies with a good epidemiological design can isolate the observed effect of an intervention. Approximately one quarter (26%) of the studies used randomization to allocate the treatments to different groups; in 1 study randomization was combined with prestratification. The remaining studies could be regarded as cohort studies, in which 26% used a prepost design and others a prospective (future) cohort or retrospective (historic) cohort to compare the interventions. Furthermore, in some instances cases were matched with controls and others a prospective (future) cohort or retrospective (historic) cohort to compare the interventions. Finally, the study by Webb et al combined before-and-after comparison with a prospective cohort, and in the study by Britton et al the diagnostic validity was assessed step by step.

Table 2 lists the other epidemiological criteria that were studied for this review. The number of patients included varied from 34 to 2009. None of the studies performed a power calculation specifically for the economic evaluation part of the study. In CVD research, the study period has to be long enough to determine whether the effect of an intervention is longstanding. The study period in the articles varied from 8 weeks to 1 year. The majority of the studies (61%) considered the costs and consequences of interventions during the hospital stay. Of the articles reviewed, 70% defined inclusion and exclusion criteria. Even with a good study design, the results can be affected by noncompletion. Protocol deviation, such as withdrawals, dropouts, contamination, and noncompliance was reported by approximately one fifth of the studies (22%). However, it should be remarked that protocol deviation is most likely to occur in randomized controlled studies and prospective cohort studies. The general consensus is that several actors (ie, patients, observers, clinicians, investigators) in the clinical trial should be “blinded,” ie, kept ignorant of which treatment the CVD

**Table 2. Main Epidemiological and Economic Characteristics of the Studies**

<table>
<thead>
<tr>
<th>Author</th>
<th>Period</th>
<th>Design</th>
<th>Groups, n</th>
<th>Protocol Deviation</th>
<th>Blinding</th>
<th>Cost Identified</th>
<th>Cost Valuation</th>
<th>Effects Identified</th>
<th>Effects Measured</th>
</tr>
</thead>
<tbody>
<tr>
<td>Back</td>
<td>Hospital</td>
<td>Pre-post cohort</td>
<td>102</td>
<td>2</td>
<td>N</td>
<td>N</td>
<td>CMA</td>
<td>Health</td>
<td>Full costs, tariffs</td>
</tr>
<tr>
<td>Bahr</td>
<td>Hospital</td>
<td>Pre-post cohort</td>
<td>112</td>
<td>2</td>
<td>N</td>
<td>N</td>
<td>CMA</td>
<td>Health</td>
<td>Tariffs</td>
</tr>
<tr>
<td>Bowen</td>
<td>Hospital</td>
<td>Pre-post cohort</td>
<td>346</td>
<td>3</td>
<td>N</td>
<td>N</td>
<td>CMA</td>
<td>Health</td>
<td>Tariffs</td>
</tr>
<tr>
<td>Britton</td>
<td>Hospital</td>
<td>Prospective cohort</td>
<td>419</td>
<td>6</td>
<td>N</td>
<td>N</td>
<td>CEA</td>
<td>Health</td>
<td>Other</td>
</tr>
<tr>
<td>Bryant</td>
<td>PRE</td>
<td>Matched control</td>
<td>50</td>
<td>2</td>
<td>N</td>
<td>N</td>
<td>CEA</td>
<td>Health</td>
<td>Tariffs</td>
</tr>
<tr>
<td>Byford</td>
<td>PRE</td>
<td>Matched control</td>
<td>148</td>
<td>2</td>
<td>N</td>
<td>N</td>
<td>CEA</td>
<td>Health</td>
<td>Full costs</td>
</tr>
<tr>
<td>Calligaro</td>
<td>Hospital</td>
<td>Pre-post cohort</td>
<td>322</td>
<td>2</td>
<td>N</td>
<td>N</td>
<td>CMA</td>
<td>Health</td>
<td>Tariffs</td>
</tr>
<tr>
<td>Falconer</td>
<td>Hospital</td>
<td>RCT</td>
<td>121</td>
<td>2</td>
<td>Drop</td>
<td>N</td>
<td>CEA</td>
<td>Health</td>
<td>Tariffs</td>
</tr>
<tr>
<td>Feigenson</td>
<td>Hospital</td>
<td>Matched control</td>
<td>439</td>
<td>2</td>
<td>N</td>
<td>N</td>
<td>CMA</td>
<td>Health</td>
<td>Tariffs</td>
</tr>
<tr>
<td>Garrard</td>
<td>Hospital</td>
<td>Prospective cohort</td>
<td>97</td>
<td>2</td>
<td>N</td>
<td>N</td>
<td>CMA</td>
<td>Health</td>
<td>Tariffs</td>
</tr>
<tr>
<td>Gladman</td>
<td>Hospital</td>
<td>Matched control</td>
<td>50</td>
<td>2</td>
<td>N</td>
<td>N</td>
<td>CMA</td>
<td>Health</td>
<td>Tariffs</td>
</tr>
<tr>
<td>Green</td>
<td>Hospital</td>
<td>Matched control</td>
<td>157</td>
<td>2</td>
<td>N</td>
<td>N</td>
<td>CMA</td>
<td>Health</td>
<td>Tariffs</td>
</tr>
<tr>
<td>Hu</td>
<td>Hospital</td>
<td>RCT</td>
<td>120</td>
<td>2</td>
<td>N</td>
<td>N</td>
<td>CEA</td>
<td>Health</td>
<td>Other</td>
</tr>
<tr>
<td>Jordan</td>
<td>Hospital</td>
<td>Matched control</td>
<td>500</td>
<td>2</td>
<td>N</td>
<td>N</td>
<td>CEA</td>
<td>Health</td>
<td>Tariffs</td>
</tr>
<tr>
<td>Keith</td>
<td>Hospital</td>
<td>Retrospective cohort</td>
<td>428</td>
<td>2</td>
<td>N</td>
<td>N</td>
<td>CMA</td>
<td>Health</td>
<td>Tariffs</td>
</tr>
<tr>
<td>Kelley</td>
<td>Hospital</td>
<td>Prospective cohort</td>
<td>53</td>
<td>2</td>
<td>With, drop</td>
<td>N</td>
<td>CMA</td>
<td>Health</td>
<td>Tariffs</td>
</tr>
<tr>
<td>Kraiss</td>
<td>Hospital</td>
<td>Prospective cohort</td>
<td>196</td>
<td>2</td>
<td>N</td>
<td>N</td>
<td>CMA</td>
<td>Health</td>
<td>Tariffs</td>
</tr>
<tr>
<td>Lanzieri</td>
<td>Hospital</td>
<td>Matched control</td>
<td>34</td>
<td>2</td>
<td>N</td>
<td>N</td>
<td>CEA</td>
<td>Health</td>
<td>Other</td>
</tr>
<tr>
<td>Larson</td>
<td>Hospital</td>
<td>Pre-post cohort</td>
<td>157</td>
<td>3</td>
<td>N</td>
<td>N</td>
<td>CEA</td>
<td>Health</td>
<td>Tariffs</td>
</tr>
<tr>
<td>Murphy</td>
<td>Hospital</td>
<td>RCT</td>
<td>352</td>
<td>2</td>
<td>With</td>
<td>Y</td>
<td>CEA</td>
<td>Health</td>
<td>Tariffs</td>
</tr>
<tr>
<td>Webb</td>
<td>Hospital</td>
<td>Combination cohort</td>
<td>2009</td>
<td>2</td>
<td>N</td>
<td>N</td>
<td>CMA</td>
<td>Health</td>
<td>Tariffs</td>
</tr>
<tr>
<td>Young</td>
<td>Hospital</td>
<td>RCT</td>
<td>95</td>
<td>2</td>
<td>N</td>
<td>N</td>
<td>CMA</td>
<td>Health</td>
<td>Full costs</td>
</tr>
</tbody>
</table>

In Design column, RCT indicates randomized controlled trial. In Protocol Deviation, drop indicates drop-out; cont, contamination; non, noncompliers; and with, withdrawals. In Cost Identified, health indicates healthcare costs; patient, patient and family costs. In Effects Identified, compl indicates medical complications; diag, diagnostic validity; disch, discharge disposition; funct, functional outcome; LOS, length of stay; and mort, mortality. In Effects Measurement, hosp rec indicates hospital records; observ, observations; and quest, questionnaire.
patients had undergone. In our review, 3 studies\(^\text{12,14,18}\) used blinding.

**Economic Quality of the Studies**

**Economic Evaluation Study Design**

Table 2 shows that overall the studies included in our review refer to a CMA (48%)\(^\text{14,15,19,21–24,27,30–32}\) or a CEA (48%)\(^\text{12,13,16–18,20,25,26,29,33,34}\). The large amount of CMA might be due to the fact that in most instances the researcher did not expect to find any differences in the consequences between the alternatives; instead, the study was performed primarily to look for the least costly effect. Furthermore, valuing effects in utilities (CUA) or in pecuniaries (CBA) is more complex, in comparison with, for instance, functional outcome measurement (CMA or CEA); therefore, CMA and CEA might be used more frequently. Finally, in our review only 1 study could be classified as a CUA,\(^\text{11}\) and in none of the studies were consequences translated into monetary terms using a CBA.

**Outcome Measurement**

In the studies examined, a variety of outcome measures was used. Almost half of the studies (48%) include mortality as an outcome measure\(^\text{14,15,18,19,21–24,31–33}\); functional outcome and medical complications were also frequently applied. Functional outcomes were measured by 43% of the studies\(^\text{12–14,17,18,25–27,29,34}\) with general and disease-specific instruments such as the Barthel Index,\(^\text{12,14,17,26,28}\) the Glasgow Outcome Scale,\(^\text{18}\) the Functional Independence Measure,\(^\text{13,29}\) the National Institute of Health Neurological Scale,\(^\text{18,25}\) and the Nottingham Health Profile.\(^\text{14,17}\) The number of medical complications was measured in 30% of the studies,\(^\text{19,21,22,24,30–32}\) Our review includes only 1 CUA,\(^\text{11}\) so a QALY measure was used rarely in trial-based economic evaluation studies concerning CVD. More than one half of the studies (65%) used hospital records to measure outcomes, or in other instances questionnaires or interviews.

**Cost Measurement**

All of the studies include healthcare costs. Only a few studies incorporate aspects regarding patient and family cost\(^\text{12,17}\); eg, Young et al\(^\text{17}\) looked at the carers’ stress and showed a significant decrease in leisure activities and an increase in domestic chores. These aspects were not valued in financial terms, but Murphy et al\(^\text{12}\) did include the cost of home assistance.

To measure costs, 87% of the studies used hospital records, but other methods were also applied, including diaries,\(^\text{14}\) measurement of resource utilization,\(^\text{15}\) expert estimation of the costs,\(^\text{12}\) and estimations from other studies.\(^\text{25}\) Only 3 studies\(^\text{14,17,26}\) calculated the actual economic cost price of the intervention examined. Although tariffs generally were not considered to be a good estimate of cost valuation, the remaining studies (70%) used tariffs to assess costs. To calculate the full costs of a program, overhead costs have to be estimated (ie, those resources that serve many different departments and programs, such as general hospital administration, central laundry, medical records, cleaning, porters, and power). Five studies\(^\text{11,14,17,26,31}\) calculated these overhead costs, and in most instances a division method was used in which the full costs of an intervention were determined by dividing the total cost by the total production. One of the studies that included productivity losses due to mortality was that of Jordan et al,\(^\text{11}\) in which a human capital approach was used, eg, calculation of the average lifetime earnings until the age of 65 years. Furthermore, Glick et al\(^\text{18}\) assessed the daily employment value for those working full-time, part-time or at home.

**Adjustments and Statistical Analysis**

Costs and benefits of CVD interventions will accrue over time and should, therefore, be discounted. Discounting was not relevant for all studies included in the review, because the study period in each case was \(<1\) year. Nevertheless, in our review 3 studies\(^\text{11,16,25}\) indexed the results to a certain year using discount rates varying between 4.5\(^\%\)\(^\text{11}\) and 7\(^\%\).\(^\text{25}\) (The latter was due to the fact that these studies collected data over a number of years.) Finally, in 4 studies, a sensitivity analysis\(^\text{11,12,14,18}\) was performed to check the influence of the assumptions made and the robustness of the conclusions.

In an economic evaluation study, the best evidence can be gathered if the statistical evidence (see Table 1) of both the effectiveness data and the cost data are tested. Close to 70% of the studies included in our review tested the differences in both costs and effects statistically. In 2 studies\(^\text{19,21}\) the statistical analysis was restricted to only the effects; in 1 study only costs were tested\(^\text{24}\); and in 4 studies\(^\text{11,20,26,33}\) neither effects nor costs were tested statistically. Furthermore, it was striking that in some studies, although no statistical significance was found, the authors concluded that the intervention was cost-effective.\(^\text{11}\)

**Incremental Analysis and Ratios**

For a meaningful comparison, it was necessary to examine the additional costs that one service or program imposes over another, compared with the additional effects, benefits, or utilities it delivers. Four studies in our review explicitly performed an incremental analysis,\(^\text{16,25,27}\) Glick et al,\(^\text{18}\) for instance, expressed the incremental costs in a ratio as the difference in cost between the 2 groups compared divided by the difference in the probability of death in these 2 groups. This study was also 1 of the 2\(^\text{11,18}\) that calculated a ratio. The other was by Jordan et al,\(^\text{11}\) who expressed the “costs per life-year saved” as a ratio.

**Conclusions**

Despite the increased interest in economic evaluation, this review shows that only a few full economic evaluations have been undertaken in the domain of CVD. Our search may not have been exhaustive, but we tried to find as many studies as possible by combining several methods. Furthermore, it has long been accepted that research with statistically significant results is more likely to be published. This so-called publication bias might influence the result of our analysis, as the review is limited to published studies. This study focuses on studies considering patients with CVD. Because of this, some preventive interventions (reduction of blood pressure, smoke cessation programs, thrombosis prevention) that focus on more general health aspects (including CVD) may not be
Another limiting factor was the fact that only trial-based, full economic evaluation studies were included in our review. Studies based on modeling were excluded. However, the authors agree that modeling55 can be used in some instances as an addition to or substitute for trial-based economic evaluation studies.

Only 2 studies included in our review were explicitly performed from a societal perspective. Regarding the epidemiological design, randomized controlled trials are generally regarded as the most scientifically rigorous method to test a hypothesis. However, randomization may not always be realistic. In our review, one quarter of the studies were based on randomized controlled trials. All studies included in the review were “piggy backed,” (ie, appendixed), and no separate power analysis was performed for the economic evaluation study. Furthermore, not all studies included a statistical analysis of both costs and effects.

Almost all of the studies used clinical outcome measures to evaluate the consequences of the interventions. One study used QALYs, although QALYs are regarded as the most holistic way of measuring effects. Especially in CVD, where intangible costs such as psychosocial consequences play an important role, QALYs should be used to quantify effects. Resource use, such as length of stay, was generally incorporated in the cost side of economic evaluation studies. It was remarkable that some studies27,30 use length of stay both as a cost measure and an effect measure. Because of the principle of not double-counting, which required that aspects included in the cost should not be included in the effect (and vice versa), we suggest that future studies avoid these duplications in order to achieve consistency. Regarding the cost measurement, only a few studies explicitly measured overhead costs and production losses. A large number of studies used charges as a proxy for costs.

The inferior quality of the studies was not unique to CVD. Previous research in other fields has also shown that sound economic evaluation generally receives little attention in current evaluation studies, in contrast to medical outcome research.2,3,36

Only a few of the articles reviewed were, in our opinion, good examples of economic evaluation. Although it was difficult to judge, we have the impression that the increasing concern for economic evaluation in CVD does not support an improvement in the quality of the economic evaluation studies performed. The quality, however, could be improved simply by using the basic principles described by experts in the field of economic evaluation.6,37

In conclusion, this review shows a significant need to improve the application of economic evaluation in the area of CVD. The initial intention of our study was to perform a meta-analysis illuminating which interventions were the most cost-effective regarding CVD. However, this was not possible because of the small number of comparable treatments, the large differences in and low quality of costing methodology, and the large difference in the CVD population, which limited the comparison between the estimates in the studies received. Therefore, the purpose of our study altered into assessing the quality of economic evaluation in the field of CVD based on systematic analysis. Thus, the conclusions of this review should be read, bearing in mind the previously mentioned shortcomings, that a decision on the cost-effectiveness of therapies for CVD is not yet possible at the moment.

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References


Economic Evaluation in Stroke Research: A Systematic Review
Silvia M. A. A. Evers, André J. H. A. Ament and Gerhard Blaauw

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