Stroke FOUNDATION

Clinical Guidelines for Stroke Management 2017

Technical Report

Contents

1. 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; and
- Raise funds from the community, corporate sector and government to continue our mission.

1.1. Purpose

The *Clinical Guidelines for Stroke Management 2017* updates and supersedes the 2010 version. Using the best available evidence, it provides a series of best-practice recommendations to assist decision-making in the management of stroke and transient ischaemic attack (TIA) in adults. 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.

1.2. 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, 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 management, 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), or
- Primary prevention of stroke (refer to *Guidelines for the management of absolute cardiovascular disease risk 2012* (National Vascular Disease Prevention Alliance) - 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) - https://www.heartfoundation.org.au/for-professionals/clinical-information/hypertension).

1.3. 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.

1.4. Structure

The Clinical Guidelines are published in eight separate chapters:

1. Pre-hospital care
2. Early assessment and diagnosis
3. Acute medical and surgical management
4. Secondary prevention
5. Rehabilitation
6. Managing complications
7. Discharge planning and transfer of care
8. 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.

2. Methodology

This *Technical Report* accompanies the *Clinical Guidelines for Stroke Management 2017*. It outlines the guideline development process and methodology, lists the clinical questions, and provides all accompanying summaries of evidence.

The Clinical Guidelines were developed according to the procedures and requirements for meeting the *2011 NHMRC standard for clinical practice guidelines*. This process updates the 2010 version of the clinical guidelines and is very similar to previous methods used. One major difference, however, was the use of the GRADE approach used to review evidence and develop the recommendations. GRADE was developed by the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) Working Group and is the Cochrane's recommended approach for grading the quality of evidence and the strength of recommendations.

The content of the Clinical Guidelines were developed by the Stroke Foundation Project Team (PT) and discipline-specific Working Parties (WPs). Leads from each of the WPs formed the Content Development Working Group (CWG). The WP Leads were responsible for leadership of their WP members and for making decisions relating to their area of expertise.

The following describes the process used to develop the Clinical Guidelines.

2.1. Define scope, clinical questions and literature search strategy

The first steps in the evidence review were to define the scope, review the clinical questions and agree on the literature search strategy.

Given that the scope of this project was to update the previous 2010 clinical guidelines, the PT used the 2010 clinical questions as its starting point. Draft clinical questions based on the 2010 version were circulated to all members of the WPs in April 2015. Comments and feedback from these members were collated and integrated into a working document. This consolidated document proposed a new set of updated clinical questions and was considered and reviewed by the CWG at its meeting of 29 September 2015.

The decision to include or exclude a clinical question was based on its clinical importance, and the availability of other evidence-based guidance to reduce duplication of effort. The majority of topics relating to organisation of care were excluded because the *National Stroke Services Frameworks* for acute and rehabilitation stroke services (2015 and 2013 respectively) provide this important information and their development used a similar systematic process as the one used for developing the Clinical Guidelines. Topics relating to lifestyle modification to prevent recurrent stroke were also excluded from the evidence review as most of the stroke evidence is in fact for primary prevention

and the CWG determined that it was appropriate to use the individual National Guidelines for these topics.

After the broad clinical questions were agreed to, these were grouped into topics, and then PICO (Population, Intervention, Comparator and Outcome) questions for each topic were specified to inform the literature search strategy.

As a result, 8 chapters, 89 clinical questions and approximately 300 PICO questions were included in the Guidelines, covering the full pathway of care following stroke or TIA. (For the list of clinical questions and their PICO questions, please refer to *Section 3* in this report).

2.2. Systematic literature search

An information specialist was engaged to undertake the literature search. The information specialist developed the search strategy based on the 2010 clinical guidelines search strategy in consultation with the PT and CWG. The search strategy was signed off by the Guidelines Advisory Committee (GAC). The search results were provided in EndNote format and the PT uploaded them into a web-based tool called Covidence. All abstracts were screened by two reviewers, either a PT member or a WP member, or two PT members. An independent third person (a member of the PT or a WP Lead) resolved conflicts. Full-text articles were screened using the same process. The use of Covidence assisted in ensuring transparency and independence between multiple reviewers during the screening stage.

The search strategy consisted of a core search string for ‘stroke’ and/or ‘transient ischaemic attack (TIA)’, search terms specific to interventions in each topic, and evidence filters to select particular study designs where relevant. A search string for ‘stroke’ used by Cochrane reviews was identified and incorporated into the search terms used in the 2010 clinical guidelines. Evidence filters were adopted from those of maximum sensitivity and specificity proposed in the Hedges Project from McMaster University [1]. They were used to identify evidence for medical therapies, diagnosis, reviews, qualitative studies of consumers’ perception and cost-effectiveness studies of resource implications. (For details of search terms, refer to *Appendix 1*).

The initial search was undertaken between November 2015 and January 2016 and the final searches completed in June and July 2016. Databases searched included Medline, Embase, Cochrane, CINAHL, EBM Review, PsycInfo and Web of Science. A separate search for Aboriginal and Torres Strait Islander populations was conducted in databases of Australian Indigenous studies in Monash University (http://guides.lib.monash.edu/subject-databases/australian-indigenous).

The following criteria were used to select studies for data extraction.

Inclusion criteria

- Population – for the first two chapters, 'Pre-hospital care' and 'Early assessment and diagnosis', the population of interest was people with suspected stroke or TIA; for the rest of the guidelines, the population of interest is people diagnosed with stroke or TIA. Where no direct evidence for stroke patients was identified, the PT and WPs considered populations in the literature adequately similar to the stroke population for the results to be transferrable.
- Intervention – specific interventions or groups of interventions were specified.
- Comparators – for diagnostic PICOs, the comparators were acceptable reference standards; for intervention PICOs, the comparators were placebo, usual care, an alternative intervention, or no intervention.
- Outcome – studies needed to report at least one of the critical outcomes pre-specified by the WPs.
- Study design – a hierarchical approach was used in selecting studies of adequate quality. For intervention PICOs, systematic reviews of randomised controlled trials (RCTs) and RCTs were used when available, and observational studies were considered if no RCTs were identified. For diagnostic studies, RCTs, observational studies with sequential sampling, and systematic reviews of them, were considered appropriate. If a high-quality systematic review with meta-analysis was identified, it was considered the highest level of evidence and only primary studies not included in the systematic review were considered in addition to the systematic review.
- For all questions being updated, the publication period searched was from 19 February 2010 to August 2016. For the three new questions it was from the inception of the databases to August 2016.

Exclusion criteria

- People under the age of 18 years.
- Patients with subarachnoid or subdural haemorrhagic stroke were excluded as they follow a different care pathway.
- Interventions unavailable or not applicable to an Australian healthcare setting were excluded.
- Non-English literature was excluded because resources did not allow for translation of such studies and the population is unlikely to be applicable to the Australian healthcare setting.
- Conference proceedings and studies published in abstracts only were excluded as the information was insufficient for assessment of the quality of the study.

Studies that did not meet the inclusion criteria and/or fit the exclusion criteria were excluded. If a study was excluded based on the criteria above but WPs deemed it relevant to inform guideline audiences, the reason for exclusion and the study's potential implication in practice were briefly discussed in the background of the relevant sections. There were no explicit criteria for reviewing literature relevant to consumers' perception and economics, and all literature relevant to the stroke population was included.

The literature search identified a total of 109,620 citations, and final list of over 800 studies was used to inform the Clinical Guidelines recommendations. (For details of search results, see *Appendix 1*).

2.3. Assessment of evidence and formulation of recommendations

2.3.1. Use of GRADE and MAGICapp

Unlike previous versions of the clinical guideline, this Clinical Guideline used GRADE methodology (Grading of Recommendations, Assessment, Development and Evaluation) [2], which was supported by an online guideline development platform known as MAGICapp (Making GRADE the Irresistible Choice). This web platform has been designed to develop and publish clinical guidelines using GRADE methodology.

The Stroke Foundation chose to use GRADE to facilitate international collaboration as it is being used by a number of international organisations including the World Health Organisation, American College of Physicians, National Institute for Health and Care Excellence in UK, and the Cochrane Collaboration. GRADE is similar to the NHMRC's methodology for assessing clinical evidence and developing recommendations. The main differences are that in GRADE, especially in combination with MAGICapp, assessment of the quality of evidence is transparent and the assessment goes beyond risk of bias, which is traditionally the focus of reviewing evidence; there is separate consideration of quality of evidence and strength of recommendation, and there is a different terminology for strength of recommendations. (For details of GRADE methodology, see *Appendix 2*).

The reasons for moving to an online guideline development platform, MAGICapp, were multifactorial and included:

- To enable collaboration between multiple authors across geographic locations,
- To ensure a standard approach in reviewing evidence and formulating recommendations consistent with GRADE methodology,
- To allow for interactive web publication format and easy access to the guidelines, and
- To facilitate future guideline updates.

MAGICapp has built-in standardised steps for evaluating evidence and developing recommendations. These include:

a. Defining population, intervention, comparator and critical outcomes;

b. Extracting relative and absolute effect estimates;

c. Assessing certainty in effects estimates/quality of evidence with the consideration of risk of bias, inconsistency, indirectness, imprecision, and publication bias;

d. Summarising results for each outcome with the consideration of both effect estimates and certainty in effects estimates;

e. Summarising the body of evidence for that combination of population, intervention and comparator, in the form of an evidence profile and/or a narrative summary of all the outcomes and other relevant literature;

f. Summarising benefits and harms, and quality of evidence across all relevant PICOs, as well as other considerations in patients' perception and resources implications; and

g. Drafting recommendations and setting their strength.

2.3.2. Data extraction and quality appraisal

The WP was primarily responsible for extracting data from the literature and assessing the quality of the evidence. For some questions, smaller groups (2-3 WP members) were given responsibility for leading the evidence review and drafting recommendations for topics relevant to their expertise. Other members of the WP then reviewed these recommendations. Experts in health economics, implementation of guidelines and consumer representatives were also involved in the reviewing of the literature.

To assist WP members to understand the GRADE methodology and MAGICapp, the PT developed documentation guides for each step required for data extraction and quality appraisal. A Word template with the same steps was developed for those WP members who preferred to complete the process offline. WP members also received standardised training sessions from the MAGIC project team (based in Norway) in the use of GRADE and MAGICapp. The MAGIC project team are experienced methodologists and members of the GRADE working group.

The evidence review process started with the PT summarising identified literature into PICO format which was then approved by the leads of each WP. The highest quality study amongst all relevant literature for each PICO was used for the evidence profile (i.e. data extraction) and other studies were described in narrative summary of each PICO so all the identified literature was available to inform the guideline readers. The study

used for the evidence profile is the one considered to be the most informative for clinical practice, for example, the most recent meta-analysis or a primary study of highest quality.

The PT then uploaded the PICOs and identified literature into MAGICapp for the author(s) to undertake data extraction and quality appraisal. Following completion of the data extraction, one member of the PT independently cross-checked the entered data based on the original articles to ensure accuracy and consistency. Any issues identified were discussed with the WP and amended as necessary.

2.3.3. Development of recommendations

The WP members were responsible for drafting the recommendations with support from the PT. As for previous steps in the process, the author(s) were provided with documentation guides for each step.

GRADE methodology considers four factors when developing recommendations:

- Benefit and harms,
- Quality of evidence,
- Confidence in patients' preferences and values, and
- Resources and related considerations such as equity and feasibility.

The benefits and harms, and quality of evidence were summarised from the evidence profile. GRADE emphasises explicit acknowledgement of patients' preference and if there is any indication of large variation. To address this requirement, qualitative studies of patients' values and perceptions were identified and reviewed by consumer representatives. Where there was no literature identified but there were potential issues in patients' preferences, consumer representatives were asked to make comments based on their own understanding and experiences for WPs to take into account. WPs also considered clinical scenarios where informed decisions may be needed. Resources and related considerations mainly consist of cost-effectiveness evidence, which the economics WP reviewed and summarised. This evidence was then considered by WPs in rating the strength of recommendations.

Based on the four factors, GRADE rates recommendations as either strong or weak. The principle for the strength of recommendations is: the strength is strong when most or all individuals will be best served by the recommended course of action, and it is weak when not all individuals will be best served by the recommended course of action, and there is a need to consider the individual patient's circumstances, preferences, and values. In addition, practical advice for implementing recommendations is given in relevant recommendations, such as contraindications, dosages, and patient selection criteria.

For some topics, a systematic review of the available evidence was conducted, but there was either a lack of evidence or insufficient quality of evidence on which to base a

recommendation. In cases where the working group determined that recommendations were important, statements and advice about topics were developed based on consensus and expert opinion (guided by any underlying or indirect evidence). These statements were labelled as 'Practice statements', and correspond to the 'consensus-based recommendations' outlined in the NHMRC procedures and requirements. These statements should be regarded with greater discretion by guideline users.

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. Examples include the lifestyle modification recommendations, where no literature search was conducted and so these Clinical Guidelines refer to existing external guidelines for these topics.

In the Clinical Guidelines, the following criteria were used in determining the strength of recommendations:

- **Strong for**: moderate to high quality evidence suggests that benefits in critical outcomes clearly outweigh the reported harms; a strong recommendation can be made in the absence of high-quality evidence if patients are expected to highly desire such practice and there are no potential harms in providing it.
- **Strong against**: moderate to high quality evidence suggests harms outweigh benefits; high quality evidence suggests lack of benefits.
- **Weak for**: moderate to high quality evidence suggests equivalent benefits and harms, patients would mostly want to receive the practice, and there is no significant resources implication in doing so; low quality evidence suggests benefits outweigh harms and there are no significant implications in patients' preferences or resources implications.
- **Weak against**: moderate to high quality evidence suggests equivalent benefits and harms, but there is expected large variation in patients' preference to receive this practice or important resource implications; low quality evidence suggests harms outweigh benefits and there are no significant implications in patients' preferences or resource implications.
- **Practice statement (consensus-based recommendation):** evidence is absent or of insufficient quality; unclear balance between benefits and harms, and there is expected large variation in patients' preferences. No formal method of reaching consensus was used but this was addressed in internal reviews.
- **Information box (Practice point):** No systematic evidence search was conducted, or the evidence was outside the scope of the systematic literature search.

Language related to the timing of interventions was standardised across the guidelines following this convention:

- *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.

In order to make changes from previous guidelines more visible, each recommendation was labelled with either an “Updated” or “New” tag. “Updated” recommendations have been updated to reflect new evidence and the GRADE format, but otherwise have not changed substantially compared to the previous guidelines. “New” recommendations were not present in previous guidelines or have seen substantial changes.

2.4. Future update of the guidelines

The Stroke Foundation is planning to move to a Living Guidelines format after the completion of this Clinical Guideline, instead of the usual five-year major clinical guideline update. The topics will be prioritised and evidence will be reviewed and updated more regularly to capture any significant changes at the time they are published. Updated recommendations will reflect the change in the evidence base.

2.5. Challenges

2.5.1. Volume of literature

The initial abstract and full-text screening was completed four weeks after schedule, which could have been significantly longer but for the mitigation strategies implemented early in the project. These mitigation strategies included review and refinement of the search strategy, and involvement of the CWP in screening literature. The main reason for the eventual delay in finalising the screening was a greater than anticipated workload due to the large volume of literature returned from the initial literature search – a 267% increase compared to the last guideline update. In addition, WP member input was delayed due to competing priorities such as NHMRC grant submission deadline in early March. The challenge was discussed at the GAC meeting on 5 April 2016 and the GAC acknowledged that the mitigation strategies were effective and noted that with additional support from the WP members the project could meet future planned milestones.

2.5.2. Use of new IT platforms, Covidence and MAGICapp

The PT used IT platforms Covidence and MAGICapp to improve efficiency in the Clinical Guideline development. The risk of using these platforms primarily revolved around lack of familiarity for both the PT and the WP members. This risk was managed by extensive

orientation of both tools by the PT and specifically the training provided to 80 WP members in the use of the MAGICapp platform. Covidence is a simple tool and training was deemed not to be required with the PT supporting WP member enquires. The MAGICapp training was completed by 80 WP members and delivered by the MAGICapp team. The training was recorded and this was made available (along with PowerPoint slides) for future reference by the WP members. In addition to addressing the challenges of adopting new IT platforms, the PT developed step-by-step instructions for WP members to extract data in MAGICapp and the MAGIC and Covidence teams were very responsive to requests from the PT.

The project experienced a number of issues within the MAGICapp platform but they were mitigated through ongoing technical and administrative support from the MAGICapp team as well as the PT. Difficulties navigating in MAGICapp were expressed by some WP members despite training and access to documentation guides. The PT provided personalised assistance to these members, and the MAGICapp team has continued to improve the user-friendly design of the platform. The capacity of MAGICapp to store and process information was challenged by the size of this Clinical Guideline and resulted in significantly slowed response in the system. The MAGICapp team resolved this by upgrading the server and splitting the Clinical Guideline into individual chapters.

2.5.3. GRADE

The GRADE framework is a new approach for the Stroke Foundation and WPs for evaluating evidence and formulating recommendations, so challenges to adopt it were expected. This risk was managed by the PT attending training about GRADE, subsequent training to all WP members about GRADE, and providing all WP members articles specifically summarising the GRADE approach. Some members were already familiar with GRADE from having used it for other guidelines, and the PT also utilised their experience in testing the optimal approach of integrating GRADE.

2.5.4. Involvement of large numbers of health professionals

This project would not have achieved the level of detail and due diligence if not for the assistance of the 96 healthcare professionals (HPs) who gave their time voluntarily. However, with this number of external volunteers came many challenges for the PT. The PT spent a lot of time engaging with and supporting each HP via email, phone and videoconference to ensure they were comfortable with their responsibilities and tasks. The challenge of managing a large working group was compounded by the aforementioned use of new methodology and IT platforms.

3. List of clinical questions

There are 8 chapters, 69 topics and 89 questions in the Clinical Guidelines related to the full pathway of care following suspected stroke or TIA. Broad clinical questions were used to specify the scope of literature searches, along with broad descriptions of the population, interventions, comparators and outcomes of greatest interest.

Based on the studies identified by the literature search and the evidence available, studies were grouped according to the population, intervention and comparator they addressed, creating structured PICO questions.

3.1. Chapter 1: Pre-hospital care

Pre-hospital care

Clinical question: What interventions by paramedics improve outcomes for people with acute stroke?

Broad description of population, intervention, comparator and outcome:

Population	Intervention	Comparator	Outcomes of most interest
All people with suspected stroke	Pre-hospital intervention	No pre-hospital intervention	Onset to treatment time Door-to-needle time Functional dependence

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with suspected stroke	Emergency medical dispatch – priority Level 1 (immediate ambulance dispatch)	Emergency medical dispatch – standard priority (Level 2 – within 30 minutes)	Thrombolysis frequency Door-to-needle time Time – call to stroke unit
Adults with suspected stroke	Pre-hospital thrombolysis	Usual care	Thrombolysis rate Secondary intracerebral haemorrhage

			7-day mortality Time to thrombolysis
Adults with suspected stroke	Pre-hospital neuroprotection (rPerC)	Usual care	Functional independence (mRS)
Adults with suspected stroke	Neuroprotection (IV magnesium sulfate)	Placebo	Functional independence (mRS ≤ 2) Serious adverse events
Adults with suspected stroke	Mobile stroke unit (MSU)	Conventional care	Functional independence (mRS ≤ 2) Alarm to therapy decision Alarm to IV tPA
Adults with suspected stroke	Pre-hospital notification system	Conventional care	Received thrombolysis Door-to-needle time – patients receiving tPA

3.2. Chapter 2: Early assessment and diagnosis

Transient ischaemic attack

Clinical question: What clinical assessment tools and investigations improve diagnostic accuracy and outcomes for people with suspected TIA?

Broad description of population, intervention, comparator and outcome:

Population	Intervention	Comparator	Outcomes of most interest
All people with suspected TIA	Investigations	Usual care	Diagnosis of TIA Readmission Stroke

Specific questions identified and evaluated:

Population	Intervention/Diagnostic tool	Comparator/Reference	Outcomes

All adults with suspected TIA	Risk prediction scores	Confirmed diagnosis of recurrent stroke	Prediction of stroke
All adults with suspected TIA in primary care setting	Decision support tool	Confirmed diagnosis of recurrent stroke	Occurrence of stroke Adverse events
All adults with suspected TIA/minor stroke	Lesion on brain imaging	Confirmed diagnosis of recurrent stroke	Prediction of recurrent stroke – multiple cerebral infarctions
All adults with suspected TIA	Rapid assessment and treatment	Control	Recurrent stroke

Rapid assessment in the emergency department

Clinical question: Do clinical assessment tools improve diagnostic accuracy in the emergency department?

Broad description of population, intervention, comparator and outcome:

Population	Intervention	Comparator	Outcomes of most interest
All people with suspected stroke	Assessment tools	Usual care	Diagnosis of stroke Speed of treatment

Specific questions identified and evaluated:

Population	Intervention/Diagnostic tool	Comparator/Reference	Outcomes
Adults with suspected stroke	Clinical scales	Confirmed diagnosis	Identification of large artery occlusion
Adults with suspected stroke	Stroke screening tool	Confirmed diagnosis	Identification of stroke or TIA
Adults with suspected stroke	Biomarkers	Confirmed diagnosis	Identification of stroke or TIA
Adults with suspected stroke	Rapid management	Usual care	None (narrative summary of available evidence)

Investigations – Imaging

Two search questions related to brain imaging and carotid/vascular imaging were originally specified, but following evidence review these questions were combined into a single topic.

Clinical question: What is the optimal modality for brain imaging for suspected acute stroke?

Broad description of population, intervention, comparator and outcome:

Population	Intervention	Comparator	Outcomes of most interest
All people with stroke	Brain imaging	Usual care	Rates of treatment with tPA and endovascular reperfusion therapies Speed of treatment

Clinical question: What is the optimal modality for carotid/vascular imaging?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with stroke or TIA	Timing of vascular imaging	Usual care	Accuracy of characterisation of carotid stenosis

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with suspected stroke	MRI	Confirmed diagnosis of stroke	Diagnosis of ischaemic stroke
Adults with suspected stroke	CT	Confirmed diagnosis of stroke	Diagnosis of ischaemic stroke
Adults with suspected stroke	Thin slice non-contrast CT	Confirmed diagnosis of vessel occlusion	Diagnosis of vessel occlusion
Adults with suspected stroke	CT perfusion imaging	Confirmed diagnosis of stroke	Diagnosis of ischemic stroke
Adults with ischaemic stroke and CT perfusion	Endovascular clot retrieval	Control	Functional independence

mismatch beyond 6hrs of stroke onset			
Adults with ischaemic stroke and MR perfusion-diffusion mismatch beyond 3hrs of stroke onset	Reperfusion achieved through intravenous thrombolysis with alteplase	Reperfusion not achieved	Functional independence
Adults with ischaemic stroke and MR perfusion-diffusion mismatch beyond 6hrs of stroke onset	Reperfusion achieved through endovascular clot retrieval	Reperfusion not achieved	Functional independence
Patients with carotid artery stenosis	Imaging	Surgical specimen	Accuracy of characterisation of carotid stenosis
Patients suspected of having carotid artery stenosis	Ultrasound, CT and MR angiography	Digital subtraction angiography	Accuracy of characterisation of carotid stenosis
Patients eligible for endovascular clot retrieval based on clinical severity	Non-invasive angiography (CT or MR)	Patients eligible for endovascular clot retrieval based on proven large vessel occlusion on non-invasive angiography	Presence of large vessel occlusion

Investigations – Cardiac investigations

Clinical question: What is the optimal modality for cardiac investigations for possible atrial fibrillation?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcome/s combined
All people with stroke or TIA	Cardiac investigations	Usual care	Detection of atrial fibrillation

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes

Adults with acute stroke	Continuous ECG monitoring	Standard ECG	Detection of atrial fibrillation
Adults with stroke	Long term ECG monitoring	Short term ECG monitoring	Detection of atrial fibrillation
Adults with cardiac conditions as potential sources of stroke or TIA	Echocardiography	Reference standard	Detection of cardiac source of stroke

3.3. Chapter 3: Acute medical and surgical management

Stroke unit care

Clinical question: Does care on a stroke unit improve outcomes for people with stroke?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with stroke	Stroke unit care	Usual care	Death Institutionalisation rate Length of stay

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Organised stroke unit care	Alternative services (less organised care)	Death by the end of scheduled follow-up Death or institutional care by the end of scheduled follow-up Death or dependency by the end of scheduled follow-up Death or dependency at 5-year follow-up Death or dependency at 10-year follow-up

			Length of stay in a hospital or institution or both
Adults with stroke	Organised stroke unit care	General medical wards	Death by the end of scheduled follow-up Death or institutional care by the end of scheduled follow-up Death or dependency by the end of scheduled follow-up Length of stay in a hospital or institution or both
Adults with stroke	Different systems of organised care: acute stroke ward	Alternative service	Death by the end of scheduled follow-up Death or institutional care by the end of scheduled follow-up Death or dependency by the end of scheduled follow-up Length of stay in a hospital or institution or both
Adults with stroke	Different systems of organised care: comprehensive stroke ward	Alternative service (mobile stroke team)	Death by the end of scheduled follow-up Death or institutional care by the end of scheduled follow-up Death or dependency by the end of scheduled follow-up Length of stay in a hospital or institution or both
Adults with stroke	Different systems of organised care:	Alternative service (mixed rehabilitation ward)	Death by the end of scheduled follow-up

	rehabilitation stroke ward		Death or institutional care by the end of scheduled follow-up Death or dependency by the end of scheduled follow-up Length of stay in a hospital or institution or both
Continuous versus intermittent physiological monitoring for acute stroke	Continuous monitoring	Intermittent monitoring of physiological variables	Death by the end of scheduled follow-up Cardiac complications Fever Length of stay (days)
Adults with stroke	Acute nursing intervention	Control	Death or dependency Functional independence (Barthel Index ≥ 95) Functional Independence (Barthel Index ≥ 60) Physical health Mental health

Palliative care

Clinical question: Do strategies to assist palliation and death improve outcomes for people with stroke and their family?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with stroke	Palliation strategies	Usual care	Quality of life Family understanding Symptom control Pain scales

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Interdisciplinary palliative care	Usual care	Advance directives ICU admissions Patient satisfaction – care environment Patient satisfaction – communication with providers Hospice length of stay

Reperfusion therapy – Thrombolysis

Clinical question: Does the administration of thrombolysis improve outcomes after acute ischaemic stroke?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with ischaemic stroke	Thrombolysis	No thrombolysis	Death Institutionalisation rate

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with acute stroke	Intravenous alteplase	Control	Death or dependency at the end of follow-up Death – 7 to 10 days Death at the end of follow-up Fatal intracranial haemorrhage – 7 to 10 days Symptomatic intracranial haemorrhage – 7 to 10 days

Adults with acute stroke treated within 3 hours	Intravenous alteplase	Control	Favourable outcome – 3 to 6 months Death – 90 days Fatal intracranial haemorrhage – 7 days
Adults with acute stroke treated at 3–4.5 hours	Intravenous alteplase	Control	Favourable outcome – 3 to 6 months Death – 90 days Fatal intracranial haemorrhage – 7 days
Adults with acute stroke treated at 4.5–6 hours	Intravenous alteplase	Control	Favourable outcome – 3 to 6 months Death – 90 days Fatal intracranial haemorrhage – 7 days
Adults with acute stroke	Low-dose intravenous alteplase	Standard-dose intravenous alteplase	Death or disability – 90 days Death – 90 days Improved functional outcome – 90 days Symptomatic intracranial haemorrhage – 90 days
Adults with acute stroke	Sonothrombolysis	Alteplase only	Death and disability – 90 days Death at follow up Cerebral haemorrhage – end of follow up

Reperfusion therapy – Neurointervention

Clinical question: Does the use of neurointerventional treatments improve outcomes in people with stroke?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with ischaemic stroke	Neurointervention	No neurointervention	Death Institutionalisation rate

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Endovascular mechanical thrombectomy	Standard medical care	Improved functional outcome – 3 months Functional independence – 3 months Mortality – 3 months Symptomatic intracranial haemorrhage – within 36 hours
Adults with stroke	Endovascular mechanical thrombectomy + intravenous thrombolysis	Intravenous thrombolysis alone	Functional independence Mortality Improved functional outcome
Adults with stroke	Stent retrievers	Merci device	Functional independence – 3 months Symptomatic intracranial haemorrhage – 24 hours Recanalisation rate
Adults with stroke ineligible for IV thrombolysis	Endovascular mechanical thrombectomy	Standard care	Improved functional outcome – 3 months Functional independence – 3 months Mortality – 3 months
Adults with stroke onset > 6 hours	Endovascular mechanical thrombectomy	Standard care	Improved functional outcome – 3 months

			Functional independence – 3 months Mortality – 3 months
Adults with stroke aged over 80 years	Endovascular mechanical thrombectomy	Standard medical care	Improved functional outcome – 3 months Functional independence – 3 months Mortality – 3 months
Adults with stroke caused by distal MCA (M2) occlusion	Endovascular mechanical thrombectomy	Standard medical care	Improved functional outcome – 3 months Functional independence – 3 months Mortality – 3 months
Adults with basilar artery occlusion	Endovascular mechanical thrombectomy	Control	None – narrative summary of available evidence

Dysphagia

Three clinical questions related to dysphagia were combined into a single topic following evidence review.

Clinical question: What is the optimal time to screen for dysphagia?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with stroke	Timing and swallow screen	Usual care	Aspiration pneumonitis Pneumonia Death Institutionalisation rate Length of stay Nutritional status Serious adverse events and complications

Clinical question: Does comprehensive swallow assessment improve outcomes for people who have failed a swallow screen?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All patients with stroke	Videofluoroscopy	Usual care	Death Institutionalisation rate Length of stay

Clinical question: Which interventions improve outcomes in stroke patients with dysphagia?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All stroke patients with dysphagia	Medical interventions	No intervention	Death Institutionalisation rate Improved swallowing function Quality of life Nutritional status Carer burden

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Early swallow screen	Usual care	Death or dependency
Adults with stroke	Swallow screen test	Reference standard (FEES or VF)	Performance in identifying dysphagia
Adults with stroke	Clinical bedside swallow exam	Instrumental swallow exam	Pneumonia Performance in identifying dysphagia/aspiration

All stroke patients with dysphagia	Surface neuromuscular electrical stimulation plus swallow therapy	Swallow therapy only	Swallowing function
All stroke patients with dysphagia	Pharyngeal electrical stimulation	Sham	Death Respiratory tract infection Severity of stroke Swallowing function
All stroke patients with dysphagia	Brain stimulation	Sham	Swallowing function
All stroke patients with dysphagia	Acupuncture	No acupuncture	Improved swallowing function
All stroke patients with dysphagia	Behavioural intervention	Control	Death Chest infection or pneumonia Presence of dysphagia Institutionalisation

Antithrombotic therapy

Clinical question: Does the use of antithrombotic therapy within first 48 hours improve outcomes in acute stroke?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with stroke	Antithrombotics within 48 hours	No antithrombotics	Death Institutionalisation rate Recurrent / secondary stroke

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes

Adults with acute ischaemic stroke	Aspirin	Placebo or no treatment	Death or dependence Death Recurrent stroke – during treatment Symptomatic intracranial haemorrhage – during treatment
Adults with acute ischaemic stroke	Anticoagulant	Placebo or no treatment	Death or dependence Death Recurrent stroke – during treatment Symptomatic intracranial haemorrhage – during treatment
Adults with acute stroke	Dual antiplatelet therapy	Mono antiplatelet therapy	Recurrent stroke Composite outcome of stroke, TIA, ACS, and all deaths Major bleeding
Adult stroke patients treated with alteplase	Early antiplatelet therapy	No additional therapy	Death Favourable outcome Symptomatic intracranial haemorrhage

Acute blood pressure lowering therapy

Clinical question: Does the use of acute blood pressure lowering therapy improve outcomes for people with stroke?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with stroke	Acute blood pressure lowering therapy	No blood pressure lowering therapy	Death Institutionalisation rate Recurrent / secondary stroke

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with ICH	Blood pressure lowering	Control	Death or dependency
Adults with ischaemic stroke	Blood pressure lowering	Control	Death or dependency
Adults with stroke	Continue pre-stroke antihypertensives	Stop pre-stroke antihypertensives	Death or dependency

Surgery for ischaemic stroke and management of cerebral oedema

Two clinical questions related to surgical interventions for acute ischaemic stroke and raised intracranial pressure were originally proposed but following evidence review these were combined into a single topic:

Clinical question: What interventions improve outcomes in acute stroke patients with raised intracranial pressure?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with stroke	Medical, surgical interventions	Usual care	Death Institutionalisation rate

Clinical question: Does the use of surgical interventions improve the outcomes for people with acute ischaemic stroke?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with stroke	Surgical interventions	No surgery	Death Institutionalisation rate

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes

Adults > 60 y.o. with malignant middle cerebral artery infarct	Hemicraniectomy	Medical treatment	Survival without severe disability at 6 months Survival at 12 months Survival without severe disability at 12 months Neurological outcome at 12 Months
Adults < 60 y.o. with malignant middle cerebral artery infarct	Hemicraniectomy	Medical treatment	Death at end of follow-up Death or disability defined as mRS > 3 at end of follow-up Death or severe disability defined as mRS > 4 at 12 months Severe disability among survivors defined as mRS 4 to 5 at 12 months
Corticosteroids for acute ischaemic stroke	Corticosteroids	Placebo	All deaths Deaths within one month

Intracerebral haemorrhage (ICH) management – Medical interventions

Clinical question: Does the administration of medical interventions improve outcomes after acute haemorrhagic stroke?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with intracerebral haemorrhage	Medical interventions	No intervention	Death Institutionalisation rate

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes

Adults with intracerebral haemorrhage	Edaravone	Usual care	Death Adverse effects Activities of daily living
Adults with intracerebral haemorrhage	Cerebrolysin	Placebo	Adverse events Activities of daily living
Adults with intracerebral haemorrhage	Tranexamic Acid	Placebo	Death Adverse events Length of stay Dependence
Adults with intracranial haemorrhage related to vitamin K antagonists	Prothrombin complex concentrate	Fresh frozen plasma	INR ≤1.2 within 3 h Death Functional independence Haematoma expansion
Adults with intracerebral haemorrhage taking antiplatelet before	Platelet transfusion	Standard care	Death or dependence Survival Serious adverse events
Adults with ICH related with DOACs	Reversal agents	No treatment	None (narrative summary of available evidence)

Intracerebral haemorrhage (ICH) management – Surgical interventions

Clinical question: Do surgical interventions improve outcomes after acute haemorrhagic stroke?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with intracerebral haemorrhage	Surgical interventions	No intervention	Death Institutionalisation rate

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes

Patients with basal ganglia/thalamic haematomas	Surgery	Conservative treatment	Unfavourable outcome
Patients with lobar haematoma	Surgery	Conservative treatment	Unfavourable outcome
Adults with intraventricular haemorrhage complicating parenchymal haemorrhage	Surgery	Conservative treatment	Unfavourable outcome
Adults with intraventricular haemorrhage complicating parenchymal haemorrhage	Intraventricular thrombolysis	Placebo	Death Adverse events – Ventriculitis Adverse events - Symptomatic bleeding

Oxygen therapy

Clinical question: Does oxygen therapy improve outcomes in stroke patients who are not hypoxic?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with stroke	Oxygen therapy	No oxygen therapy	All outcomes

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with acute ischaemic stroke	Early routine oxygen supplementation	Room air	Death – 1 week Death at 6 months Improvement in neurological outcome Disability (modified Rankin Scale ≥ 3) Quality of life
Adults with acute ischaemic stroke	Hyperbaric oxygen therapy	Standard practice	Death

			Functional outcome

Neuroprotection

Clinical question: Does the use of neuroprotective agents improve outcomes for people with acute stroke?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with stroke	Neuroprotection	No neuroprotection	Death Institutionalisation rate

Glycaemic therapy

Clinical question: Does glycaemic therapy improve outcomes in stroke patients with hyperglycaemia?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with stroke	Glycaemic therapy	No glycaemic therapy	Death Institutionalisation rate Length of stay Serious adverse events or complications Glycaemic control

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	FeSS protocol	No FeSS protocol	Death or dependency Functional dependency (Barthel Index ≥ 60) Functional dependency (Barthel Index ≥ 95)

			Length of stay
Adults with stroke with hyperglycaemia	Intravenous insulin	Subcutaneous insulin	Mortality Functional outcome Hypoglycaemia (asymptomatic or symptomatic)
Adults with stroke with hyperglycaemia	Intravenous insulin	Normal saline	Mortality Functional outcome Asymptomatic or symptomatic hypoglycaemia
Adults with stroke	Insulin for glycaemic control	Usual care	Dependency or death at the end of the follow-up Death Dependency or death – patients with diabetes mellitus Dependency or death – patients without diabetes mellitus Symptomatic hypoglycaemia Hypoglycaemia (with or without symptoms)

Pyrexia management

Clinical question: What interventions improve outcomes in stroke survivors with pyrexia?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All stroke patients with pyrexia	Medical interventions	No intervention	Death Institutionalisation rate Length of stay Infarct volume

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	FeSS protocol	No FeSS protocol	Death or dependency Functional dependency (Barthel Index ≥ 60) Functional dependency (Barthel Index ≥ 95) Length of stay
Adults with stroke	Therapeutic hypothermia	Standardized stroke unit care	Death Disability Length of stay
Adults with stroke	Paracetamol	Placebo	Disability: favourable outcome (mRS ≤ 2) Serious adverse events

3.4. Chapter 4: Secondary prevention

Lifestyle modification

Evidence for behaviour-changing strategies targeting lifestyle factors to prevent recurrence of stroke is limited and often derived from cohort studies of primary prevention. Specific guidelines focussing on each of the cardiovascular risk factors are available and these guidelines apply generically to the population including people with stroke. Therefore it was decided not to undertake a separate process to search for evidence and develop stroke-specific recommendations, but rather to refer to these overarching guidelines.

The lifestyle factors referred to in the Clinical Guidelines include:

- Smoking
- Diet
- Physical activity
- Obesity
- Alcohol.

Adherence to pharmacotherapy

Clinical question: What strategies improve concordance with medication to improve outcomes for people with stroke?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with stroke	Medication adherence strategies	No intervention	Death Institutionalisation rate Medication compliance / adherence Medication specific outcomes

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Behavioural, educational or organisations interventions designed to improve medication adherence/concordance	Usual care or modified usual care	Medication compliance – overall Medication compliance – antithrombotics Medication compliance – antihypertensives Medication compliance - statins
Adults with stroke	Organisational interventions	Usual care	Blood pressure target achievement Proportion of participants with secondary stroke or TIA Proportion of participants with vascular death Number of vascular deaths

Blood pressure lowering therapy

Clinical question: What blood pressure lowering interventions lower the risk of strokes after stroke or TIA?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with ischaemic stroke and TIA	Blood pressure lowering, exercise	No intervention	Death Institutionalisation rate Secondary stroke

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with recent stroke	Lower target of blood pressure (less than 130 mmHg)	Higher target of blood pressure (130–149 mm Hg)	Death Recurrent stroke Recurrent ischaemic stroke Recurrent intracerebral haemorrhage Adverse events
Adults with previous stroke or TIA	Blood pressure reduction medication	Control/placebo	Recurrent stroke Death (all-cause)

Antiplatelet therapy

Clinical question: What antiplatelet therapies lower the risk of stroke after stroke or TIA?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with ischaemic stroke and TIA	Antiplatelet therapy: aspirin, clopidogrel, dipyridamole	No intervention	Death Institutionalisation rate Secondary stroke Bleeding complications

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Aspirin only	Placebo	Recurrent stroke – long term – low dose (75–162mg daily) Recurrent stroke – short term – any dose Bleeding – long term – low dose (75–162mg daily) Serious vascular events – long term – low dose (75–162mg daily)
Adults with stroke	Ticlopidine only	Placebo	Recurrent stroke – long term Recurrent stroke – short term Bleeding – long term Serious vascular events – long term
Adults with stroke	Aspirin plus dipyridamole	Placebo	Recurrent stroke – long term Bleeding – long term Serious vascular events – long term
Adults with stroke	Aspirin plus dipyridamole	Aspirin alone	Recurrent stroke Death from all causes Major bleeding
Adults with stroke	Aspirin plus clopidogrel	Placebo	Recurrent stroke Bleeding Serious vascular events
Adults with stroke	Aspirin plus clopidogrel	Aspirin or clopidogrel alone	Secondary stroke – short term treatment

			Secondary stroke – long term treatment Major bleeding – short term treatment Major bleeding – long term treatment Secondary stroke, MI or vascular death – short term treatment Secondary stroke, MI or vascular death – long term treatment
Adults with stroke	Clopidogrel	Placebo	Recurrent stroke Bleeding Serious vascular events
Adults with stroke	Clopidogrel	Aspirin (75–162mg daily)	Recurrent stroke Bleeding Serious vascular events
Adults with atrial fibrillation and unsuitable for vitamin K antagonist therapy	Factor Xa inhibitor	Aspirin	All-cause death Stroke and systemic embolism Major bleeding

Anticoagulation therapy

Clinical question: What interventions improve outcomes for people with atrial fibrillation after stroke or TIA?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with stroke or TIA	Anticoagulation therapy	No intervention	Death Institutionalisation rate Secondary stroke Bleeding complications

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke with non-valvular atrial fibrillation	DOACs	Warfarin	Stroke or systemic embolic events Major bleeding
Adults with stroke	Vitamin K antagonists	Antiplatelets	Recurrent stroke All vascular events Any intracranial bleed Major extracranial bleed

Cholesterol lowering therapy

Clinical question: What cholesterol lowering therapies lower the risk of strokes after stroke or TIA?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with stroke or TIA	Cholesterol lowering therapy	No intervention	Death Institutionalisation rate Secondary stroke

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Patients with previous stroke	Fibrates	Control	Secondary stroke Secondary fatal stroke
Patients with previous stroke or TIA	Statins	Control	Death Secondary stroke – all Secondary ischaemic stroke Secondary intracerebral haemorrhage

Carotid surgery

Clinical question: What interventions improve the outcomes for patients with carotid stenosis after stroke or TIA?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with stroke or TIA	Carotid surgery	No intervention	Death Institutionalisation rate Secondary stroke

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with symptomatic carotid occlusion	Extracranial-intracranial arterial bypass surgery	Medical therapy alone	Death Death or dependency Stroke
Adults with recently symptomatic carotid stenosis	Carotid artery stenting	Carotid endarterectomy	Periprocedural death or stroke Periprocedural stroke Death or stroke – long term Stroke – long term
Adults with asymptomatic carotid stenosis	Carotid artery stenting	Carotid endarterectomy	Periprocedural death or stroke Periprocedural stroke Death or stroke – long term Stroke – long term
Adults with asymptomatic carotid stenosis	Carotid endarterectomy	Medical therapy alone	Stroke

Cervical artery dissection

Clinical question: What interventions improve outcomes for people with cervical artery dissection?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with cervical arterial dissection	Medical, surgical interventions	Usual care	Recurrent stroke Institutionalisation rate Death

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Stroke patients with cervical artery dissection	Anticoagulant	Antiplatelet	Stroke or death Death Stroke Major bleeding

Venous sinus thrombosis

Clinical question: What interventions improve outcomes for those with venous sinus thrombosis?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with venous sinus thrombosis	Medical, surgical interventions	Usual care	Death Institutionalisation rate

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with venous sinus thrombosis	Anticoagulation (heparin)	Control	Death from any cause at the end of scheduled trial follow-up Death or dependency at the end of the scheduled trial follow-up period

			Symptomatic intracerebral haemorrhage (new or increased) Any severe haemorrhage
Adults with venous sinus thrombosis	Low molecular weight heparin	Unfractionated heparin	Death Functional outcome – Poor or incomplete recovery Adverse events

Diabetes management

No specific search or evidence evaluation was conducted for diabetes management. The National Guidelines for the management of diabetes were referred to in these guidelines.

Patent foramen ovale management

Clinical question: What interventions in patent foramen ovale management lower the risk of further strokes in stroke survivors?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with stroke and patent foramen ovale	Surgical closure, medication	No intervention	Death Institutionalisation rate Secondary stroke

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Stroke patients with PFO	Closure	Medical therapy	Recurrent stroke or TIA All-cause mortality Serious adverse events
Stroke patients with PFO	Warfarin	Aspirin	Recurrent stroke or death

Hormone replacement therapy

Clinical question: Does hormone replacement therapy increase the risk of subsequent stroke in stroke survivors?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All women with stroke	Hormone replacement therapy	No hormone replacement therapy	Death Institutionalisation rate Secondary stroke

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Women with established cardiovascular disease	Hormone therapy	Placebo	Secondary stroke All-cause death

Oral contraception

Clinical question: Does oral contraception increase the risk of subsequent stroke in stroke survivors?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All women in childbearing years with stroke	Oral contraception	No oral contraception	Death Institutionalisation rate Secondary stroke

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
All women in childbearing years	Oral contraceptive use	Control	Ischaemic stroke Intracerebral haemorrhage

3.5. Chapter 5: Rehabilitation

Early supported discharge services

Clinical question: Does access to early supported discharge services improve outcomes for people with stroke?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with stroke	Early supported discharge services	Usual care	Death Institutionalisation rate Readmission

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Early supported discharge services overall	Conventional care	Death Death or requiring institutional care Death or dependency Satisfaction with services Carer satisfaction with services Activities of daily living (Barthel ADL) score Extended activities of daily living (EADL) score Subjective health status Mood status Carer subjective health status Carer mood status
Adults with stroke	Early supported discharge service with ESD team	Conventional care	Death Death or requiring institutional care

	coordination and delivery		Death or dependency Satisfaction with services Carer satisfaction with services Activities of daily living (Barthel ADL) score Extended activities of daily living (EADL) score Subjective health status Mood status Carer subjective health status Carer mood status
Adults with stroke	Early supported discharge service - ESD team coordination only	Conventional care	Death Death or requiring institutional care Death or dependency Satisfaction with services Carer satisfaction with services Activities of daily living (Barthel ADL) score Extended activities of daily living (EADL) score Subjective health status Mood status Carer subjective health status Carer mood status
Adults with stroke	Early supported discharge service - No ESD team co-ordination or delivery	Conventional care	Death Death or requiring institutional care

			Death or dependency Satisfaction with services Carer satisfaction with services Activities of daily living (Barthel ADL) score Extended activities of daily living (EADL) score Subjective health status Mood status Carer subjective health status Carer mood status

Home-based rehabilitation

Clinical question: Is home-based rehabilitation more effective than hospital-based care in reducing mortality and increasing independence amongst stroke patients?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with stroke	Home-based rehabilitation	Hospital-based rehabilitation	Death Institutionalisation rate Carer stress Length of stay Quality of life

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Home-based rehabilitation	Community-based rehabilitation	Short-term functional independence

			Medium-term functional independence Quality of life Disability

Goal setting

Clinical question: Does patient-centred goal setting improve patient outcomes?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with stroke	Goal setting	No goal setting	Health related quality of life Self-efficacy Activities of daily living (and possibly participation) Length of stay

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Patient-centred goal setting	Usual care	Quality of life Activities of daily living function Length of stay Self-efficacy

Early mobilisation

Clinical question: Do early mobilisation interventions improve outcomes in acute stroke?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with stroke	Early mobilisation	Usual care	Death and disability (mRS) Time to independent walking.

			Serious adverse events

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Very early mobilisation (<24 hrs)	Usual care	Favourable outcome (modified Rankin Scale score of 0–2) Change in functional outcome (odds of better mRS outcome) Death Time to unassisted walking Non-fatal serious adverse events
Adults with stroke	Physical rehabilitation (<3 days)	Usual care	Mortality Disability Functional outcome Complications

Sensorimotor impairment – Weakness

Clinical question: What interventions for strength improve outcomes for stroke survivors?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All stroke patients with reduced strength	Rehabilitation	No intervention	ADL Walking ability and arm function Strength Adverse events

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes

Adults with stroke	Electrical stimulation	Control	Strength
Adults with stroke	Task-oriented training	Control	Strength (lower extremities) Walking speed
Adults with stroke	Mechanical assisted training (arm)	Control	Activities of daily living Arm function Arm strength
Adults with stroke	Strength training	Control	Activities of daily living Strength Upper limb function

Sensorimotor impairment – Loss of sensation

Clinical question: What interventions increase sensation in stroke survivors?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All stroke patients with reduced sensation	Rehabilitation	No intervention	Activities of daily living Upper limb function and walking ability Sensation

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
All stroke patients with reduced sensation	Sensory-specific training	Conventional treatment	Sensation
All stroke patients with reduced sensation	Sensory-specific training plus motor function training	Conventional treatment	Improvement in activities of daily living

			Improvement in upper limb function Sensation

Sensorimotor impairment – Vision

Clinical question: What interventions (compensatory or restorative) improve visual field loss?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All stroke patients with visual field loss	Rehabilitation	No intervention	Improved visual field

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Interventions for visual field defects in patients with stroke	Restitutive interventions	Control, placebo or no intervention	Visual field
Interventions for visual field defects in patients with stroke	Compensative interventions	Control, placebo or no intervention	Activities of daily living Visual field Reading Scanning – cancellation
Interventions for visual field defects in patients with stroke	Substitutive interventions	Control, placebo or no intervention	Falls Functional activities of daily living Visual field Scanning – cancellation
Interventions for visual field	Compensative interventions	Restitutive interventions	Visual field Quality of life

defects in patients with stroke			Reading
Adults with recent stroke and visual field defect	Restorative computer-based training of border areas of the visual field	Compensatory computer-based visual scanning training	Visual field expansion Reading performance Activities of daily living
Adults with stroke with hemianopia	Serial anodal tDCS	Sham	Motion detection

Physical activity - Amount of rehabilitation

Clinical question: What is the minimum amount of task-specific practice within the first six months of a stroke to improve patient outcomes?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with stroke	Amount of practice	Usual care	Health-related quality of life Activities of daily living Walking ability and arm function Participation

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Increased scheduled therapy time	Usual care	Various function and impairment measures – pooled
Adults with stroke	Additional active practice	Usual care	Activities of daily living Walking ability Arm function and walking ability

Physical activity – Cardiorespiratory fitness

Clinical question: What interventions to improve cardiovascular fitness improve outcomes for people with stroke?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with stroke	Interventions to improve cardiovascular fitness	Usual care	Death and institutionalisation rate Aerobic fitness Health-related quality of life Adverse events

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Cardiorespiratory training	Control	Case fatality Disability Physical fitness Mobility – maximal gait speed Mobility – preferred gait speed Mobility – gait endurance Health-related quality of life Mood Cognitive function Risk factors Physical function

Physical activity – Sitting

Clinical question: What task-specific training improves outcomes for stroke survivors who have difficulties sitting?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All stroke patients	Task-specific training	No intervention	Independence in sitting

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke with difficulty with sitting balance	Sitting balance training (reaching beyond arm's length)	Control	Sitting while reaching beyond arm's length Ground reaction force

Physical activity – Standing up

Clinical question: What task-specific training improves outcomes for stroke survivors who have difficulties standing up?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All stroke patients	Task-specific training	No intervention	Ability to sit-to-stand

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Interventions for improving sit to stand	Control	Ability to sit-to-stand independently Falls Time taken to sit-to-stand or sit-to-walk Lateral symmetry

Physical activity – Standing balance

Clinical question: What task-specific training improves outcomes for stroke survivors who have difficulties standing?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All stroke patients	Task-specific training	No intervention	Activities of daily living Standing ability

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Whole body vibration	Control	Balance Mobility Gait performance
Adults with stroke	Virtual reality	Control	Balance Mobility Adverse events
Adults with stroke	Biofeedback	Control	Standing
Adults with stroke	Exercise training	Control	Balance
Adults with Stroke	Balance training on dynamic surface	Control (Balance training on stable ground)	Balance Mobility Activities of daily living
Adults with Stroke	Yoga or Tai Chi	Control	Balance

Physical activity – Walking

Clinical question: What interventions improve walking ability in stroke survivors?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All stroke patients	Interventions to improve walking	No intervention	Health related quality of life Participation Walking ability

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes

Adults with stroke	Task-specific overground walking training	Usual care	Walking speed Walking endurance Mobility Walking speed – maximum Walking speed - comfortable
Adults with stroke	Community-based ambulation	Control	Gait speed Walking endurance Participation
Adults with stroke	Circuit class therapy	Usual care	Walking speed Walking endurance Mobility
Adults with stroke	Treadmill (with or without body weight support)	Usual care (walking training without mechanical assistance)	Walking endurance Walking speed
Electromechanical-assisted training for walking after stroke	Electromechanical-assisted gait training in combination with physiotherapy	Physiotherapy (or usual care)	Ability to walk independently Adverse events – death Walking speed
Adults with stroke	Cueing of cadence	Control (walking training alone)	Walking speed
Adults with stroke	Joint position feedback	Placebo or usual therapy	Walking ability
Adults with stroke	Electrical stimulation	Control (walking training alone)	Walking speed
Adults with stroke	Virtual reality	Usual care	Walking speed
Adults with stroke	Mental practice	Control	Mobility
Adults with stroke	Orthosis	No orthosis	Walking ability Walking speed
Adults with stroke	Water-based exercises	No water-based exercises	Activities of daily living Walking speed
Adults with stroke	Whole body vibration	Control	Gait performance

Physical activity – Upper limb activity

Clinical question: What interventions improve upper limb activity in stroke patients who have difficulty using their upper limbs?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All patients with stroke with upper limb deficits	Rehabilitation	Usual care	Activities of daily living Arm function Hand function

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Constraint-induced movement therapy for upper extremities	Control	Arm motor function Perceived arm motor function Arm motor impairment Quality of life Dexterity Disability
Adults with stroke	Bilateral training	Usual care or other intervention	Performance in activities of daily living Functional movement of the upper limb – Arm functional movement Functional movement of the upper limb – Hand functional movement Performance in activities of daily living
Adults with stroke	Bilateral training	Unilateral training	Arm functional movement Everyday arm use

Adults with stroke	Biofeedback	Usual care	Arm motor function Arm and hand function
Adults with stroke	Electrical stimulation	Usual care without stimulation	Upper limb activity
Adults with stroke	Manual (hands-on) therapy	Usual care	Upper limb function
Adults with stroke	Electromechanical and robot-assisted arm training	All other interventions	Drop-outs Activities of daily living Arm function Arm muscle strength
Adults with hemiparesis after stroke	Mental practice in addition to other treatment	Other treatment	Activity – upper extremity function
Adults with stroke	Mirror therapy for improving motor function after stroke	All other interventions	Arm motor function – end of intervention Arm motor function – follow-up after 6 months Activities of daily living Arm motor function – upper extremity treatment only
Adults with stroke	Orthosis	Usual care	Arm function Range of motion of the wrist
Adults with stroke	Practice with trunk restraint	Practice without trunk restraint	Fugl-Meyer Assessment Range of motion Self-reported use
Adults with stroke	Task specific practice	Control	Arm function Hand function Activities of daily living function
Adults with stroke	Virtual reality for stroke rehabilitation	Conventional therapy	Upper limb function

Adults with stroke	Transcranial direct current stimulation	Placebo or passive control	Dropouts, adverse events and deaths Upper extremity function at the end of the intervention period Upper extremity function to the end of follow-up
Adults with stroke	Repetitive transcranial magnetic stimulation	Usual care	Motor function

Activities of daily living

Clinical question: What interventions improve activities of daily living in patients with stroke?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All stroke patients with difficulties in personal or extended activities of daily living	Interventions to improve performance of daily activities	Usual care	Death and institutionalisation rate Activities of daily living Community ambulation

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Older adults with stroke in nursing homes	Occupational therapy	Control	Activities of daily living – at 3 months Activities of daily living – at 6 months Activities of daily living – at 12 months
Adults with stroke	Occupational therapy	Control	Death or dependency Activities of daily living

			Extended activities of daily living
Adults with stroke	Cognitive rehabilitation	Control	Basic activities of daily living Instrumental activities of daily living
Adults with stroke	Transcranial direct current stimulation	Placebo or passive control	Activities of daily living
Adults with stroke	Repetitive transcranial magnetic stimulation	Control	Activities of daily living
Adults with stroke	Acupuncture	Control	Activities of daily living
Adults with stroke	Water-based exercise	Control	Activities of daily living
Adults with stroke	Amphetamine	Placebo	Death or dependency Death (all causes) Activities of daily living
Adults with stroke	Virtual reality	Conventional therapy	Activities of daily living
Adults with stroke	Motivational interviewing	Control	Improved activities of daily living Death
Adults with stroke	Mental practice	Control	Change in activities of daily living
Adults with stroke	Selective serotonin reuptake inhibitor	Control	Dependency Activities of daily living

Communication - Aphasia

Clinical question: What interventions improve outcomes for patients with aphasia?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest

All stroke patients with aphasia	Interventions to improve communication	Usual care	Improved communication Quality of life Carer burden

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke with aphasia	Speech and language therapy	Control	Functional communication General expressive language Mood
Adults with stroke with aphasia	High intensity speech and language therapy	Low intensity language and speech therapy	Functional communication Severity of language impairment Mood
Adults with stroke with aphasia	Repetitive transcranial magnetic stimulation	Sham	Severity of language impairment Naming Writing Comprehension
Adults with stroke with aphasia	tDCS plus speech and language therapy (SLT)	Sham tDCS plus SLT for improving aphasia	Accuracy of naming
Adults with stroke with aphasia	Piracetam	Placebo	Death Improvement on aphasia measures

Communication – Apraxia of speech

Clinical question: What interventions improve outcomes for people with dyspraxia of speech?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All stroke patients with dyspraxia of speech	Interventions to improve communication	Usual care	Improved communication Quality of life Carer burden

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Stroke patients with dyspraxia	Articulatory–kinematic treatment	Usual care	Improved communication
Stroke patients with dyspraxia	Rhythm/rate control methods	Usual care	Improved communication

Communication – Dysarthria

Clinical question: What interventions improve outcomes for people with dysarthria?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All stroke patients with dysarthria	Interventions to improve communication	Usual care	Improved communication Quality of life Carer burden

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Stroke patients with dysarthria and aphasia	Early, well-resourced communication therapy	Attention control	Improved communication Carer burden
Stroke patients with dysarthria	Communication therapy with non-speech oro-motor exercises	Communication therapy	Improved communication

Communication - Cognitive communication difficulties

Clinical question: What interventions improve outcome in stroke patients with cognitive communication difficulties?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All stroke patients with cognitive communication difficulties	Interventions to improve cognitive communication	Usual care	Improved cognitive communication Quality of life Carer burden

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke and cognitive communication difficulties	Interventions to improve cognitive communication	Usual care	Improved cognitive communication

Cognition – Attention and concentration

Clinical question: What interventions improve outcomes in stroke patients with attention and concentration deficits?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All stroke patients with attention and concentration deficits	Interventions to improve attention and concentration deficits	Usual care	Improved attention and concentration

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Cognitive rehabilitation	Control	Alertness Selective attention Sustained attention Divided attention

Adults with chronic stroke	Exercise training and leisure/recreation activities	Usual care	Selective attention and conflict resolution
Adults with stroke	Intensive vascular risk factor intervention	Usual care	Attention
Adults with stroke	Head-mounted display virtual reality	Desktop-based virtual reality	Attention functioning
Adults with stroke	Transcranial direct current stimulation	Sham	Selective attention

Cognition – Executive function

Clinical question: What interventions to initiate everyday activities in stroke patients improve impaired executive functioning?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All stroke patients	Interventions to initiate everyday activities	Usual care	Improved executive functioning

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Cognitive training	Control	Executive functioning
Adults with stroke	Strategy training	Attention control	Executive functioning
Adults with stroke	Intensive vascular risk factor intervention	Usual care	Executive functioning
Adults with stroke	Selegiline	Placebo	Executive functioning
Adults with stroke	Citicoline	Control	Lack of impairment in attention and executive functioning
Adults with stroke	Rivastigmine	Control	Executive functioning

Cognition and perception - Perception

Clinical question: What interventions improve perceptual impairment in stroke survivors?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All stroke patients with perceptual impairment	Interventions to improve perceptual impairment	Usual care	Improved perceptual and cognitive impairment

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with impaired perception after stroke	Perceptual interventions	Control	Perceptual impairment

Cognition – Limb apraxia

Clinical question: What interventions improve outcomes for stroke patients with limb apraxia?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All stroke patients with apraxia	Interventions to improve apraxia	Usual care	All outcomes

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Strategy training	Control	Activities of daily living Motor function Apraxia
Adults with stroke	Gesture training	Control	Ideational test of apraxia

			Ideomotor test of apraxia
Adults with stroke	Errorless learning	Control	Activities of daily living

Cognition – Neglect

Clinical question: What interventions improve the outcome of stroke patients with unilateral spatial neglect?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All stroke patients with neglect	Interventions to improve neglect	Usual care	Improved spatial awareness Improved levels of safety in the home

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke with neglect	Rivastigmine and rehabilitation	Rehabilitation	Barrage test Effectiveness on barrage test Letter cancellation Effectiveness on letter cancellation Sentence reading Effectiveness on sentence reading Wundt-Jastrow Effectiveness on Wundt-Jastrow Disability Daily life functions
Adults with stroke with neglect	Mirror therapy	Control	Activities of daily living Visuospatial neglect
Adults with stroke with neglect	Non-invasive brain stimulation	Control	Spatial awareness (Line bisection test)

			Spatial awareness (Letter cancellation test) Spatial awareness (Ota's task)
Adults with stroke with neglect	Cognitive rehabilitation	Control	Falls Activities of daily living Neglect

Cognition and perception – Memory

Clinical question: What interventions improve outcomes in stroke patients with memory difficulties?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All patients with memory difficulties	Interventions to improve memory	Usual care	Improved memory Quality of life Level of independence

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Head-mounted display virtual reality	Desktop-based virtual reality	Memory
Adults with stroke	Selegiline	Placebo	Episodic memory Logical memory Memory (Rey–Osterrieth complex figure copy)
Adults with stroke	Citicoline	Control	Memory – lack of impairment

3.6. Chapter 6: Managing complications

Nutrition and hydration – Early hydration

Clinical question: Do early means of hydration improve outcomes in acute stroke?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All stroke patients	Hydration	No intervention	Death Health-related quality of life Physical function Dehydration

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with acute stroke	Colloid parenteral fluids	Crystalloid parenteral fluids	Death Death or dependence Pneumonia Cerebral oedema Pulmonary oedema
Adults with acute stroke	Parenteral fluid of 0.9% saline	Other parenteral fluid	Death Death or dependence Pneumonia Pulmonary oedema

Nutrition and hydration – Early feeding

Clinical question: Do early means of feeding improve outcomes in acute stroke?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All stroke patients	Feeding	No intervention	Malnutrition Death Health-related quality of life Physical function Nutritional status

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes

Adults with stroke	Percutaneous endoscopic gastrostomy feeding	Nasogastric tube feeding	Death or dependence Death Chest infection or pneumonia Length of stay Nutritional status
Adults with stroke	Continuous pump feeding	Intermittent bolus feeding	Death Pneumonia
Adults with stroke	Nutrition support	No nutrition support	Death Death or dependence Length of stay Nutritional status

Poor oral hygiene

Clinical question: Do interventions to maintain good oral hygiene improve outcomes in people with acute stroke?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All stroke patients	Oral hygiene	No intervention	Mortality Health-related quality of life Physical function Fever / pneumonia

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Oral hygienic care intervention	Standard care	Pneumonia Carer knowledge Functional oral intake Dysphagia

Spasticity

Clinical question: What interventions to reduce spasticity improve the outcomes for patients with spasticity?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All stroke patients with spasticity	Interventions to reduce spasticity	Usual care	Activities of daily living Health-related quality of life Arm function (discharge functional independence measure) Spasticity adverse events including pain Pain – Modified Ashworth score Joint range of motion (Passive)

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke with upper limb spasticity	Botulinum toxin A	Control	Disability assessment scale Action Research Arm Test Generalised disability Disability (botulinum toxin specific scales) Motor function
Adults with stroke with lower limb spasticity	Botulinum toxin A	Control	Adverse events Muscle tone Gait speed Lower limb function
Adults with stroke with spasticity	Acupuncture	Control	

Adults with stroke with spasticity	Neuromuscular electric stimulation	Control	Spasticity Range of motion
Adults with stroke with spasticity	Adjunct therapies to Botox	Control	Spasticity
Adults with stroke with spasticity	Stretch	Control	Spasticity – immediate effects Spasticity – long term
Adults with stroke with spasticity	Transcutaneous electrical nerve stimulation (TENS)	Control	Spasticity

Contracture

Clinical question: What interventions to reduce contracture improve outcomes for people with stroke?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All stroke patients with contracture	Interventions to reduce contracture	Usual care	Activities of daily living Upper limb function and walking Range of motion Adverse events – pain Joint range of motion (passive)

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Passive movements	Usual care	Pain
Adults with stroke	Stretch	Usual care	Joint mobility Pain Activity limitation
Adults with stroke	Stretch and neuromuscular stimulation	Sham	Presence of pain Passive range of motion improvement

			Pain severity Activities of daily living restriction

Subluxation

Clinical question: What interventions to prevent or treat shoulder subluxation improve outcomes for people with stroke?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All stroke patients	All interventions to prevent shoulder subluxation	Usual care	Health-related quality of life Pain reduction Upper limb function Degree of subluxation

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Shoulder strapping	No strapping	Health-related quality of life Upper limb function Pain reduction
Adults with stroke	Functional electrical stimulation	Conventional therapy	Shoulder subluxation Pain Motor function
Adults with stroke	Combined arm stretch positioning and neuromuscular electrical stimulation	Conventional treatment	Pain
Adults with stroke	Shoulder joint functional orthosis + conventional treatment	Conventional treatment	Pain Limitation of movement Subluxation

Shoulder pain

Clinical question: What is the best intervention to prevent or treat shoulder pain in stroke survivors?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All stroke patients	All interventions to treat shoulder pain	Usual care	Health-related quality of life Activities of daily living Pain Adverse events Use of opiates

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Shoulder strapping	No strapping	Health-related quality of life Pain reduction Upper limb function Degree of subluxation
Adults with stroke	Functional electrical stimulation	Conventional therapy	Shoulder subluxation Pain Motor function
Adults with stroke with severe paresis of arm	Combined arm stretch positioning and neuromuscular electrical stimulation	Conventional treatment	Pain Pain medication use
Adults with stroke with shoulder pain	Acupuncture	Control	Pain Adverse events
Adults with stroke with shoulder pain	Botulinum toxin injection by any route	Placebo injection	Adverse events Pain
Adults with stroke with shoulder pain	Peripheral nerve stimulation with single implantable lead	Usual care	Pain Health-related quality of life

Adults with stroke with shoulder pain	Segmental neuromyotherapy combined with standard hospital therapy	Standard hospital therapy	Pain
Adults with stroke with shoulder pain	Suprascapular nerve block	Placebo injection	Pain
Adults with stroke with shoulder pain and with diagnosed rotator cuff syndrome (clinically and by ultrasound)	Subacromial corticosteroid injection	Placebo (lidocaine) injection	Daytime pain Pain (night) Activities of daily living Shoulder external rotation (range of motion)

Swelling of the extremities

Clinical question: What interventions are effective at managing and/or reducing oedema?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with stroke who are immobile	Interventions to improve mobility	Usual care	Health-related quality of life Activities of daily living Reduction in swelling Improved function Girth measurements of the limb or hands

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Blixembosch best practices protocol	Usual care	Mean duration of oedema Presence of oedema at baseline Presence of oedema overall

			Presence of oedema after admission
Adults with stroke	Kinesio tape + standard therapy	Standard therapy	Wrist circumference Metacarpophalangeal circumference
Adults with stroke	Dynamic pressure garments	Control (same participants)	Limb swelling – third digit Limb swelling – forearm
Adults with stroke	Continuous passive motion with elevation	Control (same participants)	Hand volume Finger circumference

Fatigue

Clinical question: What interventions improve the management of fatigue in stroke survivors?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All stroke patients with fatigue	All interventions to prevent fatigue	Usual care	Health-related quality of life Activities of daily living Fatigue Epworth Sleepiness Scale

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Interventions to treat fatigue	Control	Fatigue – self-reported presence of fatigue Fatigue severity

Incontinence – Urinary incontinence

Clinical question: What interventions improve outcomes in stroke survivors with bladder problems?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All stroke patients	All interventions to prevent bladder problems	Usual care	Decreased urinary incontinence Institutionalisation rates Improved quality of life Recurrence of urinary tract infections Catheter use Length of stay

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Stroke patients with urinary incontinence	Behavioural intervention	Control	Continence Catheter use Urinary tract infections Length of stay Health-related quality of life
Stroke patients with urinary incontinence	Specialised professional input	Control	Incontinence Urinary symptoms Quality of life
Stroke patients with urinary incontinence	Transcutaneous electrical nerve stimulation	Control	Urinary incontinence Activities of daily living (Barthel Index > 50)
Adults with overactive bladder syndrome	Anticholinergic drugs	Placebo	Withdrawal due to adverse events Leakage episodes Quality of life
Adults with suspected urinary incontinence	Diagnostic assessment of urinary incontinence	Multichannel urodynamics	Diagnosis of urinary incontinence

Incontinence – Faecal incontinence

Clinical question: What interventions improve outcomes in stroke survivors with bowel problems?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All stroke patients	All interventions to prevent bowel problems	Usual care	Decreased bowel incontinence Improved quality of life Participation levels

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Stroke patients with constipation	Daikenchuto	Conventional therapy	Bowel incontinence
Stroke patients with constipation	Daily digital stimulation	Digital stimulation every other day	Bowel regularity
Stroke patients with constipation	Morning bowel evacuation	Evening schedule of bowel evacuation	Time to achieve regular bowel movement
Stroke patients with constipation	Nurse-led intervention	Routine care	Normal bowel movements

Mood disturbance – Treatment for emotional distress

Clinical question: What general, non-pharmacological management should be undertaken to reduce emotional distress?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with stroke	Non-pharmacological interventions	No intervention	Emotional distress

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes

Adults with stroke	Pharmaceutical interventions	Placebo	Improved emotionalism Adverse events

Mood disturbance – Prevention of depression

Clinical question: What interventions prevent depression and/or anxiety?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with stroke	Medical interventions	No intervention	No depression and/or anxiety

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Pharmacotherapy for the prevention of depression	Control	Presence of depression
Adults with stroke	Psychotherapy for the prevention of depression	Control	Presence of depression Depression – continuous scores

Mood disturbance – Treatment for depression

Clinical question: What interventions manage depression and/or anxiety?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with stroke	Medical interventions	No intervention	Reduced depression and/or anxiety

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Structured exercise	Control	Depressive symptoms

			Safety
Adults with stroke with depression	Wuling capsule	No treatment	Response rate Depressive symptoms Safety
Adults with stroke	Mindfulness-based interventions	No treatment	Anxiety Depression Quality of life
Adults with stroke with depression	Non-invasive brain stimulation	Control	Depression
Adults with stroke with depression	Acupuncture therapy	Control	Response rate Changes in depression scale
Adults with stroke with depression	Selective serotonin reuptake inhibitors	Control	Depression – dichotomous outcome Depression – continuous scores
Adults with stroke with anxiety	Pharmacological interventions	No control group	Anxiety

Mood disturbance – Treatment for anxiety

Clinical question: What interventions manage depression and/or anxiety?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with stroke	Medical interventions	No intervention	Reduced depression and/or anxiety

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke with depression	Selective serotonin reuptake inhibitors	Control	Anxiety – continuous scores

Deep venous thrombosis or pulmonary embolism

Clinical question: What interventions prevent deep venous thrombosis or pulmonary embolism in stroke survivors?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with stroke	Interventions to prevent DVT/PE	No intervention	Reduced risk of DVT/PE

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Anticoagulation	Control	Deep vein thrombosis Pulmonary embolism
Adults with stroke	Intermittent pneumatic compression	Usual care	Any deep vein thrombosis Proximal deep vein thrombosis
Adults with stroke	Graduated compression stockings	Usual care	Deep vein thrombosis Symptomatic pulmonary embolism

Falls

Clinical question: What interventions are effective in preventing or reducing falls for stroke patients?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with stroke	Interventions to prevent or reduce falls	No intervention	Health-related quality of life Falls rate Falls self-efficacy Death Institutionalisation rate

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Exercise	Control	Number of fallers Rate of falls Quality of life Falls efficacy
Adults with stroke	Single lens distance glasses	Usual (multifocal) glasses	Number of fallers Rate of falls
Adults with stroke	Medication	Control	Number of fallers Rate of falls

3.7. Chapter 7: Discharge planning and transfer of care

Information and education

Clinical question: Does the provision of information and/or education improve outcomes after stroke?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All stroke patients	Information Education	No information No education	Death Institutionalisation rate Secondary stroke Readmission Quality of life Mood Participation rates

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Stroke patients and their caregivers	Information provision	Control	Death Patient anxiety Patient depression Carer psychological distress Patient activities of daily living and participation Patient quality of life

			Carer quality of life
Stroke patients and their caregivers	Active information provision	Control	Death Patient anxiety Patient depression Carer psychological distress
Stroke patients and their caregivers	Passive information provision	Control	Death Patient anxiety Patient depression Carer psychological distress

Discharge care plans

Clinical question: Does the use of discharge care plans improve outcomes after stroke?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All stroke patients	Discharge care plans	No discharge care plans	Readmission Institutionalisation rate Participation rates Quality of life Functional independence

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Standardised stroke discharge orders	Usual care	Optimal secondary prevention treatment
Adults admitted to hospitals	Discharge planning	No discharge planning	Length of stay Mortality Readmission

Patient and carer needs

Clinical question: Does assessment of patient and carer needs prior to discharge improve outcomes after stroke?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All stroke patients	Assessment of patient and carer needs	No assessment	Health-related quality of life (patient and carer) Unmet needs Healthcare utilisation Caregiver burden

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Pre-discharge assessment of patient and carer needs	No assessment	No studies reporting outcomes of interest found

Home Assessment

Clinical question: Does conducting a home assessment of the stroke patient prior to discharge improve outcomes?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All stroke patients	Home assessment	No home assessment	Death Institutionalisation rate Readmission

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Home visit	No visit	Activities of daily living Health-related quality of life Falls Readmissions

Carer training

Clinical question: Does the provision of training for carers improve outcomes after stroke?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All carers of stroke patients	Training	No training	Health-related quality of life (patient and carer) Carer burden Patient unmet needs Health care utilisation Quality of life

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Carers of adult stroke patients	Telephone-based problem-solving intervention	Information only	Carer depression Carer competence Patients' functioning
Carers of adult stroke patients	Structured training program in hospital	Usual care	Carer burden Patients' extended activities of daily living

3.8. Chapter 8: Community participation and long term care

Self-management

Clinical question: Do self-management programs improve outcomes in stroke patients once they return to the community?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with stroke	Self-management programs	No intervention	Health-related quality of life

			Participation Self-efficacy Health care utilisation

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Self-management	Control	Participation Health utilisation Medication adherence Quality of life Self-efficacy

Driving

Clinical question: Do driver retraining interventions improve a stroke survivors' ability to return to driving?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with stroke	Driver retraining interventions	No intervention	Ability/capacity to return to driving

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults post-stroke	Driving rehabilitation intervention	Control	On-road score Road sign recognition

Community mobility and outdoor travel

Clinical question: What interventions improve stroke survivors' ability to access community transport?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest

All people with stroke	Support to access community transport	No support	Increased access to community transport

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Community dwelling adults with stroke	Community ambulation	Control	Walking speed Participation
Community dwelling adults with stroke	Outdoor mobility rehabilitation training	Control	Number of outings Mobility Health-related quality of life Psychological well-being

Leisure

Clinical question: What interventions increase participation of stroke survivors in leisure and/or vocational activities?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with stroke	Targeted occupational therapy	No therapy	Increased participation in leisure activities

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Leisure therapy	Control	Leisure activity Extended activities of daily living Mobility and independence

Return to work

Clinical question: What interventions improve a stroke survivor's ability to return to work?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All stroke patients wishing to return to work	Support	No support	Ability to return to work Return to work rates

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke wanting to return to work	Workplace intervention programme	Usual stroke care	Return to work rates Activities of daily living Perceived quality of life

Sexuality

Clinical question: Does access to information and support regarding sexuality issues improve outcomes for stroke survivors?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with stroke	Information and support about sexuality issues	No information	Improved quality of life Improved sexual relationships Sexual satisfaction Sexual self-esteem

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults post stroke	Sexual rehabilitation programme	Control	Sexual functioning Psychological functioning Physical functioning Quality of life

Support – Peer support

Clinical question: Does peer support improve the outcomes of stroke survivors?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All people with stroke	Peer support	No peer support	Improved quality of life

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adults with stroke	Peer support	No peer support	Health-related quality of life

Support – Carer support

Clinical question: Do interventions to support carers improve outcomes for stroke survivors?

Broad description of population, intervention, comparator and outcome:

Patient	Intervention	Comparator	Outcomes of most interest
All carers of stroke survivors	Interventions	No intervention	Death Institutionalisation rate Improved quality of life Carer stress / burden Quality of life

Specific questions identified and evaluated:

Population	Intervention	Comparator	Outcomes
Adult caregivers of stroke survivors	Support and information	Control	Informal caregiver stress and strain Global measures of stress and strain Caregiver depression

			Health-related quality of life
Adult caregivers of stroke survivors	Psycho-educational	Control	Global measures of stress or distress Informal caregiver stress and strain Depression
Adults with stroke and adult family caregivers	Psychosocial interventions	Usual care	Caregiver burden Caregiver depression

4. References

1. Health Information Research Unit. 2016. Hedges. [cited 2016 7/10/2016]; Available from: http://hiru.mcmaster.ca/hiru/HIRU_Hedges_home.aspx.

2. Grade Working Group. 2004. Grading quality of evidence and strength of recommendations. British Medical Journal, 328(7454), p.1490-1490.

3. Middleton, S., et al. 2016. Implementation of evidence-based treatment protocols to manage fever, hyperglycaemia, and swallowing dysfunction in acute stroke (QASC): a cluster randomised controlled trial. The Lancet, 378(9804), p.1699-1706.

4. Schünemann, H., et al. 2016. Handbook for grading the quality of evidence and the strength of recommendations using the GRADE approach. [cited 2016 10/10/2016]; Available from: http://gdt.guidelinedevelopment.org/app/handbook/handbook.html.

5. Cochrane Handbook for Systematic Reviews of Interventions. 2011. J. Higgins and S. Green, Editors. The Cochrane Collaboration.

5. Appendices

Appendix 1: Search terms and search results

1. Search strings and search filters

The following search strings were used to identify relevant studies when conducting systematic literature searches. Specific search terms for each clinical question included in the guidelines are documented in the section below.

Core search string for ‘stroke’ and ‘transient ischaemic attack (TIA)’:

Medline_Core stroke

1. cerebrovascular disorders/

2. basal ganglia cerebrovascular disease/

3. brain ischemia/

4. exp brain infarction/

5. hypoxia-ischemia, brain/

6. carotid artery thrombosis/

7. carotid artery, internal, dissection/

8. infarction, anterior cerebral artery/

9. infarction, middle cerebral artery/

10. infarction, posterior cerebral artery/

11. exp "intracranial embolism and thrombosis"/

12. exp stroke/

13. vertebral artery dissection/

14. (isch?emi$ adj2 (stroke$ or apoplex$ or cerebral vasc$ or cerebrovasc$ or cva)).tw.

15. ((brain or cerebr$ or cerebell$ or vertebrobasil$ or hemispher$ or intracran$ or intracerebral or infratentorial or supratentorial or middle cerebr$ or mca$ or anterior circulation or basilar artery or vertebral artery) adj2 (isch?emi$ or infarct$ or thrombo$ or emboli$ or occlus$ or hypoxi$)).tw.

16. (ICH or ((intracerebral or intracranial or brain or cerebellum) adj2 (hemorrhag$ or haemorrhag$ or bleed$))).ti,ab.

17. exp intracranial hemorrhages/

18. or/1-17

19. limit 18 to english language

20. exp Adult/

21. 19 and 20

Embase_Core stroke

1. cerebrovascular accident/

2. brain infarction/

3. brain stem infarction/

4. cerebellum infarction/

5. exp brain ischemia/

6. exp carotid artery obstruction/

7. exp occlusive cerebrovascular disease/

8. stroke patient/

9. (isch?emi$ adj2 (stroke$ or apoplex$ or cerebral vasc$ or cerebrovasc$ or cva)).tw.

10. ((brain or cerebr$ or cerebell$ or vertebrobasil$ or hemispher$ or intracran$ or intracerebral or infratentorial or supratentorial or middle cerebr$ or mca$ or anterior circulation or basilar artery or vertebral artery) adj2 (isch?emi$ or infarct$ or thrombo$ or emboli$ or occlus$ or hypoxi$)).tw.

11. (ICH or ((intracerebral or intracranial or brain or cerebellum) adj2 (hemorrhag$ or haemorrhag$ or bleed$))).ti,ab.

12. exp brain hemorrhage/

13. or/1-12

14. exp adult/

15. and/13-14

16. limit 15 to english language

EBM Reviews_ Core stroke

1. stroke*.tw.

2. cva.tw.

3. tia.tw.

4. transient ischemic attack.mp.

5. or/1-4

6. limit 5 to last year

7. limit 6 to english language

8. limit 7 to humans

9. remove duplicates from 8

CINAHL_Core stroke

S5 S1 OR S2 OR S3

Limiters - Publication Year: 2010-2015 (2015-2016 in updated search)

S4 S1 OR S2 OR S3

S3 cerebrovascular accident OR cva AND tia

S2 (MH "Cerebral Ischemia, Transient")

S1 (MH "Stroke+")

PsycInfo_ Core stroke

1. Ischemia/ or Cerebrovascular Disorders/ or Cerebrovascular Accidents/ or Cerebral Ischemia/

2. limit 1 to last year

Medline_TIA

1. Ischemic Attack, Transient/

2. (mini adj2 stroke$).ti,ab.

3. ("TIA" or (transient adj2 (ischemi$ or ischaemi$))).ti,ab.

4. (symptomatic adj2 carotid adj2 stenosis).ti,ab.

5. or/1-4

Embase_TIA

1. transient ischemic attack/

2. (mini adj2 stroke$).ti,ab.

3. (symptomatic adj2 carotid adj2 stenosis).ti,ab.

4. ("TIA" or (transient adj2 (ischemi$ or ischaemi$))).ti,ab.

5. or/1-4

Core stroke string used in the databases of Australian Indigenous studies:

All questions were searched together.

Stroke* OR (cerebrovascular (disorder* OR accident*)) OR ischemi* OR infarc* OR (intracranial AND thrombo*)

Evidence filter:

Medline_Evidence filter

1. randomized controlled trial.pt. or random* controlled trial.mp.

2. (MEDLINE or systematic review).tw. or meta analysis.pt.

3. (cost effective or sensitivity analys:).tw.

4. or/1-3

Embase_Evidence filter

1. double-blind:.mp. or placebo:.tw. or blind:.tw.

2. (meta-analysis or systematic review).tw.

3. (cost effectiveness or sensitivity analys:).tw.

4. or/1-3

2. Search terms and results for each topic

Initial searches were conducted between November 2015 and January 2016. Updated searches were conducted in June and July 2016, including any articles published after the cut-off of the initial search.

Total numbers of search results found for each topic are shown in the table below, along with the specific search strings used for each topic. The listed search strings show the time limits applied for the initial searches conducted between November 2015 and January 2016, including articles up to 1 October 2015. For the updated searches conducted in June and July 2016, these limits were changed to find articles published between 1 October 2015 and 15 May 2016 (i.e. Medline: Limit # to ed=20151001-20160515, Embase: Limit # to dd= 20151001-20160515).

In the table below, the “Strings added” column lists the additional search strings and filters (as described above) applied to each specific topic, i.e.:

- S: Core search strings for stroke and transient ischaemic attack.
- Y: Year filter restricting searches to studies from 2010 onward (not applied for new search questions).
- E: Evidence filter restricting searches to randomized controlled trials and systematic reviews (or diagnostic studies where applicable).

Topic	Number of references found							Medline strategy	Embase strategy	Strings added
	Medline	Embase	Cochrane	Cinahl	Web of Science	PsycINFO	Total			
1.1 Pre-hospital care	87	240	402	0	149	-	877	1. Emergency Medical Technicians/ 2. Emergency Medical Services/ 3. (ambulance officer* or paramedic*).ti,ab. 4. or/1-3 5. Clinical Competence/ 6. Education/ 7. (education or training).ti,ab. 8. or/5-7 9. and/4,8 10. rapid transfer.ti,ab. 11. pre hospital.ti,ab. 12. ((LAMS or MASS or RACE) adj2 score*).ti,ab. 13. or/10-12 14. or/9,13 15. limit 14 to ed=20100211-20151001	1. paramedical education/ 2. ((ambulance or paramedic* or emergenc*) adj2 (training or education)).ti,ab. 3. rapid transfer.ti,ab. 4. pre hospital.ti,ab. 5. ((LAMS or MASS or RACE) adj2 score*).ti,ab. 6. or/1-5 7. limit 6 to dd=20100211-20151001	S,E,Y
Chapter 1 totals	87	240	402	0	149	-	877			

2.1 TIA	1583	653	37	0	577	-	2942	1. Blood Glucose/ 2. exp Carotid Artery Diseases/ 3. Echocardiography/ 4. exp Angiography/ 5. Lipids/ 6. Atrial Fibrillation/ 7. exp risk/ 8. ABCD*.ti,ab. 9. or/1-8 10. DI.fs. 11. emergency department/ 12. acute.ti,ab. 13. or/10-12 14. and/9,13 15. limit 14 to ed=20100211-20151001	1. glucose blood level/ 2. carotid artery obstruction/ and imaging/ 3. echocardiography/ 4. (fasting adj2 lipid*).ti,ab. 5. (risk* adj2 (assessment or stratification)).ti,ab. 6. ABCD*.ti,ab. 7. or/1-6 8. emergency department/ 9. acute.ti,ab. 10. or/8-9 11. and/7,10 12. limit 11 to dd=20100211-20151001	S, Y
2.2 Rapid assessment in the emergency department	1056	1031	150	0	0	-	1764	1. emergency department/ 2. acute.ti,ab. 3. or/1-2 4. "Severity of Illness Index"/ 5. (nih or nihss).ti,ab. 6. ((scandinavian or rosier) adj2 scale*).ti,ab. 7. ((clinical* or emergenc*) adj2 (tool* or assess* or measur* or test* or scale*)).ti,ab. 8. or/4-7	1. scoring system/ 2. rating scale/ 3. "National Institutes of Health Stroke Scale"/ 4. ((scandinavian stroke or rosier) adj2 scale*).ti,ab. 5. (emergenc* adj2 assess*).ti,ab. 6. ((NIH adj2 scale*) or NIHSS).ti,ab. 7. or/1-6	S,Y

								9. and/3,8 10. limit 9 to ed=20100211-20151001	8. emergency department/ 9. acute.ti,ab. 10. or/8-9 11. and/7,10 12. limit 11 to dd=20100211-20151001	
2.3 Investigations – brain imaging (later combined with carotid/vascular imaging)	394	543	582	0	67	-	1586	1. exp Neuroimaging/ 2. exp Image Processing, Computer-Assisted/ 3. exp Tomography, X-Ray Computed/ 4. exp Perfusion Imaging/ 5. exp Magnetic Resonance Imaging/ 6. (timing or mri or ct or magnetic resonanc* or Computerised Topography).ti,ab. 7. or/1-6 8. emergency department/ 9. acute.ti,ab. 10. or/8-9 11. and/7,10 12. limit 11 to ed=20100211-20151001	1. exp computer assisted tomography/ 2. exp nuclear magnetic resonance imaging/ 3. exp time/ 4. (mri or ct).ti,ab. 5. and/3-4 6. or/1-2,5 7. emergency department/ 8. acute.ti,ab. 9. or/7-8 10. and/6,9 11. limit 10 to dd=20100211-20151001	S,Y,E
2.4 Investigations – Cardiac investigations	1169	564	261	0	0	-	1994	1. Electrocardiography, Ambulatory/ 2. (holter adj2 monitor*).ti,ab.	1. holter monitor/ or holter monitoring/ 2. electrocardiogram/	S

								3. Electrocardiography/ 4. exp Telemetry/ 5. exp Arrhythmias, Cardiac/ 6. (implantable adj2 loop adj2 recorder*).ti,ab. 7. or/1-6 8. emergency department/ 9. acute.ti,ab. 10. or/8-9 11. and/7,10	3. telemetry/ 4. implantable cardiac monitor/ 5. heart atrium fibrillation/ 6. or/1-5	
2.5 Carotid/vascular imaging (later combined with brain imaging)	543	1933	186	0	128	-	2410	1. ((Duplex or doppler) adj2 ultrasound).ti,ab. 2. exp Cardiac Imaging Techniques/ 3. ((ct or mr) adj2 angiography).ti,ab. 4. or/1-3 5. emergency department/ 6. acute.ti,ab. 7. or/5-6 8. and/4,7 9. limit 8 to ed=20100211-20151001	1. Doppler echography/ or Doppler flowmetry/ 2. computed tomographic angiography/ 3. magnetic resonance angiography/ 4. or/1-3 5. emergency department/ 6. acute.ti,ab. 7. or/5-6 8. and/4,7 9. limit 8 to dd=20100211-20151001	S,Y
Chapter 2 Totals	4745	4724	1216	0	772	-	10696			
3.1 Stroke unit care	854	1426	936	0	25	-	3241	1. exp Hospital Units/ 2. (stroke adj2 unit*).ti,ab. 3. Patient Admission/ 4. (early adj2 (admit* or	1. stroke unit/ 2. (early adj2 (admit* or admissi*)).ti,ab. 3. (stroke adj2 unit*).ti,ab.	S, Y, E

								admission*)).ti,ab. 5. or/1-4 6. limit 5 to ed=20100211-20151001	4. or/1-3 5. limit 4 to dd=20100211-20151001	
3.2 Palliative care	644	549	52	-	-	-	1245	1. Palliative Care/ 2. (counsel* or communicat* or training or information*).ti,ab. 3. (palliat* or death or dying).ti,ab. 4. and/2-3 5. or/1,4 6. limit 5 to ed=20100211-20151001	1. exp palliative therapy/ 2. ((counsel* or communicat* or training or information*) and palliat*).ti,ab. 3. or/1-2 4. limit 3 to dd=20100211-20151001	S, Y
3.3 Thrombolysis	2305	3292	1155	-	111	-	6863	1. Mechanical Thrombolysis/ 2. Thrombolytic Therapy/ 3. Tissue Plasminogen Activator/ 4. (Sonothrombolysis or thrombolysis or (clot* adj2 remov*)).ti,ab. 5. or/1-4 6. limit 5 to ed=20100211-20151001	1. (Sonothrombolysis or thrombolysis).ti,ab. 2. limit 1 to dd=20100211-20151001	S, Y, E
3.4 Neurointervention	1210	3258	481	0	11	-	4960	1. Thrombectomy/ 2. Infusions, Intra-Arterial/ 3. (neurointervention* adj2 treatment*).ti,ab. 4. (endovascular adj2	1. (neurointervent* adj2 (treatment* or therap*)).ti,ab. 2. exp thrombectomy/ 3. (endovascular adj	S, Y, E

								(therap* or treatment*)).ti,ab. 5. (aspiration or aspirating).ti,ab. 6. neurothrombectomy.ti,ab. 7. (clot adj2 (retriev* or remov*)).ti,ab. 8. or/1-7 9. limit 8 to ed=20100211-20151001	(therap* or Treatment*)).ti,ab. 4. (intra-arterial or intra arterial).ti,ab. 5. neurothrombectomy.ti,ab. 6. (clot adj2 (retriev* or removal)).ti,ab. 7. aspiration/ 8. or/1-7 9. limit 8 to dd=20100211-20151001	
3.5 Antithrombotic Therapy	501	418	370	-	73	-	1362	1. Aspirin/ 2. exp Platelet Aggregation Inhibitors/ 3. acetylsalicylic acid.ti,ab. 4. ((anti platelet or antiplatelet) adj2 (therapy or treatment*)).ti,ab. 5. or/1-4 6. limit 5 to ed=20100211-20151001	1. acetylsalicylic acid/ 2. anticoagulant agent/ 3. or/1-2 4. acute.mp. 5. and/3-4 6. limit 5 to dd=20100211-20151001	S, Y, E
3.6 Acute phase blood pressure lowering therapy	384	368	453	-	21	-	1226	1. exp Antihypertensive Agents/ 2. Blood Pressure/ 3. (blood pressure adj2 (lower* or reduc*)).ti,ab. 4. or/1-3	1. antihypertensive agent/ 2. (blood pressure adj2 (lower* or reduc*)).ti,ab. 3. or/1-2 4. limit 3 to dd=20100211-20151001	S, Y, E

								5. limit 4 to ed=20100211-20151001		
3.7 Surgery for ischaemic stroke and management of cerebral oedema	256	385	12	48	413	-	1114	1. exp Brain Ischemia/ 2. (ischemic adj2 stroke).ti,ab. 3. or/1-2 4. hemicraniectomy.ti,ab. 5. (ventric* adj2 drain*).ti,ab. 6. Cranial Fossa, Posterior/ 7. Decompression, Surgical/ 8. or/4-7 9. limit 8 to ed=20100211-20151001 10. 3 and 9	1. exp brain ischemia/ 2. (ischemic adj2 stroke*).ti,ab. 3. or/1-2 4. craniectomy/ 5. (ventric* adj2 drain*).ti,ab. 6. posterior fossa/ 7. decompression surgery/ 8. or/4-7 9. limit 8 to dd=20100211-20151001 10. 3 and 9	Y, E
3.8 Raised intracranial pressure (later combined with 3.7)	173	109	71	0	0	-	353	1. exp Brain Ischemia/ 2. (ischemic adj2 stroke).ti,ab. 3. or/1-2 4. Neurosurgery/ 5. Hyperventilation/ 6. osmotherapy.ti,ab. 7. exp Hemostatics/ 8. (hemicraniectomy or craniectomy).ti,ab. 9. or/4-8 10. limit 9 to ed=20100211-	1. exp brain ischemia/ 2. (ischemic adj2 stroke*).ti,ab. 3. or/1-2 4. therapeutic hyperventilation/ 5. osmotherapy.ti,ab. 6. hemostatic agent/ 7. craniectomy/ 8. hemicraniectomy.ti,ab. 9. decompressive craniectomy/ 10. or/4-9	Y, E

								20151001 11. 3 and 10	11. limit 10 to dd=20100211-20151001 12. 3 and 11	
3.9 Intracerebral haemorrhage (ICH) management - medical	972	828	392	-	6	-	2198	1. exp Intracranial Hemorrhages/ 2. Factor VIIa/ 3. (NOVO7 or NOVO 7).ti,ab. 4. or/1-3 5. limit 4 to ed=20100211-20151001	1. exp brain hemorrhage/ and (acute or emerg*).ti,ab. 2. recombinant blood clotting factor 7a/ or recombinant erythropoietin/ or blood clotting factor 7a/ 3. (NOVO7 or NOVO 7).ti,ab. 4. or/1-3 5. limit 4 to dd=20100211-20151001	Y, E
3.10 Intracerebral haemorrhage (ICH) management - surgical	145	163	136	0	0	-	444	1. exp Intracranial Hemorrhages/ 2. ((haemorrhag* or hemorrhag*) adj2 stroke*).ti,ab. 3. or/1-2 4. exp Decompression, Surgical/ 5. surgery/ 6. (craniectomy or evacuation*).ti,ab. 7. hemicraniectomy.ti,ab.	1. brain hemorrhage/ 2. ((haemorrhag* or hemorrhag*) adj2 stroke).ti,ab. 3. or/1-2 4. (acute or emerg*).ti,ab. 5. and/3-4 6. surgery/ 7. exp craniectomy/ 8. evacuat*.ti,ab. 9. hemicraniectomy.ti,ab. 10. posterior fossa/	Y, E

								8. (fossa adj2 decompression*).ti,ab. 9. (external adj3 ventricular).ti,ab. 10. or/4-9 11. and/3,10 12. limit 11 to ed=20100211-20151001	11. decompression surgery/ 12. brain decompression/ 13. (external adj2 ventric*).ti,ab. 14. or/6-13 15. and/5,14 16. limit 15 to dd=20100211-20151001	
3.11 Oxygen therapy	231	775	246	0	131	-	1383	1. Hyperbaric Oxygenation/ or Oxygen Inhalation Therapy/ 2. (oxygen adj2 (therap* or treat*)).ti,ab. 3. or/1-2 4. limit 3 to ed=20100211-20151001	1. exp oxygen therapy/ 2. limit 1 to dd=20100211-20151001	S, Y
3.12 Glycaemic control	265	735	182	0	0	-	1182	1. Blood Glucose/ 2. exp Hyperglycemia/ 3. or/1-2 4. limit 3 to ed=20100211-20151001	1. hyperglycemia/ 2. (glycemi* adj2 (treatment* or therap*)).ti,ab. 3. or/1-2 4. limit 3 to dd=20100211-20151003	S, Y, E
3.13 Neuroprotection	989	1719	225	0	409	-	3342	1. exp Neuroprotective Agents/ 2. Cytoprotection/ 3. Uric Acid/ 4. ("NXY 059" or	1. neuroprotection/ 2. exp cell protection/ 3. uric acid/ 4. ("NXY 059" or nxy059).ti,ab.	S, Y, E

								NXY059).ti,ab. 5. Hypothermia, Induced/ 6. or/1-5 7. limit 6 to ed=20100211-20151001	5. induced hypothermia/ 6. cooling/ 7. or/1-6 8. limit 7 to dd=20100211-20151001	
3.14 Pyrexia management	528	186	122	0	178	-	1014	1. exp Fever/ 2. exp Antipyretics/ 3. Acetaminophen/ 4. or/1-3 5. limit 4 to ed=20100211-20151001	1. fever/ 2. paracetamol/ 3. exp antipyretic agent/ 4. or/1-3 5. limit 4 to dd=20100211-20151001	S, Y,E
Chapter 3 totals	7959	12236	3845	48	1353	-	25088			
4.1 Adherence to pharmacotherapy	276	262	60	0	18	-	616	1. Medication Adherence/ 2. ((medication or medicines) adj3 (comply or compliance)).ti,ab. 3. or/1-2 4. limit 3 to ed=20100211-20151001	1. medication compliance/ 2. ((medication or medicines) adj3 (comply or compliance)).ti,ab. 3. or/1-2 4. limit 3 to dd=20100211-20151001	S, E
4.2 Blood pressure lowering	596	985	1428	0	32	-	3041	1. exp Antihypertensive Agents/ 2. Blood Pressure/ 3. exp Exercise/ 4. or/1-3 5. limit 4 to ed=20100211-20151001	1. exp antihypertensive agent/ 2. exercise/ 3. or/1-2 4. limit 3 to dd=20100211-20151001	S,E, Y

4.3 Antiplatelet therapy	454	1294	442	0	106	-	2296	1. exp Antihypertensive Agents/ 2. Blood Pressure/ 3. exp Exercise/ 4. or/1-3 5. limit 4 to ed=20100211-20151001	1. exp antithrombocytic agent/ 2. limit 1 to dd=20100211-20151001	S,E,Y
4.4 Anticoagulation therapy	452	491	1289	0	8	-	2240	1. Atrial Fibrillation/ 2. (atrial adj2 fibrillat*).ti,ab. 3. or/1-2 4. exp Anticoagulants/ 5. anticoagula*.ti,ab. 6. or/4-5 7. and/3,6 8. limit 7 to ed=20100211-20151001	1. exp heart atrium fibrillation/ 2. exp anticoagulant agent/ 3. and/1-2 4. limit 3 to dd=20100211-20151001	S,E,Y
4.5 Cholesterol therapy	180	557	370	0	186	-	1293	1. exp Hydroxymethylglutaryl-CoA Reductase Inhibitors/ 2. ((cholesteroal* or lipid*) adj2 (lower* or redu*)).ti,ab. 3. or/1-2 4. limit 3 to ed=20100211-20151001	1. exp hypocholesterolemic agent/ 2. limit 1 to dd=20100211-20151001	S, Y
4.6 Carotid surgery	212	453	202	0	175	-	1042	1. Carotid Stenosis/ 2. limit 1 to ed=20100211-20151001	1. exp carotid artery obstruction/ 2. limit 1 to dd=20100211-20151001	S, E,Y

4.7 Cervical artery dissection	460	186	111	0	0	-	757	1. Vertebral Artery Dissection/ 2. (cervical arter* adj2 dissect*).ti,ab. 3. or/1-2	1. artery dissection/ 2. vertebral artery/ 3. and/1-2	S,E
4.8 Venous Sinus Thrombosis	156	157	24	0	0	-	337	1. exp Sinus Thrombosis, Intracranial/ 2. venous sinus thrombo*.ti,ab. 3. or/1-2	1. cerebral sinus thrombosis/ 2. venous sinus thrombo*.ti,ab. 3. or/1-2	S, E
4.9 Patent foramen ovale management	58	75	86	0	190	-	409	1. exp Foramen Ovale, Patent/ 2. patent foramen ovale.ti,ab. 3. or/1-2 4. limit 3 to ed=20100211-20151001	1. exp patent foramen ovale/ 2. limit 1 to dd=20100211-20151001	S,E,Y
41.0 Hormone replacement therapy	126	243	88	0	75	-	532	1. exp Hormone Replacement Therapy/ 2. (hormone* replac* adj2 therap*).ti,ab. 3. or/1-2 4. limit 3 to ed=20100211-20151001	1. exp hormone substitution/ 2. limit 1 to dd=20100211-20151001	S,Y
4.11 Oral contraception	177	111	67	0	117	-	472	1. exp Contraceptives, Oral/ 2. (oral adj2 contracepti*).ti,ab. 3. or/1-2	1. exp oral contraception/ 2. limit 1 to dd=20100211-20151001	S,Y

								4. limit 3 to ed=20100211-20151001		
Chapter 4 totals	3147	4814	4167	0	907	-	13035			
5.1 Home based rehabilitation	33	144	310	411	56	0	954	1. exp home care/ 2. exp community care/ 3. ((home or community or ancillary) adj2 rehabilitat*).ti,ab. 4. or/1-3 5. limit 3 to ed=20100211-20151001	1. exp home care/ 2. exp community care/ 3. ambulatory care/ 4. ((home or community or ancillary) adj2 rehabilitat*).ti,ab. 5. or/1-4 6. limit 5 to dd=20100211-20151001	S,Y, E
5.2 Early supported discharge services	238	753	116	11	29	0	1147	1. "length of stay"/ or patient discharge/ 2. exp Home Care Services/ 3. (early adj3 discharg*).ti,ab. 4. or/1-3 5. limit 4 to ed=20100211-20151001	1. "length of stay"/ or hospital discharge/ 2. (early adj3 discharg* adj3 hospital*).ti,ab. 3. or/1-2 4. limit 3 to dd=20100211-20151001	S, Y, E
5.3 Amount and intensity of rehabilitation	94	138	228	192	261	0	913	1. (rehabilitat* adj5 (amount* or dose or doses or intens*)).ti,ab. 2. limit 1 to ed=20100211-20151001	1. (rehabilitat* adj5 (amount* or dose or doses or intens*)).ti,ab. 2. limit 1 to dd=20100211-20151001	S,Y
5.4 Goal setting	247	521	409	40	27	0	1244	1. goals/ 2. goal*.ti,ab. 3. or/1-2	1. exp motivation/ 2. goal*.ti,ab. 3. or/1-2	S,Y

								4. limit 3 to ed=20100211-20151001	4. limit 3 to dd=20100211-20151001	
5.5 Timing of rehabilitation	19	54	120	22	16	0	231	1. Early Ambulation/ 2. (early adj3 (mobili* or ambulat*)).ti,ab. 3. or/1-2 4. limit 3 to ed=20100211-20151001	1. exp mobilization/ 2. (early adj3 (mobili* or ambulat*)).ti,ab. 3. or/1-2 4. limit 3 to dd=20100211-20151001	S,Y,E
5.6 Dysphagia – screening (all dysphagia topics later moved to acute chapter)	38	59	86	0	96	0	279	1. exp Deglutition Disorders/ 2. Dysphagia.ti,ab. 3. or/1-2 4. (assess* or diagnos* or screen*).ti,ab. 5. and/3-4 6. limit 5 to ed=20100211-20151001	1. exp dysphagia/ 2. (assess* or diagnos* or screen*).ti,ab. 3. and/1-2 4. limit 3 to dd=20100211-20151001	S,Y,E
5.7 Dysphagia – swallow assessment (all dysphagia topics later moved to acute chapter)	26	22	17	6	84	0	155	1. videofluoroscopy.ti,ab. 2. (swallow* adj3 (screen* or barium* or assess*)).ti,ab. 3. or/1-2 4. limit 3 to ed=20100211-20151001	1. videofluoroscopy.ti,ab. 2. (swallow* adj3 (screen* or barium* or assess*)).ti,ab. 3. or/1-2 4. limit 3 to dd=20100211-20151001	S,Y,E
5.8 Dysphagia interventions (all dysphagia topics later moved to acute chapter)	50	93	213	45	63	0	464	1. Dysphagia.ti,ab. 2. limit 1 to ed=20100211-20151001	1. Dysphagia.ti,ab. 2. limit 1 to ed=20100211-20151001	S,Y,E

5.9 Weakness	286	772	99	63	142	0	1362	1. "Muscle Strength"/ 2. Muscle Weakness/ 3. (strength or strong).ti,ab. 4. or/1-3 5. limit 4 to ed=20100211-20151001	1. "Muscle Strength"/ 2. Muscle Weakness/ 3. (strength or strong).ti,ab. 4. or/1-3 5. limit 4 to ed=20100211-20151001	S,Y,E
5.10 Loss of sensation	197	123	155	34	80	0	589	1. Sensation/ 2. sensory.ti,ab. 3. or/1-2 4. limit 3 to ed=20100211-20151001	1. exp sensation/ 2. sensory.ti,ab. 3. or/1-2 4. limit 3 to dd=20100211-20151001	S,Y,E
5.11 Visual field loss	181	220	355	18	86	0	860	1. exp Vision, Ocular/ 2. (visuo* or visua*).ti,ab. 3. or/1-2 4. (compensat* or restor* or prism* or glass* or training).ti,ab. 5. and/3-4 6. limit 5 to ed=20100211-20151001	1. exp vision/ 2. (visuo* or visua*).ti,ab. 3. or/1-2 4. (compensat* or restor* or prism* or glass* or training).ti,ab. 5. and/3-4 6. limit 5 to dd=20100211-20151001	S,Y
5.12-5.14 Sitting, standing up, standing balance	98	85	223	78	381	0	865	1. Posture/ 2. (sit or sitting).ti,ab. 3. standing.ti,ab. 4. or/1-3 5. limit 4 to ed=20100211-20151001	2. exp standing/ 3. (sitting or standing).ti,ab. 4. or/1-3 5. limit 4 to dd=20100211-20151001	S,Y,E

5.15 Walking	210	319	603	99	449	0	1680	1. exp Walking/ 2. (mobilis* or mobiliz*).ti,ab. 3. or/1-2 4. limit 3 to ed=20100211-20151001	1. exp walking/ 2. (mobilis* or mobiliz*).ti,ab. 3. or/1-2 4. limit 3 to dd=20100211-20151001	S,Y,E
5.16 Upper and lower limb activity – non-invasive brain stimulation	159	192	121	14	0	0	486	1. Transcranial Magnetic Stimulation/ 2. Transcranial Direct Current Stimulation/ 3. Deep Brain Stimulation/ 4. (TMS or tDCS or tACS or (random adj3 noise*)).ti,ab. 5. or/1-4 6. limit 5 to ed=20100211-20151001	1. exp transcranial magnetic stimulation/ 2. exp transcranial direct current stimulation/ 3. exp brain depth stimulation/ 4. (TMS or tDCS or tACS or (random adj3 noise*)).ti,ab. 5. or/1-4 6. limit 5 to dd=20100211-20151001	S,Y,E
5.17 Upper and lower limb activity – Upper limb interventions	619	770	1223	194	449	0	3255	1. exp Upper Extremity/ 2. (arm or arms).ti,ab. 3. or/1-2 4. limit 3 to ed=20100211-20151001	1. exp arm/ 2. (arm or arms).ti,ab. 3. or/1-2 4. limit 3 to dd=20100211-20151001	S,Y,E
5.18 Activities of daily living	518	952	1166	0	155	0	2791	1. "Activities of Daily Living"/ 2. "Quality of Life"/ 3. (adl or qol or (function* adj3 independen*)).ti,ab. 4. or/1-3	1. exp daily life activity/ 2. exp "quality of life"/ 3. (adl or qol or (function* adj3 independen*)).ti,ab. 4. or/1-3	S,Y,E

								5. limit 4 to ed=20100211-20151001	5. limit 4 to dd=20100211-20151001	
5.19 Aphasia	83	142	190	0	84	0	499	1. exp Aphasia/ 2. limit 1 to ed=20100211-20151001	1. exp aphasia/ 2. limit 1 to dd=20100211-20151001	S,Y,E
5.20 Dyspraxia of speech	4	10	8	2	112	0	136	1. exp Apraxias/ 2. dyspraxia.ti,ab. 3. or/1-2 4. limit 3 to ed=20100211-20151001	1. exp apraxia/ 2. dyspraxia.ti,ab. 3. or/1-2 4. limit 3 to dd=20100211-20151001	S,Y,E
5.21 Dysarthria	80	1133	25	4	0	0	1242	1. Dysarthria/ 2. limit 1 to ed=20100211-20151001	1. exp dysarthria/ 2. limit 1 to dd=20100211-20151001	S,Y,E
5.22 Cognitive communication deficits	671	2323	411	0	0	0	3405	1. exp Cognition/ 2. (cognition or cognitive).ti,ab. 3. or/1-2 4. (rehabilitat* or therap* or training or communication).ti,ab. 5. and/3-4 6. limit 5 to ed=20100211-20151001	1. exp cognition/ 2. (cognition or cognitive).ti,ab. 3. or/1-2 4. (rehabilitat* or therap* or training or communication).ti,ab. 5. and/3-4 6. limit 5 to dd=20100211-20151001	S,Y
5.23 Perception	664	736	116	0	0	0	1516	1. exp Perception/ 2. (percep* adj5 (improv* or impair*)).ti,ab. 3. or/1-2	1. exp perception/ 2. (percep* adj5 (improv* or impair*)).ti,ab. 3. or/1-2	S,Y

								4. limit 3 to ed=20100211-20151001	4. limit 3 to dd=20100211-20151001	
5.24 Attention and concentration	37	113	469	88	168	65	940	1. Attention/ 2. concentration.ti,ab. 3. or/1-2 4. limit 1 to ed=20100211-20151001	1. exp attention/ 2. concentration process/ or concentration loss/ 3. or/1-2 4. limit 3 to dd=20100211-20151001	S,Y,E
5.25 Memory	291	1079	103	37	85	162	1757	1. exp Memory/ 2. limit 1 to ed=20100211-20151001	1. exp memory/ 2. limit 1 to dd=20100211-20151001	S,Y
5.26 Executive functions	207	464	45	19	148	313	1196	1. Executive Function/ 2. (external adj3 cue*).ti,ab. 3. ((goal or metacognitive) adj5 training*).ti,ab. 4. or/1-3 5. limit 4 to ed=20100211-20151001	1. exp executive function/ 2. (external adj3 cue*).ti,ab. 3. ((goal or metacognitive) adj5 training*).ti,ab. 4. or/1-3 5. limit 4 to dd=20100211-20151001	S,Y
5.27 Limb apraxia	96	205	10	51	37	0	399	1. exp Apraxias/ 2. (limb adj3 apraxia*).ti,ab. 3. or/1-2 4. limit 3 to ed=20100211-20151001	1. exp apraxia/ 2. ((limb* or leg* or arm*) adj3 apraxia*).ti,ab. 3. or/1-2 4. limit 3 to dd=20100211-20151001	S,Y

5.28 Neglect	279	382	108	27	136	0	932	1. neglect.ti,ab. 2. limit 1 to ed=20100211-20151001	1. exp neglect/ 2. neglect.ti,ab. 3. or/1-2 4. limit 3 to dd=20100211-20151001	S,Y
Chapter 5 totals	5425	11804	6929	1455	3144	540	25641			
6.1 Nutrition & hydration – early feeding	488	143	459	0	67	0	1077	1. exp Feeding Methods/ 2. Intubation, Gastrointestinal/ 3. (((Nasogastric or supplementary or enteral) adj2 (feed or food*)) or (PEG or percutaneous endocopic gastrostomy) or diet*).ti,ab. 4. or/1-3 5. limit 4 to ed=20100211-20151001	1. nose feeding/ 2. percutaneous endoscopic gastrostomy/ 3. diet supplementation/ 4. enteric feeding/ 5. (((Nasogastric or supplementary or enteral) adj2 (feed or food*)) or (PEG or percutaneous endocopic gastrostomy) or diet*).ti,ab. 6. or/1-5 7. limit 6 to dd=20100211-20151001	Y, S, E
6.2 Nutrition & hydration – early hydration	39	130	316	0	190	0	675	1. exp Fluid Therapy/ 2. Drinking/ 3. ((subcutaneous or percutaneous) adj2 hydrat*).ti,ab. 4. or/1-3 5. limit 4 to ed=20100211-20151001	1. hydration/ 2. fluid intake/ 3. (hydrate or hydration).ti,ab. 4. or/1-3 5. limit 4 to dd=20100211-20151001	Y, S, E

6.3 Poor oral hygiene	23	65	435	18	6	0	547	1. oral hygiene/ 2. ((Mouth or oral) adj2 (hygiene or assessment or care)).ti,ab. 3. or/1-2 4. limit 3 to ed=20100211-20151001	1. mouth hygiene/ 2. ((Mouth or oral) adj2 (hygiene or assessment or care)).ti,ab. 3. or/1-2 4. limit 3 to dd=20100211-20151001	Y, S, E
6.4 Spasticity	301	660	321	14	322	0	1618	1. Muscle Spasticity/ 2. spastic*.ti,ab. 3. or/1-2 4. limit 3 to ed=20100211-20151001	1. spasticity/ 2. spastic*.ti,ab. 3. or/1-2 4. limit 3 to dd=20100211-20151001	Y, S, E
6.5 Contracture	123	349	198	3	106	0	779	1. exp Contracture/ 2. exp Patient Positioning/ 3. Muscle Stretching Exercises/ 4. exp Electric Stimulation/ 5. casting.ti,ab. 6. or/1-5 7. limit 6 to ed=20100211-20151001	1. exp contracture/ 2. patient positioning/ 3. exp stretching/ 4. electrostimulation/ 5. casting*.ti,ab. 6. or/1-5 7. limit 6 to dd=20100211-20151001	Y, S, E
6.6 Subluxation	17	18	20	1	37	0	93	1. Shoulder Dislocation/ 2. subluxation.ti,ab. 3. or/1-2 4. Electric Stimulation/ 5. exp orthopedic equipment/ 6. exp Physical Therapy Modalities/	1. exp subluxation/ 2. shoulder dislocation/ 3. or/1-2 4. electrostimulation/ 5. therapy/ 6. exp physiotherapy/ 7. supporti*.ti,ab.	Y, S, E

								7. (supporti* or physiotherap* or therap*).ti,ab. 8. or/4-7 9. and/3,8 10. limit 9 to ed=20100211-20151001	8. exp orthopedic equipment/ 9. or/4-8 10. and/3,9 11. limit 10 to dd=20100211-20151001	
6.7 Shoulder pain	114	117	48	4	21	0	304	1. exp Shoulder/ 2. (shoulder adj2 pain).ti,ab. 3. or/1-2 4. limit 3 to ed=20100211-20151001	1. shoulder pain/ 2. limit 1 to dd=20100211-20151001	Y, S, E
6.8 Swelling of the extremities	24	462	152	3	214	0	855	1. exp Edema/ 2. limit 1 to ed=20100211-20151001	1. exp edema/ 2. electrostimulation/ 3. elevat*.ti,ab. 4. (passive adj2 motion*).ti,ab. 5. pressure.ti,ab. 6. or/2-5 7. and/1,6 8. limit 7 to dd=20100211-20151001	Y, S, E
6.9 Loss of cardiorespiratory fitness	918	1435	447	48	90	0	2938	1. exp Exercise Therapy/ 2. Physical Fitness/ 3. (exercise* or fitness*).ti,ab. 4. or/1-3 5. limit 4 to ed=20100211-20151001	1. exp exercise/ 2. exp fitness/ 3. (aerobic adj2 (fitness or physical or training)).ti,ab. 4. or/1-3 5. limit 4 to dd=20100211-20151001	Y, S, E

6.10 Fatigue	150	1213	146	9	54	0	1572	1. exp Fatigue/ 2. fatigue.ti,ab. 3. or/1-2 4. limit 3 to ed=20100211-20151001	1. exp fatigue/ 2. fatigue.ti,ab. 3. or/1-2 4. limit 3 to dd=20100211-20151001	Y, S, E
6.11 Urinary incontinence	35	285	124	0	149	0	593	1. exp Urinary Incontinence/ 2. (catheter* adj2 (urine* or urinary)).ti,ab. 3. or/1-2 4. limit 3 to ed=20100211-20151001	1. exp urine incontinence/ 2. (catheter* adj2 (urine* or urinary)).ti,ab. 3. or/1-2 4. limit 3 to dd=20100211-20151001	Y, S, E
6.12 Faecal incontinence	12	657	46	0	51	0	766	1. Constipation/ 2. Fecal Incontinence/ 3. (bowel adj2 (dysfunction or training)).ti,ab. 4. or/1-3 5. limit 4 to ed=20100211-20151001	1. constipation/ 2. exp feces impaction/ or feces incontinence/ 3. (bowel adj2 (dysfunction or training)).ti,ab. 4. or/1-3 5. limit 4 to dd=20100211-20151001	Y, S, E
6.13 Mood disturbance – emotional distress	6	8	4	5	43	0	66	1. exp Cognitive Therapy/ 2. exp Behavior Therapy/ 3. ((cognitive adj3 therapy) or cbt).ti,ab. 4. or/1-3 5. Stress, Psychological/ 6. distress*.ti,ab. 7. or/5-6	1. distress*.ti,ab. 2. emotional stress/ 3. or/1-2 4. exp cognitive therapy/ 5. Behavior Therapy/ 6. cbt.ti,ab. 7. or/4-6 8. and/3,7	Y, S, E

								8. and/4,7 9. limit 8 to ed=20100211-20151001	9. limit 8 to dd=20100211-20151001	
6.14 and 6.15 – depression/anxiety prevention and management	855	3144	605	284	193	0	5081	1. Depression/ 2. exp Anxiety/ 3. (depression* or anxiety or anxious).ti,ab. 4. or/1-3 5. limit 4 to ed=20100211-20151001	1. exp depression/ 2. exp anxiety/. 4. or/1-2 5. limit 3 to dd=20100211-20151001	Y, S, E
6.16 Deep venous thrombosis or pulmonary embolism	372	2754	170	0	118	0	3414	1. exp Venous Thrombosis/ 2. exp Pulmonary Embolism/ 3. (dvt or pe).ti,ab. 4. or/1-3 5. limit 4 to ed=20100211-20151001	1. deep vein thrombosis/ 2. lung embolism/ 3. or/1-2 4. limit 3 to dd=20100211-20151001	Y, S, E
6.17 Falls	234	266	269	0	736	0	1505	1. exp Venous Thrombosis/ 2. exp Pulmonary Embolism/ 3. (dvt or pe).ti,ab. 4. or/1-3 5. limit 4 to ed=20100211-20151001	1. falling/ 2. limit 1 to dd=20100211-20151001	Y, S, E
Chapter 6 totals	3711	11706	3760	389	2397	0	21883			
7.1 Information and education	210	634	288	-	70	-	1202	1. exp Health Education/ 2. pamphlet/ 3. (health adj2 (information or education)).ti,ab. 4. or/1-3	1. medical information/ 2. (health adj2 (information or education)).ti,ab. 3. publication/	S, Y, E

								5. limit 4 to ed=20100211-20151001	4. or/1-3 5. limit 4 to dd=20100211-20151001	
7.2 Discharge care plans	653	328	190	-	-	-	1171	1. Patient Discharge/ 2. exp Patient Care Planning/ 3. (discharge adj2 plan*).ti,ab. 4. or/1-3 5. limit 4 to ed=20100211-20151001	1. checklist/ 2. (discharge adj2 plan*).ti,ab. 3. or/1-2 4. limit 3 to dd=20100211-20151001	S, Y
7.3 Patient and carer needs	371	638	153	-	-	-	1162	1. Needs Assessment/ 2. Occupational Therapy/ 3. ((predischarge or home) adj2 assessment*).ti,ab. 4. or/1-3 5. limit 4 to ed=20100211-20151001	1. Needs Assessment/ 2. Occupational Therapy/ 3. ((predischarge or home) adj2 assessment*).ti,ab. 4. or/1-3 5. limit 4 to dd=20100211-20151001	S, Y
7.4 Home assessment	53	175	145	-	30	-	403	1. House Calls/ 2. Homemaker Services/ 3. (home adj2 (visit* or assessment*)).ti,ab. 4. (occupational adj2 visit*).ti,ab. 5. or/1-4 6. limit 5 to ed=20100211-20151001	1. exp home care/ 2. (home adj2 (visit* or assessment*)).ti,ab. 3. (occupational adj2 visit*).ti,ab. 4. or/1-3 5. limit 4 to dd=20100211-20151001	S, Y

7.5 Carer training	119	607	86	-	147	-	959	1. Caregivers/ 2. (carer* adj2 train*).ti,ab. 3. or/1-2 4. limit 3 to ed=20100211-20151001	1. caregiver/ 2. (carer* adj2 train*).ti,ab. 3. or/1-2 4. limit 3 to dd=20100211-20151001	S, Y, E
Chapter 7 totals	1406	2382	862	-	247	-	4897			
8.1 Self-management	199	408	524	806	288	-	2225	1. exp Self Care/ 2. goals/ 3. self efficacy/ 4. or/1-3 5. limit 4 to ed=20100211-20151001	1. self care/ 2. motivation/ 3. self concept/ 4. self-directed learning/ 5. or/1-4 6. limit 5 to dd=20100211-20151001	S,Y
8.2 Driving	49	34	7	0	0	-	90	1. exp Automobile Driving/ 2. ((visual attention or percep* or driver*) adj2 (training or retraining or program)).ti,ab. 3. or/1-2 4. limit 3 to ed=20100211-20151001	1. exp car driver/ or car driving/ 2. ((visual attention or percep* or driver*) adj2 (training or retraining or program)).ti,ab. 3. or/1-2 4. limit 3 to dd=20100211-20151001	S,Y
8.3 Community mobility and outdoor travel	9	25	80	366	0	-	480	1. ((transport* or community) adj2 (access* or educat*)).ti,ab. 2. limit 1 to ed=20100211-20151001	1. ((transport* or community) adj2 (access* or educat*)).ti,ab. 2. limit 1 to dd=20100211-20151001	S,Y

8.4 Leisure	844	153	380	944	28	-	2349	1. exp Leisure Activities/ 2. ((leisure or self or community) adj2 rehabilitat*).ti,ab. 3. or/1-2 4. limit 3 to ed=20100211-20151001	1. exp leisure/ 2. ((leisure or self or community) adj2 rehabilitat*).ti,ab. 3. or/1-2 4. limit 3 to dd=20100211-20151001	S,Y
8.5 Return to work	71	52	21	76	0	-	220	1. exp work/ 2. (return* adj2 work*).ti,ab. 3. or/1-2 4. limit 3 to ed=20100211-20151001	1. return to work/ 2. work capacity/ 3. or/1-2 4. limit 3 to dd=20100211-20151001	S,Y
8.6 Sexuality	53	13	22	230	0	-	318	1. exp Sexuality/ 2. sexual*.ti,ab. 3. or/1-2 4. limit 3 to ed=20100211-20151001	1. attitude to sexuality/ or sexuality/ 2. limit 1 to dd=20100211-20151001	S,Y
8.7 Peer support	182	330	538	174	0	-	1224	1. social support/ 2. (support* adj2 (peer* or group*)).ti,ab. 3. or/1-2 4. limit 3 to ed=20100211-20151001	1. social support/ 2. (support* adj2 (peer* or group*)).ti,ab. 3. Caregivers/ 4. (education adj2 counsel*).ti,ab. 5. or/1-4 6. limit 5 to dd=20100211-20151001	S,Y
8.8 Carer support	239	58	194	24	60	-	575	1. Caregivers/ 2. (education adj2	1. social support/ 2. (support* adj2 (peer* or	S,E,Y

								counsel*).ti,ab. 3. or/1-2 4. limit 3 to ed=20100211-20151001	group*)).ti,ab. 3. Caregivers/ 4. (education adj2 counsel*).ti,ab. 5. or/1-4 6. limit 5 to dd=20100211-20151001	
Chapter 8 totals	1646	1073	1766	2620	376	-	7481			
Overall totals	28126	48979	22947	4512	9345	540	109598			

3. Aboriginal and Torres Strait Islander peoples – search strategy

Evidence regarding stroke in the Aboriginal and Torres Strait Islander population was sought using a search string that covered all stroke-related questions:

ATSI Suite_Core stroke

Stroke* OR (cerebrovascular (disorder* OR accident*)) OR ischemi* OR infarc* OR (intracranial AND thrombo*)

A search was conducted using this string in the Aboriginal and Torres Strait Islander Health Bibliography (ATSIhealth, https://www.informit.org/index-product-details/ATSIHEALTH) database. A total of 30 references were identified, although following evidence review it was decided that none provided sufficient evidence to specifically inform recommendations about treatments.

Appendix 2: GRADE methodology

The Clinical Guidelines were developed following the GRADE methodology (Grading of Recommendations, Assessment, Development and Evaluation). GRADE provides a transparent and structured approach for specifying health care questions, choosing outcomes of interest and rating their importance, evaluating the available evidence, and bringing together the evidence with values and preferences of patients as well as society to arrive at recommendations.

The description of the GRADE methodology provided here is largely drawn from the GRADE handbook [4] (available at: http://gdt.guidelinedevelopment.org/app/handbook/handbook.html), supplemented with some details about how the GRADE methodology is implemented in the MAGICapp tool for guideline development. For full details readers are encouraged to refer to the GRADE handbook, but relevant details have been summarised below.

Based on the stages of guideline development outlined in the GRADE handbook, the process of developing recommendations involved:

1. Framing the health care question.
2. Selecting and rating the importance of outcomes.
3. Summarising the evidence.
4. Assessing the quality of evidence.
5. Converting evidence to recommendations.

Framing the health care question

The GRADE methodology uses the PICO framework for framing health care questions. The emphasis is on carefully specifying four components of the clinical question being addressed. The GRADE handbook defines these four components as:

- Patient: the patients or population to whom the recommendations are meant to apply.
- Intervention: the therapeutic, diagnostic, or other intervention under investigation (e.g. the experimental intervention, or in observational studies the exposure factor).
- Comparison: the alternative intervention; intervention in the control group.
- Outcome: the outcome(s) of interest.

The patient/population of interest may be broad. However, if there are subgroups within the population with different levels of baseline risk, separate questions may be required to develop appropriate recommendations, as the benefits of treatment may differ even if the effect of the intervention is similar across the subgroups.

Selecting and rating the importance of outcomes

GRADE emphasises that all outcomes that are important or critical to patients should be considered by guideline developers. The choice of outcomes is guided by their importance to patients, rather than what is available in the existing evidence, meaning critical outcomes for which there is no evidence available should still be acknowledged.

To guide decisions about the relative importance of outcomes, the GRADE handbook suggests rating outcomes on a 1 to 9 scale where 1 represents outcomes of least importance and 9 the outcomes of most importance. This rating scale divides outcomes into three categories, with ratings of 1 to 3 representing outcomes of limited importance, 4 to 6 representing important but not critical outcomes, and 7 to 9 representing outcomes that are critical for making a decision. This 1 to 9 rating scale is implemented in the MAGICapp platform as part of the evidence profile, and was used during the Clinical Guideline development process to guide the creation of recommendations.

The process of selecting outcomes involves:

- A preliminary classification of the importance of different outcomes, before gathering evidence;
- A reassessment of the importance of outcomes after gathering evidence, and
- Judgements of the balance between desirable and undesirable health outcomes when making recommendations.

The preliminary classification of outcomes is focused on identifying the outcomes of greatest importance to the target population, through either systematic reviews of the literature, consultation with the guideline panel, or asking members of the public.

Reassessment of the outcomes after gathering evidence includes checking for outcomes reported in the evidence that were not originally included, and using the available evidence to reassess the original judgements of the importance of each outcome.

Judgements about the balance between desirable and undesirable health outcomes should be based on a summary of findings table or evidence profile and can take into account the experience of panel members, systematic reviews of the effects of the intervention, economic analyses and evidence about the value that the population places on key outcomes.

When evidence about the most important outcomes is lacking or unavailable, surrogate or substitute outcomes may be used, but as these outcomes only provide indirect evidence about outcomes that are most important to patients, this may result in the evidence being judged as lower quality.

Summarising the evidence

The GRADE Handbook emphasises that recommendations should be based on the "best available body of evidence", usually a high quality systematic review. Based on the best available evidence, a summary of evidence is created including an estimate of the treatment effect for each outcome, a rating of the quality of evidence and a summary of the evidence.

Evidence is presented in evidence tables, either **evidence profiles** with detailed information about the quality of evidence for each outcome, or **summary of findings tables** that present findings for each outcome in an accessible format that can be understood by a broad audience.

MAGICapp provides standardised evidence profile tables based on GRADE methodology, and these were used in this guideline. These provide:

- A list of outcomes evaluated for the PICO question and the timeframe over which these outcomes were assessed;
- A rating of importance for each outcome;
- Information about the number of studies and participants contributing to the evidence for each outcome;
- The relative effect of the intervention, e.g. odds ratio, relative risk, or hazard ratio for dichotomous outcomes, mean difference or standardised mean difference for continuous outcomes;
- For dichotomous outcomes, the assumed baseline risk (per 1000 people), e.g. prevalence in target population or control group risk. For this guideline the assumed baseline risk was generally the control group risk, based on the observed numbers of events in the control group;
- The corresponding risk (per 1000 people) in the intervention group. In this Clinical Guideline the corresponding risk was generally calculated from the assumed control risk and the relative effect;
- The absolute effect, e.g. for dichotomous outcomes, the absolute difference in the number of events per 1000 people based on the assumed control risk and the relative effect estimate and its confidence interval;
- Judgements about factors affecting the quality of evidence;
- Rating of the overall certainty in the effect estimates, based on the GRADE guidelines and the judgements about individual quality of evidence factors, and
- A summary of the evidence, based on the size of the effect and the quality of evidence. MAGICapp automatically suggests standard phrases for the summary based on the quality of evidence, such as "[The intervention] probably improves [the outcome] slightly" for moderate quality evidence of a small benefit.

The standardised evidence profile tables used in MAGICapp emphasise “Absolute effect estimates” for dichotomous outcomes, displaying the number of people per 1000 people expected to have the outcome in the control and intervention groups. Wherever possible, these estimates were calculated using the following procedure:

a. Obtain the relative effect estimate (odds ratio or relative risk) and corresponding confidence interval from the study (systematic review or primary study) that data is being extracted from.

b. 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).

c. Calculate an estimate of the corresponding risk per 1000 in people receiving the intervention using the relative effect estimate, using methods based on the methods for calculating absolute risk reductions in the Cochrane Handbook for Systematic Reviews of Interventions [5]. These calculations are implemented in MAGICapp, so that once the relative effect estimate and control group risk have been entered, an “Auto-calculate” button calculates the corresponding risk in the intervention group, the risk difference between intervention and control groups, and the confidence interval for this risk difference (based on the confidence interval for the relative effect estimate).

Since the estimated risk in people receiving the intervention is based on a relative effect estimate that may be adjusted (e.g. covariate-adjusted to account for baseline differences between participants), this estimated risk may differ from the raw estimate of the intervention group risk from the corresponding study. During evidence review, some WP members raised concerns about differences between the reported intervention risks in the MAGICapp evidence profiles and the raw proportions of events observed in the trials from which evidence was drawn. In order to address these concerns, an explanation of the estimated intervention risks and the process used to calculate them was added to each chapter of the guidelines.

In some cases, calculation of these absolute risks was not possible. Reasons for this included:

- Insufficient information being reported in the relevant study, or
- The reported estimate in the trial was a hazard ratio, generalised odds ratio, odds ratio from an ordinal logistic regression analysis, or some other estimate of the relative effect. While calculations of absolute risk based on these estimates are possible in some cases (e.g. hazard ratio), the relevant studies generally did not report sufficient information to allow their calculation. In other cases the absolute risk estimates could not have been reported in the standardised MAGICapp tables, such as when generalised odds ratios were used to analyse ordinal modified Rankin Scale scores.

An example MAGICapp evidence profile table from the Clinical Guidelines is shown below:

Outcome Timeframe	Study results and measurements	Absolute effect estimates Standard-dose intravenous alteplase	 Low-dose intravenous alteplase	Certainty in effect estimates (Quality of evidence)	Summary
Death or disability 90 days 9 Critical	Odds Ratio 1.09 (CI 95% 0.95 - 1.25) Based on data from 3206 patients in 1 studies	511 per 1000	533 per 1000 Difference: 22 more per 1000 (CI 95% 13 fewer - 55 more)	Low Due to serious imprecision, Due to serious indirectness	Low-dose intravenous alteplase may slightly increase death or disability
Death 90 days 9 Critical	Odds Ratio 0.8 (CI 95% 0.63 - 1.01) Based on data from 3297 patients in 1 studies Follow up: 90 days.	103 per 1000	84 per 1000 Difference: 19 fewer per 1000 (CI 95% 36 fewer - 1 more)	Low Due to serious imprecision, Due to serious indirectness	Low-dose intravenous alteplase may slightly decrease death
Improved functional outcome 90 days 8 Critical	Odds Ratio 1 (CI 95% 0.89 - 1.13) Based on data from 3206 patients in 1 studies Follow up: 90 days.	n/a	n/a	Low Due to serious imprecision, Due to serious indirectness	Low-dose intravenous alteplase may have little or no difference on improved functional outcome
Symptomatic ICH 90 days 8 Critical	Odds Ratio 0.48 (CI 95% 0.27 - 0.86) Based on data from 3297 patients in 1 studies Follow up: 90 days.	21 per 1000	10 per 1000 Difference: 11 fewer per 1000 (CI 95% 15 fewer - 3 fewer)	Low Due to serious imprecision, Due to serious indirectness	Low-dose intravenous alteplase may decrease symptomatic ICH

Assessing quality of evidence

According to the GRADE handbook, the GRADE definition of quality of evidence differs depending on whether the context is a systematic review or a guideline panel. For guideline panels, the quality of evidence "reflects the extent to which our confidence in an estimate of the effect is adequate to support a particular recommendation".

GRADE specifies four grades of evidence, as listed in the table below:

Table 1: Quality of evidence grades. Source: GRADE handbook (http://gdt.guidelinedevelopment.org/app/handbook/handbook.html)

Grade	Definition
High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Very Low	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Quality of evidence ratings are done separately for each outcome, as different factors may affect each outcome differently.

Rating the quality of evidence for a particular outcome starts with the study design – evidence drawn from randomised trials (without any other important limitations) are rated as high quality evidence, while observational studies (without particular strengths or limitations) are considered low quality evidence.

Following the initial rating based on the study design, quality of evidence is then assessed systematically by considering five factors that can reduce the quality of evidence:

- Risk of bias – factors such as lack of allocation concealment and blinding that may introduce a risk of bias.
- Inconsistency of results – differences in estimates of the treatment effect across studies that cannot be plausibly explained.
- Indirectness of evidence – whether the evidence directly relates to comparisons of the interventions of interest in the target population on the outcomes of most interest.
- Imprecision – whether "our confidence in the estimate of an effect is adequate to support a particular decision" (GRADE Handbook), e.g. whether the confidence interval for the treatment effect includes both benefit and harm.
- Publication bias – whether the treatment effect may have been over- or under-estimated due to selective publication of studies.

Based on each of these factors, reviewers might choose to downgrade the quality of evidence by one or two levels (for each factor, e.g. a reviewer may downgrade two levels based on limitations in study design, and one level for imprecision, downgrading by three levels overall).

Reviewers can also choose to rate the quality of evidence up based on three factors:

- Large magnitude of effect,
- Dose-response gradient, and
- All plausible confounding would reduce the observed effect (or increase the effect, if a null effect was observed).

However, rating the quality of evidence up is generally only recommended for observational studies.

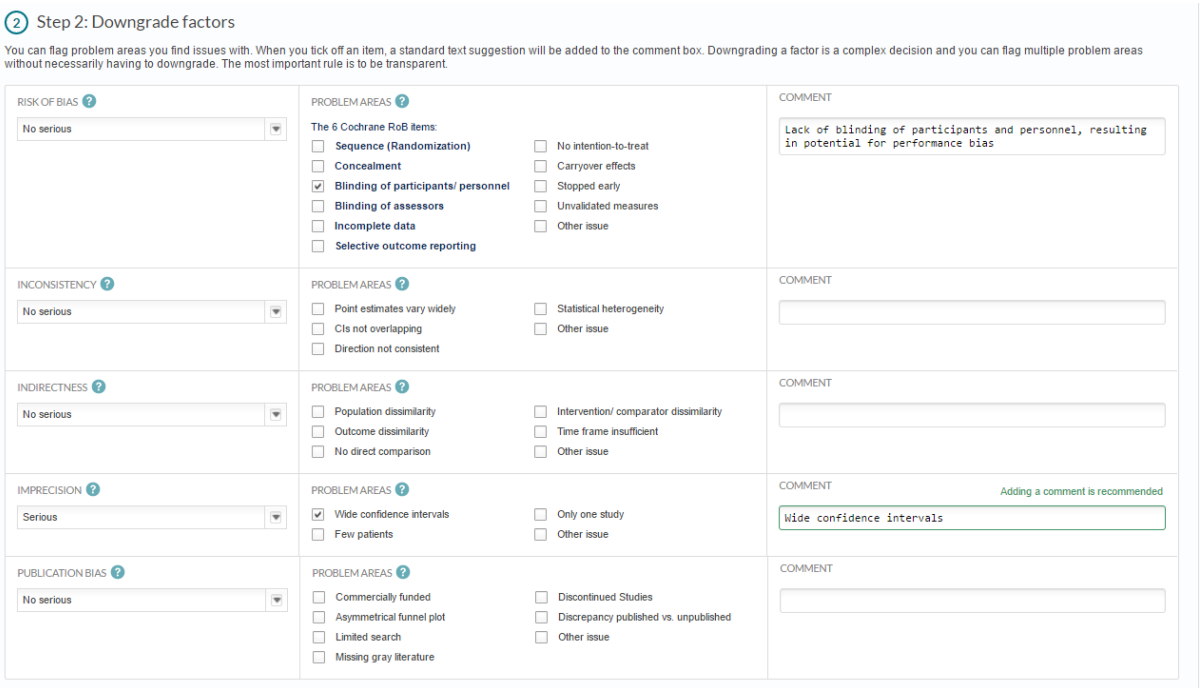
These judgements about the quality of evidence are not intended to be objective or reproducible, but reviewers and authors are encouraged to provide explicit reasons for their decisions so that the decisions are transparent to users.

In MAGICapp, this framework for rating the quality of evidence is encouraged by the use of a standardised form. Authors can mark individual "problem area" items relating to each downgrade factor listed above, and then choose whether there are "No

serious" issues relating to that downgrade factor, "Serious" issues, or "Very serious" issues. Selecting "Serious" or "Very serious" causes the overall quality of evidence rating suggested by MAGICapp to decrease by one or two levels respectively (although authors can still modify the rating based on their own judgement).

An example of this quality rating form is shown below:

Figure 1: Example quality of evidence form from MAGICapp



Going from evidence to recommendations

The GRADE process specifies 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":

- Strong recommendations, where guideline authors are certain that the evidence supports a clear balance towards either desirable or undesirable effects.
- 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.

The GRADE handbook summarises the implications of these categories of recommendations as follows:

Table 2: 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.

Guideline panels may also choose to make no recommendation regarding an intervention, or recommend that an intervention only be used in research. The GRADE handbook specifies three reasons why guideline panels might make no recommendation:

- The confidence in effect estimates is so low that the panels feel a recommendation is too speculative.
- Irrespective of the confidence in effect estimates, the trade-offs are so closely balanced, and the values and preferences and resource implications not known or

too variable, that the panel has great difficulty deciding on the direction of a recommendation.

- Two management options have very different undesirable consequences, and individual patients' reactions to these consequences are likely to be so different that it makes little sense to think about typical values and preferences (GRADE Handbook).

Recommendations to only use an intervention in research can be made when the intervention is promising but there is insufficient evidence of benefit. The GRADE handbook outlines three conditions that should be met when recommending an intervention only be used in research:

- There is thus far insufficient evidence to support a decision for or against an intervention,
- Further research has large potential for reducing uncertainty about the effects of the intervention, or
- Further research is thought to be of good value for the anticipated costs.

The four main factors used to determine the strength of recommendations are:

i. The balance between desirable and undesirable consequences
ii. Confidence in the estimates of effect (quality of evidence)
iii. Confidence in values and preferences and their variability
iv. Resource use (cost).

Judging the *balance between desirable and undesirable consequences* involves considering both the best estimates of the magnitude of desirable and undesirable effects and considering the importance of outcomes and their weight in terms of the typical values that patients and populations apply to them. If the best estimates of the effects of an intervention point to large desirable effects and no or minimal undesirable effects then the recommendation will likely be strong, but if there are large desirable and undesirable effects then a weak recommendation may be needed. These effects should be considered while taking into account patient preferences and values and how important these desirable and undesirable effects are for patients.

Rating the *confidence in the estimates of effect and quality of evidence* requires considering the same factors that are considered for individual outcomes, i.e. factors such as risk of bias and inconsistency. These factors are judged across all the relevant outcomes simultaneously, taking into account the relative importance of these outcomes so that if there is low confidence regarding critical outcomes, the recommendation will generally be weak.

For *confidence in values and preferences* and their variability, the guideline panel should consider uncertainty about values and preferences based on the available

evidence, as well as the extent to which these values and preferences are expected to differ among patients. Ideally, information about values and preferences could be obtained from systematic studies of these preferences, but given that studies of this kind are rare, this will often be based on clinicians' experience.

Considerations of *cost and resource utilisation* are similar to considerations of clinical outcomes, where the guideline panel should consider the most important resource implications, provide estimates of the difference between intervention and control and make explicit judgements about the quality of evidence informing these estimates.

A few points were considered when interpreting the cost-effectiveness evidence that informs the recommendations or practice statements.

- When an intervention is cost-saving/dominant, it has higher clinical effectiveness and less cost, thus further supporting the recommendation.
- An intervention can be cost-effective without being cost-saving. This means the additional cost for the health benefits gained from the intervention are considered worthwhile. What constitutes a cost-effective intervention is a value judgment. Currently, a widely accepted threshold for cost-effectiveness is $50,000 per quality adjusted life year (QALY) gained (http://www.nejm.org/doi/full/10.1056/NEJMp1405158). This threshold is an arbitrary value that indicates a society's willingness for a QALY gained. These cost-effectiveness thresholds vary between countries. For example, the cost-effectiveness threshold of $50,000 is commonly used in Australia and the United States of America, and the equivalent is £30,000 in the United Kingdom.
- In areas where there are no data from economic evaluations that support the recommendations or practice statements, it remains unclear whether any additional costs of providing the intervention above usual care for the additional potential benefits obtained are justified.

MAGICapp emphasises the consideration of these factors when making recommendations through a "Key info" form with separate sections for "Benefits and harms", "Quality of evidence", "Preference and values" and "Resources and other considerations" (corresponding to the four factors above), allowing authors to provide specific comments about each factor as well as selecting from a limited set of standardised phrases to reflect their judgement for each factor, i.e.:

- Benefits and harms – either:

  Small net benefit, or little difference between the alternatives, OR
  Substantial net benefits of the recommended alternative

- Quality of evidence:

  Very low
  Low
  Moderate

High

- Preference and values:

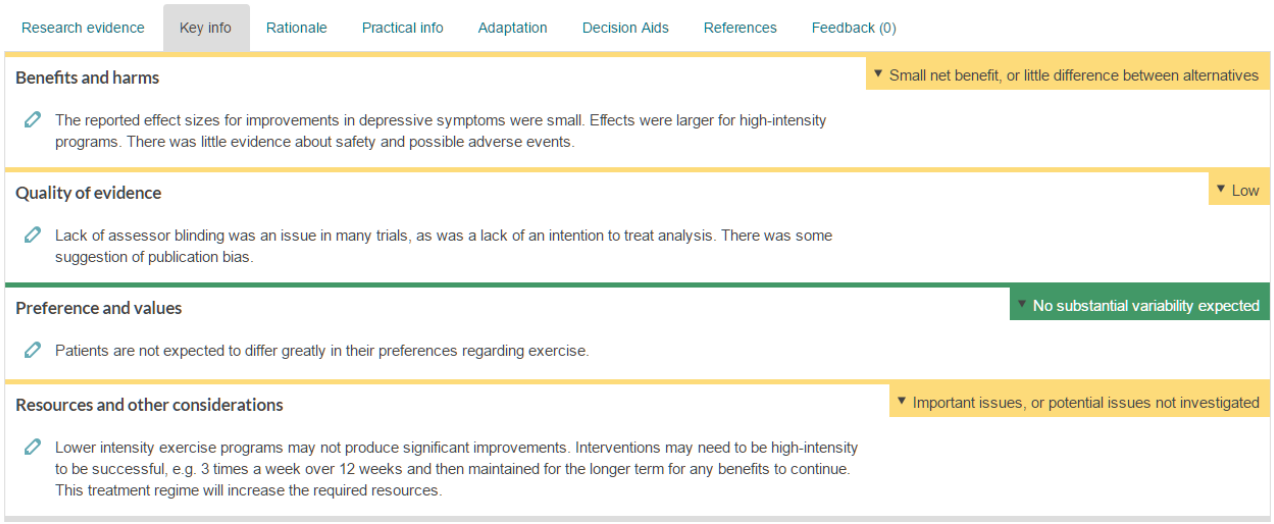
  Substantial variability is expected or uncertain
  No substantial variability expected

- Resources and considerations:

  Important issues, or potential issues not investigated
  No important issues with the recommended alternative.

An example MAGICapp evidence form from this guideline is shown below:

Figure 1: Example MAGICapp "Key info" template



In MAGICapp, guideline authors also provide a “Rationale” summarising how these factors were synthesised to decide on the final recommendation, and “Practical info” regarding the implementation of the recommended interventions.

Appendix 3: NHMRC requirements

	Location of information relevant to each requirement (i.e. guideline, administrative or technical report including page number/s).	Notes pertaining to assessment of requirement or location of information relating to the requirement.
MANDATORY REQUIREMENTS	***Guideline developer to complete***	***Methodological reviewer to complete***
Clinical questions addressed by the guideline are stated in a structured and consistent format to define the boundaries of the topic, i.e. by specifying the relevant population, intervention/s (e.g. treatment/s or diagnostic test/s), comparator/s and outcomes measured.	Must appear in guideline and must appear in the technical report	Yes / No
	Guideline: all evidence profiles are presented in PICO format Technical report: Section 3 List of clinical questions	Comment:
Systematic searches for evidence are undertaken and the search strategy is documented, including the search terms and databases searched.	Must appear in technical report	Yes / No
	Technical report: Section 2.2 Systematic literature search and Appendix 1: Search terms and search results	Comment:
The population groups specified in the search strategy include Aboriginal and Torres Strait Islander peoples and any population subgroups that have been identified (see Requirement B.4 and B.5).	Must appear in technical report	Yes / No
	Technical report: see a search specific to Aboriginal and Torres Strait Islander peoples in Section 2.2 and Appendix 1: Search terms and search results	Comment:
The publication period covered by the searches is stated, and the latest date is within 12 months of the first day of public consultation and within 20 months of submission of the final draft guideline to NHMRC for approval.	Must appear in technical report	Yes / No
	Technical report: Section 2.2 Systematic literature search and Appendix 1: Search terms and search results	Comment:
The inclusion and exclusion criteria used to select studies for appraisal are described.	Must appear in technical report	Yes / No
	Technical report: Section **Error! Reference source not found. Error! Reference source not found.**	Comment:
For each clinical question, the developer has provided an evidence table, which summarises the systematic assessment and critical appraisal of all studies that meet the inclusion criteria (i.e. the body of evidence on which a	Must appear in technical report	Yes / No
	Technical report: Appendix 4 Evidence tables. Methodology used is described in Section 2.3.2 Data extraction and quality appraisal	Comment:

recommendation will be based). Each evidence table should include information on study design, outcomes, level of evidence, the findings of meta-analysis (if performed) and other relevant information.		
For each clinical question, the developer has provided an evidence statement form, which documents the synthesis and evaluation of the body of evidence to determine the grade of each recommendation, according to an NHMRC-approved method (NHMRC grades for recommendations or GRADE).	Must appear in technical report	Yes / No
	Technical report: see Appendix 4 Evidence tables. Methodology used is described in Section 2.3.3 Development of recommendations	Comment:
For each recommendation, the developer has provided an evidence summary, which briefly states the outcomes of each clinical studies on which the recommendation was based, their level of evidence and reference details.	Must appear in guideline	Yes / No
	Guideline: see each chapter	Comment:
A recommended date for future update of the guideline is identified.	Must appear in guideline	Yes / No
	Guideline: see Introduction of each chapter	Comment:

	Location of information relevant to each requirement (i.e. guideline, administrative or technical report including page number/s).	**Notes pertaining to assessment of requirement or location of information relating to the requirement.**
DESIRABLE REQUIREMENTS: Evidence review	***Guideline developer to complete***	***Methodological reviewer to complete***
The population groups specified in the search strategy include groups such as culturally and linguistically diverse communities or other groups for whom specific sociocultural factors (including ethnicity, gender, age, disability, socioeconomic status and location) in treatment or prevention outcomes should be considered.	To appear in technical report	Yes / No
	Technical report: where relevant, search strategies for specific topics specify population groups that need special consideration. See section 2.2 Systematic literature search and Appendix 1 Search terms and search results	Comment:

Search strategies include search terms to identify evidence related to consumers' perceptions and experiences.	To appear in technical report	Yes / No
	Technical report: see section 2.2 Systematic literature search and Appendix 1 Search terms and search results	Comment:
Dependent on the guideline scope, the search strategy is designed to identify evidence for all relevant alternatives for screening, prevention, diagnosis or treatment of the condition addressed by the guideline, including relevant complementary and alternative medicine approaches.	To appear in technical report	Yes / No
	Search terms used in the literature search were broad enough to include all relevant alternatives, including complementary and alternative approaches. Technical report: see Appendix 1 2. Search terms and results for each topic	Comment:
Search strategies include search terms to identify evidence related to cost effectiveness and resource implications of practice.	To appear in technical report	Yes / No
	Technical report: see search strings documented in Appendix 1 1. Search strings and search filters	Comment:
If gaps in the evidence are identified during the evidence review, these are described in the guideline and areas for further research are noted.	To appear in guideline	Yes / No
	Guideline: see Introduction	Comment:

Appendix 4: Evidence tables

The evidence tables contained within each of the Clinical Guideline chapters are able to be viewed online in the evidence and recommendation tabs. The links for each chapter are as follows:

Chapter 1 of 8: Pre-hospital care - https://www.magicapp.org/public/guideline/NnV76E

Chapter 2 of 8: Early assessment and diagnosis - https://www.magicapp.org/public/guideline/ojmKvn

Chapter 3 of 8: Acute medical and surgical management - https://www.magicapp.org/public/guideline/QnoKGn

Chapter 4 of 8: Secondary prevention - https://www.magicapp.org/public/guideline/8L0RME

Chapter 5 of 8: Rehabilitation - https://www.magicapp.org/public/guideline/Kj2R8j

Chapter 6 of 8: Managing complications - https://www.magicapp.org/public/guideline/WE8wOn

Chapter 7 of 8: Discharge planning and transfer of care - https://www.magicapp.org/public/guideline/VLpK8j

Chapter 8 of 8: Community participation and long-term care - https://www.magicapp.org/public/guideline/6nYJxE