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Original research

Optimized density and locations of stroke centers for improved cost effectiveness of mechanical thrombectomy in patients with acute ischemic stroke

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ABSTRACT

Background Despite the proven cost effectiveness of mechanical thrombectomy (MT) in patients with acute ischemic stroke (AIS) due to large vessel occlusion, treatment within 6 hours from symptom onset remains inaccessible for many patients. We aimed to find the optimal number and location of treatment facilities with respect to the cost effectiveness of MT in patients with AIS, first by the most cost effective implementation of comprehensive stroke centers (CSCs), and second by the most cost effective addition of complementary thrombectomy capable stroke centers (TSCs).

Methods This study was based on nationwide observational data comprising 18 793 patients with suspected AIS potentially eligible for treatment with MT. The most cost effective solutions were attained by solving the p median facility location–allocation problem with the objective function of maximizing the incremental net monetary benefit (INMB) of MT compared with no MT in patients with AIS. Deterministic sensitivity analysis (DSA) was used as the basis of the results analysis.

Results The implementation strategy with seven CSCs produced the highest annual INMB per patient of all possible solutions in the base case scenario. The most cost effective implementation strategy of the extended scenario comprised seven CSCs and four TSCs. DSA revealed sensitivity to variability in MT rate and the maximum willingness to pay per quality adjusted life year gained.

Conclusion The combination of optimization modeling and cost effectiveness analysis provides a powerful tool for configuring the extent and locations of CSCs (and TSCs). The most cost effective implementation of CSCs in Sweden entails 24/7 MT services at all seven university hospitals.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Despite proven cost effectiveness of mechanical thrombectomy (MT) in patients with acute ischemic stroke (AIS), it remains under utilized and inaccessible for many patients.

⇒ Increasing the number of comprehensive stroke centers in healthcare systems may contribute to overcoming these issues and thus the cost effectiveness of MT in patients with AIS needs to be analyzed with respect to the number and locations of comprehensive stroke centers.

WHAT THIS STUDY ADDS

⇒ This study demonstrates how to optimize the density and locations of thrombectomy centers for nationwide stroke care delivery systems with regards to the cost effectiveness of MT.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE, OR POLICY

⇒ We believe this study could help improve the planning of acute stroke care delivery systems for patients with AIS.

INTRODUCTION

Ground breaking evidence on the clinical effectiveness of mechanical thrombectomy (MT) in patients with acute ischemic stroke (AIS) due to occlusion of arteries in the proximal anterior circulation, commenced reforms in acute stroke care of patients with suspected AIS.[1] Ensuing studies outlined the association of time from symptom onset to arterial puncture with diminishing odds of favorable functional outcomes in patients treated with MT.[2] Despite compelling evidence for the cost effectiveness of MT as a complementary intervention to standard care, it remains inaccessible for many eligible patients and under utilized in healthcare systems across the world.[3 4] Increasing the number of comprehensive stroke centers (CSCs) that provide 24/7 MT service constitutes a cornerstone of action plans and recommendations for improving the organization, availability, and delivery of advanced stroke care.[5]

Optimization modeling has proven useful for analysis and planning of stroke services in terms of population accessibility to, and quality of care for, acute stroke therapies.[6] Apart from the challenges posed by geographic and demographic factors, the planning and implementation of MT needs to consider aspects of patient safety and economics. Thus the aim of this study was to analyze the cost effectiveness of MT as a complementary intervention to treatment with conservative therapy (CVT) or intravenous thrombolysis (IVT) in patients with AIS, with respect to the number and locations of CSCs.

METHODS

By means of an economic model for decision analysis, this study evaluated how the number and

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locations of CSCs in Sweden impacted healthcare costs and the treatment effectiveness of MT in patients with AIS.

Data

The study material consisted of anonymized registry data on acute stroke patients between 2012 and 2017. The consolidated data set assembled the case histories of individual patients by integrating collected data in case records from different registries. The data set comprised emergency medical services (EMS) call out data from emergency call operator companies, stroke care data from the Swedish stroke registry (RIKSSTROKE), and data on inpatient healthcare episodes and eventual cause of death from the Swedish National Board of Health and Welfare.[7–10]

The merging of 220 267 case records of EMS call out data of patients with suspected stroke with 124 484 case records of patients with a confirmed stroke diagnosis at hospital discharge (encoded with ICD-10), gave coherent case histories for 72 640 stroke patient records. These had case specific registry data on individual patients, collected from symptom onset to death or the end of the study period, whichever occurred first. After removing AIS cases with confirmed posterior circulation occlusion, cerebral infarction (I63) accounted for 63 964 cases. A description of the patient characteristics and selection criteria has previously been presented in detail.[11]

In this study, patients presenting with a National Institutes of Health Stroke Scale (NIHSS) score >5 at hospital admission were considered eligible candidates for treatment with MT (n=13 519 cases); unless contraindicated, these patients were considered eligible for preceding treatment with IVT. Additionally, all patients treated with MT regardless of the presenting NIHSS score also qualified as eligible candidates for treatment. Among the 1135 cases of reported treatment with MT, 164 (14%) presented with an NIHSS score of <6, while 565 patients were treated with IVT before MT. Another 5247 patients, of whom 2971 had intracerebral hemorrhage (I61) and 2302 stroke mimics, reflected the proportion of false positives among patients assessed with the prehospital stroke triage system, termed the A2L2 test.[12] Thus the final study population for analysis was 18 793 patients with suspected AIS. The decision analysis was structured into three consecutive stages of modeling (figure 1).

Network analysis

The strategic decision problem to solve is a p median facility location–allocation problem with an imposed maximum travel time constraint for road ambulance patient transportation, and a minimum allocation of 50 MT interventions per year and CSC.[13] Let H be the set of hospitals where a CSC can be located, P is the set of patients, and T is a matrix with travels times from each patient to every hospital, where t_{ph}=the time from patient case p to hospital h. The objective is then to minimize the sum of the times to transport patients to hospitals: $\text{Min} \sum_{p\in P} \min_{h\in H} t_{ph}$, subject to the aforementioned constraints (figure 1A).

The presence of a neurosurgical clinic is set as a prerequisite for hospitals to qualify as candidate facilities for CSC location in the model; this gave seven university hospitals. Each of the 18 793 patients was represented by its point location for EMS

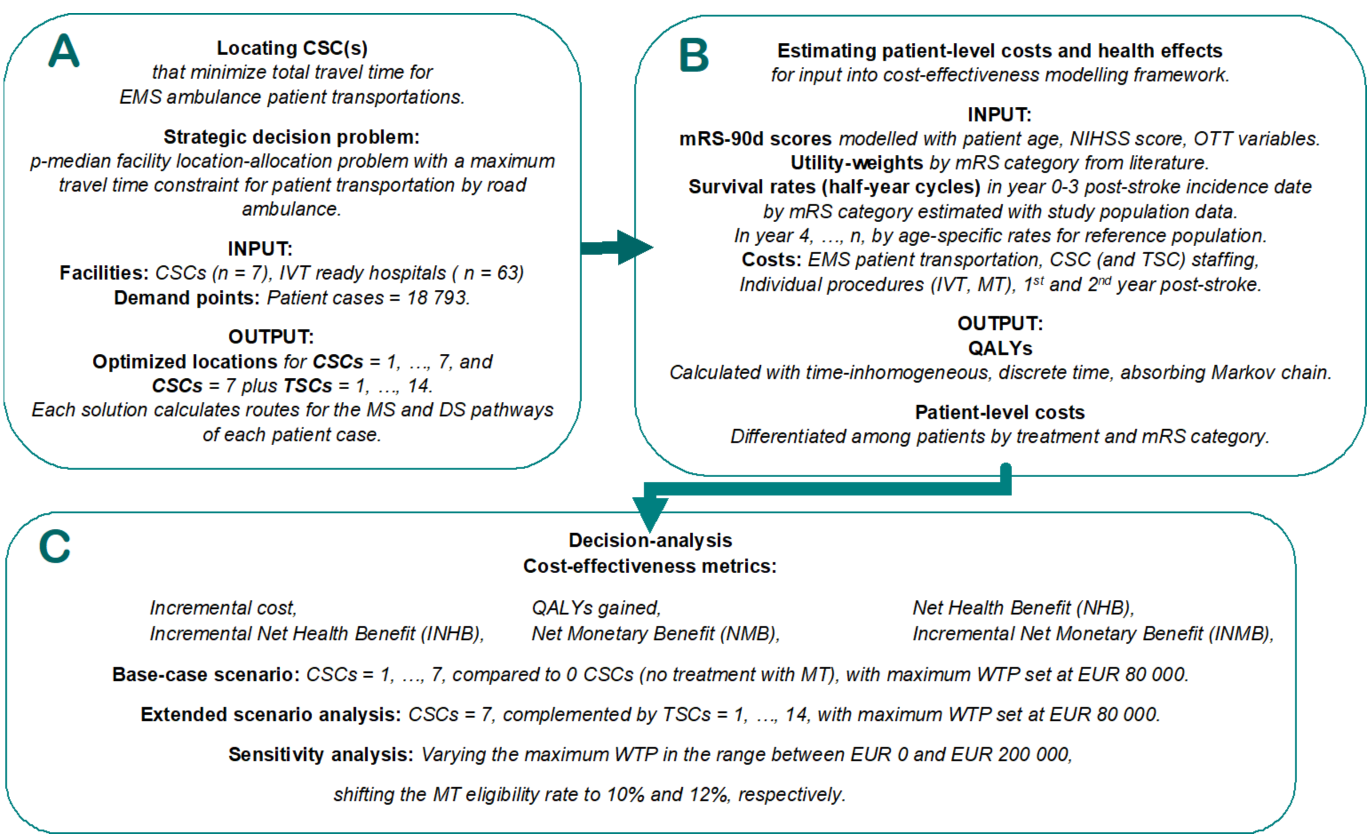

Figure 1 Schematic overview of modelling framework for decision analysis. CSC, comprehensive stroke center; DS, drip-and-ship; EMS, emergency medical services: IVT, intravenous thrombolysis; mRS, modified Rankin Scale; MS, mothership; MT, mechanical thrombectomy; NIHSS, National Institutes of Health Stroke Scale; OTT, onset to treatment time; TSC, thrombectomy capable stroke center; QALYs, quality adjusted life years; WTP, willingness to pay.

pick-up of the patient in the national road network that covers a land area of 403 865 km^2.

The model limits the symptom onset to treatment time (OTT) window for MT to 360 min. The median time from symptom onset to EMS arrival at the patient location was 62 min for the study population. The reported median time from hospital arrival to treatment start with MT is 58 min in Sweden.[14] After deducting the two latter time intervals from the OTT window for MT, 240 min remained for EMS transportation of patient from the pick-up point of location to the nearest CSC. Thus the model dismisses patients with estimated travel times beyond 240 min of road transportation to a CSC as ineligible for treatment with MT. In accordance with the fitted linear associations between OTT and the modified Rankin Scale score at 90 days (mRS-90d score) in predictive generalized linear models, the solver is set to minimize a p median objective function, which translates into minimizing the total sum of time spent on transporting patients to a CSC.[11] Thus the solutions for one and up to seven CSCs, respectively, suggest the CSC locations that minimize the overall travel time for EMS patient transportations.

Travel times were calculated using the quickest path in the network, calculated with road length and maximum allowed speed for each road link. Each solution provides the calculated travel times for the mothership (MS) and drip-and-ship (DS) pathways for each patient. The MS pathway marks the quickest path between the patient pick-up location and a CSC, while the DS pathway determines the quickest path between the patient pick-up location and an IVT ready hospital, with the quickest path between the IVT-ready hospital and a CSC.

The network analyses were conducted with ESRI ArcGIS Desktop 10.6.1. The analyses used the location–allocation tool and the national road network from the Swedish national road database. Thus the location problem was solved using ArcGIS built-in solvers, which use a range of heuristics, including semi-randomized initial solutions, a vertex substitution heuristic, and a metaheuristic, to find good solutions.

Patient level costs and health effects

The aggregated staffing costs of performing 300 MT procedures per year constitute the minimum staffing costs for running a 24/7/365 MT service in a hospital with a comprehensive neurosurgical suite (see online supplemental material and online supplemental table S1). Thus the economic model expects each interventionist to perform 75 MT each year. Moreover, the model allows hospitals to overutilize staffing resources by 25%, before prompting the installment of additional staffing resources required for performing 150 MT procedures per year (figure 1B).

The patient level cost items consisted of individually estimated EMS patient transportation costs, staffing and equipment costs associated with different treatment modalities (CVT, IVT, and/or MT), and mRS categorized first and second year costs post-stroke derived from the literature, and takes on a societal perspective (table 1).[15] Costs are expressed in year 2021 euro currency (EUR) based on the consumer price index in Sweden and the annual average exchange rate of the EUR against the Swedish kronor.

While expecting OTTs for IVT and MT to vary across the seven solutions (CSCs=1, …., 7), patient age and NIHSS score were fixed. Inserting the parameters as independent variables into the predictive GLMs returns the expected mRS-90d scores for each patient and for each solution.[11] The model selects the treatment modality and pathway that generates the lowest mRS-90d score for each patient. Utility weights from the literature apply to the expected mRS-90d scores.[16]

Retrieved from the consolidated data set, the survival outcomes of all patients with mRS-90d scores and a stroke incidence date during the first half of the study period (n=74 988), was the basis for calculation of 3 year survival rates for ischemic stroke patients according to mRS categories 0–2, 3, 4, and 5. The age adjusted annual survival rate trend for patients with ischemic stroke aligned with the reference population's survival rates within 3 years post-stroke in Sweden.[17] Thus from year 4 and onwards, the survival rates were calculated with age specific mortality rates for the Swedish reference population.[18] Accordingly, the time inhomogeneous discrete time Markov chain consisted of patient state transition probabilities from all possible initial states (mRS 0–2, 3, 4, 5, 6) to the absorbing state of mRS 6 (dead). It constructs 68 transition matrices of half year cycle lengths before process termination due to complete migration to absorption state.

Next, on basis of the age and mRS category distributions of the study population, and the underlying patient transition probability distributions of the discrete time Markov chain, simulation of a sufficiently large number of sequences (n=100 000) generated estimations of the quality adjusted life years (QALYs) remaining for patients in each mRS category.[19]

Metrics of cost effectiveness for decision analysis

The decision analysis used a bayesian statistical approach within the cost effectiveness framework.[20] The estimated outcome distributions of patient level costs and QALYs enabled calculation of the net health benefit (NHB), net monetary benefit (NMB), and incremental NMB (INMB) for each implementation strategy in the willingness to pay (WTP) range between EUR 0 and EUR 200 000 per QALY gained, and in comparison with no MT (figure 1C).

Due to the inherent property as a fixed quantity measure, the expected INMB is well suited as the primary cost effectiveness metric for determining the most cost effective implementation strategy while providing information on the relative cost effectiveness of the competing strategies by ranking them according to the expected NMB. Thus the strategy that produced the highest expected INMB in comparison with no CSCs was selected as the optimal strategy for the implementation of CSCs.

Base case scenario

The base case scenario mimics the reported national MT rate at 7% of all patients with confirmed AIS in Sweden during 2021.[14] This translates to 1708 triage positive patients per year, of whom 1229 are eligible candidates for treatment with MT due to AIS. A minimum volume of 50 MT procedures per year was set as a criterion for selecting a CSC in the model. The maximum WTP for the base case scenario (EUR 80 000) reflected the lowest cost per QALY gained for declined reimbursement of treatments of severe health conditions by the Swedish Dental and Pharmaceutical Benefits Agency.[21]

Extended scenario analysis

By relaxing the requirement of allowing only hospitals that facilitate a neurosurgical clinic to become candidates for the location of an MT facility, the scope of analysis was extended to evaluate the potential addition of one and up to 14 thrombectomy capable stroke centers (TSCs) at IVT ready hospitals, to complement the CSCs.[22] The minimum volume criteria for selecting CSCs/TSCs was lowered to 20 MT procedures per year.

Table 1 Input parameters for calculating individual patient level costs and health outcomes in life time economic model

Parameter	Estimate	Source
Prediction modeled mRS-90d scores in patients with AIS for different treatment modalities		Ennab Vogel *et al*[11]
CVT	$0.0388*age_x+0.0960*NIHSS_x$ where age_x denotes the age (in years) of patient *x* at stroke incidence date, and $NIHSS_x$ denotes the clinically assessed stroke severity score at hospital admission for patient *x*	
IVT+MT	$0.0004 * (age_x)^{\wedge 2}+0.0024 * (NIHSS_x)^{\wedge 2}+0.0022 * IVT_{OTTx}+0.0010*MT_{OTTx}$ where IVT_{OTTx} and MT_{OTTx} denote the time lapse (in min) from stroke onset to treatment start with IVT and MT, respectively, for patient *x*	
IVT only	$0.3600+0.0004*(age_x)^{\wedge 2}+0.0024*(NIHSS_x)^{\wedge 2}+0.0022*IVT_{OTTx}$	
MT only	$0.5940+0.0004*(age_x)^{\wedge 2}+0.0024*(NIHSS_x)^{\wedge 2}+0.0010*MT_{OTTx}$	
Utility weighted mRS-90d scores		Wang *et al*[16]
0	0.96633	
1	0.88979	
2	0.73767	
3	0.56522	
4	0.27721	
5	−0.08642	
6	0	
Average life expectancy (years) by mRS-90d level		Statistics Sweden[18]
0–2	11.302660	
3	8.452735	
4	6.490088	
5	4.722382	
6	0	
Discount rates		Swedish Dental and Pharmaceutical Benefits Agency
Costs	0.03	
Health outcomes	0.03	
EMS patient transportation costs		Southern Regional Board of Healthcare.
Distance based costs for EMS patient transportation	$c *(d_x(u_x, h_x))$ where c is the EMS cost per km (€8.9), and $d_x(u_x, h_x)$ represents the length (km) of the quickest path in the road network from the point location of EMS conveyance (u) to the point location of hospital discharge (h) for patient *x*, and holds true for all distance based EMS patient transportation costs exceeding the minimum fee per patient transportation (€178): $\{(c * d_x) \in R \mid 178 \leq\}$, and where	
MS pathway	$d_x(u_x, MS_x)$ denotes the road length of the quickest path between u_x and a CSC, and	
DS pathway	$d_x(u_x, IVT_x)$ and $d_x(IVT_x, DS_x)$ denotes the road length of the quickest path between u_x and an IVT ready hospital, and between the IVT ready hospital and a CSC, respectively.	
Patient level costs for individual procedures		
Staffing costs, MT	€4784	Online supplemental table S1
Stent retriever device	€2274	Board for Supply of Goods
Alteplas for IVT	€894	Stockholm Regional Council
Post-stroke costs, first and second year by mRS level		Lekander *et al*[15]
0–2	€32 883	
3	€89 117	
4	€103 634	
5	€184 299	
6	€32 002	

AIS, acute ischemic stroke; CSC, comprehensive stroke center; DS, drip-and-ship; EMS, emergency medical services; IVT, intravenous thrombolysis; mRS-90d, modified Rankin Scale score at 90 days; MS, mothership; MT, mechanical thrombectomy; NIHSS, National Institutes of Health Stroke Scale; OTT, onset to treatment time.

Deterministic sensitivity analysis

The deterministic sensitivity analysis (DSA) examined how results change when varying the maximum WTP in the range EUR 0–200 000. Furthermore, the DSA explored the impact on the results from shifting the MT rate to 10% and 12%, thereby considering the highest MT rate reported by a healthcare region

Table 2 Modelling outcomes in base case scenario (1, 2, …, 7 comprehensive stroke centers, compared with none, mechanical thrombectomy rate at 0.07, maximum willingness to pay at €80 000)

Outcomes	Strategies (No of implemented CSCs)						
(n=1229)	1	2	3	4	5	6	7
No of CSCs per 1 million inhabitants*	0.10	0.19	0.29	0.38	0.48	0.57	0.67
Patients with OTT_{MT} ≤360 min (%)	80.5	86.5	96.8	97.7	97.7	97.7	97.7
CVT (%)	18.4	17.2	10.8	5.8	3.4	3.4	2.5
IVT only (%)	27.6	24.9	13.4	8.5	4.9	4.9	3.8
MT only (%)	31.7	32.9	39.2	44.2	46.6	46.6	47.5
IVT+MT (%)	22.3	25.0	36.6	41.5	45.1	45.1	46.2
Drip-and-ship pathway, advantageous (%)	66.3	64.4	55.4	48.9	41.0	33.5	31.0
University Hospital of Umeå (n)†	0	134	89	67	67	67	67
Uppsala University Hospital (n)†	0	0	586	381	381	122	122
Karolinska University Hospital (n)†	0	0	0	0	0	309	283
Örebro University Hospital (n)†	0	0	0	347	223	175	120
Linköping University Hospital (n)†	1102	1044	0	0	0	0	141
Sahlgrenska University hospital (n)†	0	0	0	0	321	321	275
Skåne University Hospital Lund (n)†	0	0	533	414	217	215	201
QALYs gained†	568	574	625	610	654	681	690
Additional EMS transportation costs (€)‡	28 251 914	24 348 722	18 811 056	15 343 618	10 182 012	9 131 016	7 919 019
Additional CSC staffing costs (€)†	4 048 520	4 867 006	4 807 541	4 151 168	5 192 084	5 909 062	7 159 645
Additional drug and medical equipment costs (€)†	1 831 000	1 938 868	2 441 939	2 719 072	2 886 765	2 887 385	2 941 961
Additional first and second year post-stroke costs, (€)†	−6 523 588	−6 727 264	−6 856 167	−6 091 461	−6 994 158	−7 362 587	−7 469 351
Incremental cost, annual (€)	27 607 846	24 427 333	19 204 369	16 122 397	11 266 703	10 564 877	10 551 274
Incremental NMB per patient (€)	14 530	17 476	25 061	26 611	33 416	35 738	36 301

*For a population of 10 452 326 individuals (Swedish population at the end of year 2021).
†Per year.
‡Of 1708 triage positive cases per year.
CSC, comprehensive stroke center; CVT, conservative therapy; EMS, emergency medical services; IVT, intravenous thrombolysis; MT, mechanical thrombectomy; NMB, net monetary benefit; OTT, onset to treatment time; QALYs, quality adjusted life years.

in Sweden during 2021 and the reported MT rate in Bremen, Germany in 2017.[14 23]

RESULTS

Patient population access to comprehensive stroke centers

The estimated OTT for IVT at the nearest IVT ready hospital was within 270 min for all patients, with a mean OTT of 119 min. Mean age was 77.5 years and median NIHSS score was 10. Implementation of one CSC made MT within 360 min from symptom onset accessible for 80.5% of eligible candidates with AIS. With the implementation of four CSCs, accessibility to MT reached a maximum level of 97.7%. The number of CSCs per 1 million inhabitants reached 0.67 with seven CSCs, and 93.7% of eligible candidates with AIS underwent treatment with MT (table 2).

The visualized solution with seven CSCs highlights the location of patients without access to MT as yellow diamonds (online supplemental figure S1).

Health gains and costs in the base-case scenario

Compared with having only IVT ready hospitals and no MT services, implementation of one CSC would imply an annual incremental cost of EUR 27.6 million (from EUR 103.9 to 131.5 million per year) to produce health gains equal to 568 QALYs per year (from 2166 to 2734 QALYs per year). Apart from producing the largest health gain per year (690 QALYs), the strategy of seven CSCs would cause the least incremental cost and the highest annual INMB per patient (table 2). Thus the most cost effective strategy in the base case scenario was to implement all seven CSCs (aggregated INMB of EUR 44.6 million per year, figure 2A).

Deterministic sensitivity analysis

With the MT rate at 7%, only one intersection point appeared on the cost effectiveness acceptability frontier (CEAF) in the WTP range between EUR 0 and 200 000. Indeed, between EUR 0 and 15 301, the most cost effective strategy would be to not implement any CSCs. Thus the solution with seven CSCs is the most cost effective implementation strategy when the maximum WTP for a QALY gained reaches EUR 15 302 and up until EUR 200 000.

Seven CSCs was still the most cost effective implementation strategy when the MT rate was 10% or 12%, with the only noticeable difference on the CEAF being that the intersection between zero and seven CSCs appeared at EUR 12 387 and EUR 10 755, respectively.

Extended scenario analysis

With the possibility of complementing seven CSCs with up to 14 TSCs at IVT ready hospitals, the solution with 11 CSCs/TSCs was the most cost effective implementation strategy (online supplemental figure S2). The estimated INMB per patient was EUR

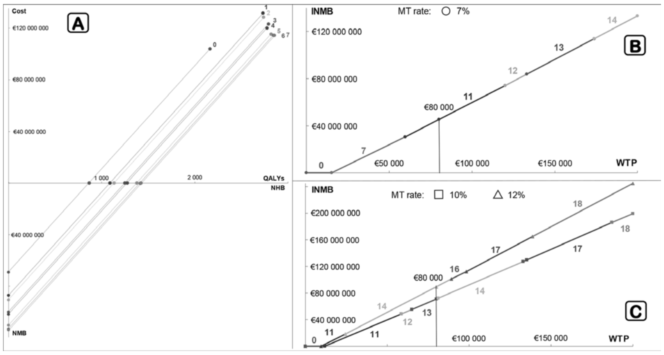

Figure 2 (A) Net benefit on the cost effectiveness plane with colour schemed indifference curves (one for each strategy) sloped at a maximum willingness to pay (WTP) of €80 000 compared with no mechanical thrombectomy (MT), with MT rate set at 7%. The net health benefit (NHB) and net monetary benefit (NMB) of each strategy is delineated by the intersection points of its indifference curve with the horizontal and vertical axis, respectively. The upper half of the chart displays the estimated yearly cost in € millions and quality adjusted life years produced with each strategy. (B) Cost effectiveness acceptability frontier (CEAF) of implementation strategies for a maximum of seven comprehensive stroke centers and 14 complementary thrombectomy capable stroke centers with MT rate fixed at 7%. It displays the highest aggregated annual incremental NMB compared with no MT in the WTP range from €0 to €200 000. (C) CEAFs when the MT rate shifts to 10% and 12%, respectively; all else as in (B).

36 863, and the CSC/TSC density reached 1.05 per 1 million inhabitants, bringing the proportion of patients with access to MT within 360 min from symptom onset up to 99.1% (online supplemental table S2). The CEAF displays how the solution with 11 CSCs/TSCs was the most cost effective implementation strategy in the maximum WTP range between EUR 59 505 and 120 083 (figure 2B). With MT rates at 10% and 12%, the most cost effective implementation strategy comprised 13 and 14 C-/TSCs, respectively (figure 2C).

DISCUSSION

This study showed that the optimal implementation strategy for CSCs in the base case scenario was 24/7 operability of MT services at all seven university hospitals in Sweden, generating substantial health gains for patients treated with MT. At four optimally located CSCs, patient accessibility to MT within 360 min from symptom onset reached the maximum level when patient transportations were handled by road ambulances.

The optimal solution for the CSC location–allocation problem depends on the objective function(s) chosen when solving it. Settling for a solution aimed at satisfying the condition of maximum population access to MT may require far fewer CSCs, but inevitably neglects the immense health gains to be made by implementing the most cost effective solution. Indeed, when making the cost effectiveness of MT the main objective, the optimal solution accounts for the diminishing clinical effectiveness of MT over the treatment time window and also the additional costs associated with worsened patient outcomes following treatment delays. Thus soaring health gains counterbalance the incremental costs of additional CSCs until reaching the most cost effective implementation solution. This was further corroborated in the extended scenario analysis. Relaxing the precondition of only including hospitals that met the required standards for CSC certification and allowing the model to solve for a maximum of 14 additional TSCs to the complete set of CSCs, revealed that the most cost effective implementation strategy comprised 11 CSCs/TSCs. Thus the optimal solution for the extended scenario represents a saturation point for health gains and cost savings to be made by the further addition of TSCs; incremental costs overshadowed expected health gains produced. Furthermore, the solutions of the extended scenario analysis improved patient accessibility to MT compared with the solutions for the base case scenario.

The analysis revealed that results were sensitive to variabilities in the maximum WTP and MT rate. The maximum WTP set for the base case scenario analysis was in line with the Swedish healthcare system settings. Because the consumption value of health varies across healthcare systems globally, and because the WTP for gaining a QALY has a great impact on the results, a cautious approach is needed for the transfer of results. A UK study concluded that when the implementation level of CSCs reached about 30%, the health benefits of MT started to exceed the costs over a 5 year period for a WTP set at £20 000 per QALY gained.[24] This breakpoint corresponds to a CSC density of roughly the same as the implementation of one CSC in the Swedish healthcare system. Indeed, NMB was positive with the implementation of only one CSC in this study.

Other cost effectiveness analyses based on pooled data from randomized controlled trials suggest that MT might be cost saving.[25] In contrast, this study explored real world patient level data and estimated for both the MS and DS pathways the cost and treatment effectiveness of CVT, IVT, MT, and IVT+MT in every patient and for each of the implementation strategies evaluated within the modelling framework of cost effectiveness analysis. Additionally, the analysis incorporated EMS transportation costs of triaging false positive patients to a CSC. This study encapsulates and quantifies the inevitable trade-off in costs and health effects between the MS and DS pathways. Taken together, the methodological novelties and the minor divergences in research approach may account for most of the observed differences in results compared with previous studies.

The MT rate was an important determinant when solving for the optimal implementation strategy after relaxing the requirement of only allowing MT services at certified CSCs, particularly when studied across the WTP range in the extended scenario analysis (figure 2B-C). Moreover, while the highest MT rate assumed in the sensitivity analyses might seem farfetched, recent evidence from regional studies demonstrate that it is achievable.[26]

In the base case scenario, both the maximum access solution and the most cost effective solution to the p median facility location–allocation problem had CSC densities well below the benchmark density of 1.0 per one million inhabitants estimated by the European Stroke Organization.[27] The CSC/TSC densities of the maximum access solution and the most cost effective solution of the extended analysis converged neatly with the benchmark density. Thus while the underlying rationale for a benchmark on implementation strategies for CSCs may rest on the incentive to maximize population access to MT, it would be further informed by the rationale of cost effectiveness analysis.

The addition of TSCs to complement the set-up of CSCs seems promising from a cost effectiveness perspective but requires further investigation. For instance, this study does not account for the potential adverse health effects that arise when patients with intracerebral hemorrhage are triaged to a TSC under the false presumption of a suspected large vessel occlusion, thereby delaying access to advanced critical care that CSCs may provide for some of these patients.[28] Moreover, with a large number of competing MT facilities, whether CSCs or CSCs/TSCs, the volume eligibility requirements for maintenance of good stroke quality of care is at risk of being undermined with potentially detrimental effects on patient outcomes following treatment with MT.[29]

To consolidate individual level registry data from several nationwide quality registers provided a solid foundation for conducting the analyses in the real world setting. This strengthens the accuracy and potential transferability of the results to inform healthcare decision making. However, lack of available registry data at the time of data collection precluded the incorporation of recent advances in the extended time window for MT up to 24 hours after stroke in the analysis of this study.[30]

Although the solvers provided by ArcGIS do not guarantee mathematically optimal solutions, it is unlikely that this had any major impact on the results; all numerical analyses were valid for the solutions presented.

Noteworthy study limitations included lack of data on MT for patients with wake-up stroke or in the extended time window, failure to account for potential adverse effects of bypassing the nearest stroke unit in triaging false positive patients, and increasing the number of CSCs/TSCs with regard to the maintenance of competencies for performing MT among neurointerventionalists.

CONCLUSION

The combination of optimization modelling and cost effectiveness analysis provides a powerful tool for configuring the extent and locations of CSCs (and TCSs). The most cost effective implementation of CSCs in Sweden was MT services at all seven university hospitals. Apart from the contextual premisses of demographics and geographics, this study showed the importance of accounting for the MT rate and the maximum WTP when solving for the optimal implementation strategy of CSCs (and TCSs) with respect to the cost effectiveness of MT in patients with AIS.

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Contributors NEV: study conceptualization and design, data acquisition, analysis and interpretation, drafting and writing of the manuscript, and guarantor for the overall content. TAG and PW: study conceptualization and design, and revision of the manuscript for intellectual content. L-ÅL: study conceptualization and design, revision of the manuscript for intellectual content, and study supervision.

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