**Mobile Stroke Unit treatment – cost effective or just an expensive hype?**

*Silke Walter MD1,2,3; Iris Q. Grunwald MD2; Stefan A. Helwig1; Andreas Ragoschke-Schumm MD1; Michael Kettner4; Mathias Fousse MD1; Martin Lesmeister1; Klaus Fassbender MD1*

1Department of Neurology, Saarland University, 66421 Homburg, Germany; 2Neurocience Unit, Faculty of Medicine, Anglia Ruskin University, Chelmsford, Essex, UK; Radiology Department, Southend University Hospital NHS Trust, Essex, UK; 3The Florey Institute of Neuroscience and Mental Health, The University of Melbourne, Melbourne, Australia; 4Department of Neuroradiology, Saarland University, 66421 Homburg, Germany

**Correspondence to:** Klaus Fassbender, Department of Neurology, University of the Saarland, Kirrbergerstrasse 1, 66421 Homburg, Germany. Klaus.Fassbender@uks.eu

**Abbreviations:** CT, computed tomography; EMS, emergency medical services; IV, intravenous; LVO, large vessel occlusion; MSU, Mobile Stroke Unit; quality-adjusted life years, QALY; POC, point-of-care; tPA, tissue plasminogen activator

**Key Words:** stroke, thrombolysis, mechanical recanalization, Mobile Stroke Unit, triage, pre-hospital treatment

**Word Count:** Total, 1900; abstract, 238; text, 1662

**List of Tables and Figures:** 1 figure

**Abstract**

*Purpose of review*

Acute stroke is a treatable disease. Nevertheless, only a minority of patients obtain guideline-adjusted therapy. One major reason is the small time window in which therapies have to be administered in order to reverse or mitigate brain injury and prevent disability. The Mobile Stroke Unit (MSU) concept, available for a decade now is spreading worldwide, comprising of ambulances, fully equipped with computed tomography, laboratory unit, and telemedicine connection to the stroke centre and staffed with a specialized stroke team. Besides its benefits, this concept adds a relevant amount of costs to health services.

*Recent findings*

The feasibility of the MSU and its impact on reducing treatment times have been proven by several research trials. In addition, pre-hospital stroke diagnosis including computed tomographic angiography analysis facilitates correct triage of patients, needing mechanical recanalization, thereby reducing the number of secondary or inter-hospital transfers. Even so, the concept is not yet fully implemented on a broad scale. One reason is the still open question of cost-effectiveness. There are assumptions based on the randomised trials of MSUs hinting towards an acceptable amount of money per quality-adjusted life years and overall cost-effectiveness. Up to now, neither a prospective analysis nor a consideration of secondary transfer avoidance is available.

*Summary*

The MSU concept is an innovative and impactful strategy to improve stroke management, especially in times of constraints in healthcare economics and health care professionals. Prospective information is needed to answer the cost-effectiveness question satisfactorily.

**Introduction**

**Need for new stroke management concepts**

Acute stroke is the most common cause for permanent disability in adults and one of the main causes of death (1••). Due to extensive research in the field, stroke treatment is possible, but treatment success is strongly dependent on an early therapy initiation.

Effective treatment options for ischemic stroke include intravenous (IV) thrombolysis with tissue plasminogen activator (tPA), as evidenced by several large randomized trials (2, 3). Moreover, if the stroke is caused by intracerebral large vessel occlusion (LVO), mechanical recanalization is a highly effective treatment (4•). Both treatments have been shown to not only improve clinical outcome but also to be highly cost-effective (14–24). However, IV thrombolysis and mechanical recanalization in the case of LVO are much more effective, the earlier they are administered, best in the first golden hour after symptom onset (5••), when the probability of survival without any disability is the highest.

Patients with intracranial haemorrhage are currently treated either symptomatically or get neurosurgical intervention (6, 7•). But, also in this field, research is developing: several clinical trials investigated the usefulness of anticoagulant reversal or reversal of effects of novel anticoagulants. Recently, the large randomised, placebo-controlled TICH-2 trial, examining the effect of tranexamic acid in acute haemorrhagic stroke did not show any significant clinical benefit (8). Nevertheless, further trials, focusing on e.g. an ultra-early drug administration (NCT03385928) are following.

However, most stroke patients arrive in the hospital too late for any type of acute stroke treatment. Only an estimated 19–60% of stroke patients present within 3 hours after symptom onset (9, 10). In addition, hospital-based pathways are also far from efficient or available 24/7; although alarm-to-door times are reduced to 45 minutes in the large national United States Get-With-The-Guidelines-Stroke-Population, door-to-tPA times are still reported to be 71 min (median; interquartile range 54–94; (5••)). This leads to dramatic underuse of the available therapies. Only 3.4–9.1% of acute ischaemic patients receive thrombolysis (11, 12) and only 1–2% (13% of patients with LVO) are treated with intra-arterial recanalizing methods (13••).

Unfortunately, just speeding up of the intra-hospital management does not present an overall solution to the evident treatment gap in acute stroke. Apart from the fact that many patients reach the hospital too late for effective treatment, endovascular and neurosurgical treatment options are only available in very few highly specialized neurovascular centres (e.g., comprehensive stroke centres). Thus, if the patient is triaged to a hospital without these advanced treatment options, secondary or inter-hospital transfers to such centres are required, thereby causing additional detrimental treatment delays and costs. On the other hand, triage of every stroke patient to a neurovascular centre would congest the emergency rooms of the neurovascular centre, increasing staff burden and causing treatment delays. Therefore, a rational triage of stroke patients according to the individual needs of the patient is of high medical and financial relevance.

**Mobile Stroke Unit concept**

Approximately 15 years ago, the concept of a Mobile Stroke Unit (MSU), an ambulance equipped with computed tomography (CT), point-of-care (POC) laboratory unit, and telemedicine connection to the closest specialised stroke centre, staffed with a team highly specialised in acute stroke treatment has been first published (25). Then, 10 years ago, the first MSU was deployed, investigating feasibility and time efficiency of pre-hospital stroke management in a randomised trial (26, 27••). Time from stroke symptom onset to treatment was reduced by 50% (27••) even when compared to an optimised in-hospital protocol that included a dedicated stroke-room, hospital pre-notification and hand-over, neurological and laboratory (POC) examination, and thrombolysis of the patient at the CT scanner [16, 17]. A second randomised trial confirmed this pronounced time efficiency (28••).

With MSU implementation, a new era in stroke treatment started, which enabled more than 50% of patients to be treated within the golden hour, first 60 minutes after symptom onset, as compared with as less than 4% in the control group or 1.3% reported in the Get-With-The-Guidelines-Stroke registry (5••).

**MSU projects worldwide**

The concept of MSU for pre-hospital acute stroke treatment is currently implemented in around 20 sites worldwide (Fig. 1). The implementation of MSUs at more sites is underway. All projects are adapted to the local emergency medical service EMS system. In most European countries, EMS operates with emergency physicians. For example, the Norwegian Air Ambulance Foundation, which is responsible for a large area of Norway’s EMS, started an MSU service in 2012 with trained anaesthesiologists on-board responsible for neurological examination and performance of CT scans (29•). In contrast, MSU projects in Anglo-American settings mainly work with paramedics or intensive care assistants, stroke nurses, radiology technicians, and telemedicine connection to the specialist physician at the specialised hospital. The first US centre, at the University of Texas Houston, demonstrated that 31% of ischemic stroke patients could be treated within the first 60 minutes after symptom onset (30). The Houston group, which initially employed a stroke physician as part of the MSU team, later replaced this with remote stroke experts in the hospital connected via telemedicine. The group also has initiated a randomized trial investigating the effects of MSU treatment on clinical outcomes (31••). The second US centre, at the Cleveland Clinic, runs the MSU with a radiology technician, paramedic, and stroke nurse. Neurologists and neuroradiologists are consulted by telemedicine connection (7, 32). The implementation of MSUs in such a variety of different regions will help to gain further understanding of best settings, e.g. answer the question of MSU usefulness in urban versus rural or remote areas.

Indeed, with the amount of variability in settings and configurations, the Pre-hospital Stroke Treatment Organization (PRESTO; (33•)) was formed to implement international high quality operating procedures of MSU use and facilitate international cooperation between sites.

**New directions of MSU use**

Hastening of acute ischemic stroke thrombolysis is not the only useful effect of MSU prehospital diagnostic work-up and treatment. In addition, MSU service can help to reduce treatment disparity in rural and remote areas without highly specialised stroke service facilities (34••). Another important benefit of MSUs is the possibility to identify and triage patients with LVO to the closest comprehensive stroke centre for intraarterial treatment based on prehospital CT angiography results or patients with stroke mimics in order to avoid unnecessary admissions to tertiary care hospitals (35••).

**Cost-effectiveness of MSU treatment**

One of the main questions for novel therapies always concerns cost efficiency. It has to be kept in mind that there are different cost-effectiveness patterns: low costs with high effectiveness in treatment optimisation usually results in a rapid and broad-scale implementation throughout health care systems. Extremely high costs or very low costs, but low clinical effectiveness usually stops or dampens treatment implementation. The decision of implementation is more difficult when costs are medium to high, but clinical effectiveness is also compelling. It then depends on real costs and ethical pressure to implement.

The MSU concept has been proven to reduce times to proven stroke treatments. Clinical effectiveness of proven stroke treatments is highly dependent on time from onset to treatment. Thrombolysis within the golden hour after symptom onset has been described to be associated with a higher probability of discharge to home (adjusted odds ratio, 1.25; 95% confidence interval, 1.07–1.45), independent ambulation at discharge (adjusted odds ratio, 1.22; 95% confidence interval, 1.03–1.45), and freedom from disability (modified Rankin Scale 0–1) at discharge (adjusted odds ratio, 1.72; 95% confidence interval, 1.21–2.46) when compared to later treatment times (5••).

The willingness to pay threshold is described with € 50,000 per quality-adjusted life years (QALY) (36). As reference point, cost-effectiveness ratio for tPA treatment has been described to be up to $48,676 per QALY, depending on the age at treatment (37). There are two published analyses concerning MSU cost-effectiveness. Both show an advantage of MSU use when incorporating savings as a result of clinical outcome improvement from earlier thrombolysis. Cost-effectiveness analysis based on the first randomised trial results were based on direct cost savings in relation to incremental direct costs associated with a pre-hospital stroke treatment on a 1-year basis. It was described that compared to the standard care control group, the MSU group had a 34% increase of patients treated within the first 90 minutes after symptom onset, leading to an assumption of 18.6 additional patients that would have benefited in the catchment area with 361,629 inhabitants and 371 acute ischemic stroke patients. Different staffing scenarios ranging from a neurologist and (neuro-) radiologist on the scene to reduced personnel with only one paramedic and one radiology technician were considered (Figure 2). Interestingly, even with the first experimental staffing configuration including 2 physicians (neurologist and neuroradiologist) onboard, cost-benefit ratio was 1.96, demonstrating cost efficiency (38••). The cost-benefit ratio further increased, if staff was reduced by replacement of onboard physicians by remote experts in the hospital connected via telemedicine. The maximal cost-benefit ratio ranged between 2.16 and 6.85 when operating radiuses between 43.01 and 64.88 km. Although efficacy apart from the radius of MSU action correlated with population density, cost-benefit ratio was >1 even in rural areas with a population density of 79 inhabitants per km2.

The second analysis is based on the Phantom-S trial results (28••). The costs of the MSU concept were calculated with €963,954 per year. Based on the pooled analysis of thrombolysis trial (3) it was assumed that due to a higher number of patients thrombolysed with the MSU concept compared to standard care (310 of 1,070 versus 225 of 1,041) and in addition an earlier treatment (48.1% versus 37.4% within the first 90 min), the number of relevant disability (disability defined by a modified Rankin Scale value of > 1) was avoided in 18 more patients compared to standard in-hospital treatment, resulting in 29.7 saved QALYs. These calculations lead to incremental cost-effectiveness ratio of €32,456 per QALY (39••), which is well within the accepted pay threshold.

Both of these cost-effectiveness analyses base their findings on data from the large thrombolysis trials and assume, based on this, a potential clinical benefit of MSUs. A first trial that is gathering prospective data on cost efficiency is the BEST-MSU trial, coordinated at Houston, Texas, USA (40•). It is expected that important questions on cost efficiency will be answered by this trial, although in the future there is much room for reduction of MSU costs. This could be achieved for example by reduction of costs of still very expensive ambulances if there were a larger demand and competition among producers. In addition, MSU staffing costs can be reduced, if the MSU doctors or radiology technicians are involved in routine clinical work while waiting for the next pre-hospital MSU job.

**Conclusions**

The MSU concept is a useful strategy to improve stroke management, leading to a dramatic reduction in symptom onset to treatment times and thrombolysis rates. Moreover, it may be relevant in ensuring the correct triage decision is made in regard to the most appropriate destination hospital for suspected acute stroke patients. Nevertheless, cost efficiency has so far only been modelled by analysis of results of the first two MSU studies’ results and current knowledge of the time-dependent clinical benefits of stroke treatment. Results of ongoing prospective trials specifically with economical endpoints are eagerly awaited.

**Compliance with Ethical Standards**

**Human and Animal Rights and Informed Consent**

All reported studies with human subjects performed by the authors have been previously published and complied with all applicable ethical standards (including the Helsinki declaration and its amendments and national research committee standards).

**Conflict of Interest** Iris Q. Grunwald is the co-founder and Medical Director of Brainomix Ltd., UK. There are no conflicts regarding this paper. All other authors declare no conflicts of interest.

**Figure legends**

**Figure 1: World map of** stroke centres using MSU service. Blue circles represent centres with active service, red triangles centres with MSU in planning.

**Figure 2:** Different on-scene staffing models and their cost-benefit ratio in correlation to the catchment area. (Scenario 1: MSU staffed with 1 neurologist, 1 neuroradiologist, 1 paramedic supported by general EMS ambulance staffed with 1 emergency physician, 3 paramedics; Scenario 2: MSU: staffed with 1 neurologist, 1 radiographer, 1 paramedic supported by general EMS ambulance staffed with 2 paramedics; Scenario 3: MSU alone staffed with 1 physician, 1 radiographer, 1 paramedic; Scenario 4: MSU alone staffed with 1 radiographer, 2 paramedics; Scenario 5: MSU alone staffed with 1 radiographer, 1 paramedic). Permission granted by S. Karger AG, Basel.

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