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Economic Evaluation of Home-Based Stroke Care – A systematic review

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Master's thesis in Public Health HEL-3950 August 2023

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Acknowledgement:

The process of conducting this systematic review has been equally challenging and rewarding. It would not have been possible without the encouragement, love, and patience of several people.

Firstly, I would like to thank my supervisor Hans Olav Melberg, professor in Health Economics at the Institute of Community Medicine at the UiT, the Arctic University of Norway. Your knowledge and guidance during the Health Economics course and during this thesis process was valuable for my deeper understanding of health economics and for the execution of this thesis.

I would like to thank UiT- The Norwegian Artic University and the Department of Community Medicine for providing me the opportunity to work on this dissertation. I would like to express my sincere gratitude to lecturers both at UiT and at Gothenburg University for their contribution to my academic journey. This also applies to the great librarians at both universities, who helped me to develop my search strategy and assisted me in gaining a greater understanding of how to navigate the different databases. Thank you so much.

Furthermore, I would like to express my appreciation to fellow classmates throughout these two years. I am so grateful for all the shared moments, laughter and frustration, collaboration, and uplifting conversations during this master's programme. Lastly, I would like to acknowledge my sincerest gratitude to my family and friends. Especially to my dear twin sister who has been my biggest support, while writing her own master thesis.

Thank you!

Feben Dawit Teklezghi

Abstract:

Background:

The Global Burden of Disease (GBD) of 2019 ranked stroke, as both the second-leading cause of death and the third-leading cause of death and disability worldwide. As the burden of stroke has risen the past three decades, stroke has emerged as one of the current greatest public health issues worldwide of growing importance. During the past 40 years, healthcare expenditure has increased dramatically throughout the world. Home-based rehabilitation has the protentional to be an beneficial alternative to the conventional existing hospital-and institution-based rehabilitation programmes in the healthcare sector. Home-based rehabilitation for stroke has shown to have a significant effect and a clinical impact when compared to both hospital-based and institution-based rehabilitation.

Objectives:

The objective was to conduct a systematic review on the research question: Is home-based rehabilitation cost-effective compared to conventional rehabilitation in adult stroke patients?

Method:

MEDLINE, EMBASE, CINAHL, Web of Science and Scopus was searched in February 2023, reference list included publications and relevant systematic reviews to were screened for eligibility. Study selection, data extraction and assessment of methodological quality was carried out by one independent author. Outcome data were synthesized narratively due to heterogeneity in the outcomes.

Results:

Five full economic evaluations were included in this review. Narrative synthesis showed that all of the included studies found home-based rehabilitation to be a more cost-effective option for stroke patients based on health outcomes, such as Barthel index, mRS index, quality of life, mortality and hospitalization. The overall methodological quality in the included EEs was high/ good based on Drummonds 10 checklist and the QHES- instrument. Results of sensitivity analysis in the studies, also demonstrated results in favor of home-based rehabilitation.

Conclusions:

Due, to the limitations in this systematic review further research is needed according to the context of each country and based on clinical trials reporting outcomes that can improve the quality of evidence and give implication for future policy. If the cost-effectiveness of home-based rehabilitation suggested in this review is supplemented with further knowledge supporting these results, these findings could be an important contributor to policy makers and the current knowledge regarding stroke-rehabilitation.

Abbreviations:

GBD	Global Burden of Disease
BI	Barthel Index
QALY	Quality adjusted life years
WHO	The World Health Organization
HBR	Home-based rehabilitation
HR	Hospital-based rehabilitation
IR	Institution-based rehabilitation
SR	Systematic Review

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1 Background

1.1 Description of the condition

The Global Burden of Disease (GBD) of 2019 ranked stroke, also known as brain attack or cerebrovascular accident (CVA) as both the second-leading cause of death and the third-leading cause of death and disability worldwide (1). From 1990 to 2019 the global stroke incidence increased by 70%, and the prevalence and mortality by 85% and 43%, respectively (2) . World Stroke Organization (WSO) estimated that over 101 million people living had experienced stroke and projected that one in four people worldwide over the age of 25 will be subjected to stroke in their lifetime (3). As the burden of stroke has risen the past three decades, stroke has emerged as one of the current greatest public health issues worldwide of growing importance (2) .

Stroke is a medical condition that occurs when the blood supply to a part of the brain is interrupted or reduced, and it is often classified into two main types: ischemic and hemorrhage stroke (4) . Ischemic stroke is the most common type accounting for 62% of all incidents of stroke (3). Blood clots or cellular debris (organic waste left over after a cell dies) that blocks blood vessels in the brain is the most common cause of ischemic strokes. These blood blockages lead to lack of oxygen and nutrients in millions of nerve cells and other brain cells (5) . Hemorrhagic stroke accounts for 28% of all strokes(3) and occurs when an artery in the brain raptures and causes bleeding into and around the brain tissue. As a result, pressure inside the skull rises as blood enters the brain, causing significant damage to the surrounding tissue (5).

Both ischemic strokes and hemorrhagic strokes prevent the brain from accessing the oxygen and nutrients it depend to function properly (4). When the blood supply is interrupted or reduced even for a short time braincells die, leading to loss of brain function (6). This may lead to temporary or permanent disability depending on how long the brain lacks blood supply (6). Stroke is recognized as a medical emergency that require immediate medical attention since duration is a factor in the health outcomes. Every minute counts, hence, the expression “time is brain” that highlights importance of early treatment and care (4). Treatment options for stroke depend on the type and severity of the stroke and usually fall into three approaches which entail emergency medical or surgical treatment, post-acute care treatment, and rehabilitation.

Loss of brain function can be mild or severe depending on the magnitude and location of the stroke (7). Individuals who have had a stroke experience a wide range of disabilities that may affect their ability to perform daily activities and live a normal life. One of the most common consequences following a stroke is motor impairments, that affect physical functions including the ability to move, control and coordinate muscles. This can lead to difficulties with walking, balance and performing simple everyday tasks such as dressing, using the bathroom, grooming, and eating (5). Sensory impairments including numbness, weakness, or pain, due to stiff joints, paralysis or a disabled limbs are also seen. Stroke survivors may experience fatigue or lack of energy (5). Other effects that are common are cognitive impairments including memory loss, difficulties learning and judging, attention deficits and difficulties in speaking and understanding language. Emotional impairments and difficulties controlling emotions might also occur after a stroke, which can lead to depression, anxiety, irritability, or other emotional effects (5) . In addition, behavioral changes such as impulsivity, agitation or disinhibition can also be experienced after a stroke (5). Living with these stroke-related disabilities can be challenging, due to limitation in activities and participation.

Stroke typically occurs in adults over the age of 65 (8) , and the risk of getting stroke increases with age (9). However, there is an increasing trend in incidence of stroke in younger age groups that is concerning (3). Sixteen percent of all the cases occur in people 15-49 years of age (3). It is particularly concerning because it can have a significant impact on the quality of life and can lead to long-term disability in an otherwise young and healthy age group. Consequently, the extent of stroke is now making a severe impact on a wide range of age groups.

Despite the increasing trends in the incidence (3), it has in recent years been set global preventative actions aiming to reduce the burden of stroke by reducing the risk factors among people. In addition to the nonmodifiable risk factors, such as age and gender there are a list of modifiable risk factors associated with stroke (10). The most important risk factors are high blood pressure, high cholesterol, diabetes, heart disease, obesity, smoking, and high red blood cells counts. Some of these risk factors can be controlled thought lifestyle changes and medications, and there are several global actions aiming at preventing stroke by reducing these risk factors (10).

The World Health Organization (WHO) have developed guidelines for prevention of hypertension, which include promoting healthy diets, increasing physical activity, and reducing salt intake (11). Policies have been implemented by governments around the world, aiming at reducing smoking rates. Advertising bans taxes on tobacco products and smoke-free laws have shown to be effective in reducing smoking rates, especially in high-income countries (12). Several guidelines for the control of diabetes, high cholesterol and obesity have also been developed (13). These guidelines promote population-wide strategies on healthy diets, physical activity, and strategies on providing access to healthcare and medications. However, the implementation has shown to be slow and non-universal (2) .

The burden of stroke is still continuously growing despite preventative efforts being made. This implies that the economic burden of stroke will also likely increase and put more pressure on the future healthcare budgets. Demographic projections have shown that the population is aging(14) and as people living with stroke-related disability increases there is a substantial need for rehabilitation assisting patients in recovery.. It has been estimated that the global cost of stroke is over USD 891 billion (3). The overall stroke burden has an impact on both individuals, families, healthcare systems and societies in both developing and developed countries. There is, therefore, strong incentives for policymakers to commission stroke interventions that provide good value for the money.

1.2 Description of the intervention

A variety of rehabilitation strategies for stroke patients have emerged throughout the decades. Home-based rehabilitation has been recognized as a potentially effective programme for stroke patients (15). Home-based rehabilitation makes it possible to deliver healthcare services provided by healthcare personnel in the patient's home (15). In recent years it has gained recognition as an alternative to conventional rehabilitation for stroke patients (16).

Different definitions and terms have been applied to define rehabilitation or care provided in the patient's home (17). When referring to this form of rehabilitation, this systematic review will use the term home-based rehabilitation (HBR). This includes rehabilitation in the form of therapy or care provided by healthcare personnel in a patient home that aims to assist stroke patients in regaining as much function as possible. The goal of this rehabilitation is to enable these patients to live as independently as possible and regain as much function as possible.

Conventional hospital rehabilitation (HR) or inpatient rehabilitation (IR) generally offers therapy and care outside of the patient's home. However, these programmes are found insufficient for some patients because the patients are separated from familiar social and physical surroundings and settings (18). Healthcare personnel have expressed concerns that recovery of physical function in HR often focus on discharge as the endpoint in the rehabilitation and it has been emphasized that little attention has been given towards psychosocial issues that stroke patients may experience after discharge (19).

Health disparities among stroke patients is highlighted with higher incidence, prevalence, worse rehabilitation outcomes and lower utilization of rehabilitation services (20). These health disparities in stroke outcomes illustrates a need for more suitable and targeted rehabilitation interventions. Increased trends in stroke incidence and prevalence the last decades highlight a demand towards rehabilitation for stroke patient. This can be tackled by increasing individuals' ability to better regain function in the comfort of their own home.

HBR has the protentional to reduce barriers such as geographical differences in specialized conventional rehabilitation services for stroke patients. In doing so it allows patients to stay in the safe comfort of their home. It eliminates the need to stay in an unfamiliar physical and social setting and the need to travel to outpatient hospital clinics. Being in a familiar surrounding can help stroke patients feel more comfortable and motivated to participate in rehabilitation activities and exercises. It can help stroke patients regain their independence faster by teaching them skills needed to preform daily activities in their own home environment (18). Home-based rehabilitation can involve family members or caretakers in the therapy process, which can provide emotional support and encourage adherence to the therapy programs.

However, home-based rehabilitation might have some underlying challenges. There might be limited availability of specialized equipment and resources in the home environment, that patients otherwise would have access to in traditional rehabilitation settings (21). This can make it difficult to provide appropriate therapy activities and exercises necessary for optimal recovery. Patients may experience difficulties in adhering to therapy programmes and hard times preforming exercises correctly independently without the presence of healthcare personnel. This might especially apply to those lacking adequate support from family members assisting them in the recovery (22). These challenges highlight a need for individually tailored

home-based rehabilitation programmes that address these issues and provide patients with the necessary resources, support, and motivation to ensure successful and efficient recovery.

1.3 How the intervention might work

Home-based rehabilitation has the protentional to be an beneficial alternative to the traditional existing hospital-and institution-based rehabilitation programmes in the healthcare sector (23). However, it is important to highlight that rehabilitation cannot substitute acute care provided in hospitals, which is necessary in the immediate aftermath of a stroke. Furthermore, it is important to note that HBR may not be suitable for all stroke patients, as the level of disability and complexity of medical needs can vary greatly among individuals. This rehabilitation programme may therefore be more appropriate for less complex patients with moderate or milder disabilities who do not require extensive and excessive medical supervision.

As an alternative to conventional rehabilitation interventions and an extension to acute stroke care, HBR allows for an interactive health service programme (15). This involves health personnel delivering traditional therapy typically involving a combination of exercises and activities practiced in a real home environment. It has the advantage that it can be designed to allow patients tailored rehabilitation in accordance with their own surroundings which has shown to increase patients' satisfaction (15). These programmes are typically provided by a multidisciplinary team that provide the patients with therapy that may include occupational therapy, physical therapy, speech therapy and cognitive rehabilitation, among other forms of therapy (23).

1.4 Description of economic evaluation in healthcare

During the past 40 years, healthcare expenditure has increased dramatically throughout the world (24). In a health service with competing and increasing demands for limited resources, simply demonstrating the efficacy of an intervention is no longer sufficient. However, key questions in the resource allocation can be answered by economic evaluations. Economic evaluation involves "the comparative analysis of alternative courses of action", in terms of both their costs and consequences (25). The task of economic evaluations is to identify, measure, value and compare the two sets of variables (1) costs, which is the recourse use; and (2) consequences, that is the outcomes, benefits, effects, and any cost savings of the alternatives

being considered (26). Economic evaluations can therefore also be applied and useful when comparing costs and consequences of stroke rehabilitation interventions. It can enable decision-makers to assess the cost-effectiveness of alternative interventions within a well-established analytical framework, and answer questions on the cost-effectiveness of home-based stroke rehabilitation.

However, not all studies that measure costs are economic evaluations. There exists a large literature on studies that describe the societal costs of disease. These studies are known in the literature as cost of illness or burden of illness studies and are not described as full economic evaluations because alternatives are not compared (26). On the other hand, some studies only consider costs when comparing alternatives and fall into the category of cost analysis. These are also not considered full economic evaluations (26).

Economic evaluations can be conducted alongside randomized controlled trials or can combine existing information from a variety of sources to provide estimates (27). Different perspectives can be adopted in the retrieval of information on resource use. When an economic evaluation accounts for resource use and consequences of the whole society rather than solely those of the institution that provides the service and the individuals that receive the intervention, it takes a societal perspective (25). When doing so societal costs such as out of pocket expenditure costs, patient's travel cost and productivity loss are accounted for (27). The primary costs of an intervention tend to be the direct medical costs, including resource use of medicines, equipment, and staff time. A narrower healthcare perspective usually restricts the resource use to these direct medical costs and the resulting consequences and is commonly chosen. Most economic evaluations identify various types of costs measured in monetary units. However, the way that the consequences are measured may differ considerably. Therefore, the evaluations can be used to answer different decision questions (25).

Cost-benefit analysis (CBA) is a common economic evaluation and is the only method that quantifies both the costs and benefits in monetary terms (26). This implies placing a value on life and health trough translating consequences such as life-years gained, or disability days avoided into a monetary value that can be interpreted alongside the costs. Results in CBAs may be expressed as a ratio of costs to benefits, or a simple sum that represents the net benefit (loss) of one alternative over the other, a trade-off. When answering policy questions on whether an intervention is worth implementing, the present value of the future stream of benefits is

compared with the future stream of costs, calculating the net present value (NPV). If the NPV is greater than zero, the programme is considered to be beneficial. However, difficulties in assigning a money value to health outcomes makes this method pragmatic in health care. Other methods of economic evaluations that do not require outcomes to be valuated monetarily are therefore applied to a more extent in the health care sector (26).

Cost-minimization analysis (CMA) is a more basic form of economic evaluation (Sampson). CMA is preformed when two or more interventions under consideration are believed to achieve the same extent of the outcome. Therefore, what distinguishes the interventions are reduced to the difference in costs. Drummond (26) stated that it is not appropriate to view CMA as a full economic evaluation due to the uncertainty related to the estimates of costs and effect. The views that the alternatives under consideration are equivalent is based on researchers professional opinion which may lead to uncertainty in estimates. Hence, there might be questions regarding the basis on how the view was formed. Alternative interventions are however rarely clinically equivalent, and it is therefore usually more appropriate to combine information about both the costs and the consequences when comparing interventions and preforming an economic evaluation (27).

Cost-effectiveness analysis (CEA) is therefore the most common type of economic evaluation in the health sector. These analyses are commonly used to assess whether current practice should be replaced when evaluating new interventions (26). CEAs can inform either prolonging or termination of a current intervention or demonstrate uncertainty in the current understanding of the intervention. The costs in a CEA are related to a single, common effect that may differ dependent on the interventions under evaluation. The analysis can therefore be applied to many different types of health interventions as the outcome measures used can easily vary. The results in a CEA comparison can be expressed in terms of incremental cost per unit of effect or effects per unit of cost (e.g., the extra cost per life-year gained of the more effective and more costly intervention). Using the information provided by the cost-effectiveness analysis decision makers can determine whether the incremental benefits justify the incremental cost (26) . However, one of the limitations with CEA is the way the outcome is measured. The outcome is often not calculated in ratios, and it rather focuses on the single outcome common to the interventions being evaluated. Hence, it cannot be used to compare interventions that affect different outcomes without missing several off the effects. A common outcome may therefore not be considered the primary outcome of interest to both interventions.

What is often referred to in the literature as cost-utility analysis (CUA), is variant of CEA. In contrast to CEA, CUA has been developed to be used in health care specifically. The largest difference between the two methods is that CUAs use a generic measure of health gain when measuring the consequences (25). The use of this measure enables the opportunity cost (the value of the next best alternative forgone as a result of the decision made) to be assessed. Meaning that decision-makers can make informed decisions where they can compare the benefits gained from introducing new interventions with the loss from replacing any of the current existing programmes. The measures are developed to estimate individuals or societies preferences for a given health outcome (e.g., a particular health state or a period of states throughout time) or the extent to which an intervention affects one's general well-being or "utility" (26).

The generic measure of the outcome is usually expressed as Quality adjusted life years (QALY)(26). When calculating QALYs, the information about quality of life and length is combined. Information on an individual's quality of life is retrieved from a measure of health-related quality-of-life (HRQOL) on a scale of states from 0 to 1, where 1 is representing "full health" and 0 is representing "death". An individual's value of HRQOL is than multiplied by the number of years in this health state to create the number of QALYs. Typically, the results of CUAs are the costs per QALYs gained by introducing an intervention instead of another. The QALYs are further used to estimate a ratio to compare the cost-effectiveness of the evaluated interventions. The cost-effectiveness of the intervention under comparison is usually presented as the incremental cost-effectiveness ratio (ICER). The ICER represent the cost per-benefit of the intervention and is calculated by dividing the incremental cost by the incremental benefit of the intervention. In the case of CUA the benefit will be the QALYs gained. When ICERs of different interventions are compared to one another the cost-effectiveness between the evaluated interventions can be assessed. This comparison provides policy relevant information that healthcare decision-makers can benefit from when being faced with the decisions between interventions. Guidelines have developed emphasizing to choose the "current best practice" or the most cost-effective alternative (26).

Economic evaluations have the past two decades had an increasingly important role in the health care sector. The explicitly design can provide decision-makers with information about the best available research evidence by measuring the efficiency and allocation of resources.

This information is of relevance when assessing implementation of strategies, comparing interventions and can be relevant for providers and patients. These methods are therefore highly appropriate to apply when comparing different interventions and programmes(26), especially in light of the growing concerns about quality of care and limits of resources in the health sector.

1.5 Why it is important to do this review

Home-based rehabilitation for stroke has shown to have a significant effect and a clinical impact when compared to both hospital-based and institution-based rehabilitation. However, in the advent of rising costs, health care resource allocation has become increasingly important (25) and the costs of interventions for stroke rehabilitation is no exception. It is therefore important to define cost-effective and evidence-based intervention for rehabilitation of stroke patients.

Economic evaluations have been applied when assessing the cost-effectiveness of stroke rehabilitation interventions in research. However, only two reviews aim at evaluating the cost-effectiveness of home-based rehabilitation for stroke patients by synthesizing economic evaluations. Khoramrooz et al. (28) conducted a systematic review in 2021 aiming at reviewing economic evaluations of home care compared to hospital care for stroke patients. Based on five studies the review concluded that home care was a more a cost-effective option than hospital care for stroke patients, but that few studies had been published and that there is a need for further research. The conclusion in these systematic reviews raises question on whether home-based rehabilitation is cost-effective compared to a conventional intervention.

Since the publication of the prior review two larger economic evaluations evaluating on cost effectiveness of home-based stroke rehabilitation have been published (18, 29). To my knowledge no systematic review have assessed the cost-effectiveness of home-based rehabilitation compared to institution-based rehabilitation. This knowledge gap is important to investigate, as it could affect future healthcare services, increasing health benefits and may be cost saving. It is important for policy makers to know if this intervention is not only clinically effective, but weather it is cost-effective compared to the variety of rehabilitation interventions offered today. This information can contribute by ensuring that resources are allocated efficiently, and that health care sector deliver the most cost-effective interventions.

This systematic review of economic evaluations aims at investigating the cost-effectiveness of home-based rehabilitation when compared any form of conventional rehabilitation for stroke patients.

2 Method

This systematic review followed a pre-specified protocol that has not been published and the Preferred Reporting Items for Systematic Reviews and Meta- Analysis (PRISMA) statement and checklist (30). The PRISMA 2020 checklist for this review is presented in appendix 1. Research that reported cost-effectiveness outcomes associated with home-based stroke rehabilitation were included in the review. Economic evaluations evaluating the cost-effectiveness of home-based rehabilitation or care in adult stroke patients who had been discharged from the hospital to their homes were included. Eligible comparisons were adult stroke patients who had been subjected to conventional rehabilitation or care in other settings than in their home. This systematic review had no funding, and no funders were involved in any aspect of the review.

2.1 Objective

The objective was to conduct a systematic review on the research question: Is home-based rehabilitation cost-effective compared to conventional rehabilitation in adult stroke patients?

2.2 Literature search

MEDLINE, EMBASE, CINAHL, Web of Science and Scopus was searched in February 2023 for studies meeting the inclusion criteria for this review. These search strategies are presented in appendix 2. In addition, reference lists of relevant systematic reviews that were identified through the electronic searches and the reference list of the included studies in this systematic review were searched. The search was limited to English publications between January 1990 and February 2023 due to the time limitation.

Search specialists at The Artic University of Norway (UiT) and The University of Gothenburg (GU) assisted and advised me on how preform searches in the databases. The search strategies were however developed and conducted by the author independently. The searches strategies

were divided into three categories; i) related to the population, stroke patients, ii) related to the intervention, home-based rehabilitation, iii) related to the study type and outcome, economic evaluation and cost-effectiveness. Given the extent of different home-based rehabilitation programmes a variety of search terms were used to procure all relevant studies evaluating the aimed research question. There exists a large variety of terms describing conventional stroke rehabilitation in different healthcare systems. Including these terms as a comparator category in the search strategy was not justifiable as it could reduce the quality of the search strategy by missing relevant publications. The comparator intervention was therefore manually screened for in accordance with the preset inclusion criteria.

2.3 Inclusion and exclusion criteria

Study design: Full economic evaluations (studies in which both the costs and the outcomes of the alternatives were examined and in which a comparison of two or more interventions are undertaken) were included in this SR following the classification of economic studies by Drummond (26). This includes cost-benefit analysis (CBA), cost-utility analysis (CUA), cost-effectiveness analysis (CEA) . Trial-based, decision models, trial-based models and simulation-model based conducted full economic evaluations were included. Studies where a full economic evaluation was conducted as a part of the larger study were included if they met the eligibility criteria. In the case that very few full economic evaluations would meet the inclusion criteria partial economic evaluations like cost-minimization analysis (CMA) would be included. Protocols, qualitative evaluations, short notes, comments, editorial and conference abstracts were excluded.

Study setting: No restrictions were enforced on country setting, meaning that the studies could be carried out in low-, middle-, high-income countries.

Population: Adults (18 years and older) who experienced stroke. No restrictions were enforced on the gender, severity or type of the stroke or the level of dilatability following the stroke.

Intervention: The intervention was home-based rehabilitation. Therapy or care aiming at enabling patients to live as independently as feasible after a stroke by assisting them in regaining as much function as possible. It was provided either by family members, domiciliary workers, or healthcare personnel. The intervention had to be offered in the patient's own home,

and could include therapy like speech therapy, occupational therapy and physiotherapy. The intervention could also be provided through tele health or e-health solutions if the patient received the intervention in his or her home. The intervention could also be home-based rehabilitation in combination with conventional rehabilitation.

Comparison: The comparison could be any form of conventional rehabilitation where the intervention was provided outside of the patient's home. This would include rehabilitation or care provided in hospitals, out-patient clinics or in facilities.

Outcome: Cost-effectiveness outcomes, assessing both clinical primary outcomes and costs associated with the alternative interventions. E.g., expressed in cost per single natural units (disease or life years) gained or cost per QALY gained.

2.4 Article selection

The retrieved records were imported into EndNote 20.4. EndNote was further used to check and consequently remove duplicate records of the same reports. Titles and abstracts of the identified records were then imported and screened based on the inclusion criteria in the web-tool Rayyan. Obviously irrelevant reports according to the inclusion criteria was then removed. The title and abstract screening were generally over-inclusive and carried out twice by one author independently. This was accomplished by importing the retrieved reports into two separate screening projects in the Rayyan. This was preformed to avoid removing relevant reports in the screening process. Discordances between the two screening projects were resolved by re-examining the record. Publications that were found to be relevant were then appointed for full text reading using a pre-designed form to assess eligibility of the studies. The pre-designed form was used to assure consistency in the screening process and is presented in appendix 3. Figure 1 illustrates the article selection process.

2.5 Data extraction and management

Two pre-designed forms were created independently by the author and used to extract data from the elected studies, see appendix 4 and 5. These forms were created to ensure standardization of the data extracted. Based on the inclusion criteria both model simulated EEs and trial-based EEs would be eligible for this SR. These methods of conducting EEs often differentiate in terms of methodology, analysis, and source of data. Therefore, creating one form that would fit both

methods would be inexpedient. This is because the form would not be exhaustive or comprehensive enough to extract all the relevant data and multiple categories in the form would be left blank because the category were not applicable for the study. Thus, two different extraction forms were crated and used to extract the relevant data from the included studies in this SR.

Using the extraction form for model simulated EEs (appendix 4) following characteristics were extracted: i) Study characteristics: study title, author, year of publication, country of study, study setting (location) and study aim, ii) Study method: type of Economic Evaluation, model type, study perspective, model cycle length, time horizon, currency of cost, year of costing valuation, discount rates, outcome, sensitivity analysis, iii) Economic model input parameters: description of population, source of population data, description of intervention, description of comparator, description of health measures, source of health measures, description of included costs and source of cost data, iv) Study outcomes: unit measurement, threshold measurement for cost effectiveness, results and sensitivity analysis.

The following characteristics were extracted from the included studies using the extraction form for trial-based EEs: i) Study characteristics: study title, author, year of publication, country of study, study setting (location), study design and study aim, ii) Study methods: type of Economic Evaluation, study perspective, year of data collection, time horizon, price year of collected cost data, description of included costs, currency of cost, cost type, discount rates, health measure, outcome measure and sensitivity analysis, iii) Participant characteristics: description of participants, total number from population and population (where from), iv) Information about the intervention: number in the intervention group, description of intervention, duration, frequency and deliverer of intervention, v) Information about the comparator: number in the comparator group, description of the comparator, duration , frequency and deliverer of intervention, vi) Study outcomes: result, sensitivity analysis. Two studies: Candio et al. (29) and Allen et al. (31) had had supplementary material, which was used in the data extraction to fill out the extraction forms.

2.6 Assessment of methodological quality

Studies were appraised for methodological quality using conventional methodological assessment tools in health economics (32). Similar to the data extraction, two tools had to be used to assess the quality of the included studies. This is because these tools are usually appropriate for checking methodological quality of either model-based or trial-based economic evaluations. A conclusion was therefore drawn to use two separate tools to assess the quality rather than using one tool that would not be applicable for both methods. This would ensure that all the included studies would be properly assessed for methodological quality. The quality assessment was done by one author independently. Each study was quality assessed twice to ensure consistency in the quality assessment. Discordances between the two was solved by quality assessing the studies a third time.

For model-based economic evaluation The Quality of Health Economic Studies (QHES) instrument was used (33). It consists of a list with16 criterias, where each criteria have an assigned weight in scores. The tool assesses the study objectives, perspectives, variable estimates, data sources, costs, outcome measures, model structure and description of analysis. The format of the criteria's are "Yes" or "No" and a study meets or fails to meet each criterion. Thus, scoring either the full weighted value or zero. The perfect score for a study is 100 and the lowest score is 0. Evidently, a standard metric for ranking QHES scores is lacking in the literature. However, earlier previous studies adapting the QHES instrument in quality assessment have used cutoff scores to grade studies into quartile groups where a score of; (0-24) indicate extremely poor quality, (25-49) poor quality, (50-74) fair quality and (75-100) high quality.

Trail-based economic evaluations were assessed for methodological quality using what is known as Drummond's 10-point checklist or Drummond 10 Point (26). This checklist contains of 10 questions considering the research question, description of the study/intervention, study design, identification, measurement, valuation of cost and consequences, discounting, incremental analysis, presentation of results and sensitivity analysis and discussion of the results in the context of policy relevance and existing literature. A ranking metrics is also lacking with the Drummond checklist, and so several a ranking scales have been developed by scholars. This systematic review applied a ranking scale developed by Doran (34). A protentional score of 1 was attributed to each item on the checklist. The economic quality appraisal aggregates a result as poor (1–3 points), average (4–7) and good (8–10).

2.7 Data analysis

Outcome measures are expressed as they were presented. Meaning that costs were expressed in the currency the study reported them in. This also applies for the primary health outcomes. It was planned to pool sufficiently similar outcomes by doing a meta-analysis.

It was assumed that the intervention and comparisons of the studies would vary, and that heterogeneity would be present. It was therefore decided to do a meta- analysis with a random effects model using inverse variance. The random effects model assumes that the different studies are estimated different, yet related, intervention effects. The random effect model creates wider confidence intervals for the intervention effect. Thus, statistical significance will be more conservative. Review Manager 5.4 was planned to be used when pooling data values and heterogeneity would be examined in accordance with the Cochrane Handbook for Systematic Reviews of Interventions. A rough guide would be used to interpret heterogeneity (I^2) between the studies; might not be important (0% to 40%), may represent moderate heterogeneity (30% to 60%), may represent substantial heterogeneity (50% to 90%) and considerable heterogeneity (75% to 100%).

However, it was revealed that study specific heterogeneity existed among the studies when similarities and differences among the studies where inspected. EEs have many sources of heterogeneity, and many methodological issues therefore making it challenging to conduct a meta-analysis of EEs outcomes compared to outcomes of clinical studies. SR of EEs does therefore often not pool the effects. Sources of heterogeneity found in the included studies for this SR included study characteristics such as (setting, country, country currency) and methodology including (time horizon, perspective, model type, data source, input parameters, reporting of outcome and assumptions). Because of the heterogeneity observed among the included studies conducting a meta-analysis would not be justifiable. A narrative synthesis was therefore preformed, reporting the findings of the included studies without applying a meta-analysis estimating the pooled effect measures. Tables were created to present the study outcomes.

3 Results

3.1 Description of the search results

In total 532 references were obtained through electronic searches in MEDLINE (247), EMBASE (49), CINAHL (42), Web of Science (52) and Scopus (142). 157 duplicates were removed using Endnote 20.4. One reference was found through reference lists. Thus, 375 references were assessed by title and abstract. Seven-teen publications were promoted from title and abstract screening to full-text screening. Twelve of the 17 full-text assessed articles were excluded. Reason for exclusion is stated and listed in appendix 7. In total, five studies met the inclusion criteria and were included in this review (31), (29), (35), (18) and (36) .

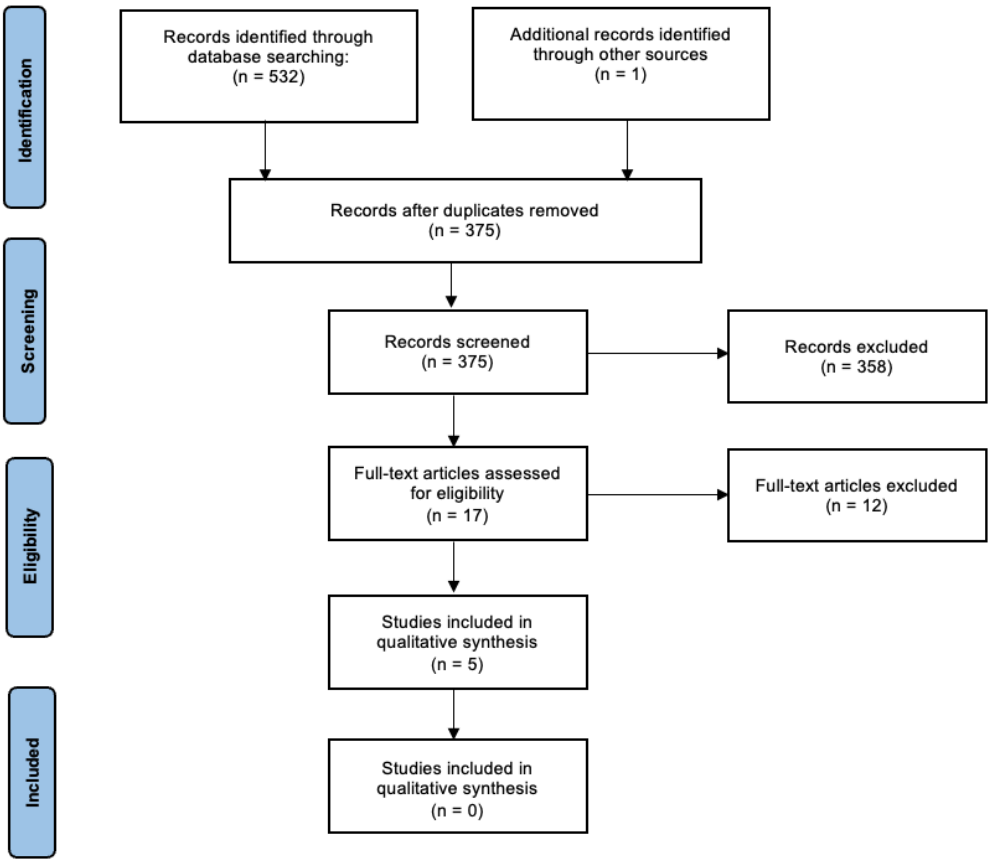

Figure 1 – PRISMA flow diagram of Search results

3.2 Description of the included studies

The studies included in this SR were published between 2002 and 2021. Two are model-based EEs while three were trial-based EEs. Two of the studies were conducted in The UK (29) (35), one in Canada (31), one in Thailand (36) and one in Taiwan (18). A cost-utility analysis was performed in two of the studies, while a cost-effectiveness analysis was performed in the remaining two studies. Patel et al. (35) performed both cost-utility analysis and cost-effectiveness analysis. Table 1 presents a brief description of the included studies. Further details of the included studies will be presented in the following sections.

Table 1 – Description of the included studies

Author/ year	Country	Economic evaluation	Population	Intervention	Comparison
Allen et al., 2018	Canada	Cost- utility analysis	164 adult stroke survivors from Canada	HBR: Individualized services, therapy, and support	Usual care, no or limited rehabilitation
Candio et al., 2022	UK	Cost- utility analysis	855,000 adult patients survived the acute stroke phase from 32 European countries	HBR: a package of physiotherapy, occupational therapy, and speech therapy	Conventional hospital-based care (inpatient and outpatient).
Patel et al., 2003	UK	Cost- utility analysis and Cost-effectiveness analysis	457 adult stroke survivors from The UK	HBR: Investigation on outpatient basis, therapy, and personal care.	Stroke unit and stroke team
Tung et al., 2021	Taiwan	Cost-effectiveness analysis	197 adult stroke survivors from Taiwan	HBR: task-oriented rehabilitation training	Hospital rehabilitation and therapy
Sritipsukho et al., 2010	Thailand	Cost-effectiveness analysis	60 adult stroke survivors from Thailand	HBR: home-based exercise program together with conventional care	Conventional hospital care

3.2.1 Type of Economic Evaluation

Three of the studies were trial-based EEs. This includes Patel et al. (35) and Sritipsukho et al. (36) that both conducted the economic evaluation alongside an RCT, and Tung et al. (18) that was carried out alongside a retrospective study. Two of the included studies were model-based (31) (29). Allen et al. simulated the natural history of stroke survivors and the impact of the intervention in a Markov model with six-month cycles. The model consisted of four possible health states: nondisabled (able to live independently in activities of daily living), disabled (live in one's own home, requires assistance for activities of daily living), long-term care (LTC) (residents in a LTC or assisted living facility), or death. Candio et al. simulated the impact of the intervention in a Decision tree followed by a Markov model with 3-month cycles. In the decision tree part of the model, stroke survivors were all assumed to remain alive between two weeks and 3 months from hospital admission. Functional independence was measured using the modified Ranking Scale, with effectiveness of the intervention measure as a change in mRS ranging from 0 (no disability) to 5 (confined to bed). In the Markov model, the risk of death was estimated over the remaining years conditional on the 3-month mRS score, age, and gender.

Time horizon

The time horizon varied greatly among the included studies. Outcomes were simulated for 35 years or until death in Allen et al., 5 years in Candio et al. In Sritipsukho et al. the time horizon was set to 3 months and 12 months in Patel et al. Time horizon was measures as mean length of intervention utilization in the intervention and comparator groups respectively in Tung et al. The mean length of rehabilitation was 35.65 days in the home-based cohort and 27.00 days in the comparator cohort.

Cost perspective and measure of cost and resource use

Two of the studies were EEs with a societal perspective, including both direct and indirect costs (29) (35). While three of the studies had a narrower provider perspective (36), (18) and (31).

Candio et al.,(29) included estimated unit costs for rehabilitation treatment, inpatient costs, outpatient costs, accident and emergency costs and nursing home costs, informal care costs and costs associated with productivity loss. The intervention cost was measured by multiplying the mean number of therapy sessions by their respective unit costs for each type of therapy, which was based on national UK refence cost. Weighting costs were obtained by dividing the unit cost for an outpatient care visit in each country by the same type of visit in the UK. This was

performed to capture country-heterogeneity in the intervention costs. Health and societal care costs including hospital stay and day cases (inpatient costs), outpatient visits, accidents and emergencies (A&E) visits, and nursing and residential care costs (for patients $\geq$ 65 years) were derived from a primary study. Country-specific resource weights were applied for 31 European countries to adjust for UK estimates. For informal care costs it was assumed that 50% of the stroke patients with moderate to severe disability at 3 months following the stroke would require informal care. Based on expected level of independence, informal care cost was estimated using age/gender specific numbers of days of received care, based on the Survey of Health, Aging and Retirement in Europe (SHARE) study, the average of the macro-region to which the country belongs (i.e. Central Europe, Eastern Europe, Southern Europe and Scandinavia).

Mortality related productivity losses were estimated as the number of working years lost due to premature death multiplied by the country- specific employment rate. Country-specific average days of work due to stroke was applied to measure morbidity related productivity losses. It was assumed that absence from work would be temporary in stroke patients that had slight to no symptoms or disability at 3 months. For patients with moderate to severe disability at 3 months it was assumed that absent from work would be permanent. For these patients, the first 90 days of work absence were considered, and work time was valued using country-specific, gender-stratified earnings.

Patel et al. (35) included cost of health services, other formal care agencies and informal caregivers. Health service costs included hospital resource use and therapy costs that was measured on an ongoing basis. Data on the use of informal care and other public sector services were collected retrospectively at 12 months after the stroke onset. Supplementary information from families or caregivers, health and social services records and direct observations of services provided.

Annual estimation of informal care inputs was based on the number of weeks in a year over which care was utilized. Costs were calculated for each patient and the unit costs were obtained from local services whenever possible to approximate actual intervention costs. Informal care costs were calculated using two methods: i) based on the UK minimum wage rate using the opportunity cost method, and ii) based on unit cost of social services home help worker, the replacement cost method. Cost of medication were not included.

Allen et al.(31) adopted a narrower public payer perspective, hence only included direct costs. Cost associated with health service resources were measured by multiplying the frequency of utilization by the price of the service. Individual-level data from Markle Rein et al. (7), derived from responses to the Health and Social Services Utalisation Survey were used to measure costs of healthcare usage for both the home-based cohort and the comparator arm in the model. These costs included physician visits (emergency room and specialists), other healthcare professionals/services, hospitalizations and surgeries, diagnostic tests and laboratory expenses, devices and special treatment, household help, and travel costs. Visit costs for the intervention group were provided by the intervention programme. Visit cost calculations were specific to therapist type. For long-term projections a cost per visit was applied based on costing in the intervention programme study.

Sritipsukho et al. (36) also adopted a narrower provider perspective including costs of hospital services. Cost of medical services received by patients in both the intervention and control groups included costs of hospital care and rehabilitation services. The costs of teaching material development of CDs for the intervention group were considered as capital costs. The annual cost of development of the teaching material production and the costs of home visits by physical therapist were calculated for individual patients. Macro-costing was applied to calculate the cost of conventional hospital care received by an individual patient. Thus, the number of hospital services were quantified and multiplied by their unit costs. The unit costs were based on the reimbursement rate for the Civil Servant Medical Benefit Scheme paid by the Ministry of Finance in Thailand. The reimbursement rate was to be the actual hospital costs because the study hospital was a government hospital. Like Sritipsukho et al. and Allen et al., Tung et al. also applied a narrower health system perspective. The total cost of rehabilitation of each patient was extracted from declared medical expenses, which was calculated using a payment standard based on Taiwan national health insurance rules. The costs included in the study were direct costs of resource use of services offered.

Discount rates

Three of the included studies discounted the results, both costs and primary health outcomes (29) (31) (36). Candio et al. applied an annual discount rate of 3.5% for both cost and QALY, while Allen et al. discounted costs and QALY at a 3% rate per year. Sritipsukho et al. applied a 3% discount rate, but only to the economic costs and not to the effects measure. Patel et al. and Tung et al. neither discounted cost nor effects.

Table 2 – Description of methodology in the Economic Evaluation

Author/ year	Study perspective	Economic evaluation	Model type	Time horizon	Cost type	Discount rates	Outcome measure
Allen et al., 2018	Public payer perspective	Cost-utility	Model-based	35-year or until death	Direct costs	3%	Incremental QALYs and Incremental costs
Candio et al., 2022	Societal perspective	Cost-utility	Model-based	5-year	Direct and indirect	3.5%	ICER, generated additional QALYs and cost savings
Patel et al., 2003	Societal perspective	Cost-utility and Cost-effectiveness	N/A Trial-based	1 year	Direct and Indirect	-	ICER per QALY gained and per (%) death and institutionalization averted
Tung et al., 2021	Health system perspective	Cost-effectiveness	N/A Trial-based	Not mentioned	Direct costs	-	The total cost/ improvement in BI, IADL, ED5Q and MNA scores.
Sritipsukho et al., 2010	Provider perspective	Cost-effectiveness	N/A Trial-based	3 months	Direct costs	3%	ICER per Disability averted

3.2.2 Population

All the included studies had participants that had survived a stroke. Three out of the five studies had population data extracted from a clinical trial. However, not all the EEs reported the age distribution among the participants. Those that did, had a middle-aged to older population with a mean age ranging from 66.2 to 76.52 years.

Patel et al. (35) undertook the EE utilizing participants from a previously published RCT on 457 patients from a suburban district in the UK with a stroke diagnosis defined by WHO's definition (). Participants with moderately severe stroke, who could be supported at home with nursing, therapy and social services were included in the study (). This EE had three study arms

and so the gender distribution was measured for the three patient cohorts respectively. There were (47%), (51%) and (46%) female in the cohorts respectively.

Tung et al. (18) used primary clinical data collected on 197 patients while conducting the EE. Patients were recruited from Chi Mei Medical Center for post- acute stroke in Taiwan and were included in the study if they had a relatively stable medical condition with an mRS score of 3 (moderate disability) or 4 (moderate to severe disability). The intervnetion group had 45.76% female and 54.24% male, while the comparison group had 44.9% female and 55.1% male.

Sritipsukho et al. (36) was conducted alongside a prospective RCT, where 60 ischemic stroke patients were recruited from inpatient wards at Thammasat teaching university hospital in Thailand. Ischemic stroke was diagnosed by clinical diagnosis or exclusively using CT or MR scanning. Patients with a stroke from middle cerebral artery infarction was included. In the home-based group there was 47% male and 53% female and in the comparator group there was 43% male and 57% female. Participants in this study had major strokes and were severely disabled based on baseline measures. All participants in the study had baseline mRS (3-5), which they classified as major strokes. The mean score on the baseline Barthel Index was 31.7 for the intervention and 33.2 which was interpreted as severely disabled.

Allen et al., (31) is a model-based EE, thus the methodology differentiates from the trial-based studies. The population in this study were simulated in a Markov model. This is a model that predicts future outcome variable based on current states. Several sources of data were used to populate the parameters in this model and two RCTs were used to populate the participants in the intervention and comparator cohorts. The RCT populating the intervention cohort was conducted in Ontario, Canada. The intervention participants were 164 patients of whom 59.1% were males and 40.9% were female. Mean age was 66.2 and severe stroke was seen in 82 (50%) of the participants. The RCT populating the control cohort was conducted in Toronto, Canada. Thirty-nine participants with a confirmed diagnosis of stroke (first ever or recurrent) or transient ischemic attack (TIA) within the previous 18 months were included in the usual care cohort. Mean age was 70.6, and (24) 62% of the participants were male, while 15 (38%) were female.

The population in Candio et al. were from 32 European countries, including 27 State members of the European Union, Iceland, Israel, and the United Kingdom. These 855,083 country-specific simulated participants were identified from the Global Burden of Disease study. This

population consisted of patients who had survived the acute stroke phase (between 24 h and two weeks from symptoms onset) and had a confirmed diagnosis of intracerebral hemorrhages, ischemic stroke, or strokes of unknown type, were aged ≥20 years old and admitted to the hospital. Gender and age distribution was not presented in the study nor in sources in the reference list.

Table 3 - Description of the population

Author/year	Population
Allen et al., 2018	Intervention group: N=164 stroke survivor from Ontario, Canada. Mean age: 66.2. 59.1% male, 40,9% female. Severe stroke seen in 50%. Control group: N =39 patients from Toronto, Canada with confirmed diagnosis of stroke. Mean age: 70.6. 62% male, 38% female.
Candio et al., 2022	N= 855,083 stroke participants from 32 European countries. Mean age and gender proportion is unknown. Participants eligible for rehabilitation.
Patel et al., 2003	N=457 (152/152/153) stroke patients from a suburban district in the UK, Mean age: 76. 52% male, 48% female in all participants. Baseline median Barthel Index placed all participants at moderately to severely disabled level.
Tung et al. 2021	N=197 (59/138) stroke patients from Tainan, Taiwan. Median age: 68.0 (intervention), 67.5 (comparator). 54.24% male and 44,76% (intervention), 55.10% male and 44.9% female (control). Baseline mRS 3 = 39.98% (intervention) and 28.26% (comparator), mRS 4 = 61.02% (intervention) and 71.74% (comparator).
Sritipsukho et al., 2010	N=60 (30/30) stroke patients from Thammasat University Hospital, Thailand. Mean age: 67 (intervention), 66 (comparator). 24.8% male (intervention), 75.2% female (intervention), 24.6% male (comparator), 75.4% (comparator). Baseline mRS (3-5) for all participants (major strokes). Baseline mean Barthel Index: 31.7 (intervention) and 33.2 (comparator)

3.2.3 Intervention

All the included studies had a home-based intervention that focused on regaining maximum level of function after a stroke by providing a variety of rehabilitation services. All the studies had interventions that provided individualized services or tailored plans. Two of the studies had a simulated population using several studies populate long-term models, and so individual level measures including length or frequency of intervention were not stated (Allen and Candio).

The interventions differed in the services that was provided for the patients. Two of the studies provided a combination of physiotherapy, occupational therapy and speech or language therapy (29) (35). The simulated population in Allen et al. (31) received in-home physical rehabilitation as well as social and emotional support, education system navigation and community re-integration. In addition, caregiver support was provided. The participants in Tung et al. (18) received therapy and task- oriented training using domestic tools and by merging training programmes with daily practical, real life circumstances, creating familiar environments. Feasible and easy-to practice activities and community engagement was also offered. The participants in Sritipsukho et al. received exercise programs based on physiology and motor learning, therapy sessions as well as audio material of rehabilitation procedures for self-care.

Home-based rehabilitation and care were the sole intervention in three of the included studies (Allen, Candio, Tung). However, the patients in Patel et al. received tomography scans (CT scans) in outpatient clinics, and patients in Sritipsukho et al. received conventional hospital services in addition to the intervention received at home.

The deliverer of the intervention also differed between the studies. Type of healthcare personnel and their experience related to stroke varied among the studies. Four of the studies (31) (29) (35) (18) stated that healthcare personnel were provided while Candio et al. did not mention the deliverer of the intervention in the study. In Allen et al. (31) the intervention was delivered by an interdisciplinary team with registered nurses, occupational therapists, physiotherapists, speech-language pathologists, therapeutic recreation therapists or rehabilitation therapists as well as social workers. In Patel et al. (35) a multidisciplinary specialized stroke team including a general practitioner, a stroke physician, a physiotherapist, an occupational therapist, a speech and language therapist provided the intervention. In addition, support from district nursing and social services were provided. In Tung et al. (18) the healthcare personnel were therapists, however their occupational therapy background was not stated in the study. Family members

were also invited to participate in the rehabilitation. In Sritipsukho et al. stroke experts, stroke patients, physical therapists, occupational therapists, and speech therapists developed the exercise program that was delivered to the patient. However, the home visits were done by a physical therapist.

The length of the interventions also differed among the included studies. Two of the studies (35) (18) had a 3-month intervention length. In Tung et al. the length of the intervention was according to the patient's needs, meaning that the length varied amongst the participants. The mean length was 35.65 days in the intervention cohort, not much longer than the length seen in Patel et al and Sritipsukho et al. In Allen et al. and Candio et al. neither the length nor the frequency of the interventions is mentioned.

The frequency of the therapy sessions varied from six 50-minute sessions per week in Tung et al. (18) to one therapy session a month in Sritipsukho et al. In addition to once-a-month therapy sessions Sritipsukho et al., patients were also provided with exercise programs and standard audiovisual materials that were be utilized outside of the therapy sessions. The intervention in Patel et al. (35) was individualized and so the frequency was based on each patient's needs. Table 3 presents a full description of the interventions in the included studies.

Table 4 – Description of the intervention

Author/ year	Intervention delivered	Frequency/Length	Delivery
Allen et al., 2018	Home-based rehabilitation (CSRT). Individualized services including physical rehabilitation, social and emotional support, education, system navigation, community re-integration, and caregiver support.	N/A Simulated population and projected intervention	Registered nurses, occupational therapists, physiotherapists, speech-language pathologists, social workers, therapeutic recreation therapists or rehabilitation therapists working together in an interdisciplinary team.
Candio et al., 2022	Home-based rehabilitation. A package of care including physiotherapy, occupational therapy and speech therapy at the patient's home.	N/A Simulated population and projected intervention	Simulated population and projected intervention
Patel et al., 2003	Home-based rehabilitation. Individualized tailored care plan outlining activities and the objectives of treatment, reviewed weekly in multidisciplinary	3 months, frequency was individual	Multidisciplinary specialized stroke team including general practitioner, stroke physician, physiotherapist,

	meetings. Including physiotherapy, occupational therapy, and speech and language therapy provide in the patient's home. Investigations, including tomography scans, were done on an outpatient basis.		occupational therapist, speech and language therapists and support from district nursing and social services for personal care.
Tung et al. 2021	Home-based post-acute stroke care (PAC), therapy using domestic tools for task-oriented training, merging training programmes with daily practical, real-life circumstances, inviting family participation, reassuring caregivers regarding their performance, creating a familiar environment , offering feasible and easy-to-practice activities, and encouraging community engagement.	50 min sessions 6 times per week. Length according to the patients needs. Mean length was 35.65 days.	Therapists and family participation.
Sritipsukho et al., 2010	Home-based exercise program based on principles of exercise physiology and motor learning. Standard audiovisual materials of rehabilitation procedures were also given to patients and caregivers for self-care. Home-based exercise programme together with conventional hospital services.	One visit per month for 3 months	Exercise program was developed by experts, stroke patients, physical therapists, occupational therapists and speech therapists. Home visit by physical therapist.

3.2.4 Comparison

Three of the studies had hospital-based rehabilitation services for the control group (patel, tung, stri). The control group in Allen et al. (31) received usual care, which was no or limited rehabilitation services. The content of the hospital-rehabilitation varied among the studies. The simulated population in Candio et al. (29) received centre-based rehabilitation, containing conventional hospital care including inpatient and outpatient care. Patel et al. (35) was a three-armed study, thus there was two comparator cohorts in this study. Both cohorts received rehabilitation in a hospital setting, one cohort in a stroke unit and one in a general medical ward

(stroke team). The stroke unit cohort got joint assessments, goal settings, treatment and discharge planning, while the cohort in the stroke team received stoke management, investigation and discharge planning. The control group in Tung et al. () received intensive inpatient physical, occupation and speech therapy. While the control group in Sritipsukho et al received conventional hospital care including outpatient rehabilitation at the discretion of their physicians and follow-up visits at an outpatient clinic.

The deliverer of the comparison intervention also differed between the studies. Three of the included studies stated that the comparator intervention was provided by healthcare personnel (35) (18) (36). Allen et al. (31) and Candio et al. (29) had no description of the deliverer. The stroke team cohort in Patel et al. had a multidisciplinary team including specialist stroke physician and staff with specialist stroke experience, while the cohort in the medical ward had general physicians, nonspecialized nurses, and therapy staff, advised by a specialist stroke team. In Tung et al (18) a multidisciplinary team including physiatrists, therapists, nurses, phycologists, social workers, nutritionists, and medical technicians provided the rehabilitation. Hospital staff and physician provided the control group in Sritipsukho et al. (36). There was no detailed description of the hospital staff's specifical health occupation.

Length of the interventions in the control groups also varied. Two of the studies (35) (36) had a 3-month intervention length. In Tung et al. the length of the intervention was according to the patents needs, meaning that the length varied amongst the participants. Mean length in the control group was 27 days. In the simulated populations in Allen et al. (31) and Candio et al. (29) neither the length nor the frequency of the interventions is mentioned in the control group. The frequency of the therapy sessions varied from 3-hour sessions five days a week in Tung et al. (18) to care based on patients needs in Sritipsukho et al. (36). This was carried out at discretion to the patient's physician. The control group in Sritipsukho et al. (36) also had follow up- visits scheduled once a month. In Patel at al. (35) frequency of the intervention in the control group was individualized. Table 4 presents a full description of the comparisons in the included studies.

Table 5 – Description of the comparator

Author/ year	Intervention delivered	Frequency	Delivery
Allen et al., 2018	Usual care. Assumed to receive no or limited rehabilitation services.	N/A Simulated population and projected intervention	N/A Simulated population and projected intervention
Candio et al., 2022	Centre-based rehabilitation: Including conventional hospital-based rehabilitation (inpatient and outpatient)	N/A Simulated population and projected intervention	N/A Simulated population and projected intervention
Patel et al., 2003	Hospital-based rehabilitation: Stroke unit: including joint assessment, goal setting, treatment, and discharge planning utilizing guidelines for stroke management. Stroke team: care in general medical wards including management, investigation and discharge planning	Frequency was individual. Length was 3 months.	Stroke unit care: a multidisciplinary team including specialist stroke physician and staff with specialist experience in stroke. Stroke team care: general physicians, nonspecialized nurses and therapy staff, advised by specialist stroke team.
Tung et al. 2021	Hospital-based rehabilitation: Intensive inpatient hospital rehabilitation. Physical, occupational, and speech therapy.	Three hours per day on weekdays (5 days a week). Length according to the patients' needs. Mean length was 27 days.	Multidisciplinary team including physiatrists, therapists, nurses, phycologists, social workers, nutritionists, and medical technicians.
Sritipsukho et al., 2010	Hospital-based rehabilitation: including outpatient rehabilitation at the discretion of their physicians and follow-up visits at an outpatient clinic.	Hospital care at discretion of physicians. Follow-up visits scheduled monthly for 3 months.	Hospital staff and physician.

3.2.5 Outcomes

Four of the studies calculated incremental cost-effectiveness ratio (ICER) (31) (29) (35) (36). In three of these studies, QALY was used to measure the value of the health outcomes including length of life and quality of life as the benefits of the interventions.

Allen et al. (31) calculated incremental costs per QALY gained for both the intervention and the comparator. This cost-effectiveness outcome measure was calculated using expected value calculations. The total expected value of cost and accumulated QALYs for patients in the different health states in the model were estimated and accumulated for each cohort. The Markov model was used to simulate the population in the health states and calculate NMB for the intervention and comparator. The NMB was determined at a willingness to pay threshold of $20.000 per QALY and home-based rehabilitation was considered to be a desirable outcome of in terms of cost-effectiveness NMB was >0.

Candio et al. (29) also had QALY as their primary health outcome and calculated ICER, cost per QALY gained to determine the cost-effectiveness. The ICER was obtained by dividing the between-intervention difference in mean cost by the between difference in mean QALYs. Estimates were calculated for the whole EU and for all the 32 countries combined. Two perspectives were applied in their analysis. Under base case scenario, a societal perspective was adopted, and home-based rehabilitation were considered to be cost-effective if the ICER was below the country GPD per capita. In the narrower health and social care perspective a €22.727 (£20.000) threshold per QALY gained were used to determine cost-effectiveness.

Patel et al. (35) conducted both an CEA and a CUA. The primary health outcome in the CEA part of the study was percent point of deaths and institutionalization avoided. The primary outcome was combined with mean cost to compute ICERs, representing additional costs per additional percentage point in deaths and institutionalizations avoided for home-based rehabilitation and the two comparators. In the CUA part of the study cost, length and quality of life was compared across the groups by computing QALYs. EQ-5D responses from the participants from stroke onset were modelled statistically used to measure QALY gain. ICERs for the CUA were calculated representing incremental cost per QALY gained and compared between the interventions.

The primary health outcome in Tung et al. was improvement in the Barthel Index (BI), the Lawton-Brody instrumental activities of daily life scale (IADL), EQ-5D and the mini nutritional assessment (MNA). These health measures were evaluated in each participant at the beginning and the end of the interventions. Improvement in the scores of these measures were defined as the differences in mean scores in the groups after intervention completion and before intervention completion. Cost-effectiveness outcome was calculated as the total cost divided by the improvement in these primary health outcome scores, and comparison of this measurement was done to determine the cost-effectiveness of the home-based intervention.

Sritipsukho et al. (36) employed two primary health outcomes, BI and modified Ranking Scale (mRS). These outcomes were expressed as disability averted and represented successful cases after interventions were completed. Goal achievement using the BI were expressed as achieving mild or no disability (BI 1) or achieving no disability (BI 2). While a patient was classified as a success case with (mRS) if clinical outcome improved from major stroke to minor stroke. Cost-effectiveness was evaluated calculating ICERs, which defined as cost per case in achieving the treatment goal and was calculated for both the intervention group and the comparator group. ICERs were calculated by dividing the total costs of the patient group by the number of successful cases.

Table 6 – Description outcome measures in the included studies

Author/ year	**Primary health outcome**	**Cost-effectiveness outcome**
Allen et al., 2018	QALY	Incremental cost per QALY gained using
Candio et al., 2022	QALY	Societal perspective: ICER was below/over country GDP per capita
		Health and social care perspective: cost per QALY gained
Patel et al., 2003	CEA: Death/institutionalization avoided (%)	CEA: ICER cost per (%) point in Death/institutionalization avoided
	CUA: QALY	CUA: ICER cost per QALY gained

Tung et al. 2021	Improvement in BI, IADL, ED5Q and MNA scores	Total medical costs divided by improvement in BI, IADL, ED5Q and MNA scores
Sritipsukho et al., 2010	BI and mRS	ICER: cost per achieved successful cases based on BI and mRS treatment goals

3.3 Quality assessment of the included studies

Quality assessment of the included EE studies was done using The Quality of Health Economic Studies (QHES)(33) instrument and Drummond's 10-point checklist (26). The QHES instrument was used for model-based EEs (31) and (29), while the Drummond's 10-point checklist was used for trial-based EEs (35) (36) (18). More detailed description of the quality assessment for each study is presented in appendix 8. Table 6 and table 7 presents the results of the quality assessment of model-based and trial-based included EEs, respectively.

3.3.1 Results of the Quality assessment

The two included model-based EEs had scores between 75 to 100 in the Drummond's 10-point checklist, equivalent to high quality when applying the quartile group cutoffs. Allen et al. had a total score of 86 while Candio et al. had a score of 79 out of 100. Allen et al. did not gain scores on items 2. The reason for this was because the reasoning for selecting a public payer perspective was not stated. Candio et al. did not gain scores on items 8 and 12 because they only applied a 5-year time horizon, which in the literature has been stated to be too short to allow all relevant and important outcomes of stroke rehabilitation to be estimated (36). Scores were also not gained on item 12 because the component of the numerator and denominator in the cost-utility analysis was not displayed in clear and transparent manner. Both Allen at al. and Candio et al. did not gain scores on item 10 and 14 because there was not given any justification for the measure of the primary outcome and because the magnitude and direction of protentional biases were not discussed.

Using the ranking scale developed by Doran et al. (34) it was concluded that one of the trial-based EEs had an average methodological quality with a score between (4-7) (18), while two were classified as having good quality with a score between (8-10) (36) (35). Patel et al. (35) received a score of 8/10 and Tung et al. (18) a score of 6/10, while Sritipsukho et al. (36) had a

score of 9/10. According to the relative weight on item scores, studies scored relatively lower quality regarding measurement of cost or the choice of included costs in the studies. Patel et al. and Tung et al. did not gain scores on item 4. Patel et al. for not including all relevant costs, and Tung for not stating a clear description of the including costs (18). Tung et al. also did not gain scores item 5 for the same reason and item 7 for not adjusting for differential timing by applying a discount rate to cost and primary health outcome.

In addition, Tung et al. did not adequately perform uncertainty in the estimates of costs and consequences by performing sensitivity analysis. Uncertainty in the estimated was done by calculating mean and standard deviation (SD). Thus, scores were not gained on item 9. Patel et al. did not gain scores on item 2 because there was no description of the frequency in rehabilitation of the intervention and comparator, and Sritipsukho et al. did not gain scores on item 10 for not comparing the results of the cost-effectiveness of the study with prior research on the topic. However, despite these shortcomings the three included trail-based EEs included in this systematic review were rated as having average to good methodological quality.

Table 6 – Quality assessment, QHES-insutiment for model-based Economic evaluations

Item/ Study	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Method. Quality
Allen et al., 2018	Y	N	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	N	Y	Y	86/100
Candio et al., 2022	Y	Y	Y	Y	Y	Y	Y	N	Y	N	Y	N	Y	N	Y	Y	79/100

Y = Yes, N = No

Table 7 – Quality assessment, Drummond's 10-point checklist for trial-based Economic evaluations

Item/ Study	1	2	3	4	5	6	7	8	9	10	Method. Quality
Patel et al., 2003	Y	N	Y	N	Y	Y	Y	Y	Y	Y	8/10
Tung et al. 2021	Y	Y	Y	N	N	Y	N	Y	N	Y	6/10
Sritipsukho et al., 2010	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	9/10

Y = Yes, N = No

3.4 Data analysis

The aim of this systematic review was to investigate whether home-based rehabilitation for stroke patients was cost-effective compared to any conventional rehabilitation. It was concluded that there was a strong heterogeneity amongst the included EEs after assessing the similarities among the studies. Disparities was observed by assessing PICO and the methodology of the studies. Based on the observed variation among the studies it was concluded that performing meta-analysis would not be justifiable due to the EEs being too heterogeneous to pool. Despite several of the studies reporting results on the same primary health outcome, they were presented differently. In example both Tung et al. and Sritipsukho et al. reported the effectiveness of the alternatives using improvement in BI and mRS scores as health outcome. However, Tung et al. simply assessed the improvements in scores while Sritipsukho et al. assessed successful cases based on pre-set treatment goals. In addition, the studies were conducted in different countries and so costs were also reported in different currencies and was therefore also heterogeneous. Due to the variation in the way outcome measure were reported, it would not be certain that the observed effect measure in the included studies would give a true overall pooled effect estimate. Since the outcome data were not reported in a manner that made meta-analysis possible, the outcome data for the results is therefore summarized narratively by text and tables for each cost-effectiveness outcome presented in table 5.

3.5 Results

All in all, the five EEs reported on four eligible outcomes of cost-effectiveness. Four studies did an incremental analysis resulting in calculating ICERs. However, the calculation of the ICERs differentiated among the included studies. Thus, the cost-effectiveness outcomes were reported differently among the studies. Some of the studies calculated ICER as cost per QALY gained, while others calculated ICERs as cost per (%) point in death/institutionalization avoided, and cost per achieved successful cases on BI and MRS treatment goals.

3.5.1 Cost per QALY gained

Allen et al. (31), Candio et al. (29) and Patel et al. (35) were all a cost-utility analyses and all three studies measured cost per QALY gained as the cost-effectiveness outcome of home-based stroke rehabilitation. All the studies had consistent results in favor of home-based rehabilitation. Candio et al. had a larger simulated sample size of 855,00 participants, while Allen et al. and Patel et al. had smaller sample sizes of 203 and 459, respectively.

The cost-utility analysis in Allen et al. revealed that home-based rehabilitation through the CSRT programme was both less costly with an incremental cost of -$17.255 and more effective with an incremental effect of 1.65 QALYs gained when compared to usual care. These results were robust, demonstrated with several uncertainty analysis. Two-way sensitivity analysis revealed that the home-based CSRT programme had a NMB > 0 in the majority of the instances, which was considered to be a desirable outcome. The scenario analysis revealed that the home-based intervention remained cost-effective at a $20.000 willingness to pay threshold at higher discount rates. A willingness to pay threshold of $20.000 per QALY was considered to be a conservative threshold. In the probabilistic sensitivity analysis, the mean cost of the home-based CSRT programme was $171,484 (SD $5596) and the mean utility was 11.63 (SD 0.23). The mean cost in the usual care was higher at $188,636 (SD $6057), while the mean utility gain was lower at 9.99 (SD 0.22) The probabilistic sensitivity analysis revealed that the incremental cost-effectiveness of the home-based rehabilitation was superior in 100% of the iterations when compared to usual care. Results of this probabilistic sensitivity analysis are consistent with those of the two-way and the scenario analysis. Based on these results it was concluded that home-based rehabilitation was cost-effective compared to usual care.

Candio et al. (29) had the largest population simulated from 32 European countries consisting of 855,083 cases. Similarly, to Allen et al. (31), Candio et al. (29) also found the home-based rehabilitation intervention to be cost-effective compared to centre-based rehabilitation. In all the 32 European countries, home-based rehabilitation generated higher QALYs on average, when compared to centre-based rehabilitation. For the whole Europe home-based rehabilitation generated additional 61,888 QALYs. However, incremental estimates of QALYs were only significant in six countries (Austria, Belgium, Croatia, Estonia, Ireland and Italy). The home-based intervention also found to generate 5-years cost savings to society when compared to centre-based rehabilitation with €44.1 billion vs. €43.8 billion respectively. In 26 of the 32 countries, the implementation of home-based rehabilitation was associated with cost savings in a societal perspective. When a health and a social care perspective was considered this number declined to 21, due to Cyprus, Israel and the United Kingdom bearing additional costs.

Home-based rehabilitation found to provide good value for the money when a societal perspective (including informal care costs and productivity losses) was adopted, using the country's per- capita GDP as the cost effectiveness threshold. Home-based rehabilitation was

found to be dominant in generating cost savings and more effective in generating QALYs over the comparator for the whole European Union, Europe as a whole and for the majority of the individual countries (24/32) and cost-effective in the remaining eight countries. The probability of home-based rehabilitation to being cost-effective, when compared to centre-based rehabilitation was found to be 0.95 for Europe as a whole, and rage from 0.85 to 0.98 across the 32 European countries. Similar results were also seen when a UK-based €22,727 (£20,000) per QALY gained cost-effectiveness threshold was considered. Comparable probabilities were estimated except for Sweden (0.62) and Finland (0.77). Sensitivity analysis applying extreme values revealed that home-based rehabilitation remained the most cost-effective option across most scenarios and parameters variations teste. In example assuming that the type of rehabilitation had no effect on mortality on post stroke still showed home-based rehabilitation to be cost-effective compared to centre-based rehabilitation. Only when the lower bound of the confidence interval concerning the effectiveness of home-based rehabilitation, centre-based rehabilitation was found to be cost effective at a 94% probability. Evidence from Candio et al. () suggest that a shift from centre-based to a home-based approach to stroke rehabilitation is cost-effective and likely to be good value for the money with estimated additional QALY gains of 61,888 and a cost saving of €237 million (95% CI: -237 to 1,764) and €352 million (95% CI: -340 to 2,237) in health- and societal costs, respectively.

Patel et al (35) performed both a cost-utility analysis and a cost-effectiveness analysis. For the cost- utility analysis, QALYs gained were measured for the three intervention cohorts. Mean QALYs gained were 0.297, 0.216 and 0.221 for stroke unit, stroke team and home-based rehabilitation. ICERs were calculated using rules of dominance, where the alternatives were ranked by cost, from least to most expensive. If an intervention was more expensive and less effective than the previous strategy it was said to be dominated and was therefore excluded from the calculation of ICERs. Mean QALYs gained in the stroke team was 0.216 and 0.221 in the home-based intervention. For total costs when informal care was excluded, the stroke team cohort and home-based cohorts had mean costs of £95237 and 6840£, respectively. The stroke team also had higher mean costs than the home-based rehabilitation cohort when informal care was included, both based on a minimum wage rate (£12 512 vs. £10 296) and when it was based on home help rate (£18 498 vs. £17 226). Based on this practice, the stroke team intervention was dominated by home-based rehabilitation on primely health outcomes and from all cost

perspective. The comparison of interventions cost-effectiveness was therefore reduced to stroke unit versus home-based rehabilitation.

However, the stroke unit cohort did not dominate the home-based rehabilitation cohort and so ICERs were calculated to indicate the additional outcomes obtained for the additional costs of stroke unit. ICERs per additional QALY gained was £67 323 when only immediate care costs were included, £64 097 when total health and social care costs were calculated, £89 132 total care costs were calculated including informal care costs based on minimum wage rate and £136 609 when total costs were calculated including informal care costs based on home help rate.

Uncertainty around the decisions based on the ICERs were done by estimating the probability of each strategy being cost-effective for a range of protentional maximum values for health/social services. This was done by applying several willingness to pay thresholds for an additional QALY gained. Results of uncertainty analysis revealed that there was a 59% probability that home-based rehabilitation would be the most cost-effective intervention out of the three interventions if decision makers were willing to pay nothing for additional QALY gains. The probabilities that the stroke unit and stroke team would be the most cost-effective intervention was 16% and 26%, respectively.

However, the probability that home-based rehabilitation was the most cost-effective alternative decreased with increased levels of willingness to pay thresholds for QALY gains, leveling out at about the £60 000 threshold, but did still remain higher than the two alternative interventions across a full range of specified values. Home-based rehabilitation remained the most cost-effective alternative at a £30 000 threshold value per QALY gained. This was the current willingness to pay threshold in the UK during the publication of this EE in 2003. Based on this threshold the probability that stroke unit and stroke team was the most cost-effective alternative was equal to 29%, while home-based rehabilitation had a probability of 42%. Thus, cost per QALYs gained in this cost-utility analysis revealed that home-based rehabilitation was the cheapest intervention and that it generated second most QALYs out of the three alternatives. The uncertainty analysis in this study also revealed that home-based rehabilitation was the most cost-effective alternative.

3.5.2 Cost per (%) point in death/institutionalization avoided

In addition to, calculating cost per QALY gained, Patel et al. (35) also calculated additional cost per percentage of patients who avoided death/ institutionalization in their cost-effectiveness analysis. The percentages of patients who avoided death/ institutionalization were 87%, 69% and 78% in the stroke unit, stroke team and in the home-rehabilitation cohorts, respectively.

Due to the rules of dominance the comparison of interventions cost-effectiveness was therefore reduced to stroke unit versus home-based rehabilitation. Additional cost of avoiding an additional 1% of death and institutionalizations in the stroke unit group was £534 based on immediate care costs alone and £496 from a total healthcare and social care cost perspective. This further increased to £682 when informal care costs based on minimum wage rates were added to healthcare and social care costs. It doubled to £1033 on the basis of the broadest cost perspective incorporating the higher informal rates based on home help rates. However, no threshold was applied for decision making in the cost-effectiveness analysis and no uncertainty analysis was conducted on this outcome measure.

3.5.3 Costs by improvement in BI, IADL, ED5Q and MNA scores

Tung et al. (18) found improvements in BI score and its subdomains, 24.239 ±16.610 in the hospital-based rehabilitation cohort and 25.66 ±15.140 in the home-based rehabilitation cohort (p=0.530). Similar outcomes were found in both cohorts in several of the BI domains: feeding (p=0.265), transfer (p=0.717), ambulation (p= 0.843), stairs climbing (p= 0.953), bladder control (p= 0.659), bowel control (p=0.157) and toilet use (p=0.113). In domains regard dressing oneself (p=0.003), self-hygiene (p=0.013) and showering (p=0.001) the home-rehabilitation cohort exhibited significantly greater improvements than those of the hospital-based rehabilitation cohort. However, the total improvement in BI scores and most of the domains were not significantly different between the two interventions. Similar results were also seen in the improvement of IADL (p =0.527), ED5Q (p= 0.769) and MNA (p = 0.792).

The total rehabilitation costs were however significantly different between home-based and hospital-based cohorts ($p < 0.001$). The cost based on improvements in BI, IADL, EDQ5 and MNA scores were also significantly different in both cohorts with p-value of ($p < 0.001$) in all

outcomes. The mean rehabilitation costs of the hospital-based programme for each patient with stroke was NTD 80,975.54 ± NTD 33,213.72 ($2699.19 ± 1107.12), which was significantly higher than those of the home-based programme (NTD 31,617.71 ± NTD 12,557.57) ($1053.92 ± $418.59). This cost-effectiveness analysis revealed that the home-based rehabilitation programme costs NTD 1445.51 ± NTD 1050.53 ($48.18 ± $35.02) per 1-point increase in BI score, whereas the hospital-based rehabilitation costed NTD 4574.21 ± NTD 4939.84 ($152.474 ± $164.66) per 1-point increase in BI score. In other words, to reach the same functional poststroke recovery outcome home-based rehabilitation required considerably lower medical expenses, approximately one-third lower. Home-based rehabilitation was therefore concluded to be more cost effective than the hospital-based alternative.

3.5.4 Cost per achieved success cases on BI and MRS treatment goals

Sritipsukho et al. (36) had classified three levels of successful clinical outcomes based on the BI (BI 1 = achieving mild or no disability), (BI 2 = achieving no disability) and mRS (improvement from major to minor stroke). Costs were however only calculated in Thai baht. ICER of the BI1 and mRS of the hospital rehabilitation cohort were 25.849 THB and 42.081 THB, respectively. There were no successful cases of BI 2 in the control group. Thew costs were lower in the home-based rehabilitation cohort than those of the hospital-based cohort. For the home-based rehabilitation group costs were 16.218 THB, 33.595THB and 16.798 RHB for the BI 1, BI 2, and mRS, respectively. ICER for the home-based rehabilitation group was the lowest for the mRS measurement at 13.644 THB, followed by those of the BI 1 and BI 2 of 14.212 THB and 24.364 THB, respectively.

The authors argued that there does not exist a willingness to pay threshold for the clinical effect measures that was measured in this study, but that there however are guidelines for economic evaluation in Thailand stating that an intervention is considered cost-effective if the intervention adds one additional QALY for less than 100.000 THB (gross domestic product per capita). Based on the BI 2, a disability avoided in one additional patient would cost 24.364 THB. Thus, it was concluded that the home-based rehabilitation programme in the study was cost-effective comparted to the alternative. For sensitivity analysis the scenario was composed of variations in the number of patients and the payment of physical therapists who conducted home visits. As scenario 1 and 2, 8000THB and 1,500 THB were estimated, respectively. Both

scenarios resulted in greater cost-effectiveness of home-based rehabilitation than those of the base case measure.

4 Discussion

4.1 Aim of the review

This systematic review summarizes the results of five EEs evaluating the cost-effectiveness of home-based rehabilitation for adult patients who have had a stroke. These results include an assessment of both clinical primary health outcomes and cost outcomes.

4.2 Main findings

4.2.1 Cost-effectiveness of home-based stroke rehabilitation

The results in this SR are based on data from five unique economic evaluations, where a cost-effectiveness analysis was performed in three and cost-utility analysis was undertaken in three of the included studies. Overall, the results in all the included studies suggest that home-based rehabilitation for stroke patients is a cost-effective intervention compared to the conventional alternatives based on four cost-effectiveness outcome measure. Allen et al. (31) found home-based rehabilitation to be less costly and more effective in gaining QALYs. The same applies for Candio et al. that found the intervention generate cost savings and higher QALYs on average in Europe as a whole. Patel et al. (35) found the intervention to generate second most QALYs out of the three alternatives under consideration and to be the less costly alternative. Tung et al. found a significant difference in total rehabilitation costs between home-based and hospital-based rehabilitation. They found that home-based rehabilitation required considerably lower costs than the alternative (one-third) per 1-point increase in BI.

Four of the five included EEs had good/ high methodological quality while one had an overall average quality. (31) (29) (35) (36). Domains that some of the studies did not gain scores on were regarding uncertainty estimates, reason for choosing perspective or justification for choice of primary health outcomes, as well as measurements of costs and choice of included costs. See section 3.3, and table 6 and 7.

4.3 Implication for search

4.3.1 Population

The participants in this review were from or were simulated from 32 European countries, Canada, Thailand, and Taiwan. The participants were all from high to upper-middle income countries and were generally an older population with a mean age ranging from 66.2 to 76 years old. Thus, it would not be applicable to draw a conclusion on cost-effectiveness of the intervention on a younger or middle-aged population. Consequences of stroke may differ in different age groups and create a larger productivity loss among younger age groups, which could have an impact on the study outcomes, especially in those undertaking a societal perspective including societal costs such as productivity losses.

The studies also differed in the number of participants included in the study, all from 855,083 participants simulated in Candio et al. (29) to 60 participants in Sritipsukho et al. (36). There, also seems to be a variation in several characteristics for the participants included in the EEs. A difference in participants levels of disability or severity of the stroke is observed. Two of the included studies had included participants with either moderate or moderate severe disability levels (mRS 3-4) (35) (29). One of the studies included participants with moderate, moderate severe and severe disability (36). While one study had 50% severe stroke cases in their participants. The remaining study did not state any disability level in their simulated sample. However only participants eligible for rehabilitation were included in the study. All in all, it seems to be quite a variation in the disability levels for the participants included and it is possible that a more similar baseline disability level in the participants would lead to a greater consistency in the primary clinical health outcomes observed in the studies. Thus, lead to a greater comparability across the studies and to more conclusive results.

4.3.2 Intervention

All the included studies favored the home-based rehabilitation intervention. However, variations are seen amongst the interventions introduced as home-based rehabilitation. All the studies in this review had interventions that were individualized or tailored for each patient either by providing individualized services or tailored plans. However, in two of the interventions conventional hospital services were received in addition to the home-rehabilitation (35) (36). I question whether these additional services might have had an impact on the primary health outcomes seen the participants in these Patel et al. (35) and Sritipsukho

et al. (36). Sritipsukho et al. was the only intervention that used any form of audiovisual materials of rehabilitation procedures. These were also given to patients and caregivers for self-care for independent use. This can have impacted a greater participation of rehabilitation exercises independently.

The frequency and the duration of the interventions also differed among the studies. The interventions in our review had a duration of 35.65 days to three months. In the model-based EEs lengths of the intervention was not stated.

The length of the interventions also differed among the included studies. Two of the studies (35) (36)) had a 3-month intervention length. In Tung et al. the length of the intervention was according to the patient's needs, meaning that the length varied amongst the participants. The mean length was 35.65 days in the intervention cohort. In Allen et al. (31) and Candio et al. (29) neither the length nor the frequency of the interventions is mentioned. The frequency of the therapy sessions varied from six 50-minute sessions per week in Tung et al. (18) to one therapy session a month in Sritipsukho et al. In Sritipsukho et al., the patients were also provided with exercise programs and Standard audiovisual materials in addition to once-a-month therapy sessions. The intervention in Patel et al. was individualized and so the frequency was based on each patient's needs. Table 3 presents a full description of the interventions in the included studies.

4.3.3 Comparison

The control groups received different rehabilitation interventions than the intervention group. Three of the studies had hospital-based rehabilitation as intervention for the control group, one had centre-based rehabilitation. The comparison cohorts overall received a more intensive rehabilitation than the intervention groups. In In four of the comparator cohorts, participants were admitted to the hospital and received the rehabilitation in a hospital setting with the care of health personnel. However, the intervention in Allen et al. stuck out, as the comparative cohort received a less intensive rehabilitation than those in the intervention group. The control group received usual care defined as no or limited rehabilitation. Providing a less intensive rehabilitation in the cohort group might have been a factor that contributed to the home-based group being more effective in terms of gaining more QALYs.

4.3.4 Outcome

All appropriate cost-effectiveness outcomes common in full economic evaluations were eligible for this SR. Overall, four appropriate cost-effectiveness outcomes were reported in the included studies. These outcomes were reported and calculated using common health outcome measures used to measure disability in patients.

4.4 Future research

Few economic evaluations have attempted to compare home-based stroke rehabilitation to alternative rehabilitation in terms of cost-effectiveness, as observed by the low numbers of EEs included in this SR. There is a need for more research on both the primary health effects of home-based rehabilitation and on cost-effectiveness of the intervention. Even though the existing published research on this field lean towards home-based rehabilitation being a cost-effective rehabilitation alternative it is still difficulty to draw conclusion. Heterogeneity among the published research make it difficult to pool outcomes in a meta-analysis. Thus, there is a need for more standardized reporting of outcomes in future EEs assessing this research topic. Preferably using a generic health outcome such as QALYs that can be pooled in a meta-analysis and give more power to the results in future SR on this topic.

4.5 Implications for practice

The systematic review offers valuable insights into an alternative rehabilitation intervention that could be of interest for policy makers and stakeholders in healthcare, and healthcare personnel. It could also be of interest for patients and family members especially since the intervention allows for rehabilitation in the patient's own home. Despite all the included studies reporting results in favor of home-based rehabilitation, this review is insufficient to make strong recommendations on clinical practice of stroke rehabilitations. However, the results imply that offering home-based rehabilitation as an alternative to conventional rehabilitation can be beneficial both for patients, but also in terms of economics. Further research is however needed to support these results.

4.6 Current evidence and agreement with other studies or systematic reviews

To the best of my knowledge, this is the first systematic review that strictly includes full economic evaluations when investigating the cost-effectiveness of home-based rehabilitation in adult stroke patients where the control group received any form of conventional rehabilitation. The results of this SR suggest that home-based rehabilitation in stroke patients is a cost-effective alternative based on outcomes including cost per QALY gained, cost per (%) point in death/institutionalization avoided, cost per improvement in BI, IADL, EQ5D and MNA scores, and cost per achieved success on BI and MRS scores.

A SR published in 2021 included partial economic evaluations and investigated the cost-effectiveness of home-based care in stroke patients, when it was strictly compared to hospital-based care (28) . This review included partial economic evaluations such as cost-comparison analyses and cost-minimization analysis which does not take clinical health outcomes into consideration when a comparison is made. However, similarly to this SR, the review found evidence that home care was a more cost-effective option than hospital care for stroke patients with regards to clinical outcomes such as BI, MRS, QALY, mortality and institutionalization. The authors of the previous systematic review stated that few economic evaluations on home-based care as an alternative to hospital services in stroke patients had been published, and so a small number of studies were included. I also observed this throughout the screening process. However, two full EEs assessing the cost-effectiveness of home-based rehabilitation in stroke patients was published after the publication of the previous systematic review (29) (18), including Candio et al. (29) that had simulated a large sample of 855, 000 stroke survivors in 32 European countries. The authors of the previous SR however stated that there were exceptions to their conclusion due to study limitations such as heterogeneity of the interventions in the included studies and methodological differences among the studies.

4.7 Ethical considerations

In order to handle the resources and costs spent on stroke, we need a new way to handle the health-related consequences following strokes. By introducing a home-based rehabilitation alternative, we can deliver health services in and follow up of the patients with stroke-related disability in their recovery process the patient's home. Home-based rehabilitation can increase

patients' functional outcomes by providing individualized therapy, encouraging patients to execute daily tasks in a familiar environment with family participation, which can contribute to an increased self-management and overall improvement in health status.

Most of the studies had no conflict of interest, but not all the studies had such information reported. One of the studies did not provide information regarding conflict of interest (36), while one of the studies recognized that one of the main authors was a former coordinator of the Community Stroke Rehabilitation Teams, which was the team providing the home-based rehabilitation to the intervention group. I would not consider this to have biased the results as the researcher no longer holds a position with the team, and thus would not receive any economic gain from results favoring the home-based rehabilitation provided. However, there might be a conflict of interest in the study that did not provide this information that could bias the results.

Regarding the financial support, the studies received funding from university hospitals, stroke networks, non-profit organizations such as Stroke Alliance of Europe and Stroke associations or grants from Health Technology Assessment Programmes. No, bias was observed in any of the included studies regardless of financial support. See appendix 6 for a more detailed description of funding source.

4.8 Overall completeness and applicability of evidence

Most of the included studies had similar inclusion and exclusion criteria in participants. The studies provided a reasonable representation of an average stroke population. However, there was a considerable difference observed in the interventions and the comparators setting, as well as the currency reported on costs. The studies' were conducted on participants in several countries. Thus, the contexts also differed, and comparing high-income countries to the upper-middle income countries may raise some issues about due to differences in the quality of healthcare services and the organization. However, Candio et al. (29) reported results on 32 European countries, and so these results might be generalizable other settings targeting recovery of stroke patients.

4.9 Timestamp

Five months have passed since the literature search were conducted until the submission of this systematic review. It is unlikely that a sufficient number of new studies could alter the results in this systematic review.

4.10 Strengths and limitations in the review process

There are several strengths in this review that raises its significance and protentional contribution. There are several reviews assessing the cost-effectiveness of stroke rehabilitation. However, this is the first systematic review to investigate the cost-effectiveness of home-based stroke rehabilitation, by comparing it to any conventional rehabilitation alternative. It is also the only systematic review on this topic that only includes full EEs in which a comparison of both primary health outcomes and cost outcomes of the alternatives are conducted. One of the strengths of this SR is that it is conducted in line with the Cochrane Handbook for Systematic Reviews of Interventions, chapter 20 regarding economic evidence (37) and the PRISMA- 2020 checklist (30) which ensures consistency, transparency, and accuracy in the methodology.

The database searches were planned and conducted systematically. The search was conducted in five international databases using a planned search strategy created and conducted by the author. Different concepts were used for the same search terms and a variety of MeSH terms and subject headings were applied in the searches. This minimized the risk of missing relevant studies. The author was not experienced in in systematic searches but had assistance from experienced librarians. Database searches were supplemented by searches in the reference lists of relevant identified primary studies and systematic reviews which also minimized the risk of missing relevant papers. Studies were appraised for methodological quality using conventional checklist tools in health economics. Two separate tools were used for trial-based and modelled-based EEs, which ensured consistency and accuracy in the quality assessment results.

There are however some limitations in this systematic review. One author worked on this systematic review independently. The absence of a co-author is a limitation because it might have decreased the methodological quality in this systematic review. Certain steps in a systematic review especially the screening process and selection of studies for inclusion and the quality assessment of included studies should be conducted by preferable to authors. This

would have brought strength to the systematic review. The absence of a co-author was however handled by systematically conducting the screening process and quality assessment twice, as to lower the risk of decreased methodological quality.

Limitations regarding the heterogeneity in the included studies such as differences in the interventions, in patients' characteristics including disability level, and difference in perspectives, outcomes and overall methodology in the economic evacuations, as well as in the healthcare systems of the countries excluded the possibility of conducting a meta-analysis of the outcomes.. There therefore exists a limitation in the power of the results itself.

Another possible limitation is the restriction to English-language and Nordic-language publications, due to the author not having the skills to read scientific paper in other languages. Thus, studies published in other languages than those mentioned were not assessed for eligibility. No Nordic articles identified or eligible for this SR and so only English- language publications were included. The number of included studies in this SR was five. However, the number of included studies in this SR could have been increased if the publications in other languages could have been included. Due to the limitation in time conducting this SR grey literature was not searched for. Thus, all the studies in this SR were published. It therefore is a possibility that unpublished research papers or grey literature have been missed. Including a grey literature search could possibly also have increased the number of included studies in this SR and brought more power to the results.

4.11 Conclusion

This systematic review summarizes and presents results that suggests benefits in terms of cost-effectiveness of home-based rehabilitation, in comparison to conventional rehabilitation for stroke patients. All of the included studies found home-based rehabilitation to be a more cost-effective option for stroke patients based on health outcomes, such as Barthel index, mRS index, quality of life, mortality and hospitalization. The overall methodological quality in the included EEs was high/ good based on Drummonds 10 checklist and the QHES- instrument. Results of sensitivity analysis in the studies, also demonstrated results in favor of home-based rehabilitation. However, there were limitations in this systematic review such as heterogeneity of the interventions and comparators in the included studies, variation in patients' level of disabilities, difference in health outcomes and currency of costs. As well as differences in setting including the variation of health systems in the different countries where the participants were drawn form and overall methodological differences. Due, to the limitations in this systematic review further research is needed according to the context of each country and based on clinical trials reporting outcomes that can improve the quality of evidence and give implication for future policy. If the cost-effectiveness of home-based rehabilitation suggested in this review is supplemented with further knowledge supporting these results, these findings could be an important contributor to policy makers and the current knowledge regarding stroke-rehabilitation.

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Appendix

Appendix 1: PRISMA Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Front page
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	II
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	p. 1-9
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	p. 9
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	p. 11-12
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	p. 10
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	p. 53-55
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	p. 12
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	p. 14
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	p.11-12
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	p.11-1
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	p. 14
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	p. 15
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	p.15
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	p.15
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	p.14 &18
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	p.17
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	p. 17
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	p. 15
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	-

Section and Topic	Item #	Checklist item	Location where item is reported
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	-
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	p. 18
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	p. 75
Study characteristics	17	Cite each included study and present its characteristics.	p- 18-29
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	p. 31-55
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	p. 18-32
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	p. 35-40
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	N/A
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	p. 35
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	N/A
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	N/A
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	p. 41
	23b	Discuss any limitations of the evidence included in the review.	p.47-48
	23c	Discuss any limitations of the review processes used.	p. 47-48
	23d	Discuss implications of the results for practice, policy, and future research.	p. 44
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	N/A
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	
Competing interests	26	Declare any competing interests of review authors.	
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: http://www.prisma-statement.org/

Appendix 2: Search strategies

OVID Medline 1946 – present

Date of search: 27/02/2023

(247) References

1. exp Stroke/
2. stroke*.ti,ab,kw.
3. "cerebrovascular accident*".ti,ab,kw.
4. CVA*.ti,ab,kw.
5. "cerebrovascular apoplexy".ti,ab,kw.
6. apoplex*.ti,ab,kw.
7. "brain vascular accident*".ti,ab,kw.
8. "cerebrovascular stroke*".ti,ab,kw.
9. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8
10. exp Home Care Services/
11. "home care service*".ti,ab,kw.
12. "domiciliary care".ti,ab,kw.
13. exp Home Nursing/
14. "home nurs*".ti,ab,kw.
15. (home* adj2 care).ti,ab,kw.
16. (home* adj2 rehabilitation).ti,ab,kw.
17. exp Stroke Rehabilitation/
18. "stroke rehabilitation".ti,ab,kw.
19. 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18
20. exp Cost-Benefit Analysis/
21. "cost effectiveness".ti,ab,kw.
22. "cost effectiveness analys*".ti,ab,kw.
23. "economic evaluation".ti,ab,kw.
24. 20 or 21 or 22 or 23
25. 9 and 19 and 24
26. limit 25 to (english language and yr="1990 -Current")

EMBASE Classic + EMBASE 1974 – present

Date of search: 27/02/2023

(49) References

1. exp Stroke/
2. stroke*.ab,kw,ti.
3. "cerebrovascular accident* ".ab,kw,ti.
4. CVA*.ab,kw,ti.
5. "cerebrovascular apoplexy".ab,kw,ti.
6. apoplex*.ab,kw,ti.
7. "brain vascular accident* ".ab,kw,ti.
8. "cerebrovascular stroke* ".ab,kw,ti.
9. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8
10. exp Home Care Services/
11. "home care service* ".ab,kw,ti.
12. "domiciliary care".ab,kw,ti.
13. exp Home Nursing/
14. "home nurs* ".ab,ti,tw.
15. (home* adj2 care).ab,ti,tw.
16. (home* adj2 rehabilitation).ab,ti,tw.
17. (home adj2 rehabilitation).ab,ti,tw.
18. exp Stroke Rehabilitation/
19. "stroke rehabilitation".ab,ti,tw.
20. 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19
21. exp Cost-Benefit Analysis/
22. "cost effectiveness".ab,ti,tw.
23. "cost effectiveness analys*".ab,ti,tw.
24. "economic evaluation* ".ab,ti,tw.
25. 21 or 22 or 23 or 24
26. 9 and 20 and 25
27. limit 26 to (english language and yr="1990 -Current")

EBSCOhost CINAHL Plus with Full Text

Date of search: 27/02/2023

(42) References

1. (MH "Stroke+")
2. stroke*
3. "cerebrovascular accident*"
4. “cerebrovascular stroke”
5. cva
6. apoplex*
7. "brain vascular accident"
8. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7
9. (MH "Home Rehabilitation+")
10. "home rehabilitation"
11. “home based rehabilitation”
12. “home care”
13. “home care service*”
14. “homecare service”
15. “home health care”
16. (MH "Home Nursing")
17. "home nursing"
18. 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17
19. (MH "Cost Benefit Analysis")
20. "cost effectiveness"
21. "cost effectiveness analys*"
22. "cost utility analys*"
23. "economic evaluation"
24. 19 OR 20 OR 21 OR 22 OR 23
25. 8 AND 18 AND 24
26. limit 25 to (english language and yr="1990 -Current")

Web of Science Core Collection

Date of Search: 27/02/2023

(52) References

1. (ALL=("Stroke*" OR "Cerebrovascular accident*" OR "Cerebrovascular apoplexy" OR "Apoplexy" OR "CVA" OR "Brain vascular accident*"))

2. (ALL=("Home nursing" OR "Domiciliary care" OR "Home health" OR “Home health care” OR "Home care" or "Home care service*" OR "Home rehabilitation" OR "Home based rehabilitation" OR "Home-based rehabilitation"))

3. (ALL=("Cost effectiveness" OR "Cost-effectiveness" OR "Cost-utility analys*" OR "Cost utility analys*" OR "Economic evaluation*"))

4. 1 AND 2 AND 3

Scopus Elsevier Co.

Date of Search: 27/02/2023

(142) References

(TITLE-ABS-KEY (stroke* OR "Cerebrovascular accident*" OR "Cerebrovascular apoplexy" OR apoplexy OR cva OR "Brain vascular accident*") AND TITLE-ABS-KEY ("Home nursing" OR "Domiciliary care" OR "Home health" OR "Home health care" OR "Home care" OR "Home care service*" OR "Home rehabilitation" OR "Home based rehabilitation" OR "Home-based rehabilitation") AND TITLE-ABS-KEY ("Cost effectiveness" OR "Cost-effectiveness" OR "Cost-utility analys*" OR "Cost utility analys*" OR "Economic evaluation*"))

Appendix 3: Article selection form

Title:_____

Author: _____

Year: _____

Type of economic evaluation: _____

Selection criteria:

Study design:

Is the study a full economic evaluation? Yes/No

Is the study an economic evaluation alongside a trial ? Yes /No

Population:

Have the targeted population survived a stroke? Yes/No

Does the targeted population have a confirmed diagnosis of stroke? Yes/ No

Are the included participants 18 years of age or older? Yes/No

Were the participants discharged from the hospital? Yes/No

Intervention:

Did the intervention group receive rehabilitation or care in their home? Yes/No

Was the intervention delivered by healthcare personnel? Yes/ No

Control:

Did the control group receive rehabilitation or care outside of their home? Yes/No

Outcome:

Is the health outcome measured appropriate in accordance with the study design? Yes/ No

Is the outcome measured in:

i) Single natural units (e.g. life-years gained, disease averted) Yes/ No

ii) Quality-adjusted life-years (QALYs) / disability-adjusted life-years (DALYs) Yes/ No

iii) In monetary terms individuals' willingness to pay Yes/ No

Appendix 4: Data extraction form: model-based economic evaluations

	Description in report or supplementary literature	Location in report
Study characteristics		
Study title		
Author(s)		
Year of publication		
Country of study		
Study setting (location)		
Study Aim		
Study methods		
Type of economic evaluation		
Model type		
Study perspective		
Model cycle length		
Time horizon		
Currency of cost		
Year of costing valuation		
Discount rates		
Outcome		
Sensitivity analysis		
Economic model input parameters		
Description of population		
Source of population data		
Description of intervention		
Description of comparator		
Description of health measures		
Source of health measures		
Description of included costs		
Source of included cost data		
Study outcomes:		

Units of measurement		
Threshold measurement for cost-effectiveness		
Results		
Sensitivity analysis		
Other:		
Funding source		
Conflict of interest		

Appendix 5: Data extraction form trial-based economic evaluations

	Description in report or referenced supplementary literature	Location in report
Study characteristics		
Study title		
Author(s)		
Year of publication		
Country of study		
Study setting (location)		
Study design		
Study Aim		
Study methods		
Type of economic evaluation		
Study perspective		
Years of data collection		
Time horizon		
Price year of collected cost data		
Description of included costs		
Currency of cost		
Cost type		
Discount rates		
Health measure		
Outcome measure		
Sensitivity analysis		
Participants characteristics		
Description of participants		
Total number from population		

Population (where the cases or participants are drawn)		
Information about intervention		
Number in the intervention group		
Description of intervention		
Duration		
Frequency		
Deliverer of intervention		
Information about the comparator		
Number in comparator group		
Description of the comparator		
Duration		
Frequency		
Deliverer of intervention		
Study outcomes:		
Results		
Sensitivity analysis		
Other:		
Funding source		
Conflict of interest		

Appendix 6: Data extraction of included studies

Allen et al., 2018

	Description in report or supplementary literature	Location in report
Study characteristics		
Study title	Assessing the impact of home-based stroke rehabilitation programme: a cost-effective study	p.2060
Author(s)	Allen, L,. John-Baptiste, A,. Meyer, M,. Richardson, M,. Speechley, M,. Ure, D,. Markle-Reid, M,. Teasell, R,.	p.2060
Year of publication	2018	p.2060
Country of study	Canada	p.2060
Study setting (location)	Ontario	p.2060
Study Aim	The purpose of this study was to perform a 1-year prospective evaluation of utility outcomes and costs among clients of The Community Stroke Rehabilitation Teams (CSRT) model to no formal rehabilitative care for patients recovering from stroke.	p.2060
Study methods		
Type of economic evaluation	Cost utility analysis	p.2062
Model type	Markov model	p.2061
Study perspective	Public payer perspective	p.2061
Model cycle length	6-month cycles	p.2061
Time horizon	35 years or until death	p.2061
Currency of cost	US dollars ($)	p.2062
Year of costing valuation	Not mentioned	
Discount rates	3% per year after the first year	p.2062
Outcome	Cost-effectiveness	
Sensitivity analysis	One-way and two-way sensitivity analysis, scenario analysis and probabilistic sensitivity analysis were applied.	p. 2062
Economic model input parameters		
Description of population	Adult stroke survivors who are unable to access traditional outpatient rehabilitation services. Intervention group: N=164 stroke survivor from Ontario, Canada. Mean age: 66.2. 59.1% male, 40,9% female. Severe stroke seen in 50%.	p. 2061-2062

	Control group: N =39 patients from Toronto, Canada with confirmed diagnosis of stroke. Mean age: 70.6. 62% male, 38% female.	
Source of population data	Two RCTs	p. 2061
Description of intervention	The Community Stroke Rehabilitation Teams (CSRTs) deliver individualized services, which may include physical rehabilitation, social and emotional support, education, system navigation, community re-integration, and caregiver support, based on the Canadian best-practice recommendations for stroke.	p. 2060
Description of comparator	Controls were assumed to have received no, or limited rehabilitation services (usual care)	p. 2061
Description of health measures	Quality of life	p. 2061
Source of health measures	Two RCTS + population based studies	p. 2061
Description of included costs	Costs included physician visits (Emergency Room and specialists), other health care professionals/ services, hospitalizations and surgeries, diagnostic tests and laboratory expenses, devices and special treatments, household help and travel cost.	p. 2061
Source of included cost data	Health care usage costs for both CSRT and usual care arms, using individual- level data from Markle Reid et al., were derived from responses to the Health and Social Services Utilisation Survey. - Visit costs for the CSRT programme were provided by the programme. - For the long-term projection of costs a cost per visit was applied based on costing data used in the CSRT study. - Mean weekly costs of LTC (nursing/ personal care, physician costs, other), hospitalizations, emergency department visits, and diagnostic tests were totaled and a 6-month cost estimated from the weekly cost reported in an Ontario-based study of LTC residents	p. 2061
Study outcomes:		
Units of measurement	Incremental cost, Incremental QALYs	p. 2063
Threshold measurement for cost-effectiveness	Willingness to pay threshold of $20,000	p. 2063
Results	The CSRT programme dominated usual care, as it resulted in a cost savings. The analysis showed that providing home-based rehabilitation through the CSRT is both less costly (incremental cost: -$17,255) and more effective (incremental effect: -$1.65 QALYs) when compared to usual care. At a	p. 2063

	Willingness to pay threshold of $20,000, CSRT had a NMB of $43,655 when compared with usual care.	
Sensitivity analysis	In the one-way sensitivity analysis, NMB was assessed . Two-way sensitivity analysis. In scenario analysis, cost per QALY for at a Willingness to pay threshold of $20,000 In the probabilistic sensitivity analysis -	p. 2063
Other:		
Funding source	The Ontario Stroke Network	p. 2064
Conflict of interest	David Ure is the former coordinator of the Community Stroke Rehabilitation Teams	p. 2064

Candio et al., 2022

	Description in report or supplementary literature	Location in report
Study characteristics		
Study title	Cost-effectiveness of home-based stroke rehabilitation across Europe: a modelling study	p. 183
Author(s)	P, Candio,. M, Violato,. R, Luengo-Fernandez,. J, Leal,.	p. 183
Year of publication	2022	p. 183
Country of study	United Kingdom	p. 183
Study setting (location)	32 European countries (members of the European Union + Iceland, Israel, Norway Switzerland, and the United Kingdom)	p. 184
Study Aim	“To explore the cost-effectiveness of home-based rehabilitation compared to center-based rehabilitation for stroke survivors across European countries.”	p. 183
Study methods		
Type of economic evaluation	Cost-utility analysis	p. 183
Model type	Cohort-level Markov model and an imbedded decision tree	p. 184
Study perspective	Societal perspective and health and social care perspective	p. 183
Model cycle length	1 year following the first 12 months of simulation	p. 184
Time horizon	5 years	p. 183
Currency of cost	Euros (€)	p. 184
Year of costing valuation	2017	p.184
Discount rates	3.5% annually (Costs and QALYs)	p. 184
Outcome	Cost-effectiveness	p. 185

Sensitivity analysis	A series of deterministic and a probabilistic sensitivity analysis were perfumed. In probabilistic terms, a thousand iterations were simulated to represent the full distribution of uncertain parameters and to assess the likelihood of the intervention being cost effective.	p. 185
Economic model input parameters		
Description of population	Patients who: - survived the acute stroke phase (between 24h and two weeks from symptoms onset) - had a confirmed diagnosis of intracerebral hemorrhages, ischemic stroke, or strokes of unknown type - were aged ≥ 20 years old - admitted to the hospital	p. 184
Source of population data	Country-specific, age- and gender-stratified adult stroke cases were derived identified from the Global Burden of Disease study	p. 184
Description of intervention	The targeted population received home-based rehabilitation. Defined as a package of care whereby a stroke patient would receive physiotherapy, occupational therapy, and speech therapy at their home.	p. 184
Description of comparator	Centre-based rehabilitation where the patient would receive conventional hospital-based care (inpatient and outpatient).	p. 184
Description of health measures	Intervention effectiveness was based on Barthel Index. Barthel Index of score 0-20 was linked to the modified Rankin Scale (mRS) varying from 0, no disability to 5, confined to bed, so that any given Barthel Index would represent a certain proportion of mRS scores. - Quality of life were derived from Euroqol-5 dimensions-3 levels collected from stroke patients at: 1 to 3, 6, 12 and 60 months and converted into utilities using UK population tariffs. - all-cause mortality risks were estimated.	p. 184
Source of health measures	Intervention effectiveness using Barthel Index was based on results of a meta- analysis. All-cause mortality risks were estimated based on data from Oxford Vascular Study (OXVASC) Data from Oxford Vascular Study was	p. 184
Description of included costs	Societal costs included health and social care costs, informal care costs and productivity losses.	p. 184
Source of included cost data	i) Country- specific unit costs obtained from a study evaluating the costs of stroke in all 32 countries. “Economic burden of stroke across Europe: a	p. 184-185

	population-based cost analysis" ii) Health and societal care costs and resources use was derived from Oxford Vascular study iii) Informal care costs were estimated based on the Survey of Health, Aging and Retirement in Europe (SHARE). For countries not included in the SHARE study, the average of the macro-region to which the country belongs (i.e., Scandinavia, Central Europe, Eastern Europe and Southern Europe) was assigned. iiii) Productivity losses were calculated in terms of mortality and morbidity in stroke patients under the age of 65 years.	
Study outcomes:		
Units of measurement	Incremental QALYs and LYs, cost savings, ICER (incremental cost effectiveness ratio) – costs per QALY gained	p. 185
Threshold measurement for cost effectiveness	National Institute of Health and Care Excellence threshold Countries per- capita Gross Domestic Product (GPD) as cost-effectiveness threshold	
Results	Home-based rehabilitation generated higher numbers of incremental QALYs, on average, when compared to CB, in all the 32 European countries. For the whole of Europe, home-based rehabilitation generated additional 61,888 QALYs (3609 to 118,679).. Home-based rehabilitation generated 5-years cost savings when compared to CB-rehabilitation. The probability of HB being cost-effective, when compared to CB, was found to be 0.95 for Europe as a whole and range from between 0.85 and 0.98 across the 32 European countries. When a UK-based threshold of cost-effectiveness was considered, comparable probabilities were estimated except for Sweden (0.62) and Finland (0.77).	p. 185
Sensitivity analysis	Sensitivity analysis showing that HB remained the most cost-effective option across most scenarios and parameters variations tested. For example, assuming that the type of rehabilitation had no effect on mortality post stoke still showed HB to be cost-effective, compared to CB. Only when we used the lower bound of the confidence interval concerning the effectiveness of HB (0.12), we found CB to be cost-effective at a 94% probability.	p. 185-189
Other:		
Funding source	The study was funded by an unrestricted grant from the Stroke Alliance for Europe.	p.188

Patel et al., 2003

	Description in report or referenced supplementary literature	Location in report
Study characteristics		
Study title	Alternative Strategies for Stroke Care – Cost-Effectiveness and Cost-Utility Analysis From a Prospective Randomized Controlled Trial	p. 196
Author(s)	A, Patel,. M, Knapp,. I, Perez,. A, Evans,. L, Kalra,.	p. 196
Year of publication	2003	p. 196
Country of study	United Kingdom	
Study setting (location)	Not mentioned	
Study design	Prospective Randomized Controlled Trial	p. 196
Study Aim	To describe comprehensive service use and informal care patterns, associated costs, and corresponding outcomes for a 12-month follow up period for each of three trial groups (stroke unit, stroke team and domiciliary care)	p. 196
Study methods		
Type of economic evaluation	Cost-effectiveness and Cost-utility analysis	
Study perspective	Societal perspective	p. 198
Years of data collection	Not mentioned	
Time horizon	12 months	p. 196
Price year of collected cost data	All costs were standardized to 1997-1998 prices by using the NHS Executive hospital and community health services inflation index.	p. 198
Description of included costs	Direct costs	p. 200
Currency of cost	Pounds sterling (£)	p.198
Cost type	Direct costs (Study appendix)	
Discount rates	Not mentioned	
Health measure	Number of deaths, institutionalizations, and QALYs gained	p. 199
Outcome measure	Cost- effectiveness analysis: ICER per avoided death/institutionalization Cost-utility analysis: ICER per additional QALY gained	p. 199
Sensitivity analysis	Cost-effectiveness analysis: Was examined by reporting a range of ICERs based on the inclusion and exclusion of key cost components (immediate care for stroke episode, follow-up care informal based on 2 different costing approaches). Cost-utility analysis: trough cost-effectiveness acceptability curves using the net benefit approach (based on total health and social care costs over 12 months). The curve show the probability of each strategy being cost-effective (or optimal) compared with the others for a range of values that a decision	p. 199

	maker would be willing to pay for an additional QALY.	
Participants characteristics		
Description of participants	Acute stroke patients withing 72 hours of stroke onset.	p. 194
Total number from population	457	p. 194
Population (where the cases or participants are drawn)	Not mentioned	
Information about intervention		
Description of intervention	Patients in domiciliary care were managed in their own homes. Intervention included investigation on outpatient basis, therapy, and personal care.	
Duration	12 months	p. 196
Frequency (if trial-based EE)	Not mentioned	
Deliverer of intervention (if trial-based EE)	Stroke physician, general practitioner, specialist staff; districting nursing and social services	p. 198
Information about the comparator		
Number in comparator group	Stroke unit (147) Stroke team (147)	
Description	Stroke unit: included guidelines for stroke management, joint assessment, goal setting, treatment and discharge planning were incorporated. Stroke team: patients were on general medical wards and under the care of general physicians; assessments were done by a roving specialist stroke team that advised on management, investigation, and discharge planning; a nonspecialist nursing and therapy staff were available	p. 197 and p. 198
Duration	12 months	p. 194
Frequency	Not mentioned	
Deliverer of intervention	Stroke unit: specialist stroke physician, multidisciplinary staff with specialist experience in stroke Stroke team: general physicians, roving specialist stroke team and nonspecialist nursing and therapy staff	p. 197 and p. 198
Study outcomes:		

Results	Total health and social care costs: Per additional 1% of deaths/institutionalizations avoided: 496. Per additional QALY gained: 64,097. Total costs including informal care: Per additional 1% of deaths/institutionalizations avoided: 682. Per additional QALY gained: 89,132. The percentages of patients who avoided death/ institutionalization were 87%, 69% and 78% in the stroke unit, stroke team, and domiciliary care groups, respectively. Mean QALY gained were 0.297, 0.216 and 0.221. Stroke team was dominated by domiciliary care on both outcome measures and from all cost perspectives. Stroke unit did not dominate domiciliary care. Of the 3 strategies evaluated, stroke unit was the most expensive, and domiciliary care was the cheapest. Home care was a more cost-effective option than the stroke team services in reducing mortality and institutionalization of stroke patients, but the costs and effectiveness of the stroke unit were higher than home care. This pattern remained unchanged in incremental-cost effectiveness and cost-utility analysis and home care was therefore considered as the most cost-effective option.	p. 199 and p. 200
Sensitivity analysis	The inclusion of informal care costs increased overall costs considerably. Total costs were highest for patients managed in the stroke unit and lowest for those managed at home, regardless of how costings were undertaken. If decision makers were willing to pay nothing for QALY gains, there is a 59% probability that domiciliary care is the most cost-effective option of the 3 strategies (and a 16% and 26% probability that the stroke unit and stroke team, respectively, are the most cost-effective. The probability that domiciliary care is the most cost-effective strategy decreases with increasing levels of willingness to pay for QALY gains, leveling out at the £60,000 threshold, but remains higher than the other 2 strategies. At a willingness to pay of £30,000 per additional QALY (the implicit current threshold value per QALY in the United Kingdom), the probability that the stroke unit and the stroke team are most optimal of the 3 strategies is equal at 29% and higher for domiciliary care at 42%.	p. 199 and p. 200

Other:		
Funding source	NHS R&D Executive's Health Technology Assessment Programme and Bromley Health Authority	p. 202
Conflict of interest	Not mentioned	

Sritipsukho et al., 2010

	Description in report or referenced supplementary literature	Location in report
Study characteristics		
Study title	Cost-effectiveness analysis of home rehabilitation programs for Thai stroke patients	p. 262
Author(s)	P, Sritipsukho,. A, Riewpaiboon,. P, Chaiyawat,. K, Kulkantrakorn,.	p. 262
Year of publication	2010	p. 262
Country of study	Thailand	p. 262
Study setting (location)	Teaching hospital	p. 263
Study design	Prospective Randomized Controlled Trial	p. 263
Study Aim	To compare costs and effects of a home rehabilitation program versus conventional hospital care for ischemic stroke patients in a Thai healthcare setting	p. 263
Study methods		
Type of economic evaluation	Cost-effectiveness analysis	p. 264
Study perspective	Provider perspective	p. 264
Years of data collection	May 2007 to June 2018	p. 263
Time horizon	3 months	p. 264
Price year of collected cost data	2008	p.266
Description of included costs	Direct costs	p. 264
Currency of cost	Thai Baht (THB)	p. 262
Discount rates	3% Annually	p. 265
Cost type	Direct costs	p. 265
Health measure	Disability averted evaluated by: 1) the Barthel Index categorized based on scores: - (0-20) very severely disabled - (>20-45) severely disabled - (>45-70) moderately disabled - (>70-95) mildly disabled - (>95) no disability Goal achievement: (BI 1) achieving mild or no disability, (BI 2) achieving no disability	p.264

	2) The Modified Rankin Scale categorized into levels: - (0-2) minor stroke - (3-5) major stroke - (6) fatal stroke Successful case (MRS) if clinical status improves from major stroke to minor stroke.	
Outcome measure	Incremental cost-effectiveness ratio (ICER) per Disability averted	p.264-265
Sensitivity analysis	Conducted by varying parameters (number of patients and payments for physical therapists who provided home visits) one at a time, considering other parameters to be constant at a base-case level.	p. 265
Participants characteristics		
Description of participants	Ischemic stroke patients were recruited from inpatient wards at a teaching hospital. They were screened for eligibility around three days after stroke onset. Screening was either based on a clinical diagnosis or was performed exclusively with or aided CT or MRI scanning. The main inclusion criteria of the trial were: - stroke from middle cerebral artery infarction - patient and caregiver's willingness to participate - ability to provide informed consent - living within 50 miles of the hospital	p.264
Population (where the cases or participants are drawn)	Not mentioned	
Information about intervention		
Number in intervention group	30	p. 264
Description of intervention	Home rehabilitation programme was based on principles of exercise physiology and motor learning, and was developed by experts, stroke patients, physical therapists, occupational therapists, and speech therapists. It consisted of a home-based exercise program together with conventional hospital services. Standard audiovisual materials of rehabilitation procedures were also given to patients and caregivers for self-care.	p. 264
Deliverer	Physical therapist	p. 264
Frequency	One visit per month, approximately 1 hour	p. 264
Duration	3 months	p. 264
Information about the comparator		

Number in control group	30	p. 264
Description	The control group received conventional hospital care, which included outpatient rehabilitation at the direction of their physician.	p. 264
Duration	3 months	p. 264
Frequency	Monthly	p. 264
Deliverer of intervention	Staff at outpatient clinic	p. 264
Study outcomes:		
Results	Home rehabilitation imposed more direct costs than conventional hospital care, but it was more effective in reducing the patients' disabilities. The overall cost in the intervention group was 470,333 THB and control group was 129,243 THB. ICER (BI 1): were 16,218 TBH for the intervention group and 25,849 TBH for the control group. ICER (MRS): were 33,595 for the intervention group and 43,081 THB for the control group. Based on BI 2, a disability avoided in one additional patient costs 24,364 THB. This cost is only one-fourth of the Thai national guidelines of 100,000 THB (gross domestic product per capita). Therefore, the home-rehabilitation program was considered cost-effective.	p. 266 and p. 267
Sensitivity analysis	Both scenarios resulted in greater cost-effectiveness than the base case. Sensitivity analysis showed that if the program were expanded to cover more patients, the cost of teaching materials per patient would be decreased due to their being a part of the fixehud cost of development. Thus the intervention would be even more cost-effective.	p. 267
Other:		
Funding source	Thammasat University	p. 268
Conflict of interest	Not mentioned	

Tung et al., 2021

	Description in report or referenced supplementary literature	Location in report
Study characteristics		
Study title	Comparison of Cost-Effectiveness between Inpatient and Home-Based Post-Acute Care Models for Stroke Rehabilitation in Taiwan	p. 1
Author(s)	Y, Tung,. W, Lin,. L, Lee,. H, Lin,. C, Ho,. W, Cho,.	p. 1
Year of publication	2021	p. 1
Country of study	Taiwan	p. 1
Study setting (location)	Chi Mei Medical Center for post-acute stroke rehabilitation	
Study design	Retrospective study	
Study Aim	To compare the current inpatient PAC model with the novel home-based PAC model in cost-effectiveness and functional recovery for stroke patients in Taiwan.	p. 1
Study methods		
Type of economic evaluation	Cost-effectiveness analysis	p. 1
Study perspective	Health system perspective	p. 4
Years of data collection	June 2015 to December 2020	p. 2
Time horizon	Not mentioned	
Price year of collected cost data	Not mentioned	p. 4
Description of included costs	Medical expenses	p. 4
Currency of cost	USD$	p. 4
Cost type	Direct costs	p. 4
Discount rates	Not mentioned	
Health measure	Barthel index (BI), Lawton-Brody instrumental activities of daily life scale (IADL) EuroQoL EQ-5D (ED5Q) Mini nutritional assessment (MNA)	p. 4
Outcome measure	The total cost/ improvement in BI, IADL, ED5Q and MNA scores.	p. 4
Sensitivity analysis	Not mentioned	
Participants characteristics		
Description of participants	Patients with stroke referred to Chi Mei Medical Center for post-acute stroke rehabilitation. Eligibility for the study was: (1) Acute onset of stroke (≤ 1 month) (2) Relatively stable medical condition, with no neurological or hemodynamic deterioration in the past 3 days and no progression of diseases or complications	p. 2

	3) Modified Ranking scale (mRS) score of 3 or 4 (4) Rehabilitative protentional, including high motivation, fair consciousness and adequate physical fitness (being able to sit for 1h).	
Total number population	261	p. 3
Population (where the cases or participants are drawn)	Not mentioned	
Information about intervention		
Number in comparator group	59	p. 3
Description of intervention	Home-based PAC, rehabilitation set in a domestic, familiar environment, in which patients with stroke receive task-oriented rehabilitative training in their homes from therapists delivering remedial courses. In the home-based PAC model, the patients stayed at home, receiving rehabilitative training sessions. This model emphasized the use of domestic tools for task-oriented training, merging training programmes with daily practical , real-life circumstances, inviting family participation, reassuring caregivers regarding their performance, creating a familiar environment, offering feasible and easy-to-practice activities, and encouraging community engagements.	p. 3
Duration	Not clear if there was a preset duration for programme. Mean duration was 35.65 days in home-based group.	
Frequency	50-min sessions six times per week (5h total per week)	p. 3 and p. 4
Deliverer of intervention	Therapists	p. 3
Information about the comparator		
Number in comparator group	138	p. 2
Description	In the inpatient PAC model, patients with stroke were hospitalized for intensive rehabilitation. They received physical, occupational, and speech therapy.	p. 3
Duration	Not clear if there was a preset duration for programme. Mean duration was 29.4 days in home-based group	
Frequency	3 hours per day on weekdays according to their needs (15h total per week)	p. 3
Deliverer of intervention	Physiatrists, therapists, nurses, psychologists, social workers, nutritionists, and medical technicians formed a multidisciplinary team for these patients.	p. 3

Study outcomes:		
Results	The cost-effectiveness versus BI, IADL, ED5Q and MNA were significantly different in both groups. Cost-effectiveness analysis revealed that home-based PAC model costs were (USD 48.18 ± USD 35.02) per 1-pont increase in BI score, whereas the inpatient model costs were (USD 152.474 ± USD 164.66) per 1-point increase BI score. The medical expenses required in the home-based PAC model were considerably lower (approximately one-third lower) than those in the inpatient PAC model to reach the same functional poststroke recovery outcome. The study found similar functional recovery in both models, with the home-based PAC model being more cost-effective	p. 7 and p. 8
Sensitivity analysis	Not mentioned	
Other:		
Funding source	No external funding	p. 10
Conflict of interest	No conflict of interest	p. 11

Appendix 7: Reason for excluding studies

Excluded studies that were full text screened

Author, (number in references)	Reason for exclusion
Byrne et al. ()	Intervention is not home-based rehabilitation, and it is not a full economic evaluation (cost-consequence)
Chiu et al. ()	Not a full economic evaluation
Elia et al. ()	Intervention is not home-based rehabilitation
Gao et al. ()	Intervention is not home-based rehabilitation. It is telestroke aiming at diagnosis and treatment.
Gladman et al. ()	Not a full economic evaluation (cost-comparison)
Rodgers et al. ()	Intervention is not home-based rehabilitation (cost- minimization)
Saka et al. ()	Intervention is not home-based rehabilitation
Sampson et al. ()	Intervention is not home-based rehabilitation
Tam et al. ()	Intervention is not home-based rehabilitation
Teng et al. ()	Not a full economic
Young et al. ()	Home-based rehabilitation is the comparator not the intervention
Wallut et al. ()	Intervention is not home-based rehabilitation. It is telestroke aiming at diagnosis and treatment.
Weiss et al. ()	Not an economic evaluation

Appendix 8: Quality assessment of the included studies

Allen et al. 2022 - using The Quality of Health Economic Studies (QHES) instrument

Item no.	Questions for critical appraisal	Points	Yes	No	Support for jugement
1	Was the study objective presented in a clear, specific, and measurable manner?	7	X		Yes. The objective of this study was to evaluate the cost-effectiveness of the CSRT programme with a "Usual Care" cohort.
2	Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	4		X	The economic analysis was conducted from a public payer perspective. No reasoning for its selection.
3	Were variable estimates used in the analysis from the best available source (i.e., randomized control trial - best, expert opinion - worst)?	8	X		Yes. Large population-based studies, and economic evaluation and RCT.
4	If estimates came from a subgroup analysis, were the groups prespecified at the beginning of the study?	1	X		Estimates came from a study were subgroup analys was done as an addition, hence was not included in the main analysis. No mentioning of the subgroup analysis in this study.
5	Was uncertainty handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions?	9	X		Two-way sensitivity analysis, Scenario analysis and probabilistic sensitivity analysis was used to address random events and uncertainty
6	Was incremental analysis performed between alternatives for resources and costs?	6	X		Yes, presented as incremental costs in both the study and supplementary readings.

7	Was the methodology for data abstraction (including the value of health states and other benefits) stated?	5	X		Stated the values of the health states of the model and source of estimate inputs of the health benefits, in both study and supplementary readings (in more detail)
8	Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3% to 5%) and justification given for the discount rate?	7	X		The model time horizon was 35 years or until death which is an appropriate horizon for important outcomes. Costs and utilities after the first year were discounted at a rate of 3% per year and was chosen to reflect the chronic nature of stroke disabilities.
9	Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	8	X		They measured costing of health services by multiplying the frequency of utilization of health services by the price.
10	Were the primary outcome measure(s) for the economic evaluation clearly stated and did they include the major short-term was justification given for the measures/scales used?	6		X	The primary outcome was incremental cost of the CSRT programme per Quality Adjusted Life Year (QALY) gained when compared to usual care. No justification.
11	Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	7	X		Stroke Impact Cale (SIS), Quality of life (QALY) by the Euro-QoL 5 Dimension (EQ5D-5 L) are valid and reliable measures.

					No justification given for the measures/scales used.
12	Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	8	X		It is displayed clear manner in the online supplementary
13	Were the choice of economic model, main assumptions, and limitations of the study stated and justified?	7	X		Yes
14	Did the author(s) explicitly discuss direction and magnitude of potential biases?	6		X	No
15	Were the conclusions/recommendations of the study justified and based on the study results?	8	X		Yes
16	Was there a statement disclosing the source of funding for the study	3	X		Yes by the Ontario Stroke Network
	Total points	100	86		

Candio et al. 2022 - using The Quality of Health Economic Studies (QHES) instrument

Item no.	Questions for critical appraisal	Points	Yes	No	Support for jugement
1	Was the study objective presented in a clear, specific, and measurable manner?	7	X		Their aim was to explore the cost-effectiveness of home-based versus centre-based rehabilitation in stroke patients across Europe.
2	Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	4	X		They included a societal perspective in costs and effects, that is relevant to different areas of European societies, including informal carers and employers.
3	Were variable estimates used in the analysis from the best available source (i.e., randomized control trial - best, expert opinion - worst)?	8	X		Estimates used were from: global burden of disease study, OXVASC (population-based

					study), a systematic review of RCTs,
4	If estimates came from a subgroup analysis, were the groups prespecified at the beginning of the study?	1	X		Yes
5	Was uncertainty handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions?	9	X		Yes
6	Was incremental analysis performed between alternatives for resources and costs?	6	X		Yes
7	Was the methodology for data abstraction (including the value of health states and other benefits) stated?	5	X		Was clearly stated. Transition states were addressed in appendix.
8	Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3% to 5%) and justification given for the discount rate?	7		X	Only a 5-year time horizon was estimated which does not allow for all relevant and important outcomes. Costs and QALYs were discounted at an annual rate of 3.5%
9	Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	8	X		Yes
10	Were the primary outcome measure(s) for the economic evaluation clearly stated and did they include the major short-term was justification given for the measures/scales used?	6		X	No justification was given
11	Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	7	X		Yes
12	Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	8		X	Components of the calculation not displayed
13	Were the choice of economic model, main assumptions, and limitations of the study stated and justified?	7	X		Yes

14	Did the author(s) explicitly discuss direction and magnitude of potential biases?	6		X	No discussion regarding biases
15	Were the conclusions/recommendations of the study justified and based on the study results?	8	X		Yes
16	Was there a statement disclosing the source of funding for the study	3	X		Yes
	Total points	100	79		

Patel et al. 2003 – using Quality of Included Studies Based on Drummond Checklist (Drummond 1996)

Item no.	Questions for critical appraisal	Yes	No	Can't tell	Support for jugement
1	Was a well-defined question posed in answerable form?	X			Study examined both costs and effects of the programmes, a comparison of the programmes and a societal perspective was adopted.
2	Was a comprehensive description of the competing alternatives given (i.e., can you tell who did what to whom, where, and how often)?		X		Alternatives, deliverer, and setting is clear. Frequency is however not as clear. Not stated how often the alternatives were given.
3	Was the effectiveness of the programmes and services established?	X			Yes, measure of mortality or institutionalization over a 1-year period and the proportion of patients alive without severe disability at 1 year for all the programmes.
4	Were all the important and relevant costs and consequences for each alternative identified?		X		No, the paper states to have a societal perspective and included health service and other service costs, and informal care cost, but not production loss or other societal cost besides
5	Were costs and consequences measured accurately in appropriate	X			Yes, measured per hour, per min, per day

	physical units (e.g. hours of nursing time, number of physician visits, lost work-days, and gained life years)?				or per visits. While consequences were measured
6	Were the cost and consequences valued credibly?	X			Yes, hospital resource use and therapy inputs were recorded on an ongoing basis, while use of other public sector services were collected retrospectively at 12 months after stroke onset. Annual estimation of informal care inputs was based on the number of weeks in the year over which care was received
7	Were costs and consequences adjusted for differential timing?	X			They did discount cost or consequences, which is not necessary because the follow-up period was 1 year.
8	Was an incremental analysis of costs and consequences of alternatives performed?	X			Yes, ICER, incremental cost per QALY gained and per percentage point in deaths or institutionalizations.
9	Was uncertainty in the estimates of costs and consequences adequately characterized?	X			Yes, cost-effectiveness acceptability curves showing the probability that each strategy is cost-effective for a range of protentional maximum values for decision makers willingness to pay for an additional QALY.
10	Did the presentation and discussion of study results include all issues of concerns to user?	X			Yes
	Total score out of 10	8			

Sritipsukho et al. 2010 – using Quality of Included Studies Based on Drummond Checklist (Drummond 1996)

Item no.	Questions for critical appraisal	Yes	No	Can't tell	Support for jugement
1	Was a well-defined question posed in answerable form?	X			The study aimed to compare costs and effects of a home rehabilitation program versus conventional hospital care for ischemic stroke patients in a Thai healthcare setting.
2	Was a comprehensive description of the competing alternatives given (i.e., can you tell who did what to whom, where, and how often)?	X			Yes, deliverer, setting and frequency is clearly stated.
3	Was the effectiveness of the programmes and services established?	X			Yes, in disability averted based on Barthel Index, Modified Rankin Scale, absolute risk reduction (ARR), Number Needed to Treat (NNT), quality of life and generic health status using EQ-5D
4	Were all the important and relevant costs and consequences for each alternative identified?	X			Yes, hospital service cost and cost of individual home health care and important consequences in commonly used scales were identified
5	Were costs and consequences measured accurately in appropriate physical units (e.g. hours of nursing time, number of physician visits, lost work-days, and gained life years)?	X			Hospital costs were measured using micro-costing, cost of individual home health care was allocated equally among the study patients, composed of training material (payment for creating by staff cost is working

					days/months) , and production (cost of development) and home visits (per visit). Consequences were measured using The Barthel Index and Modified Rankin Scale.
6	Were the cost and consequences valued credibly?	X			
7	Were costs and consequences adjusted for differential timing?	X			Only the teaching material was discounted for (3% discount rate) because it was assumed to be useful for five years.
8	Was an incremental analysis of costs and consequences of alternatives performed?	X			Yes, ICERs (Incremental cost/ Barthel Index and Modified Rankin Scale)
9	Was uncertainty in the estimates of costs and consequences adequately characterized?	X			Yes, one-way sensitivity analysis by varying parameters one at time (number of patients and payment for physical therapists who provided home visits)
10	Did the presentation and discussion of study results include all issues of concerns to user?		X		The conclusions of the analysis were based on overall ratio of costs to consequences (ICERs). But results of the study were not compared with those of others who have investigated the same question. Only a list of measures of effectiveness used in stroke rehabilitation were sited. Generalizability of the results to other settings and

					patient/client groups was discussed.
	Total score out of 10		9		

Tung et al. 2021– using Quality of Included Studies Based on Drummond Checklist (Drummond 1996)

Item no.	Questions for critical appraisal	Yes	No	Can't tell	Support for jugement
1	Was a well-defined question posed in answerable form?	X			The study examines both costs and effects of the programmes, involving a comparison of the alternatives from a health system perspective.
2	Was a comprehensive description of the competing alternatives given (i.e., can you tell who did what to whom, where, and how often)?	X			Yes, deliverer, setting and frequency is clearly stated.
3	Was the effectiveness of the programmes and services established?	X			Effectiveness of the programmes was established from the retrospective study conducted.
4	Were all the important and relevant costs and consequences for each alternative identified?		X		Relevant consequences were identified, but no clear description of the included costs.
5	Were costs and consequences measured accurately in appropriate physical units (e.g. hours of nursing time, number of physician visits, lost work-days, and gained life years)?		X		No clear description of the included costs, other than that it was extracted from declared medical expenses and that it was measured as costs per rehabilitative day per patient.
6	Were the cost and consequences valued credibly?	X			Consequences were valued based on scores BI, IADL, ED5Q and MNA evaluated before and after introducing the

					programmes. Costs for each individual were valued based on extracted declared medical expenses and were valued as costs per rehabilitative day per patient.
7	Were costs and consequences adjusted for differential timing?		X		No discount rate
8	Was an incremental analysis of costs and consequences of alternatives performed?	X			Cost-effectiveness was calculated as the total cost divided by the improvement in BI, IADL, ED5Q and MNA scores.
9	Was uncertainty in the estimates of costs and consequences adequately characterized?		X		No, sensitivity analysis was conducted. Uncertainty in the estimates of cost-effectiveness were mean $\pm$ standard deviation.
10	Did the presentation and discussion of study results include all issues of concerns to user?	X			The conclusion of the analysis was based on cost-effectiveness (total cost divided by the improvement in BI, IADL, ED5Q and MNA scores). Results of the study were compared with those of others who have investigated the same question. Generalizability of the results was discussed.
	Total score out of 10	6