Journal of Stroke and Cerebrovascular Diseases 33 (2024) 107906

Contents lists available at ScienceDirect

Journal of Stroke and Cerebrovascular Diseases

journal homepage: www.elsevier.com/locate/jstroke

A systematic review of the socioeconomic impact of mechanical thrombectomy for acute ischemic stroke

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ARTICLE INFO

Keywords:
Ischemic stroke
Mechanical thrombectomy
Socioeconomic impact
Systematic review

ABSTRACT

Background: Mechanical Thrombectomy (MT) is an efficacious treatment for severe acute ischemic stroke patients. However, access to MT is limited in many parts of the world, partly due to economic barriers. The purpose of this systematic review is to provide an updated frame about the socioeconomic impact of MT.
Methods: To carry out this systematic review we used the PRISMA guidelines. We included scientific articles analyzing the socioeconomic impact of MT for acute ischemic stroke, in which MT was compared to best medical therapy (BMT). The online databases of Pubmed, Scopus and Web of Science were used as main sources of information. To carry out the comparative analysis, the incremental cost-effectiveness ratio (ICER) was used, relating the cost to quality-adjusted life-year (QALY). Risk of bias was assessed with the Consensus Health Economic Criteria (CHEC) and the Consolidated Health Economic Evaluation Reporting Standards (CHEERS).
Results: Eight hundred thirty-two studies were identified in this systematic review. As a result, studies that used cost-effectiveness analysis show that MT saves costs in the long term and cost-utility analysis show that the cost per QALY is reasonable with a mean ICER value of $14242.36/QALY.
Conclusions: MT has a favorable socioeconomic impact, as derived from cost-effectiveness and cost-utility analyses. Therefore, public policies should encourage the implementation of MT for stroke patients around the world.

Introduction

Stroke is the second leading cause of death worldwide and the leading cause of disability in adults, with about 15 million new cases of stroke per year, of which 5 million result in death and another 5 million result in permanent disability, and its incidence will continue to increase in the future.[1] Strokes are classified into two types according to their cause: ischemic and hemorrhagic, but ischemic strokes are the most prominent because they account for around 80-85% of all stroke cases in Western countries.[2] Among ischemic strokes, those caused by an acute intracranial large-vessel occlusion (LVO), are associated with the worst functional outcomes and the highest mortality and morbidity rates.[3,4]

Currently, stroke is the most common cause of hospital admission worldwide and its healthcare costs after diagnosis are high due to in-hospital care and subsequent rehabilitation.[5] In the United States, total costs for stroke are expected to rise to $142.9 billion by 2035, of which $94.3 billion is estimated as direct costs, increasing for patients aged 65-79 years.[6] In countries such as Spain, stroke causes an annual direct health expenditure of close to €2000 million and more than €6500 million in social costs after hospital discharge, mostly assumed by the patient directly. In this sense, the socioeconomic impact of stroke has increased in the last decade and will continue to increase by 40% in the next 20 years.[7]

The recent development of new cerebral reperfusion therapies has

Abbreviations: BMT, Best Medical Therapy; CHEC, Consensus Health Economic Criteria; CHEERS, Consolidated Health Economic Evaluation Reporting Standards; EVT, Endovascular thrombectomy; ICER, Incremental Cost Effectiveness Ratio; ICTRP, International Clinical Trial Research Platform.; IVT, intravenous thrombolysis; tPA, Tissue-type plasminogen activator; LVO, Large Vessel Occlusion; MeSH, Medical Subject Headings.; MT, Mechanical Thrombectomy; NHS, National Health System; NHI, National Health Insurance; PRISMA, Preferred Reporting Items for Systematic review and Meta-Analysis; QALY, Quality-Adjusted Life Year; WoS, Web of Science.

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https://doi.org/10.1016/j.jstrokecerebrovasdis.2024.107906
Received 7 December 2023; Received in revised form 25 July 2024; Accepted 29 July 2024
Available online 8 August 2024

led to improved outcomes in patients with ischemic stroke.[8,9] Thus, endovascular treatment (EVT) with mechanical thrombectomy (MT) produces early cerebral reperfusion which allows the rescuing of brain tissue at risk by preventing its conversion into irreversibly damaged infarcted tissue.[10,11] The subsequent reduction in the volume of infarcted brain tissue is associated with a significant improvement in the patient's functional outcome and better quality of life.[12]

In this regard, endovascular reperfusion therapy with MT has proven a solid superiority in clinical efficacy as compared to best medical therapy (BMT), including intravenous thrombolysis (IVT) using tissue-type plasminogen activator (tPA).[13,14] Although multiple economic analyses of the use of MT in patients with ischemic stroke have been performed in high-income countries,[15] there are still economic and organizational barriers that result in the lack of access or availability of MT in many countries around the world. Therefore, up-to-date analyses are needed to guide health authorities in implementing MT services to make such an effective treatment more accessible to more patients.

Currently, approaches such as Value-Based Medicine, introduced by Michael Porter in 2006, aim to guide care practice by emphasizing the systematic measurement of the relationship between health outcomes and costs.[16] Specifically, the model considers four types of value: allocative value (payers and managers), technical value (professionals), personalised value (patients) and social value (society).[17] Thus, it is essential to assess the socioeconomic impact of the stroke care process holistically, from the perspective of care effectiveness and economic efficiency.[12]

To relate the cost associated with medical intervention to its health outcomes, analysis methodologies such as cost-effectiveness, cost-utility or cost-benefit are often used.[18] For the estimation of long-term results, the concept of quality-adjusted life years (QALY) expresses the number of additional years that a person lives as a result of a health intervention taking into account the quality of life.[19] In this way, to relate the cost of a health intervention to the QALY gained, the mean value of the incremental cost-effectiveness ratio (ICER) can be analysed.[20]

The purpose of this systematic review is to provide an updated frame about the evaluation of the socioeconomic impact of MT for the treatment of ischemic stroke. Specifically, we aimed to determine the main characteristics of the studies published to date, to synthesize the methodologies of analysis used and to expose the results obtained from the point of view of health effectiveness and economic efficiency. Given the importance of the use of MT, other systematic reviews have been conducted in recent years, with a focused perspective on the effectiveness and safety of MT,[40] and cost-effectiveness and cost-utility analysis.[41,42] However, our systematic review adopts a broader approach based on analyzing the socioeconomic impact of MT, including a broad search for economic analysis techniques used in published studies.

Methods

To conduct this systematic review, we followed the procedure according to the Preferred Reporting Items for Systematic review and Meta-Analysis (PRISMA) guidelines.[21] It should be noted that ethical approval was not required because no sensitive data were used and all materials were collected from open and published sources. In addition, this systematic review was registered in Prospero in February 2023 (ID: CRD42023397320).

Eligibility criteria

In this systematic review, we have included scientific articles analysing the socioeconomic impact of MT compared to BMT for acute ischemic stroke. Specifically, studies dealing with cost analysis, cost allocation, cost-benefit, cost control, cost of illness, cost sharing, and cost-effectiveness analysis have been included. Healthcare costs and health expenditures have also been considered. Studies dealing with the economic impact from the hospital, medical, nursing and pharmaceutical point of view, as well as the financial approach in terms of management and financial support have also been included. Studies with a healthcare sector perspective have also been considered, in terms of investments and public expenditures.

Sources of information

Online databases were used as a main source of information, searching for scientific articles in Pubmed, Scopus and Web of Science (WoS). A search for clinical trial registries was also carried out in clinicaltrials.gov and the International Clinical Trials Registry Platform (ICTRP) Search Portal. The date of the search was January 2023 in all online sources.

Search strategy

Search terms were established according to Medical Subject Headings 2023 (MeSH) of the National Library of Medicine, with the following being determined: Stroke, Brain Infarction, Ischemic Stroke, Reperfusion, Thrombectomy, Costs and Cost Analysis, Cost Allocation, Cost-Benefit Analysis, Cost Control, Cost of Illness, Cost Sharing, Cost-Effectiveness Analysis, Health Care Costs, Health Expenditures, Economics Hospital, Economics Medical, Economics Nursing, Economics Pharmaceutical, Financial Management, Financial Support, Health Care Sector, Investments, Public Expenditures. The search strategy of databases is presented in Supplementary File 1, and, in the case of the trials, search terms were entered into advanced search sections.

Selection process

During the search process, a total of eight hundred thirty-two results were identified. All these results were exported to EndNote20 for collation and automatic removal of duplicate records, leaving a total of five hundred sixty-eight unique results. Thereafter, two reviewers (LLV and AMG) independently screened titles and abstracts to identify potential articles for inclusion, and disagreements were resolved by a third reviewer to reach a consensus (MBCM). Then, one hundred eighteen records remained to be searched for retrieval and after eliminating missing non-full-text open-access studies, eighty-eight remained to be assessed for eligibility.

An exclusion process was then performed for studies not published in English. In addition, not original studies, commentary, grey literature or abstract only, as well as those not adjusted for the intervention or comparison were excluded. In addition, an identification of studies via other methods was carried out but none were selected as valid for inclusion. Then, a total of twenty-eight results were finally included (fourteen studies and fourteen registers). To explain the process following PRISMA guidelines, a flowchart is presented in Fig. 1.

Data extraction process

All data extraction was carried out independently by two reviewers (LLV and AMG), analysing each study in detail to record the information. To achieve consensus, the information was collated by the MBCM reviewer. Specifically, the following information was collected for each study (Supplementary File 2): author, year of publication, region, intervention, sample size, economic analysis, perspective, cost structure, discount rate and source of funding. In addition, average values have been extracted according to the cost-effectiveness or cost-utility analysis methodology used. On the other hand, the information on trial registers was collected in Supplementary File 3.

Risk of bias assessment

To assess the risk of bias in the included studies, the Consensus Health Economic Criteria (CHEC)[22] and the Consolidated Health

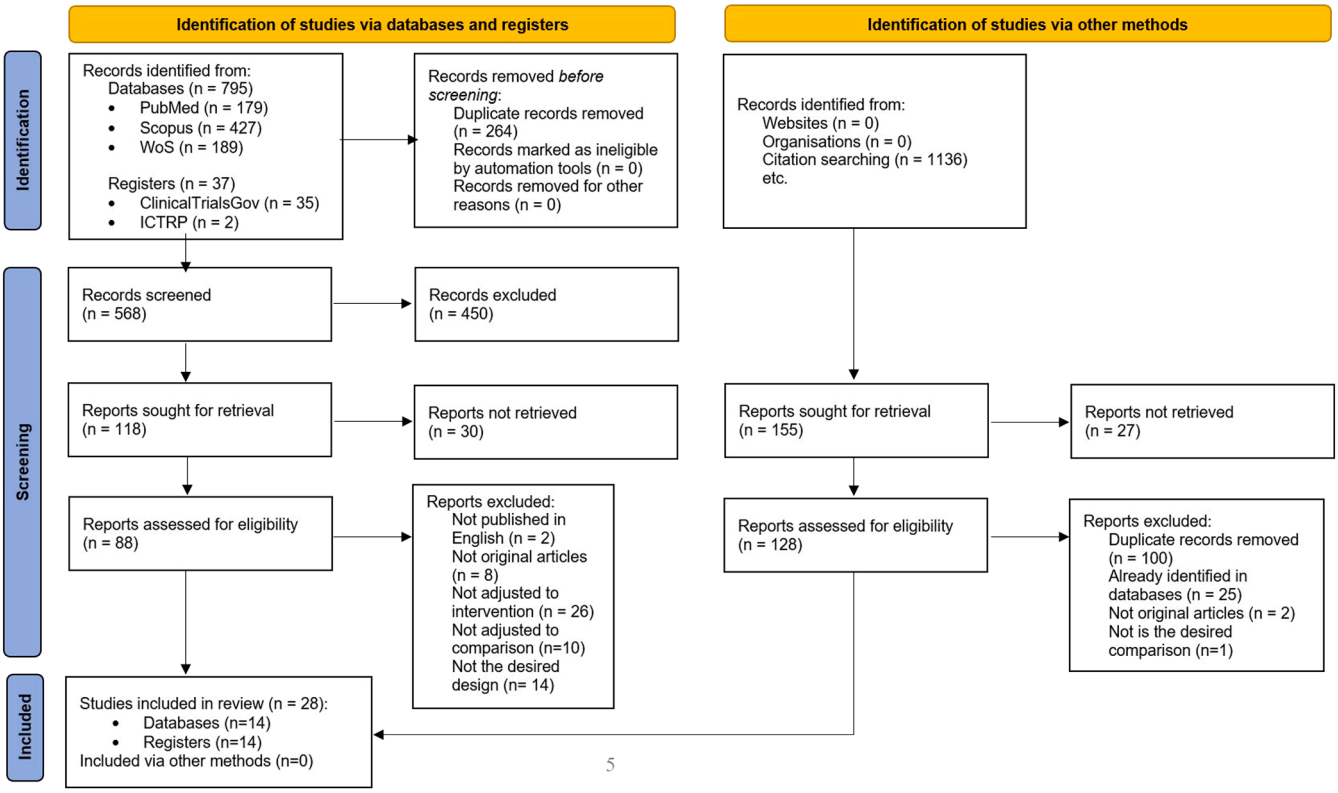


Fig. 1. PRISMA Flow Diagram for systematic reviews, including searches of databases, registers and other sources.
PRISMA: Preferred Reporting Items for Systematic review and Meta-Analysis. WoS: Web of Science. ICTRP: International Clinical Trial Research Platform.

Economic Evaluation Reporting Standards (CHEERS)[23] checklists were used. In this regard, two reviewers (JFAL and MBCM) evaluated the studies by scoring each of the items with 1 if it complied and 0 if it did not comply, achieving consensus among all reviewers. Bar graphs were then created with the relative frequencies of each of the evaluation responses (1=Yes, 0=No) for both CHEC and CHEERS, aggregated across all studies. In addition, the individual compliance rate for each study was analysed and compared with the mean compliance rate. Then, the information was statistically analysed and presented in an SPSS boxplot.

Results

Characteristics of results

After carrying out the search and selection process, a total of fourteen studies[24–37] and fourteen trial registers (Supplementary File 3) were included in this systematic review. It should be noted that, once the selection process was completed, the fourteen included registers were analysed in detail, but all of them were excluded due to the lack of available results. Thus, only the fourteen studies identified by the online database search were considered for data summarisation of characteristics in Table 1.

The year of publication of the studies was between 2011 and 2022, with five studies (36%) published in 2022, followed by three (21%) published in 2018. About the region, six studies (43%) were in Europe, specifically in Italy, France Belgium and the UK. It is also noted that there were three studies in North America and one study in South America. On the other hand, there were two studies from Asia and two from Oceania.

The economic analysis that was mostly carried out was cost-effectiveness in nine studies (64%), and five studies (36%) carried out cost-utility analysis. Regarding the sample size, the most common is between 1000 and 2000 individuals in nine studies (64%). The perspective followed was NHS in five studies (36%), followed by four studies followed the payer perspective in four studies (29%). In terms of cost structure, seven the studies followed a direct cost structure, and the other seven studies followed a direct and indirect cost structure. Regarding the discount rate understood as the interest used to determine the present value of a subsequent cash flow over time, the most used is 3%, in seven studies (50%).

Description of studies

Some studies carried out a cost-effectiveness analysis concluding that MT produces a long-term cost reduction. For example, in the UK in 2022, it was concluded that MT produces better outcomes in comparison with BMT, about discharge to home (60% vs 28%), discharge to nursing homes (4% vs 16%), residential homes (0% vs 12%), rehabilitation centres (8% vs 20%), concluding a cost reduction in the long term with MT (£22444) compared to BMT (£39664).[24] In Italy, in 2018 it was concluded that use of MT had an estimated long-term cost of €31798, lower compared to BMT (€34855).[31] In addition, in North America, in 2020 it was concluded that the use of MT beyond 6 hours was >99.9% cost-effectiveness than BMT.[25] In Australia in 2018, it was concluded that the use of MT resulted in lifetime cost savings of more than $8000 per patient.[27] In China, a cost-effectiveness analysis of MT was conducted in 2022, concluding that MT had a lower total cost and higher effectiveness.[34]

Other studies conducted a cost utility analysis. For example, in Belgium in 2022 it was concluded that MT generating an additional 1.31 QALYs and a lifetime cost saving of €10216 per patient.[29] In the UK in 2020, the incremental cost with MT was $1564 after 12h, $5253 after 16h and $3712 after 24h.[30] Also in the UK, in 2015 it was concluded that MT was more expensive in short term but it improved patient's quality of life expectancy.[35] In addition, in North America in 2011, it was concluded that the use of MT had a higher mean recanalisation with the

BMT.[36] On the other hand, in South America, in Argentina in 2022, it was concluded that MT had overall savings of 0.96% over three years, 2.6% over four years and 4.4% over five years.[37]

On the other hand, studies which calculated the necessary expense per QALY demonstrated that the investment is reasonable. For example, in France in 2019, the use of MT resulted in a cost of $14715 per QALY gained.[32] In North America in 2022 it was obtained a cost-effective ratio of $18835 per QALY when MT is used as a treatment.[26] In Australia in 2021, MT was more effective treatment for patients with $11608 to $34416 per QALY.[28] In China, a study was conducted in 2018 and concluded that the use of MT had a cost of $9690 per QALY gained.[33]

Synthesis of studies

To perform a comparative analysis of the results obtained in the studies, an analysis of the incremental cost-effectiveness ratio (ICER) was performed considering eleven studies which had that parameter available considering the valuation of the investment required to carry out the treatment with MT. Table 2 shows the ICER value extracted from each study. It should be noted that ICER values are presented in dollars, converting those data that were presented in other currencies according to the currency exchange rate at the date of each study. Then, the mean ICER values are represented along a timeline in Fig. 2.

The aggregated results indicated a mean ICER value of $14242.36/QALY (S.D.: 6933.07), with values ranging from $5892/QALY[37] to $28771/QALY.[24] This mean value can be considered reasonable because it is below the value generally accepted as a limit to recommend the adoption of health interventions.[38,39]

Risk of bias

The risk of bias in all included studies was assessed according to the degree of compliance for each of the proposed items for CHEC and CHEERS, stablishing 1 when the study comply the condition and 0 when it did not comply that condition. (Yes=1 or No=0). From this, the average percentage of studies complying with each of the items was assessed and the results were plotted in Figs. 3 and 4.

The studies mostly complied with all the CHEC proposed items, except for items: number 13 about the incremental analysis of costs and outcomes of alternatives performed, item 15 about all important variables appropriately subjected to sensitivity analysis, item 17 about the generalizability of the results to other settings and patient/client groups, and item 18 about the indication of potential conflict of interest of study researchers and funders. In addition, it should be noted that the highest degree of non-compliance was in the item number 19 about discussion of ethical and distributional issues.

The studies mostly complied with all the CHEERS proposed items, except for items: number 2 of abstract, item 9 of time horizon, item 10 of discount rate, item 15 about price rational and description of the model, item 20 about characterization of uncertainty, item 21 about approach to engagement with patients and others affected by the study, item 24 about effect of uncertainty, item 25 about effect of engagement with patients and others affected by the study, and item 28 about conflicts of interest. In addition, it should be noted that the highest degree of non-compliance was in the item 18 about characterization of heterogeneity.

Subsequently, a statistical analysis was performed in SPSS to see which studies had a smaller value for their degree of compliance in comparison with the rest of the studies. Specifically, compliance rate of each study was calculated with the mean of the CHEC and CHEERS items ratings (Yes=1 or No=0). The compliance rate according to CHEC expressed a median of 0.9474, and the compliance rate according to CHEERS expressed a median of 0.9643. Table 3 present the complete list of studies with their degree of compliance in CHEC and CHEERS, and Fig. 5 present the boxplot analysis.

According to these results, most studies were around the median values. Also, there were studies above the median because they had the highest degree of compliance in CHEC,[27,30,33,37] and CHEERS.[25,37] However, there were extreme cases of studies below the median in CHEC[36] and CHEERS,[29,36], although it should be note that they were above the 0.80 compliance value.

Discussion

The use of MT in stroke care is an increasingly widespread treatment in the clinical practice of healthcare centres around the world, leading to improved patient outcomes. However, there is a problem of insufficient access to MT treatment, due to the financial constraints of health authorities that may appear especially in low-medium income countries and in some regions with difficult health coverage. It is therefore essential to promote broader access to MT worldwide, also in emerging economies and low-median income countries where stroke strikes severely and at younger ages.

In this sense, the availability of updated systematic analyses can contribute to guide policy makers to favour the implementation of MT,

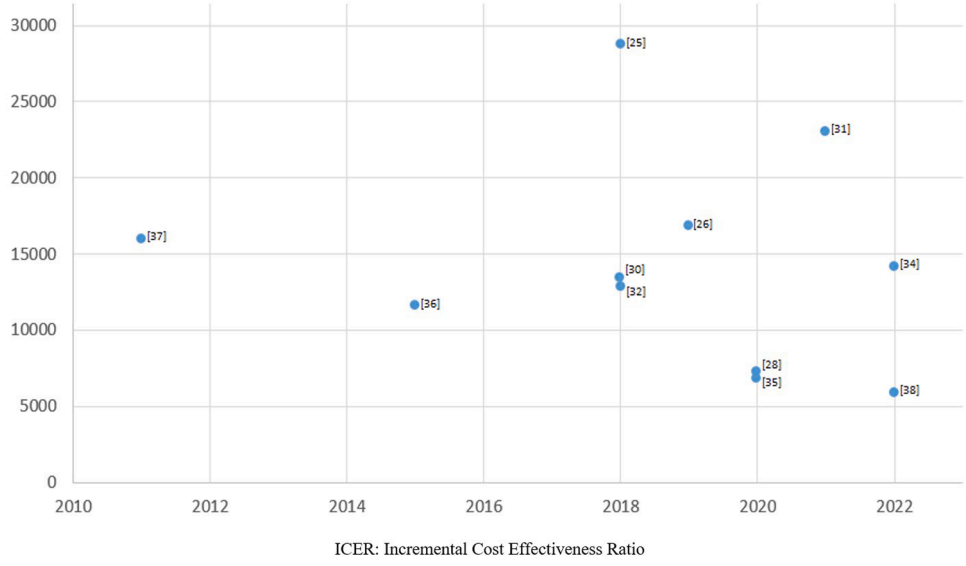
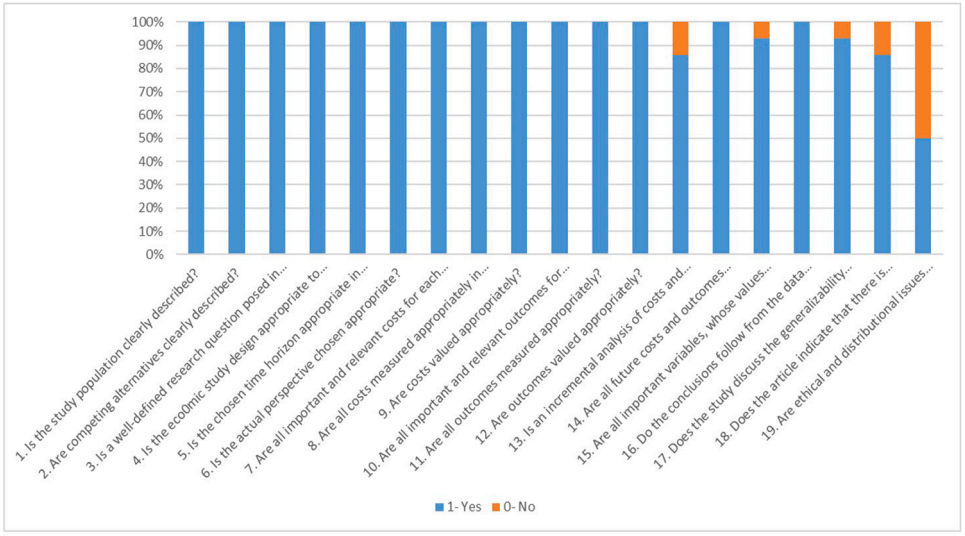
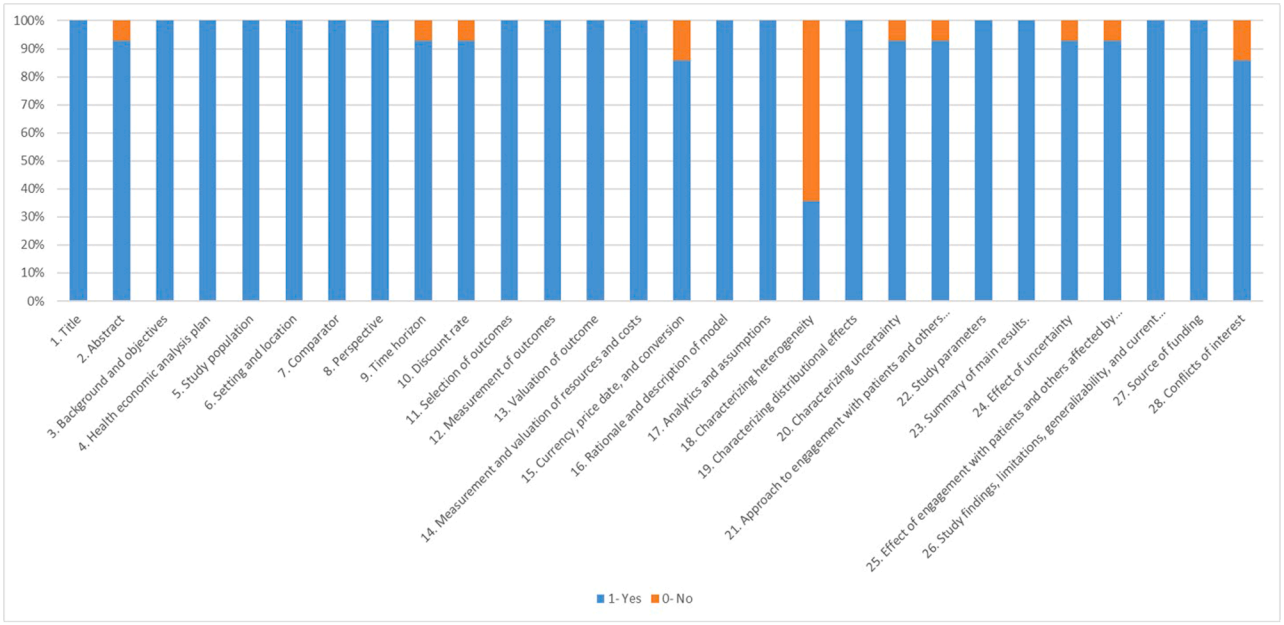


Fig. 2. Timeline comparison of ICER values.
ICER: Incremental Cost Effectiveness Ratio. QALY: Quality-Adjusted Life Year.



CHEC: Consensus Health Economic Criteria

Fig. 3. Global CHEC assessment representation.
CHEC: Consensus Health Economic Criteria.



CHEERS: Consolidated Health Economic Evaluation Reporting Standards

Fig. 4. Global CHEERS assessment representation.
CHEERS: Consolidated Health Economic Evaluation Reporting Standards.

so that more and more stroke patients around the world benefit from it. Our systematic review provides a broad approach to the socioeconomic impact of the use of MT as a treatment for ischemic stroke, which advances the knowledge with respect to other recent systematic reviews that focus more on the effectiveness and safety of MT,[40] and cost-effectiveness and cost-utility analysis.[41,42]

Our systematic review showed that there has been increasing interest in researching the benefits derived from the use of MT, both from a health and economic point of view. Included studies of MT compared with BMT determined that the use of MT produced better health outcomes, due to higher average early recanalisation rates. In addition, studies results indicated that the use of MT leads to better outcomes in discharged homes, discharged nursing homes, residential homes and rehabilitation centres.

Our review also showed that the use of MT causes a better overall economic balance in comparison with BMT. Studies using cost-effectiveness analysis show that MT saves costs in the long term, with the outcome becoming increasingly favourable over patient years. Studies using a cost-utility analysis show that the cost per QALY is reasonable compared to BMT, taking into account aspects related to neuroradiology materials, use of infrastructure, intubation and mechanical ventilation, as well as the cost of professionals such as anaesthesiologists or neuroradiologists.

The comparative analysis shows an acceptable overall ICER, because all the studies analysed were below the value generally accepted as a limit to recommend the adoption of health interventions, being around

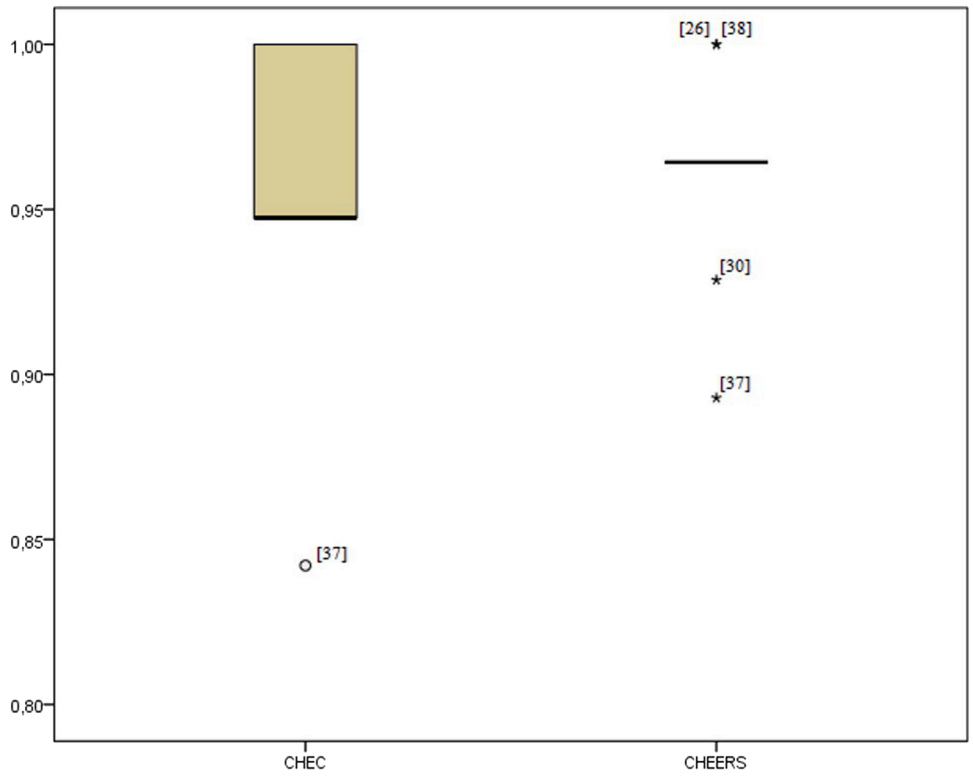


Fig. 5. Boxplot analysis for CHEC and CHEERS values.
CHEC: Consensus Health Economic Criteria. CHEERS: Consolidated Health Economic Evaluation Reporting Standards.

$30000/QALY gained in countries such as Spain[38] and around $50000/QALY gained in international contexts.[39] For this, it can be concluded that the use of MT is the dominant strategy for saving money because the investment required to achieve a QALY is reasonable.

In this way, the systematic measurement of the outcomes and costs of MT use is related to the concept of Value-Based Medicine, which seeks to orient healthcare practice towards those activities that generate the best possible health outcomes for the patient and place value on each unit of expenditure produced in the healthcare system. Therefore, the benefits derived from the use of MT improve the society health status as a whole and reduce the socioeconomic impact of stroke.

Our systematic review has the strength of having applied a broad approach, considering a variety of types of economic analysis, instead of focusing on one in particular like other systematic reviews on cost-effectiveness or cost-utility analysis. Another strength of our review is the pre-registration of the methodology in an external repository to guarantee its quality. Likewise, our review presents a robust methodology to reduce the risk of bias following standardised criteria based on CHEC and CHEERS, highlighting that, although two studies had lower compliance, the overall median value was very high and the standard deviation was small among all studies.

However, there are some limitations in this systematic review, such as the exclusion of studies not published in English, as this may result in the loss of some interesting studies written only in their native language. In addition, another limitation is the exclusion of all registries as they do not yet present results. These limitations can be addressed in future research on this topic. Nevertheless, other systematic reviews often focus on a single type of economic analysis, such as cost-effectiveness or cost-utility; but our review has included, as a search criterion, a variety of types of economic analysis rather than focusing on one in particular, which is remarkable in this field of knowledge.

The results achieved by this systematic review are oriented to provide further reasons to encourage the widespread use of MT in the daily clinical practice. We find that investment in MT has health benefits for society that translate into a lower socioeconomic impact of stroke in the long term. In this sense, it seems economically rentable for health authorities to implement tertiary stroke centers capable of providing MT to stroke patients within the countries' health regions, always placing patients and their health status at the middle of the intervention.

Likewise, the results represent an interesting way for further research about the advantages of using MT for stroke treatment. In this way, the introduction of digital health tools represents an opportunity to allow the collection of real-time information on different health and social cost variables of the care process for stroke patients. In addition, it will be essential to know the functional prognosis of the patient and its impact on the overall economic cost, to identify which parts of the care process provide the most value.

Conclusions

This systematic review shows that the socioeconomic impact of MT is crearly favourable, as the cost-effectiveness analysis demonstrates a reduction in long-term costs compared to BMT and the cost-utility analysis shows that the investment needed to obtain a QALY is reasonable. Thus, this systematic review justifies the need for public health policies to support the implementation of MT-capable stroke centers within a certain health region, since the necessary investment is reasonable compared to the high benefits in terms of patient quality of life.

Furthermore, there is great interest in the research of the economic efficiency of acute ischemic stroke treatments with MT and this will continue to increase in the coming years. Future research should employ

digital health tools to provide real-time information on the economic cost of each phase of the stroke care process, to identify where the efficiency of the investment needs to be improved.

CRediT authorship contribution statement

Adrián Martín-Gutiérrez: Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Luis Leal-Vega:** Writing – original draft, Methodology, Investigation, Conceptualization. **María Begoña Coco-Martín:** Writing – review & editing, Visualization, Validation, Supervision, Methodology, Conceptualization. **Juan F. Arenillas-Lara:** Writing – review & editing, Visualization, Validation, Supervision, Project administration, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper "A systematic review of the socioeconomic impact of mechanical thrombectomy for acute ischemic stroke".

Source of Funding

The Stroke Program HCU Valladolid receives funding from the Spanish Cooperative Network for Research in stroke (RICORS-ICTUS, Instituto de Salud Carlos III, Madrid).

Grant support

The Stroke Program HCU Valladolid receives funding from the Spanish Cooperative Network for Research in stroke (RICORS-ICTUS, Instituto de Salud Carlos III, Madrid).

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jstrokecerebrovasdis.2024.107906.

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