Stroke FOUNDATION

Clinical Guidelines for Stroke Management

Chapter 1 of 8:
Pre-hospital care

This is the first in a series of eight chapters that provide evidence-based recommendations for management of stroke and TIA in adults.

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Disclaimer

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Strong recommendation

All stroke patients potentially eligible for reperfusion therapies should have an ambulance dispatched as an immediate response and be managed as a time critical emergency. (Berglund et al 2012 *[9]*)

Strong recommendation Updated evidence, no change in recommendation

a. Ambulance services should preferentially transfer suspected stroke patients to a hospital capable of delivering reperfusion therapies as well as stroke unit care. (Chowdhury et al 2021 *[23]*)
b. Ambulance services should pre-notify the hospital of a suspected stroke case where the patient may be eligible for reperfusion therapies. (Chowdhury et al 2021 *[23]*)

Info Box

Practice point

- General practitioners are encouraged to educate reception staff in the FAST stroke recognition message and to redirect any calls about suspected acute stroke to 000.
- Regular stroke education may improve patient identification by clinicians. (Oosteama et al 2019*[25]*; Chowdhury et al 2021*[23]*)

Strong recommendation New

For patients in major cities with suspected stroke who are potentially eligible for reperfusion therapies, pre-hospital treatment in a mobile stroke unit is recommended. (Turc et al 2022 *[32]*)

Remark:
Approved by NHMRC August 2022.

Glossary and abbreviations

Introduction

The Stroke Foundation is a national charity that partners with the community to prevent, treat and beat stroke. We stand alongside stroke survivors and their families, healthcare professionals and researchers. We build community awareness and foster new thinking and innovative treatments. We support survivors on their journey to live the best possible life after stroke.

We are the voice of stroke in Australia and we work to:

- Raise awareness of the risk factors, signs of stroke and promote healthy lifestyles.
- Improve treatment for stroke to save lives and reduce disability.
- Improve life after stroke for survivors.
- Encourage and facilitate stroke research.
- Advocate for initiatives to prevent, treat and beat stroke.
- Raise funds from the community, corporate sector and government to continue our mission.

The Stroke Foundation has been developing stroke guidelines since 2002 and in 2017 released the fourth edition. In order for the Australian Government to ensure up-to-date, best-practice clinical advice is provided and maintained to healthcare professionals, the NHMRC requires clinical guidelines be kept current and relevant by reviewing and updating them at least every five years. As a result, the Stroke Foundation, in partnership with Cochrane Australia, have moved to a model of living guidelines, in which recommendations are continually reviewed and updated in response to new evidence. This approach was piloted in a three year project (July 2018 - June 2021) funded by the Australian Government via the Medical Research Future Fund.

This online version of the *Clinical Guidelines for Stroke Management* updates and supersedes the Clinical Guidelines for Stroke Management 2017. The Clinical Guidelines have been updated in accordance with the *2011 NHMRC Standard for clinical practice guidelines* and therefore recommendations are based on the best evidence available. The Clinical Guidelines cover the whole continuum of stroke care, across 8 chapters.

Review of the Clinical Guidelines used an internationally recognised guideline development approach, known as GRADE (**G**rading of **R**ecommendations **A**ssessment, **D**evelopment and **E**valuation), and an innovative guideline development and publishing platform, known as MAGICapp (**Ma**king **G**rade the **I**rresistible **C**hoice). GRADE ensures a systematic process is used to develop recommendations that are based on the balance of benefits and harms, patient values, and resource considerations. MAGICapp enables transparent display of this process and access to additional practical information useful for guideline recommendation implementation.

Purpose

The *Clinical Guidelines for Stroke Management* provides a series of best-practice recommendations to assist decision-making in the management of stroke and transient ischaemic attack (TIA) in adults, using the best available evidence. The Clinical Guidelines should not be seen as an inflexible recipe for stroke management; rather, they provide a guide to appropriate practice to be followed subject to clinical judgment and patient preferences.

Scope

The Clinical Guidelines cover the most critical topics for effective management of stroke, relevant to the Australian context, and include aspects of stroke management across the continuum of care including pre-hospital, assessment and diagnosis, acute medical and surgical management, secondary prevention, rehabilitation, discharge planning, community participation, and management of TIA. Some issues are dealt with in more detail, particularly where current management is at variance with best practice, or where the evidence needs translation into practice.

The Clinical Guidelines do not cover:

- Subarachnoid haemorrhage;
- Stroke in infants, children and youth, i.e. <18 years old (refer to Australian Childhood Stroke Advisory Committee, *Guideline for the diagnosis and acute management of childhood stroke – 2017*, and Victorian Subacute Childhood Stroke Advisory Committee, *Guideline for the subacute management of childhood stroke – 2019*, https://informme.org.au/Guidelines/Childhood-stroke-guidelines); or
- Primary prevention of stroke. (Refer to *Guidelines for the management of absolute cardiovascular disease risk 2012* (National Vascular Disease Prevention Alliance *[5]*) - https://informme.org.au/en/Guidelines/Guidelines-for-the-assessment-and-management-of-absolute-CVD-risk, and *Guideline for the diagnosis and management of hypertension in adults 2016* (Heart Foundation *[6]*) - https://www.heartfoundation.org.au/for-professionals/clinical-information/hypertension).

Target audience

The Clinical Guidelines are intended for use by healthcare professionals, administrators, funders and policy makers who plan, organise and deliver care for people with stroke or TIA during all phases of recovery.

Development
The Guidelines are published in eight separate chapters:
Pre-hospital care
Early assessment and diagnosis
Acute medical and surgical management
Secondary prevention
Rehabilitation
Managing complications
Discharge planning and transfer of care
Community participation and long-term care
The Clinical Guidelines have been developed according to processes prescribed by the National Health and Medical Research Council (NHMRC) under the direction of an interdisciplinary working group. Refer to the document on InformMe that details the Interdisciplinary Working Group Membership and Terms of Reference.

Use
The primary goal of the Clinical Guidelines is to help healthcare professionals improve the quality of the stroke care they provide.

Guidelines differ from clinical or care pathways (also referred to as critical pathways, care paths, integrated care pathways, case management plans, clinical care pathways or care maps). Guidelines are an overview of the current best evidence translated into clinically relevant statements. Care pathways are based on best practice guidelines but provide a local link between the guidelines and their use.

In considering implementation of the Guidelines at a local level, healthcare professionals are encouraged to identify the barriers, enablers and facilitators to evidence-based practice within their own environment and determine the best strategy for local needs. Where change is required, initial and ongoing education is essential and is relevant to all recommendations in the Guidelines.

Aboriginal and Torres Strait Islander People
Refer to the document on InformMe for information regarding Aboriginal and Torres Strait Islander people.

Decision-making
Stroke survivors should be treated in accordance with the principles of shared decision-making contained within the *Acute Stroke Care Clinical Standard*, *Acute Stroke Services Framework 2019* and *Rehabilitation Stroke Services Framework 2013*, which include, among other things, that treatment should be patient-centred. Therefore, stroke survivors should be involved in decisions about their care at all times; but where they do not have capacity, or have limited capacity, family members should be involved in the decision-making.

Consent
The principles of informed consent underpin these Clinical Guidelines and therefore the wording of the recommendations are directed at the healthcare professional; that is, the intervention should/may be used, rather than offered, for the stroke patient. For patients with aphasia and/or cognitive disorders requiring formal consent, easy English or aphasia-friendly written versions of an information sheet and consent form should be offered and clearly explained to patients and their families in order to assist understanding and agreement.

Endorsement
The Clinical Guidelines have been endorsed (based on the 2017 version) by a number of organisations and associations. Refer to the document on InformMe that details the organisations formally endorsing the Clinical Guidelines.

Evidence gaps
Refer to the document on InformMe that details the gaps in evidence identified, noting areas for further research.

Reports
Refer to documents on InformMe - Technical Report, Administrative Report and Dissemination and Implementation Report.

Resources
Refer to documents on InformMe that provide supporting resources to assist with implementation of the Clinical Guidelines.

Publication Approval

Australian Government

National Health and Medical Research Council

The 2017 guideline recommendations were approved by the Chief Executive Officer of the National Health and Medical Research Council (NHMRC) on 25 July 2017 under Section 14A of the National Health and Medical Research Council Act 1992 with a subsequent amendment approved on 22 November 2017. Since moving to a continual (living) guideline model, further updates have been approved:

- 9 July 2018 (updated recommendations for neurointervention)
- 7 November 2019 (updated recommendations for thrombolysis, acute antiplatelet therapy, and patent foramen ovale management)
- 11 February 2021 (updated recommendations for oxygen therapy, cholesterol lowering targets, new acute antiplatelet agent, shoulder pain and weakness)
- 7 July 2021 (updated recommendations for standing, antiplatelet therapy, and activities of living)
- 22 December 2021 (updated recommendations for pre-hospital care, acute telehealth, head position, telehealth for rehabilitation, swelling of extremities, memory, management of atrial fibrillation, lifestyle modifications, and virtual reality for arm function)
- 5 August 2022 (updated recommendations for pre-hospital care [mobile stroke unit], assessment for rehabilitation, aphasia, dysarthria, prevention and treatment for depression, treatment of anxiety, personality and behaviour, pressure injury)
- 6 December 2022 (updated recommendations for aphasia and incontinence).
- 27 July 2023 (updated recommendations for driving, neurointervention, oxygen therapy, and central post-stroke pain).

In approving the guidelines recommendations the NHMRC considers that they meet the NHMRC standard for clinical practice guidelines. This approval is valid for a period of five years.

NHMRC is satisfied that the guideline recommendations are systematically derived, based on identification and synthesis of the best available scientific evidence and are developed for health professionals practising in an Australian health care setting.

This publication reflects the views of the authors and not necessarily the views of the Australian Government.

Disclaimer

These Clinical Guidelines are a general guide to appropriate practice, to be followed subject to the clinician's judgment and the patient's preference in each individual case. The Clinical Guidelines are designed to provide information to assist decision-making and are based on the best evidence available at the time of development.

Funding

The Stroke Foundation gratefully acknowledges the financial assistance provided to establish the living guidelines between 2018-2021 by the Australian Government, Medical Research Future Fund. Funding is currently being provided by the Australian Living Evidence Consortium (https://livingevidence.org.au) to assist the continuation of the Stroke Living Guidelines. The development of the final recommendations are not influenced by the views or interests of any funding body.

Citation

Stroke Foundation. Clinical Guidelines for Stroke Management. Available at https://informme.org.au/en/Guidelines/Clinical-Guidelines-for-Stroke-Management. Accessed [insert date, month and year and if applicable specific sections or chapters].

Methodology

Development of questions

Questions have been extensively developed and reviewed over the four iterations of the guidelines. In this 'living' phase the Content Steering Group reviews the PICO questions on an annual basis. The clinical questions are listed at the start of each chapter. Individual PICOs (population, intervention/s, comparator, outcomes) are listed in the research evidence section as related to each topic or recommendation.

Literature identification

On a monthly basis, we monitor the literature for relevant, new evidence by screening all randomised controlled trials or systematic reviews related to stroke published in the Pubmed database. One member of the project team initially screens all abstracts and excludes clearly irrelevant studies. Potentially included studies are allocated to relevant topics covered by the guidelines and a second member of the project team reviews and confirms included studies prior to sending to the relevant working group members. In addition, each month new economic studies and studies related to patient values and preferences are also captured.

Clinical expert review

Where new evidence has been identified by the project team a summary is sent to content experts who review and make a final decision to include or exclude the study and also to assess the potential impact of the new evidence on current recommendations. As a result of this assessment one of two options will be communicated for each topic:

a. New evidence is unlikely to change current recommendations: review and potentially integrate information in the next review cycle; or
b. New relevant evidence may change current recommendations: rapidly review.

Data extraction, updating evidence summary and GRADE profile

For rapid updates, the project team incorporates the new evidence into the existing body of evidence by:

- Updating the Summary of Findings table including the risk of bias assessment
- Review any additional studies related to Preferences and values of patients on the topic

Concurrently members of the economic working group review newly published economic studies.

The project team then drafts changes to the overall summary (GRADE profile). This profile is then reviewed and modified by clinical content experts and people with relevant lived experience (consumers). Finally changes to the changes to the recommendation, rationale and practical considerations are considered, discussed and agreed.

Draft changes are then circulated to the wider expert working groups (including consumer panel) for internal review. Once signed off by the Steering Group a period of public consultation is undertaken. Feedback is then reviewed and any changes made in response to feedback before finally submitting to the National Health and Medical Research Council (NHMRC) for approval.

Brief summary of GRADE

The Guidelines were developed following the GRADE methodology (Grading of Recommendations, Assessment, Development and Evaluation).

GRADE 'evidence to decision' framework includes a minimum of four factors to guide the development of a recommendation and determine the strength of that recommendation:

1.
The balance between desirable and undesirable consequences.
2.
Confidence in the estimates of effect (quality of evidence).
3.
Confidence in values and preferences and their variability (clinical and consumer preferences).
4.
Resource use (cost and implementation considerations).

For full details of how GRADE is used for developing clinical recommendations, refer to the GRADE handbook, available at: http://gdt.guidelinedevelopment.org/app/handbook/handbook.html.

Strength of recommendations

The GRADE process uses only two categories for the strength of recommendations, based on how confident the guideline panel is that the "desirable effects of an intervention outweigh undesirable effects [...] across the range of patients for whom the recommendation is intended" (GRADE Handbook):

- **Strong** recommendations: where guideline authors are certain that the evidence supports a clear balance towards either desirable or undesirable effects; or
- **Weak** recommendations: where the guideline panel is uncertain about the balance between desirable and undesirable effects.

These strong or weak recommendations can either be for or against an intervention. If the recommendation is against an intervention this means it is recommended NOT to do that intervention. There are a number of recommendations where we have stated that the intervention may only be used in the context of research. We have done this because these are guidelines for clinical practice, and while the intervention cannot be recommended as standard practice at the current time, we recognise there is good rationale to continue further research.

The implications of a strong or weak recommendation for a particular treatment are summarised in the GRADE handbook as follows:
Table 1: Implications of GRADE recommendation categories (for a positive recommendation) for patients, clinicians and policy makers. Source: GRADE Handbook (http://gdt.guidelinedevelopment.org/app/handbook/handbook.html)

	Strong Recommendation	**Weak Recommendation**
For patients	Most individuals in this situation would want the recommended course of action and only a small proportion would not.	The majority of individuals in this situation would want the suggested course of action, but many would not.
For clinicians	Most individuals should receive the recommended course of action. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.	Recognise that different choices will be appropriate for different patients, and that you must help each patient arrive at a management decision consistent with her or his values and preferences. Decision aids may well be useful helping individuals making decisions consistent with their values and preferences. Clinicians should expect to spend more time with patients when working towards a decision.
For policy makers	The recommendation can be adapted as policy in most situations including for the use as performance indicators.	Policy making will require substantial debates and involvement of many stakeholders. Policies are also more likely to vary between regions. Performance indicators would have to focus on the fact that adequate deliberation about the management options has taken place.

For topics where there is either a lack of evidence or insufficient quality of evidence on which to base a recommendation but the guideline panel believed advice should be made, statements were developed based on consensus and expert opinion (guided by any underlying or indirect evidence). These statements are labelled as 'Practice statements' and correspond to 'consensus-based recommendations' outlined in the NHMRC procedures and requirements.

For topics outside the search strategy (i.e. where no systematic literature search was conducted), additional considerations are provided. These are labelled 'Info Box' and correspond to 'practice points' outlined in the NHMRC procedures and requirements.

Explanation of absolute effect estimates used
The standardised evidence profile tables presented in the Clinical Guidelines include "Absolute effect estimates" for dichotomous outcomes. These represent the number of people per 1000 people expected to have the outcome in the control and intervention groups. This estimated risk in people receiving the intervention is based on a relative effect estimate which might be adjusted, e.g. to account for baseline differences between participants or when effect estimates have been pooled from different studies in a systematic review and adjusted to account for the variance of each individual estimate. Therefore, this estimated risk in the intervention group may differ from the raw estimate of the intervention group risk from the corresponding study. The estimated risk reflects the best estimate of the risk in the relevant population, relative to the risk observed among patients receiving the control or comparator intervention.

Wherever possible (i.e. when the relevant study reported enough information to allow the calculation to be done), these estimates were calculated using the following procedure:
1.
Obtain the relative effect estimate (odds ratio or relative risk) and confidence interval from the best available study (systematic review or primary study) providing evidence about the effects of the intervention.
2.
Use the observed number of events in the control group of the same study to calculate a baseline risk per 1000 people (or "assumed

control risk").
3.
Calculate an estimate of the corresponding risk per 1000 in people receiving the intervention using the relative effect estimate. This can be done using methods based on the formulas for calculating absolute risk reductions provided in the *Cochrane Handbook for Systematic Reviews of Interventions* (http://handbook.cochrane.org/). Applying the same calculations to the upper and lower bounds of the confidence interval for the relative effect estimate gives a confidence interval for the risk in the intervention group, which is then used to calculate the confidence interval for the difference per 1000 people, reported in the evidence tables.

Cost effectiveness summaries
There are several important points to consider when interpreting the cost-effectiveness information provided in the *Resources and Other Considerations* sections of the Clinical Guidelines.

Firstly, an intervention can be cost-effective without being cost-saving. This means that although there is an additional cost for the health benefits gained from the intervention, the intervention is still considered worthwhile. The incremental cost-effectiveness ratios (ICER) presented (e.g. cost per quality adjusted life year gained) are an indication of the cost-effectiveness or "value-for-money", with lower ICERs indicating better cost-effectiveness of an intervention.

Secondly, whether or not the intervention is cost-effective is a judgment call; and should reflect a society's willingness-to-pay to have the intervention for the potential outcomes achieved. An ICER that is approximately or equivalent to US$50,000 has been commonly used by researchers in the past as a threshold for judging an intervention as being cost-effective (http://www.nejm.org/doi/full/10.1056/NEJMp1405158#t=article). However, no scientific basis for this threshold exists and actual willingness-to-pay may differ. For example, in a survey of 1000 Australian respondents conducted in 2007, the willingness-to-pay for an additional quality adjusted life year in Australia was estimated to be $64,000 (https://www.ncbi.nlm.nih.gov/pubmed/19382128).

Thirdly, there is no absolute threshold for determining whether an intervention should be funded based on the ICER (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5153921/). ICERs are only one of the major factors considered in priority setting (the process to decide which interventions should be funded within a given resource constraint). Other considerations include affordability, budget impact, fairness, feasibility and other factors that are important in the local context (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5153921/).

Lastly, in areas where there are no data from economic evaluations that support the recommendations or practice statements, it remains unclear whether the additional costs of providing the intervention above usual care for the additional potential benefits obtained is justified. However, this should not detract from implementing the Clinical Guideline recommendations.

Use of language related to timing of interventions
***Immediate*:** without delay, or within minutes, not hours (life critical action required).
***Urgent*:** minutes to several hours (immediate action but not life critical).
***Very early*:** within hours and up to 24 hours.
***Early*:** within 48 hours.

For all Clinical Guideline recommendations we make the assumption that healthcare professionals will be appropriately qualified and skilled to carry out the intervention.

Clinical question

1. What interventions by paramedics improve outcomes for people with stroke?

Pre-hospital care

Early recognition of stroke symptoms, the subsequent response of individuals to having a stroke or transient ischaemic attack (TIA), and the timing and method by which people are transferred to hospital are critical to ensuring optimal outcomes for patients.

In this hyper-acute phase of care, the ambulance service has a central coordinating role as typically 70% of stroke patients arrive by ambulance (Stroke Foundation 2015 *[20]*). In 2015, hospitals reported only 34% of patients arrived at hospital within 3-hours of stroke onset (Stroke Foundation 2015 *[20]*). Stroke patients should not only receive a high triage priority, comparable to other similarly lethal or disabling medical emergencies, but the ambulance service should also facilitate early notification to the receiving hospital and ensure that a hospital with a stroke unit is selected, where possible.

Currently, 60% of Australian hospitals report arrangements with local ambulance services for emergency/rapid transfer to hospital for stroke patients with acute stroke over and above the regular system, and 7% report no arrangements but have agreement to bypass a hospital for another stroke specific service (Stroke Foundation 2015 *[20]*). Ambulance services throughout Australia are state-based and have differing geographic, clinical and administrative arrangements. Ambulance services should continue to work closely with their local clinical networks to establish pre-notification strategies for stroke.

Strong recommendation

All stroke patients potentially eligible for reperfusion therapies should have an ambulance dispatched as an immediate response and be managed as a time critical emergency. (Berglund et al 2012 *[9]*)

Practical Info

Suspected stroke patients potentially eligible for reperfusion therapies should have an ambulance dispatched as an immediate response and managed accordingly. Factors to consider are the time from stroke onset to likely arrival in hospital – large vessel occlusion patients may be treated up to 24h after the time the patient was last known to be well. Thrombolysis may be appropriate up to 9 hours after the time last seen well or the midpoint of sleep. Large vessel occlusion triage scores may assist in identifying likely large vessel occlusion patients in late time windows who should receive prioritised transport. Premorbid functional status should also be considered as severely disabled patients are unlikely to receive reperfusion therapies. Local stroke networks and emergency services should develop protocols that operationalise this recommendation with respect to regional resources.

Evidence To Decision

Benefits and harms

Substantial net benefits of the recommended alternative

A single study, well conducted, terminated early having reached statistical significance (Berglund et al 2012 *[9]*). The study supports dispatching suspected stroke cases as priority one and supports upgrading to priority one when suspected cases are encountered by ambulance crews. No harms were identified, specifically no adverse impact on response times for the rest of the ambulance service.

Certainty of the Evidence

Moderate

Good quality single randomised controlled trial terminated early as it reached statistical significance. We are moderately confident the effect estimates are a true representation of the results.

Values and preferences

No substantial variability expected

It is expected that all suspected stroke patients would want to be managed with highest level of priority.

Resources and other considerations

No important issues with the recommended alternative

<u>Resources considerations</u>

No literature to understand or describe the potential economic implications of this recommendation was identified.

Implementation considerations

There are clinical indicators collected in the National Stroke Audit on the median time from stroke onset to the patient's arrival in the emergency department, and whether or not patients arrived by ambulance. There is also an organisational indicator collected on whether hospitals have arrangements in place with local ambulance services for the rapid transfer of patients with acute stroke over and above the regular system. For hospitals where there are no arrangements in place, an organisational indicator is collected to determine whether there is an agreement to bypass the hospital for another stroke-specific service.

Rationale

Ambulances dispatched as an immediate response will result in reduced time to hospital arrival and allow for more patients to be considered for reperfusion therapies.

Clinical Question/ PICO

Population:	Adults with suspected stroke
Intervention:	Emergency medical dispatch - priority Level 1 (immediate ambulance dispatch)
Comparator:	Emergency medical dispatch - standard priority (Level 2 - within 30 minutes)

Summary

A single, well-conducted study by Berglund et al (2012) *[9]*, was terminated as it reached statistical significance early. The study supports dispatching suspected stroke cases priority one and supports upgrading to priority one when non-suspected cases are encountered by ambulance crews. No harms were identified, specifically no adverse impact on response times for the rest of the ambulance service.

NB: Berglund et al (2012) did not report an odds ratio for the thrombolysis frequency outcome. The relative effect estimate used here was manually calculated from the reported numbers of events.

Outcome Timeframe	**Study results and measurements**	**Comparator** Level 2 - within 30 minutes	**Intervention** Immediate ambulance dispatch	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Thrombolysis frequency [1] On arrival of Stroke Unit 7 Critical	Odds ratio 2.8 (CI 95% 1.68 — 4.68) Based on data from 496 participants in 1 studies. [2] (Randomized controlled) Follow up: On arrival at stoke unit.	105 per 1000 Difference:	247 per 1000 **142 more per 1000** (CI 95% 249 more — 60 more)	**Moderate** Due to serious imprecision [3]	Immediate ambulance dispatch increases thrombolysis rate
Door to needle time Time to thrombolysis 7 Critical	Measured by: Time Lower better Based on data from 52 participants in 1 studies. [4] (Randomized controlled) Follow up: Discharge.	57 Minutes (Median) Difference:	58 Minutes (Median) **MD 1 higher** CI 95%	**Moderate** Due to serious imprecision [5]	Immediate ambulance dispatch may have little or no difference on door to needle time
Time - call to stroke unit Stroke Unit arrival 7 Critical	Measured by: Time Lower better Based on data from 245 participants in 1 studies. [6] (Randomized controlled) Follow up: Discharge.	132 Minutes (Median) Difference:	106 Minutes (Median) **MD 26 lower** CI 95%	**Moderate** Due to serious imprecision [7]	Immediate ambulance dispatch decreases time - call to stroke unit

1. Assessment with Face-Arm-Speech-Time (FAST)
2. Primary study[9]. **Baseline/comparator:** Primary study.
3. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Only data from one study. **Publication bias: no serious.**
4. Primary study[9]. **Baseline/comparator:** Control arm of reference used for intervention.
5. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Only data from one study. **Publication bias: no serious.**
6. Primary study[9]. **Baseline/comparator:** Control arm of reference used for intervention.
7. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Only data from one study. **Publication bias: no serious.**

Attached Images

Strong recommendation

Updated evidence, no change in recommendation

a. Ambulance services should preferentially transfer suspected stroke patients to a hospital capable of delivering reperfusion therapies as well as stroke unit care. (Chowdhury et al 2021 *[23]*)
b. Ambulance services should pre-notify the hospital of a suspected stroke case where the patient may be eligible for reperfusion therapies. (Chowdhury et al 2021 *[23]*)

Practical Info

Agreed catchment areas that balance travel distance versus time benefits need to be established for each State or Regional Emergency care system. A shared rapid notification system working across the hospital and prehospital environments needs to be designed, resourced and implemented on an individual Emergency care system basis.

Paramedic crew should remain professional and aware of what they are saying in the presence of the patient. Some studies have

reported that around one fifth of patients with acute stroke symptoms may exhibit an alternative 'mimic' diagnosis, due to seizures, migraines and/or psychiatric disorders. However, these do not exclude the possibility of stroke and can create challenges to prompt identification of stroke in prehospital environment. *[8]*

Evidence To Decision

Benefits and harms

Substantial net benefits of the recommended alternative

Access to hospitals with stroke unit care and capable of delivering reperfusion therapies ensures that stroke patients have the opportunity of benefiting from the full range of therapy. Several ~~non-randomised~~ studies have shown that early notification by ambulance services reduces the time to administration of reperfusion therapies for those patients who may be eligible (Chowdhury et al 2021 *[23]*~~O'Brien et al 2012 ; De Luca et al 2009 ; Quain 2008~~).

Certainty of the Evidence

Low

The quality of the evidence is considered low as most of the studies were observational, however results were consistent across the various trials in different settings.

Values and preferences

No substantial variability expected

Suspected stroke patients are likely to prefer to be transferred to hospitals with reperfusion therapies and stroke unit care which have been proven to improve patients' outcome (see Reperfusion therapy and Stroke unit care sections in Acute Medical and Surgical Management), as well as prior notification that enables quick access to reperfusion therapies.

Resources and other considerations

No important issues with the recommended alternative

Resources considerations

There is evidence that pre-hospital triage interventions to improve access to thrombolysis may be cost-effective. Economic simulation modelling using prospective (n=309) and historical control (n=551) data from Australia was conducted to evaluate the potential cost-effectiveness of a pre-hospital acute stroke triage (PAST) intervention (Lahiry et al. 2018 *[22]*). Costs to health services (ambulance, acute hospitalisation costs and rehabilitation) were estimated (cost reference year 2014). Disability adjusted life years (DALYs) avoided were estimated by applying the benefit of additional patients receiving thrombolysis and treatment in a stroke unit taken from the literature. The PAST intervention was found to be cost-effective, costing an estimated AU$ 10,921 per DALY avoided when compared to the historical control. A limitation of the economic evaluation was that estimates for DALYs were taken from published literature rather than derived directly from patients.

Implementation consideration

There is a clinical indicator collected in the National Stroke Audit to determine the total number of patients with stroke who were transported by ambulance to a hospital able to provide thrombolysis. This indicator is included in the Acute Stroke Clinical Care Standard, excluding in-hospital strokes and where the time of arrival to the emergency department was greater than 4.5 hours from the time of the patient's stroke onset.

Rationale

Delivery of the right patient to the right treatment facility with prior notification enables access to reperfusion therapies in the shortest length of time.

Clinical Question/ PICO

Population: Adults with suspected stroke
Intervention: Pre-hospital workflow optimisation
Comparator: Conventional care

Summary

A review by Chowdhury et al (2021)*[23]* examined the pre-hospital stroke workflow optimisations which were divided in to three categories: improved intravenous thrombolysis (IVT) triage, large vessel occlusion (LVO) bypass and mobile stroke unit (MSU). Twenty six studies, including 4 randomised control trials, and 117,051 participants were included; (16 for IVT triage, 9 for MSU, 3 for LVO bypass). Aspects of trials that aimed to improve IVT triage included changed assessment documentation, education, pre-notification to stroke team, stroke team pager activation, hospital bypass and offload direct to CT. Improved IVT triage strategies significantly improved rate of IVT (RR 1.80, 95% CI 1.18 to 2.75; 10 studies, n= 11,045; high heterogeneity I^2= 92.7%), but MSU did not (RR 1.22; 95% CI 0.98 to 1.52; 5 studies, n= 2520). Improved IVT triage (SMD -0.82, 95% CI -1.32 to -0.17; 10 studies; high heterogeneity 96%), LVO bypass (SMD -0.80, 95% CI -1.13 to -0.47; 3 studies; moderate heterogeneity I^2= 79%) and MSU (SMD -0.87, 95% CI -1.57 to -0.17; 2 studies; moderate heterogeneity I^2= 65%) significantly reduced door to needle time for IVT. Overall, interventions to improve pre-hospital stroke workflow did not change the rate of good functional outcome (RR 1.06, 95% CI 0.97 to 1.12; 5 studies, n= 2068), mortality at 90 days (RR 1.00, 95% CI 0.76 to 1.31; 5 studies, n= 4039; moderate heterogeneity I^2= 57%) or the rate of symptomatic intracerebral hemorrhage (RR 0.98, 95% CI 0.65 to 1.46; 11 studies, n= 4923).

A cluster study (n= 1214) by Price et al (2020)*[26]* found no significant difference in thrombolysis rates in patients with enhanced paramedic acute stroke treatment assessment (PASTA) group compared to standard care (39.4% vs 44.7%, aOR 0.81, 95% CI 0.61 to 1.08). The PASTA intervention involved additional prehospital information collection, a structured hospital handover, practical assistance up to 15 minutes after handover, a predeparture care checklist, and clinician feedback. Poor health outcomes did not differ significantly between the groups (64.0% vs 66.8%, aOR 0.86, 95% CI 0.60 to 1.20). Timeframes to complete patient assessment was longer (MD 13.4, 95% CI 9.4 to 17.4) in the PASTA group compared to conventional care as was times from paramedic on scene to thrombolysis (mean (SD) 98.1(37.6) vs 89.4(31.1), p= 0.01).

Mohamed et al. (2022) *[35]* identified 19 studies (n= 7,824 ; 12 retrospective studies, 2 RCTs, 5 prospective studies) comparing direct to comprehensive center (mothership model) or stopping at primary centre for thrombolysis before transfer to comprehensive centre (drip-and-ship model). Time from symptom onset to puncture time and symptom onset to successful recanalisation was significantly shorter in the mothership group compared to the drip-and-ship group (mean 159.69 ± 44.55 vs 223.89 ± 85.10min and 206.08 ± 85.10 vs 286.58 ± 129.66, respectively). There was no difference in time for symptom onset to IV thrombolysis between the mothership and drip-and-ship models (117.0 ± 19.95 vs 128.25 ± 26.05). Compared to the mothership model, the drip-and-ship model had significantly worse functional outcome at 90 days (mRS 3-6: OR 1.47, 95% CI 1.13 to 1.92; 18 studies, n= 7,586; moderate heterogeneity I2= 79%), less likelihood of good functional outcome at 90 days (mRS 0-2; OR 0.74, 95% CI 0.65 to 0.84; 18 studies, n= 7,579) and increased chance of symptomatic intracerebral hemorrhage (OR 1.49, 95% CI 1.22 to 1.81; 16 studies, n= 6,852). The drip-and-ship model did not increase proportions of mortality (OR 1.16, 95% CI 0.87 to 1.55; 16 studies, n= 7,658; moderate heterogeneity I2= 68%) and successful recanalisation (OR 1.12, 95% CI 0.76 to 1.65; 15 studies, n= 4,378; moderate heterogeneity I2= 77%).

Pérez de la Ossa et al (2022) *[36]* included 1401 patients which did not find any overall differences of a bypass strategy direct to comprehensive centres vs initial primary stroke centre in patients selected using the RACE prehospital triage scale. However, REVASCAT was performed in a large geographical area with longer transfer times than would apply in metropolitan regions and only 216 patients had transport times to the endovascular-capable centre of <30min. This study was terminated early due to futility at the second interim analysis. Further studies are needed to determine the efficacy of this model.

Scott et al (2022) *[39]* studied (n = 76) whether pre-hospital telestroke improves diagnostic accuracy compared with paramedic assessments. In-ambulance telestroke was more accuracte, sensitive and specific in positively predicting stroke (OR 3.56 95% CI: 1.7 to 7.6) than paramedic assessments (OR 3.11 95% CI: 1.1 to 8.8). Telestroke showed 100% accuracy (95% CI: 90 to 100), 100% sensitivity (95% CI: 69.2 to 100) and 100% specificity (95% CI: 86.3 to 100) in diagnosing eligibility for reperfusion, compared to paramedic assessments (Accuracy 70.7%, 95%CI: 54.5 to 83.90, sensitivity 76.5% 95% CI: 50.1 to 93.2, specificity 66.7% 95% CI: 44.7 to 84.4).

It appears the most important aspects of pre-hospital services that impact on access to thrombolyisis include paramedic training, pre-notification and hospital bypass to thrombolytic centres.

Outcome Timeframe	**Study results and measurements**	**Comparator** Conventional care	**Intervention** Pre-hospital workflow optimisation	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Received thrombolysis 9 Critical	Relative risk 1.8 (CI 95% 1.18 — 2.75) Based on data from 11,045 participants in 10 studies. [1] (Observational (non-randomized))	138 per 1000 Difference:	248 per 1000 **110 more per 1000** 25 more — 242 more	Very low Due to serious risk of bias, Due to very serious inconsistency, Due to serious publication bias [2]	Pre-hospital notification probably improves thrombolysis rate
Functional outcome (mRS 0-2) 90 days 8 Critical	Relative risk 1.08 (CI 95% 0.93 — 1.26) Based on data from 1,287 participants in 2 studies. [3] (Observational (non-randomized)) Follow up: 90 days.	337 per 1000 Difference:	364 per 1000 **27 more per 1000** (CI 95% 24 fewer — 88 more)	Very low Due to serious indirectness, Due to serious inconsistency, Due to serious risk of bias, Due to serious publication bias [4]	We are uncertain whether pre-hospital notification improves or worsen functional outcome (mRS 0-2)
Door to needle time - patients receiving tPA 8 Critical	Measured by: Door-to-needle time (minutes) High better Based on data from 8,543 participants in 8 studies. [5] (Observational (non-randomized))	Difference:	**SMD 0.82 lower** (CI 95% 1.32 lower — 0.32 lower)	Very low Due to serious risk of bias, Due to very serious inconsistency, Due to serious publication bias [6]	Pre-hospital notification may decrease door to needle time

1. Systematic review [23] . **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of Bias: serious.** Non-randomised trial but unlikely to see randomised trials of this protocol, control (same period 12 months prior) seems reasonable. **Inconsistency: very serious.** The magnitude of statistical heterogeneity was high, with I^2:92.7%., Point estimates vary widely, The confidence interval of some of the studies do not overlap with those of most included studies/ the point estimate of some of the included studies., The direction of the effect is not consistent between the included studies. **Indirectness: no serious. Imprecision: no serious. Publication bias: serious.** Asymmetrical funnel plot.
3. Systematic review [23] . **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of Bias: serious. Inconsistency: serious. Indirectness: serious.** Differences between the intervention/comparator of interest and those studied. **Imprecision: no serious. Publication bias: serious.** Asymmetrical funnel plot.
5. Systematic review [23] . **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of Bias: serious. Inconsistency: very serious.** The magnitude of statistical heterogeneity was high, with I^2:96.2%., Point estimates vary widely, The confidence interval of some of the studies do not overlap with those of most included studies/ the point estimate of some of the included studies.. **Indirectness: no serious. Imprecision: no serious. Publication bias: serious.** Asymmetrical funnel plot.

Attached Images

Info Box

Practice point

- General practitioners are encouraged to educate reception staff in the FAST stroke recognition message and to redirect any calls about suspected acute stroke to 000.
- Regular stroke education may improve patient identification by clinicians. (Oosteama et al 2019*[25]*; Chowdhury et al 2021*[23]*)

Rationale

Education of paramedics usually forms one part of complex interventions to improve thrombolysis (Chowdhury et al 2021 *[23]*). In one study a brief education intervention along with performance feedback improved stroke recognition, prehospital notification and early thrombolysis but results were not sustained beyond 3 months, suggesting regular education is needed (Oosteama et al 2019 *[25]*). Similarly, in another study the effects of a brief online training package increased correct stroke identification in the months after training but dropped off after 5 months, reinforcing the need for ongoing education (Brown et al 2019*[28]*).

Strong recommendation

New

For patients in major cities with suspected stroke who are potentially eligible for reperfusion therapies, pre-hospital treatment in a mobile stroke unit is recommended. (Turc et al 2022 *[32]*)

Approved by NHMRC August 2022.

Practical Info

The establishment costs and staffing demands of an MSU in Australia are substantial. As such, the current MSU configuration is relevant for major cities where population density leads to sufficient stroke case load within the feasible operational area. In the European and North American experience, the benefit of MSU was driven solely by earlier administration of IV thrombolytic. However, the Australian configuration of mixed primary and comprehensive stroke centres (24/7 ECR available) in metropolitan areas means that definitive triage of patients with large vessel occlusion to a comprehensive centre (bypassing a potentially closer primary centre and markedly reducing time to thrombectomy) is likely to contribute at least as much as earlier IV thrombolytic to the overall benefit of MSUs.

The Melbourne MSU planning was modelled on a radius of 20kms from the comprehensive stroke services. Most international MSUs operate in densely-populated cities, although some are in rural (Saarland) or suburban (Colorado) areas. (Navi et al 2022 *[33]*) Based on the early randomised trial data in Germany Dietrich et al (2014)*[21]* modelled estimates of transport ranges based on population densities and found that that MSUs would be cost-effective for population densities of at least 79 inhabitants per kilometer, whereby their operating distances for optimal efficiency ranged from 43 to 65 km. However, benefit-cost ratio's increased substantially with reduced staff and higher population densities. Clearly, modelling is needed based on local factors.

The MSU has been shown to help with making appropriate decisions for transporting patients to either a comprehensive stroke centre (e.g. for LVO or ICH) compared to a primary stroke centre. In one German study (Helwig et al 2019 *[24]*) 70% of patients in one group were accurately transported to the most appropriate centre using a clinical score by paramedics (Los Angeles Motor Scale; cut-point >3), however, 100% of patients in the MSU group were transported appropriately.

Further research is underway by the Australian Stroke Alliance (Home - Australian Stroke Alliance (austrokealliance.org.au)) to develop smaller brain imaging solutions for standard road and air ambulances in the future.

Evidence To Decision

Benefits and harms

Substantial net benefits of the recommended alternative

Patients treated in a MSU had improved outcomes, quicker access to reperfusion and improved access to tertiary stroke centres for further advanced treatments than conventional ambulances. There was no impact on safety metrics (mortality, sICH).

Certainty of the Evidence

Moderate

A small number of randomised and well conducted non-randomised, interventional studies with moderate certainty for important outcomes. Some outcomes had very low certainty.

Values and preferences

No substantial variability expected

It is expected that all suspected stroke patients would want to be managed with a dedicated MSU if available.

Resources and other considerations

No important issues with the recommended alternative

Resources considerations

Australian economic analysis found the Melbourne MSU to cost an additional $30,982 per DALY avoided 95% CI $21,142 to $47,517) compared to standard care. (Kim et al 2021 *[30]*) This is under the normal $50,000 threshold for acceptable interventions.

Rationale

Suspected stroke patients potentially eligible for reperfusion therapies should have an ambulance dispatched as an immediate response and managed accordingly.

Mobile stroke units (MSU) are ambulances equipped with a CT scanner, point-of-care lab, telemedicine and are staffed with a stroke specialised medical team. The use of a mobile stroke unit has been shown to improve rates of thrombolysis and transfer and access to endovascular therapy for patients with ischaemic stroke and also improve functional outcome compared to conventional pre-hospital care. There are 25 MSU's reported across the world with only one currently available in Melbourne with planning underway for one in Sydney. The costs of MSUs are an important consideration. As such MSUs are only appropriate in large metropolitan areas with agreed criteria for use (e.g. clinical and time based criteria to ensure specificity of treatment). Establishment of other MSUs across Australia will need to undertake local modelling based on population densities, demographics, road infrastructure and travel times, workloads and existing networks and clinical practice, and the number and location of comprehensive and primary stroke services.

Clinical Question/ PICO

Population: Adults with suspected stroke eligible for thrombolysis
Intervention: Mobile stroke unit (MSU)
Comparator: Conventional care

Summary

Turc et al (2022)*[32]* identified 13 studies including three RCTs and 10 non-randomised studies mostly for patients with ischaemic stroke patients (including the recent quasi-randomised controlled trials by Grotta et al 2021 and Ebinger et al 2021). Compared with usual care, care in a mobile stroke unit (MSU) increased the chance of an excellent outcome (adjusted odds ratio [aOR], 1.64; 95%CI, 1.27-2.13; 5 studies, n=3228; moderate heterogeneity I^2=48%), reduced disability over the full range of the mRS (aOR, 1.39; 95%CI 1.14-1.70; 3 studies, n=1563), and increased the chance of a good outcome (mRS score of 0 to 2: crude OR, 1.25; 95%CI 1.09-1.44; 6 studies, n=3266). MSU care also resulted in shorter onset-to-intravenous thrombolysis (IVT) times (median reduction, 31 mins; 95%CI 23-39 mins; 13 studies, n=3322; moderate heterogeneity I^2=47%), increased delivery of IVT (crude OR, 1.83; 95%CI 1.58-2.12; 7 studies, n=4790), and increased the proportion of delivery of IVT within 60 minutes of symptom onset (crude OR, 7.71; 95%CI, 4.17-14.25; 8 studies, n=3351; high heterogeneity I^2=75%). MSU may also reduce the onset to mechanical thrombolysis but there was high heterogeneity and results non-significant (mean reduction, 27 mins; 95%CI -17 to 71; 5 studies, n=666; very high heterogeneity I^2=86%). MSU did not increase the risk of all-cause mortality at 7 days (OR 0.74, 95%CI 0.51 to 1.09; 9 studies, n=8599) or at 90 days (OR 0.82, 95%CI 0.58 to 1.17; 7 studies, n=3924). MSU use also did not increase proportions of symptomatic intracranial hemorrhage (sICH) after IVT (OR 0.80, 95%CI 0.52 to 1.24; 5 studies, n=1977). There was no publication bias found.

Walter et al (2022)*[29]* used the review by Turc et al for the European Stroke Organisation Guidelines on mobile stroke units (MSU) but had one less observational study (Larsen et al 2021). Data was also presented slightly differently to the Turc review which used adjusted odds ratios. MSU management compared to conventional pre-hospital management improved

excellent (mRS 0-1, OR: 1.37; 95%CI 1.17-1.61, 4 studies, n=3157), good (mRS 0-2, OR: 1.23; 95%CI 1.07-1.42, 5 studies, n=3195) and any better functional outcome at 90 days (ordinal shift analysis of mRS of 1, cOR 1.28; 95%CI 1.08-1.52, 5 studies) in patients with acute ischaemic stroke (AIS). MSU care increased the proportion of ischaemic patients receiving thrombolysis (OR: 2.28; 95%CI 1.43-3.64; 7 studies, n=4633; high heterogeneity I^2=85%). MSU care did not increase the likelihood of receiving treatment with clot retrieval in ischaemic stroke patients (OR: 1.48; 95%CI 0.62-3.52; 3 studies, n=401). But MSU care did increased the rate of large vessel occlusion patients that were primarily transported to thrombectomy-capable centres (OR: 4.30; 95%CI 1.16-15.87; 2 studies, n=61). There was no difference in 90-day mortality among all ischaemic stroke patients (OR: 0.98; 95%CI 0.53-1.84; 6 studies, n=2128) irrespective of being treated with thrombolysis or not. There was also no difference in symptomatic intracranial haemorrhage (sICH) among all ischaemic stroke patients (OR: 0.81; 95%CI 0.52-1.25; 4 studies, n=1889). There was no increase with major extracranial bleeding with those treated with IVT (OR: 0.38; 95%CI 0.02-9.54). The effects were similar removing non-interventional studies.

Analysis of a small number of studies with ICH found MSU increased the proportion of patients transported to tertiary care stroke centres, with neurosurgery available (OR: 6.44; 95% CI 2.96–14.01; 2 studies, n=242). There was no difference in 7-day (OR: 1.05; 95% CI 0.28–3.89) or 90-day (OR: 1.14; 95% CI 0.24–5.50) mortality among ICH patients.

Chen et al. (2022)*[34]* with 16 studies (n= 22,766) identified 4 different studies compared to the review by Turc et al. and included 4 economic analysis. Compared with usual care, care in a MSU reduced time from onset to therapy decision (mean reduction 32.64 min, 95% CI 23.38 to 41.89; 7 studies, n= 7,657). MSU did not increase risk of in-hospital mortality (OR 1.11, 95% CI 0.83 to 1.50; 6 studies, n= 19,542) or stroke-related or neurological events (OR 0.94, 95% CI 0.70 to 1.27; 6 studies, n= 16,202). Four studies (n= 4,165) reported excellent outcome measured with modified Rankin Scale (mRS) and only a distribution of mRS at 90 days from onset was reported with a significant difference for mRS 0-2 was reported ($p<0.05$).

Another review by Chowdhury et al (2021)*[23]* examined the pre-hospital stroke workflow optimisations which were divided in to three categories: improved intravenous thrombolysis (IVT) triage, large vessel occlusion (LVO) bypass and mobile stroke unit (MSU). Twenty six studies, including 4 randomised control trials, and 117,051 participants were included, 9 studies specifically to MSU. MSU did not improve rates of IVT (RR 1.22; 95% CI 0.98 to 1.52; 5 studies, n= 2520). MSU significantly reduced door to needle time for IVT(SMD -0.87, 95%CI -1.57 to -0.17; 2 studies; moderate heterogeneity I2=65%), reduced call to needle (SMD -1.41, 95% CI -1.94 to -0.88; 6 studies; high heterogeneity I^2= 95%), and onset to needle (SMD -1.15, 95% CI -1.74 to -0.56; 3 studies) times for IVT. MSU also significantly reduced call to perfusion time (SMD -0.73, 95% CI -1.08 to -0.38; 2 studies) for EVT. Overall, interventions to improve pre-hospital stroke workflow did not significantly improve good functional outcome (RR 1.06, 95% CI 0.97 to 1.12; 5 studies, n= 2068), mortality at 90 days (RR 1.00, 95% CI 0.76 to 1.31; 5 studies, n= 4039; moderate heterogeneity I^2= 57%) or the rate of symptomatic intracerebral hemorrhage (RR 0.98, 95% CI 0.65 to 1.46; 11 studies, n= 4923).

Australian data similarly found MSU reduced all time metrics: dispatch to thrombolysis 42.5 minutes shorter, hospital arrival time 26 minutes shorter, hospital door to needle time 17 minutes shorter, dispatch to endovascular therapy 51 minutes shorter.(Zhao et al 2020 *[31]*)

Economic review
One cost-benefit analysis of a mobile stroke unit (consisting of an ambulance staffed by one paramedic and one emergency assistant and another ambulance staffed with one physician and one paramedic) has been undertaken based on data from a randomised controlled trial (Dietrich et al 2014 *[21]*). They found that that the mobile stroke unit resulted in direct cost savings of €17872 per patient, and was cost-efficient starting from an operating distance of 15.98km or from a population density of 79 inhabitants per km^2.

An Australian Analysis by Kim et al (2021)*[30]* estimated the Melbourne MSU to cost an additional $30,982 per DALY avoided (95% CI $21,142 to $47,517) compared to standard care.

Outcome Timeframe	**Study results and measurements**	**Comparator** Conventional care	**Intervention** MSU	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Mortality at 90 days 8 Critical	Odds ratio 0.82 (CI 95% 0.58 — 1.17) Based on data from 3,924 participants in 7 studies. [1] (Observational (non-randomized)) Follow up: 90 days.	**112** per 1000 Difference:	**94** per 1000 **18 fewer per 1000** (CI 95% 44 fewer — 17 more)	**Low** Due to serious risk of bias [2]	Mobile Stroke Unit may have little or no difference on mortality at 90 days

Outcome Timeframe	**Study results and measurements**	**Comparator** Conventional care	**Intervention** MSU	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Excellent functional outcome at 90 days (mRS 0-1) [3] 9 Critical	Odds ratio 1.64 (CI 95% 1.27 — 2.13) Based on data from 3,228 participants in 5 studies. [4] Follow up: 90 days.	451 per 1000 Difference:	574 per 1000 **123 more per 1000** (CI 95% 60 more — 185 more)	**Moderate** Due to serious risk of bias [5]	MSU probably improves excellent functional outcome at 90 days (mRS 0-1) in patients eligible for thrombolysis
sICH rate 7 Critical	Odds ratio 0.8 (CI 95% 0.52 — 1.24) Based on data from 1,977 participants in 5 studies. [6] (Observational (non-randomized))	51 per 1000 Difference:	41 per 1000 **10 fewer per 1000** (CI 95% 24 fewer — 11 more)	**Low** Due to serious risk of bias [7]	MSU may have little or no difference on sICH rate
LVO patients transported to ECR centre 7 Critical	Odds ratio 4.3 (CI 95% 1.16 — 15.87) Based on data from 61 participants in 2 studies. [8] (Observational (non-randomized))	359 per 1000 Difference:	707 per 1000 **348 more per 1000** (CI 95% 35 more — 540 more)	**Very low** Due to serious risk of bias, Due to serious imprecision [9]	MSU may increase ischaemic stroke patients with LVO to be transported to ECR centre
Call to needle (IVT) time 9 Critical	Measured by: Time (mins) Lower better Based on data from 3,322 participants in 13 studies. [10]	Difference:	**MD 31 lower** (CI 95% 23 lower — 39 lower)	**Moderate** Due to very serious risk of bias, Upgraded due to Very large magnitude of effect [11]	MSU probably decreases call to needle (IVT) time

1. Systematic review. **Baseline/comparator:** Control arm of reference used for intervention. **Supporting references:** [32],
2. **Risk of Bias: serious.** Two of three RCTs recruitment of participants were aware of cluster allocation, three observational studies used historical controls, one had major imbalance at baseline.. **Inconsistency: no serious.** The magnitude of statistical heterogeneity was moderate, with I^2: 55.8 %., The direction of the effect is not consistent between the included studies. **Indirectness: no serious. Imprecision: serious.** Wide confidence intervals. **Publication bias: no serious.**
3. Adjusted ORs used
4. Systematic review. **Baseline/comparator:** Control arm of reference used for intervention. **Supporting references:** [32],
5. **Risk of Bias: serious. Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Upgrade: large magnitude of effect.**
6. Systematic review. **Baseline/comparator:** Control arm of reference used for intervention. **Supporting references:** [32],
7. **Risk of Bias: serious. Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious.** Wide confidence intervals. **Publication bias: no serious.**
8. Systematic review. **Baseline/comparator:** Control arm of reference used for intervention. **Supporting references:** [29],
9. **Risk of Bias: serious.** One randomised and one non-randomised study included. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Wide confidence intervals, Low number of patients. **Publication bias: no serious.**
10. Systematic review. 3 studies were RCT and 2/5 non-randomised studies were experimental. **Baseline/comparator:** Control arm of reference used for intervention. **Supporting references:** [32],
11. **Risk of Bias: very serious. Inconsistency: serious. Indirectness: no serious. Imprecision: no serious.** Wide confidence intervals. **Publication bias: no serious. Upgrade: very large magnitude of effect.**

Attached Images

Glossary and abbreviations

Glossary

Activities of daily living: The basic elements of personal care such as eating, washing and showering, grooming, walking, standing up from a chair and using the toilet.

Activity: The execution of a task or action by an individual. Activity limitations are difficulties an individual may have in executing activities.

Agnosia: The inability to recognise sounds, smells, objects or body parts (other people's or one's own) despite having no primary sensory deficits.

Aphasia: Impairment of language, affecting the production or comprehension of speech and the ability to read and write.

Apraxia: Impaired planning and sequencing of movement that is not due to weakness, incoordination or sensory loss.

Apraxia of speech: Inability to produce clear speech due to impaired planning and sequencing of movement in the muscles used for speech.

Atrial fibrillation: Rapid, irregular beating of the heart.

Augmentative and alternative communication: Non-verbal communication, e.g. through gestures or by using computerised devices.

Central register: collection of large dataset related to patients' diagnoses, treatments and outcomes

Cochrane: Cochrane is a worldwide, not-for-profit organisation that produces systematic reviews of medical research. Systematic reviews summarise all the research that has been done on a given topic, so that health professionals, patients and policy-makers can make evidence-based decisions.

Cochrane are partnering with the Stroke Foundation on the Living Stroke Guidelines project.

Cochrane review: a comprehensive systematic review and meta-analysis published online in Cochrane library, internationally recognized as the highest standard in evidence-based health care resources

Conflict of Interest (COI) form: A conflict of interest form is signed by all working group members (including all members of the consumer panel). It highlights whether there is any risk of the person's professional judgement (eg. their assessment of research) being influenced by a secondary interest they may have, such as financial gain or career advancement.

Covidence: Covidence is computer software that Cochrane uses to help identify research for systematic reviews. It reduces the workload by allowing the person using it to quickly scan-read and screen scientific papers for relevance, make a summary of their main findings, and assess how well the research was done and whether there is a risk of bias.

Covidence will be used to screen all stroke-related research articles so that only the most accurate ones go into the Living Stroke Guidelines.

Deep vein thrombosis: Thrombosis (a clot of blood) in the deep veins of the leg, arm, or abdomen.

Disability: A defect in performing a normal activity or action (e.g. inability to dress or walk).

Drip and ship: A model of thrombolysis service provision that involves assessment of patients at a non-specialist centres with telemedicine support by stroke specialists, commencing thrombolysis (if deemed appropriate) and subsequent transfer to the stroke specialist centre.

Dyad: involvement of both patients and their caregivers

Dysarthria: Impaired ability to produce clear speech due to the impaired function of the speech muscles.

Dysphagia: Difficulty swallowing.

Dysphasia: Reduced ability to communicate using language (spoken, written or gesture).

Emotionalism: An increase in emotional behaviour—usually crying, but sometimes laughing that is outside normal control and may be unpredictable as a result of the stroke.

Endovascular thrombectomy (also called mechanical thrombectomy or endovascular clot retrieval): a minimally invasive procedure performed via angiogram, in which a catheter passes up into the brain to remove the clot in the blocked blood vessel.

Enteral tube feeding: Delivery of nutrients directly into the intestine via a tube.

Evaluation (of project): An evaluation is an assessment of a project. The aim of an evaluation is to determine the project's effectiveness, efficiency, impact and sustainability.

Evidence-based decision-making: Evidence-based decision-making is a process for making decisions about an intervention, practice etc, that is grounded in the best available research evidence.

Evidence summary: An evidence summary is a short summary of the best available evidence for a particular (guidelines') question. It aims to help clinicians use the best available evidence in their decision-making about particular interventions.

Executive function: Cognitive functions usually associated with the frontal lobes including planning, reasoning, time perception, complex goal-directed behaviour, decision making and working memory.

Family support / liaison worker: A person who assists stroke survivors and their families to achieve improved quality of life by providing psychosocial support, information and referrals to other stroke service providers.

GRADE: The GRADE approach (Grading of Recommendations Assessment, Development and Evaluation) is a standardised way of assessing research (also known as the *quality of evidence*) and determining the strength of recommendations. It was designed to be transparent and rigorous and has become the leading method used for guideline development.

GRADE will be applied to the Living Stroke Guidelines to ensure that their recommendations are accurate and robust.

Impairment: A problem in the structure of the body (e.g. loss of a limb) or the way the body or a body part functions (e.g. hemiplegia).

Infarction: Death of cells in an organ (e.g. the brain or heart) due to lack of blood supply.

InformMe: InformMe is the Stroke Foundation's dedicated website for health professionals working in stroke care.
Inpatient stroke care coordinator: A person who works with people with stroke and with their carers to construct care plans and discharge plans and to help coordinate the use of healthcare services during recovery in hospital.
Interdisciplinary team: group of health care professionals (including doctors, nurses, therapists, social workers, psychologists and other health personnel) working collaboratively for the common good of the patient.
Ischaemia: An inadequate flow of blood to part of the body due to blockage or constriction of the arteries that supply it.
MAGICapp: MAGICapp is an online platform for writing (authoring) and publishing guidelines and evidence summaries. MAGIC stands for MAking GRADE the Irresistible Choice.
The platform guides authors through the different stages of planning, authoring, and publishing of information. It then publishes the guidelines online for clinicians and their patients to access. People can dig as deep into the information as they need, in order to make well-informed healthcare decisions.
MAGICapp is the technology that will be used to write and publish the Living Stroke Guidelines.
Neglect: The failure to attend or respond to or make movements towards one side of the environment.
NHMRC: The National Health and Medical Research Council (NHMRC) is the Australian Government agency that provides most of the funding for medical research. It develops health advice for the Australian community, health professionals and governments, and develops and maintains health standards. It also provides advice on ethical behaviour in health care and in conducting health and medical research.
The NHMRC are responsible for approving the stroke clinical guidelines.
Participation: Involvement in a life situation.
Participation restrictions: Problems an individual may experience in involvement in life situations.
Penumbral-based imaging: brain imaging that uses advanced MRI or CT angiography imaging to detect parts of the brain where the blood supply has been compromised but the tissue is still viable.
Percutaneous endoscopic gastrostomy (PEG): A form of enteral feeding in which nutrition is delivered via a tube that is surgically inserted into the stomach through the skin.
Pharmaceutical Benefits Scheme (PBS): A scheme whereby the costs of prescription medicine are subsidised by the Australian Government to make them more affordable.
Phonological deficits: Language deficits characterised by impaired recognition and/or selection of speech sounds.
PICO: PICO is a common way to define what research you are looking for to answer a clinical or healthcare question. Each systematic review of research is based on a specific PICO, or group of similar PICOs. PICO stands for:
P – patient, problem or population
I – intervention
C – comparison, control or comparator
O – outcome.
For example, for the question, "does care on a stroke unit improve outcomes for people with stroke?" the PICO is:
P: all people with stroke
I: care on a dedicated stroke unit (the systematic review defines what a stroke unit actually is)
C: care on a general ward
O: death, institutionalisation rate, dependency by the end of a defined follow-up period, or length of stay in a hospital or institution
Each recommendation in the Living Stroke Guidelines will be broken down into its PICO components. The scientific papers searched will need to match as closely to the PICO elements as possible.
Public consultation: Public consultation is a process by which the public's input on matters affecting them is sought. Its main goals are to improve the efficiency, transparency and public involvement, in a project – in this case in the update of the stroke guidelines.
Pulmonary embolism: Blockage of the pulmonary artery (which carries blood from the heart to the lungs) with a solid material, usually a blood clot or fat, that has travelled there via the circulatory system.
Qualitative research: Qualitative research is about words. It aims to answer questions of 'why'. It is best used to explore perspectives, attitudes and reasons.
Quantitative research: Quantitative research is about numbers. It is best used to answer questions of 'what' or 'how many'.
Randomised control trial: A controlled trial is a clinical study that compares the results of a group of people receiving a new treatment that is under investigation, against a group receiving a placebo treatment, the existing standard treatment, or no treatment at all. These comparison groups are examples of 'control' groups.
Rehabilitation: Restoration of the disabled person to optimal physical and psychological functional independence.
Research Ethics Committee: A Research Ethics Committee is a group that reviews all research proposals involving human participants to ensure that the proposals are ethically acceptable.
Research wastage:
Risk factor: A characteristic of a person (or people) that is positively associated with a particular disease or condition.
Retiring (a question): A guidelines' question is 'retired' when it is removed from the guidelines' list – this means that we will no longer search for new research (evidence) for that particular question.
Stroke unit: A section of a hospital dedicated to comprehensive acute and/or rehabilitation programs for people with a stroke.
Stroke: Sudden and unexpected damage to brain cells that causes symptoms that last for more than 24 hours in the parts of the body controlled by those cells. Stroke happens when the blood supply to part of the brain is suddenly disrupted, either by blockage of an

artery or by bleeding within the brain.
Systematic review: Systematic reviews summarise all the research that has been done on a given topic, so that health professionals, patients and policy-makers can make evidence-based decisions.
Task-specific training: Training that involves repetition of a functional task or part of the task.
Transient ischaemic attack: Stroke-like symptoms that last for a short time period. While TIA is not actually a stroke, it has the same cause. A TIA may be the precursor to a stroke, and people who have had a TIA require urgent assessment and intervention to prevent stroke.

Abbreviations

ACE	Angiotensin-converting enzyme
ADL	Activities of daily living
AF	Atrial fibrillation
AFO	Ankle foot orthosis
BAO	Basilar artery occlusion
BI	Barthel Index
BMI	Body mass index
BP	Blood pressure
CEA	Carotid endarterectomy
CEMRA	Contrast-enhanced magnetic resonance angiography
CI	Confidence interval
CIMT	Constraint induced movement therapy
CT	Computed tomography
CTA	Computed tomography angiography
CVD	Cardiovascular disease
DALY	Disability-adjusted life years
DBP	Diastolic blood pressure
DOAC	Direct oral anticoagulant
DSA	Digital subtraction angiography
DUS	Doppler ultrasonography
DVT	Deep vein thrombosis
DWI	Diffusion-weighted imaging
ECG	Electrocardiography
ED	Emergency department
EMG	Electromyographic feedback
EMS	Emergency medical services
ESD	Early supported discharge
ESS	European Stroke Scale
FAST	Face, Arm, Speech, Time

FEES	Fibre-optic endoscopic examination of swallowing
FeSS	Fever, Sugar, Swallowing
FFP	Fresh frozen plasma
FIM	Functional independence measure
GP	General practitioner
HR	Hazard ratio
HRQOL	Health related quality of life
HRT	Hormone replacement therapy
IA	Intra-arterial
ICH	Intracerebral haemorrhage
ICU	Intensive care unit
INR	International normalised ratio
IPC	Intermittent pneumatic compression
IV	Intravenous
LMWH	Low molecular weight heparin
LOS	Length of stay
MCA	Middle cerebral artery
MD	Mean difference
MI	Myocardial infarction
MNA	Mini Nutritional Assessment
MR	Magnetic resonance
MRA	Magnetic resonance angiography
MRI	Magnetic resonance imaging
mRS	Modified rankin scale
MST	Malnutrition screening tool
MUST	Malnutrition universal screening tool
N	Number of participants in a trial
NASCET	North American Symptomatic Carotid Endarterectomy Trial
NG	Nasogastric
NHMRC	National Health and Medical Research Council
NIHSS	National Institutes of Health Stroke Scale
NMES	Neuromuscular electrical stimulation
NNH	Numbers needed to harm
NNT	Numbers needed to treat
OR	Odds ratio

OT	Occupational therapist
PBS	Pharmaceutical Benefits Scheme
PE	Pulmonary embolism
PEG	Percutaneous endoscopic gastrostomy
PFO	Patent foramen ovale
PPV	Positive predictive value
QALYs	Quality-adjusted life years
QOL	Quality of life
RCT	Randomised controlled trial
rFVIIa	recombinant activated factor VII
RHS	Right hemisphere syndrome
ROC	Receiver operator curve
ROM	Range of motion
ROSIER	Recognition of stroke in the emergency room
RR	Relative risk
RRR	Relative risk reduction
rTMS	repetitive transcranial magnetic stimulation
rt-PA	Recombinant tissue plasminogen activator
SBP	Systolic blood pressure
SC	Subcutaneous
SD	Standard deviation
SE	Standard error
SES	Standardised effect size
SGA	Subjective global assessment
sICH	symptomatic intracerebral haemorrhage
SMD	Standardised mean difference
SSS	Scandinavian stroke scale
TEE	Transoesophageal echocardiography
TIA	Transient ischaemic attack
TOE	Transoesophageal echocardiography
TOR-BSST	Toronto Bedside Swallowing Screening test
tPA	Tissue plasmogen activator
TTE	Transthoracic echocardiography
UFH	Unfractionated heparin
UK	United Kingdom

UL	Upper limb
VF or VFS	Videofluoroscopy
VR	Virtual reality
VTE	Venous thromboembolism
WMD	Weighted mean difference

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