Stroke FOUNDATION

Clinical Guidelines for Stroke Management

Chapter 6 of 8:
Managing complications

This is the sixth in a series of eight guideline chapters that provide evidence-based recommendations for recovery from stroke and TIA in adults.

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Sponsors/Funding

The Stroke Foundation gratefully acknowledges the previous financial assistance provided by the Australian Government, Medical Research Future Fund. The development of recommendations has not been influenced by the views or interests of the funding body.

Disclaimer

Sections

Summary of recommendations

Introduction

Methodology

Clinical questions

Managing complications - overview

Nutrition and hydration

Early hydration

Strong recommendation

- All stroke patients should have their hydration status assessed, monitored, and managed throughout their hospital admission.
- Where fluid support is required, crystalloid solution should be used in preference to colloid solutions as the first option to treat or prevent dehydration. (Visvanathan et al. 2015 *[10]*)

Early feeding

Strong recommendation

All stroke patients should be screened for malnutrition at admission and on an ongoing basis (at least weekly) while in hospital. (Dennis et al 2005 *[26]*)

Strong recommendation

For stroke patients whose nutrition status is poor or deteriorating, nutrition supplementation should be offered. (Geeganage et al 2012 *[19]*; Dennis et al 2005 *[26]*)

Weak recommendation

- For stroke patients who do not recover a functional swallow, nasogastric tube feeding is the preferred method of feeding in the short term. (Geeganage et al 2012 *[19]*; Gomes et al 2015 *[23]*; Dennis et al 2005 *[26]*)
- For stroke patients, there is no preference with regard to continuous pump (meaning using a pump for greater than or equal to 16 hrs out of 24 hrs for less than or equal to 80 ml/hr) feeding versus intermittent bolus feeding (meaning 250-400 mls/hr for 4-5 times/day) therefore practical issues, cost and patient preferences should guide practice. (Lee et al 2010 *[20]*)

Weak recommendation against

For stroke patients who are adequately nourished, routine oral nutrition supplements are not recommended. (Geeganage et al 2012 *[19]*; Dennis et al 2005 *[26]*)

Info Box

Practice points

- For patients with acute stroke food and fluid intake should be monitored.
- Stroke patients who are at risk of malnutrition, including those with dysphagia, should be referred to an Accredited Practising Dietitian for assessment and ongoing management.

Oral hygiene

Strong recommendation

All stroke patients, particularly those with swallowing difficulties, should have assistance and/or education to maintain good oral and dental (including dentures) hygiene. (Campbell et al 2020 *[33]*)

Strong recommendation

Staff and carers of stroke patients (in hospital, in residential care and home settings) should be trained in assessment and management of oral hygiene. (Campbell et al 2020 *[33]*)

Weak recommendation

For stroke patients, chlorhexidine in combination with oral hygiene instruction, and/or assisted brushing may be used to decrease dental plaque and gingiva bleeding. Caution should be taken, however, for patients with dysphagia. (Lam et al 2013 *[31]*; Yuan et al 2020 *[37]*)

Spasticity

Weak recommendation

For stroke survivors with ***upper*** limb spasticity, Botulinum Toxin A in addition to rehabilitation therapy may be used to reduce spasticity, but is unlikely to improve activity or motor function. (Foley et al 2013 *[39]*; Gracies et al 2014 *[43]*)

Weak recommendation

For stroke survivors with ***lower*** limb spasticity, Botulinum Toxin A in addition to rehabilitation therapy may be used to reduce spasticity but is unlikely to improve motor function or walking. (Wu et al 2016 *[51]*; McIntyre et al 2012 *[52]*; Olvey et al 2010 *[53]*)

Weak recommendation against

For stroke survivors with spasticity, acupuncture should not be used for treatment of spasticity in routine practice other than as part of a research study. (Lim et al 2015 *[54]*)

Weak recommendation

For stroke survivors with spasticity, adjunct therapies to Botulinum Toxin A, such as electrical stimulation, casting and taping, may be used. (Stein et al 2015 *[57]*; Mills et al 2016 *[63]*; Santamato et al 2015 *[64]*)

Weak recommendation against

For stroke survivors, the routine use of stretch to reduce spasticity is not recommended. (Harvey et al 2017 *[76]*)

Contracture

Strong recommendation against

For stroke survivors at risk of developing contracture who are receiving comprehensive, active therapy the routine use of splints or stretch of the arm or leg muscles is not recommended. (Harvey et al 2017 *[76]*)

Good practice statement

Consensus-based recommendations

- For stroke survivors, serial casting may be trialled to reduce severe, persistent contracture when conventional therapy has failed.
- For stroke survivors at risk of developing contracture or who have developed contracture, active motor training or electrical stimulation to elicit muscle activity should be provided.

Subluxation

Weak recommendation

For stroke survivors at risk of shoulder subluxation, electrical stimulation may be used in the first six months after stroke to prevent or reduce subluxation. (Vafadar et al 2015 *[80]*; Lee et al 2017 *[83]*)

Weak recommendation against

For stroke survivors at risk of shoulder subluxation, shoulder strapping is not recommended to prevent or reduce subluxation. (Appel et al 2014 *[79]*)

Good practice statement

Consensus-based recommendation
For stroke survivors at risk of shoulder subluxation, firm support devices (e.g. devices such as a laptray) may be used. A sling maybe used when standing or walking.

Good practice statement

Consensus-based recommendation
To prevent complications related to shoulder subluxation, education and training about correct manual handling and positioning should be provided to the stroke survivor, their family/carer and health professionals, and particularly nursing and allied health staff.

Pain

Central post-stroke pain

Consensus recommendation New

Consensus-based recommendations

For stroke survivors with central post-stroke pain tricyclic antidepressant or antiepileptic medication may be trialed to reduce pain. Any trial of medications to reduce pain needs to be undertaken with caution with planned follow up to minimise risks. Any non-pharmacological interventions trialed are strongly encouraged to be used within a research framework.

Remark:
Update approved by NHMRC July 2023.

Shoulder pain

Weak recommendation

For stroke survivors with shoulder pain, shoulder strapping may be used to reduce pain. (Appel et al 2014 *[79]*)

Weak recommendation

For stroke survivors with shoulder pain, electrical stimulation may be used to manage pain. (Qiu et al 2019 *[102]*)

Weak recommendation

For stroke survivors with shoulder pain, shoulder injections (either sub acromial steroid injections for patients with rotator cuff syndrome, or methylprednisolone and bupivacaine for suprascapular nerve block) may be used to reduce pain. (Adey-Wakeling et al. 2013 *[93]*; Rah et al. 2012 *[95]*)

Weak recommendation

For stroke survivors with shoulder pain and upper limb spasticity, Botulinum Toxin A may be used to reduce pain. (Singh et al 2010 *[97]*)

Weak recommendation

For stroke survivors with shoulder pain, acupuncture in addition to comprehensive rehabilitation may be used to reduce pain. (Liu et al 2019 *[98]*)

Good practice statement

Consensus-based recommendations
For stroke survivors with severe weakness who are at risk of developing shoulder pain, management may include:

- shoulder strapping;
- education of staff, carers and stroke survivors about preventing trauma;
- active motor training to improve function.

Info Box

Practice point
For stroke survivors who develop shoulder pain, management should be based on evidence-based interventions for acute musculoskeletal pain.

Swelling of the extremities

Good practice statement

Consensus-based recommendations
For stroke survivors with severe weakness who are at risk of developing swelling of the extremities, management may include the following

- passive mobilisation;
- elevation of the limb when resting.

Good practice statement

Consensus-based recommendations
For stroke survivors who developed swelling of the hands or feet, management may include the following:

- passive mobilisation;
- elevation of the limb when resting.

Fatigue

Consensus recommendation

Consensus-based recommendations

- Therapy for stroke survivors with fatigue should be organised for periods of the day when they are most alert.
- Stroke survivors and their families/carers should be provided with information, education and strategies to assist in managing fatigue.
- Potential modifying factors for fatigue should be considered, including avoiding sedating drugs and alcohol, and screening for sleep-related breathing disorders and depression.
- While there is insufficient evidence to guide practice, possible interventions could include cognitive behavioural therapy (focusing on fatigue and sleep with advice on regular exercise), exercise and improving sleep hygiene.

Incontinence

Urinary incontinence

Weak recommendation

- All stroke survivors with suspected urinary continence difficulties should be assessed by trained personnel using a structured functional assessment. (Martin et al 2006 *[129]*)
- For stroke survivors, a portable bladder ultrasound scan should be used to assist in diagnosis and management of urinary incontinence. (Martin et al 2006 *[129]*)

Weak recommendation Updated

- Stroke patients in hospital with confirmed continence difficulties, should have a structured continence management plan formulated, documented, implemented and monitored. (Wikander et al 1998 *[202]*)
- If incontinence persists the stroke survivor should be re-assessed and referred for specialist review once in the community. (Thomas et al 2019 *[125]*)

Remark:
Update approved by NHMRC December 2022.

Weak recommendation

For stroke survivors with urge incontinence:

- anticholinergic drugs can be tried (Nabi et al 2006 *[128]*; Abrams et al 2017 *[222]*);
- a prompted or scheduled voiding regime program/ bladder retraining can be trialled (Thomas et al 2015 *[124]*; Thomas et al 2019 *[125]*; Abrams et al 2017 *[222]*);
- if continence is unachievable, containment aids can assist with social continence.

Good practice statement

Consensus-based recommendations
For stroke patients with urinary retention:

- The routine use of indwelling catheters is not recommended. However if urinary retention is severe, intermittent catheterisation should be used to assist bladder emptying during hospitalisation. If retention continues, intermittent catheterisation is preferable to indwelling catheterisation.
- If using intermittent catheterisation, a closed sterile catheterisation technique should be used in hospital.
- Where management of chronic retention requires catheterisation, consideration should be given to the choice of appropriate route, urethral or suprapubic.
- If a stroke survivor is discharged with either intermittent or indwelling catheterisation, they and their family/carer will require education about management, where to access supplies and who to contact in case of problems.

Good practice statement

Consensus-based recommendation
For stroke survivors with functional incontinence, a whole-team approach is recommended.

Good practice statement

Consensus-based recommendation
For stroke survivors, the use of indwelling catheters should be avoided as an initial management strategy except in acute urinary retention.

Faecal incontinence

Weak recommendation

- All stroke survivors with suspected faecal continence difficulties should be assessed by trained personnel using a structured functional assessment. (Harari et al 2004 *[135]*)
- For stroke survivors with constipation or faecal incontinence, a full assessment (including a rectal examination) should be carried out and appropriate management of constipation, faecal overflow or bowel incontinence established and targeted education provided. (Harari et al 2004 *[135]*)

Weak recommendation

For stroke survivors with bowel dysfunction, bowel habit retraining using type and timing of diet and exploiting the gastro-colic reflex should be used. (Venn et al 1992 *[136]*; Munchiando et al 1993 *[137]*)

Good practice statement

Consensus-based recommendations
For stroke survivors with bowel dysfunction:

- Education and careful discharge planning should be provided.
- Use of short-term laxatives may be trialed.
- Increase frequency of mobilisation (walking and out of bed activity) to reduce constipation.
- Use of the bathroom rather than use of bed pans should be encouraged.
- Use of containment aids to assist with social continence where continence is unachievable.

Mood disturbance

Mood assessment

Practice points

- Stroke survivors with suspected altered mood (e.g. depression, anxiety, emotionalism) should be assessed by trained personnel using a standardised and validated scale for use in people with stroke.
- Diagnosis should only be made following clinical interview.

Treatment for Emotionalism

Weak recommendation

For stroke survivors with emotionalism, antidepressant medication such as selective serotonin reuptake inhibitors (SSRIs) or tricyclic antidepressants may be used. (Allida et al 2022 *[143]*)

Prevention of depression

Weak recommendation Updated

For stroke survivors, antidepressant medication may be used to prevent depression. (Allida et al 2020 *[145]*)

Remark:
Update approved by NHMRC August 2022.

Weak recommendation

For stroke survivors, psychological therapies (e.g. problem solving, motivational interviewing) may be used to prevent depression. (Allida et al 2020 *[145]*)

Treatment for depression

Weak recommendation Updated

For stroke survivors with depression, antidepressants, which includes SSRIs should be considered. There is no clear evidence that particular antidepressants produce greater effects than others and will vary according to the benefit and risk profile of the individual. (Allida et al 2020 *[155]*)

Remark:
Update approved by NHMRC August 2022.

Weak recommendation New

For stroke survivors with depression or depressive symptoms, psychological therapy may be provided. (Allida et al 2020 *[155]*)

Remark:
Update approved by NHMRC August 2022.

Weak recommendation Updated

For stroke survivors with depression or depressive symptoms, structured exercise programs, particularly resistance training or programs of high intensity, may be used. (Eng et al 2014 *[151]*; Saunders et al 2020 *[154]*)

Remark:
Update approved by NHMRC August 2022.

Weak recommendation Updated

For stroke survivors with depression, non-invasive brain stimulation (repetitive transcranial magnetic stimulation [rTMS]) may be used. (Allida et al 2020 *[155]*)

Remark:
Update approved by NHMRC August 2022.

Weak recommendation Updated evidence, no change in recommendation

For stroke survivors with depression or depressive symptoms, acupuncture may be used. (Zhang et al 2010 *[153]*)

Treatment for anxiety

Consensus recommendation New

Consensus-based recommendations

For people with anxiety after stroke, psychological therapy and/or relaxation strategies, such as yoga may be trialed to reduce levels of anxiety. The addition of pharmacotherapy should be very carefully considered taking into account higher risk of harms.

Remark:
Approved by NHMRC August 2022.

Personality and behaviour

Consensus recommendation New

Consensus-based recommendations

a. Behavioural changes after stroke can impact on a person's ability to engage in meaningful activities and also their quality of life. Therefore, the impact of any behavioural changes on relationships, employment and leisure should be assessed and addressed across the lifespan.
b. Stroke survivors and their families/carers should be given access to individually tailored interventions for personality and behavioural changes. This may include positive behaviour support programs, anger-management therapy and rehabilitation training and support in management of complex and challenging behaviour.

Remark:
Approved by NHMRC August 2022.

Deep venous thrombosis or pulmonary embolism

Weak recommendation

For acute ischaemic stroke patients who are immobile, low molecular weight heparin in prophylactic doses may be used in the absence of contraindications. (Sandercock et al 2015 *[166]*; Sherman et al 2007 *[173]*)

Weak recommendation

For acute stroke patients who are immobile, intermittent pneumatic compression may be used, either as an alternative to low molecular weight heparin or in those with a contraindication to pharmacological DVT prophylaxis (including patients with intracerebral haemorrhage or within 24 hours of thrombolysis). (Dennis et al 2013 *[171]*)

Strong recommendation against

Antithrombotic stockings are not recommended for the prevention of DVT or PE post stroke. (Naccarato et al 2010 *[172]*)

Info Box

Practice points

- For stroke patients, pharmacological prophylaxis should not be used in the first 24 hours after thrombolysis until brain imaging has excluded significant haemorrhagic transformation.
- For acute stroke patients, early mobilisation and adequate hydration should be encouraged to help prevent DVT and PE.
- For stroke patients receiving intermittent pneumatic compression, skin integrity should be assessed daily.
- For patients with intracerebral haemorrhage, pharmacological prophylaxis may be considered after 48-72 hours and once haematoma growth has stabilised, although evidence is limited.

Falls

Consensus recommendation

Consensus-based recommendations

- For stroke patients, a falls risk assessment, including fear of falling, should be undertaken on admission to hospital. A management plan should be initiated for all patients identified as at risk of falls.
- For stroke survivors at high risk of falls, a comprehensive home assessment for the purposes of reducing falling hazards should be carried out by a qualified health professional. Appropriate home modifications (as determined by a health professional) for example installation of grab rails and ramps may further reduce falls risk.

Weak recommendation

For stroke survivors who are at risk of falling, multifactorial interventions in the community, including an individually prescribed exercise program and advice on safety, should be provided. (Denissen et al 2019 *[179]*; Gillespie et al 2012 *[181]*)

Pressure injury

Info Box New

Practice point

Staff and carers of patients with stroke at risk of pressure injuries (in hospital, in residential care and home settings) should be trained to assess skin, provide appropriate pressure area care, and treat pressure injuries consistent with existing guidelines such as the International Guidelines for the Prevention and Treatment of Pressure Ulcers/Injuries. (EPUAP, NPIAP and PPPIA 2019 *[201]*)

Remark:
Approved by NHMRC August 2022.

Glossary and abbreviations

Introduction

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

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

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

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

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

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

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

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

The Clinical Guidelines do not cover:

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

Target audience

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

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

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

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

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

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

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

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

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

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

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

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

Publication Approval

Australian Government

National Health and Medical Research Council

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

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

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

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

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

Disclaimer

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

Funding

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

Citation

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

Methodology

Development of questions

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

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

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

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

Data extraction, updating evidence summary and GRADE profile
For rapid updates, the project team incorporates the new evidence into the existing body of evidence by:

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

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

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

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

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

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

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

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

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

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

These strong or weak recommendations can either be for or against an intervention. If the recommendation is against an intervention

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

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

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

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

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

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

Wherever possible (i.e. when the relevant study reported enough information to allow the calculation to be done), these estimates were calculated using the following procedure:
1. Obtain the relative effect estimate (odds ratio or relative risk) and confidence interval from the best available study (systematic review or primary study) providing evidence about the effects of the intervention.
2. Use the observed number of events in the control group of the same study to calculate a baseline risk per 1000 people (or “assumed control risk”).
3. Calculate an estimate of the corresponding risk per 1000 in people receiving the intervention using the relative effect estimate. This can be done using methods based on the formulas for calculating absolute risk reductions provided in the *Cochrane Handbook for Systematic Reviews of Interventions* (http://handbook.cochrane.org/). Applying the same calculations to the upper and lower bounds of the confidence interval for the relative effect estimate gives a confidence interval for the risk in the intervention group, which is then used to calculate the confidence interval for the difference per 1000 people, reported in the evidence tables.

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

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

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

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

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

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

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

Clinical questions

6.1 Do early means of feeding improve outcomes in acute stroke?

6.2 Do early means of hydration improve outcomes in acute stroke?

6.3 Do interventions to maintain good oral hygiene improve outcomes in people with acute stroke?

6.4 What interventions to reduce spasticity improve the outcomes for patients with spasticity?

6.5 What interventions to reduce contracture improve outcomes for people with stroke?

6.6 What interventions to prevent or treat shoulder subluxation improve outcomes for people with stroke?

6.7 What interventions to prevent or treat shoulder pain improve outcomes for people with stroke?

6.8 What interventions are effective at managing and/or reducing oedema?

6.9 What interventions improve the management of fatigue in stroke survivors?

6.10 What interventions improve outcomes in stroke survivors with bladder problems?

6.11 What interventions improve outcomes in stroke survivors with bowel problems?

6.12 Mood assessment

6.13 What interventions should be undertaken to reduce emotional distress/emotionalism/emotional lability?

6.14 What interventions prevent depression and/or anxiety?

6.15 What interventions manage depression and/or anxiety?

6.16 What interventions manage personality and behaviour changes?

6.17 What interventions prevent DVT/PE in stroke survivors?

6.18 What interventions are effective in preventing or reducing falls for stroke patients?

6.19 What interventions improve the outcomes for stroke survivors with central post-stroke pain?

Managing complications - overview

Management of secondary complications involves initial efforts at prevention. Where this is not successful, management involves strategies to reduce impairments. This chapter presents evidence for both prevention and reduction strategies. Importantly, many of the topics included in this Chapter should commence immediately in the acute phase (e.g. nutrition and hydration, incontinence management) as well as being considered during post-acute and long-term care.

Nutrition and hydration

After a stroke, a number of stroke-specific and generic factors can result in decline in nutrition and hydration status. The most notable cause of poor oral intake (aside from altered consciousness) is oropharyngeal dysphagia. Additional factors could include fatigue, hemiplegia, depression, visual spatial neglect, reduced mobility and ability to self-feed, taste changes, reduced appetite and poor oral health (Gomes et al. 2014 *[27]*).

Early hydration

Dehydration on admission (measured as elevated blood urea nitrogen to creatinine ratio) was shown to be associated with poor outcomes in acute ischaemic stroke patients, including higher infection rate, worse function (measured using Barthel index or modified Rankin Scale), death, institutionalisation and higher admission cost (Schrock et al. 2012 *[12]*; Liu et al. 2014 *[11]*). Observational studies show that hospitalised stroke patients rarely meet the standard of fluid intake, with dysphagic patients considered at particular risk of inadequate intake (McGrail and Kelchner 2012 *[13]*; Whelan 2001 *[14]*; Murray et al. 2014 *[15]*). Therefore it is critical to monitor, assess and manage patients' hydration status. The most recent National Stroke Audit of Acute Services indicated 14% of stroke patients had impaired hydration on admission (Stroke Foundation 2019 *[9]*).

There is consensus that the hydration status of stroke patients should be routinely assessed, monitored and managed throughout hospital admission. One hundred and five out of 120 hospitals reported having locally agreed management protocols for hydration (Stroke Foundation 2019 *[9]*). However, evidence is limited in guiding the optimal volume, duration, or methods for fluid supplementation.

Strong recommendation

- All stroke patients should have their hydration status assessed, monitored, and managed throughout their hospital admission.
- Where fluid support is required, crystalloid solution should be used in preference to colloid solutions as the first option to treat or prevent dehydration. (Visvanathan et al. 2015 *[10]*)

Practical Info

There was no evidence available to guide the best volume, duration, or route of administration of parenteral fluids in adults with acute stroke.

Where additional hydration is required for patients unable to swallow, fluid can be administered via intravenous, subcutaneous or enteral routes (using a nasogastric [NG] tube or percutaneous endoscopic gastrostomy [PEG]), with NG being the preferred initial method (see section Early feeding). There are several studies that suggest oro-oesophageal feeding tube may be equal if not superior to nasogastric tubes (Juan et al 2020 *[28]*) but bigger and high quality studies are needed.

Stroke patients are at risk of malnutrition and also dehydration. Although used therapeutically to address aspiration and choking risk, the use of texture modified diets and thickened liquids is known to be associated with increased risk of both malnutrition and dehydration (Vivanti et al 2009 *[16]*; Foley et al 2009 *[17]*).

Emerging evidence suggests that Free Water Protocols are safe and make positive contributions to hydration, patient satisfaction and quality of life for carefully selected inpatients in rehabilitation settings (refer to Dysphagia section of Chapter 3 - Acute medical and surgical management).

Evidence To Decision

Benefits and harms

Small net benefit, or little difference between alternatives

People with acute stroke given crystalloids (including 0.9% saline) had about the same risk of death or dependence as people given other fluid types, and a lower risk of pulmonary oedema (Visvanathan et al. 2010 *[10]*).

Certainty of the Evidence

Low

The overall quality of evidence is low based on the Cochrane review (Visvanathan et al. 2015 *[10]*), due to high statistical heterogeneity and high risk of bias.

Values and preferences

No substantial variability expected

It is expected all patients would want their hydration status to be assessed, monitored and managed. There are no identified or perceived patient preferences or values with respect to different parenteral fluids used.

Resources and other considerations

No important issues with the recommended alternative

Resources considerations

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

Implementation considerations

There is a clinical indicator collected in the National Stroke Audit on the total number of patients with an identified hydration impairment on admission to acute care and/or rehabilitation. There is also an organisational indicator collected on whether hospitals have locally agreed management protocols in place for hydration.

Rationale

Dehydration on admission (measured as elevated blood urea nitrogen to creatinine ratio) was shown to be associated with poor outcomes in acute ischaemic stroke patients, including higher infection rate, worse function, (measured using Barthel index or modified Rankin Scale), death, institutionalisation and higher admission cost (Schrock et al 2012 *[12]*; Liu et al 2014 *[11]*). Observational studies show that hospitalised stroke patients rarely meet the standard of fluid intake, with dysphagic patients considered at particular risk of inadequate intake (McGrail and Kelchner 2012 *[13]*; Whelan 2001 *[14]*; Murray et al 2014 *[15]*). Therefore it is critical to monitor, assess and manage patients' hydration status.

We believe that intravenous or subcutaneous fluid replacement with crystalloid solutions is appropriate for most patients as there was no evidence to suggest that the use of colloids improved patient outcome. The possible increased risk of pulmonary oedema with the use of colloid solutions, indicates a higher risk of harm than benefit with these fluids over crystalloid solutions.

Clinical Question/ PICO

Population: Adults with acute stroke
Intervention: Colloid parenteral fluids
Comparator: Crystalloid parenteral fluids

Summary

Based on a Cochrane Review of 12 trials (Visvanathan et al 2015 *[10]*) there is no evidence that colloids were associated with lower odds of death or dependence in the medium term after stroke compared with crystalloids, and colloids were associated with greater odds of pulmonary oedema. There were no relevant completed trials that addressed the effect of volume, duration, or mode of fluid delivery on death or dependence in people with stroke.

Outcome Timeframe	**Study results and measurements**	**Comparator** Crystalloid parenteral fluids	**Intervention** Colloid parenteral fluids	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Death 3-12 month follow-up 9 Critical	Odds ratio 1.02 (CI 95% 0.82 — 1.27) Based on data from 2,351 participants in 12 studies. [1] (Randomized controlled) Follow up: 3-12 months.	202 per 1000 Difference:	205 per 1000 **3 more per 1000** (CI 95% 30 fewer — 41 more)	**Moderate** Due to serious imprecision [2]	Colloid parenteral fluids probably have little or no difference on death compared to crystalloid fluids
Death or dependence 3-12 month follow-up 9 Critical	Odds ratio 0.97 (CI 95% 0.79 — 1.21) Based on data from 1,420 participants in 5 studies. [3] (Randomized controlled) Follow up: 3-12 month follow-up.	589 per 1000 Difference:	582 per 1000 **7 fewer per 1000** (CI 95% 58 fewer — 45 more)	**Low** Due to serious imprecision, Due to serious inconsistency [4]	Colloid parenteral fluids may have little or no difference on death or dependence compared to crystalloid fluids
Pneumonia 8 Critical	Odds ratio 0.58 (CI 95% 0.17 — 2.01) Based on data from 416 participants in 2 studies. [5] (Randomized controlled)	33 per 1000 Difference:	19 per 1000 **14 fewer per 1000** (CI 95% 27 fewer — 31 more)	**Moderate** Due to serious imprecision [6]	Colloid parenteral fluids probably have little or no difference on pneumonia compared to crystalloid fluids
Cerebral Oedema 3 months (median) 8 Critical	Odds ratio 0.2 (CI 95% 0.02 — 1.74) Based on data from 200 participants in 1 studies. [7] (Randomized controlled) Follow up: 3 months (median).	49 per 1000 Difference:	10 per 1000 **39 fewer per 1000** (CI 95% 48 fewer — 33 more)	**Low** Due to very serious imprecision [8]	Colloid parenteral fluids may have little or no difference on cerebral oedema
Pulmonary Oedema 90 days (median) 8 Critical	Odds ratio 2.34 (CI 95% 1.28 — 4.29) Based on data from 730 participants in 3 studies. [9] (Randomized controlled) Follow up: 90 days.	45 per 1000 Difference:	99 per 1000 **54 more per 1000** (CI 95% 12 more — 123 more)	**Low** Due to very serious imprecision [10]	Colloid parenteral fluids may increase risk of pulmonary oedema compared to crystalloid fluids

1. Systematic review [10] with included studies: Yu 1992, Ginsberg 2013, Matthews 1976, Fawer 1978, Larsson 1976, Borenstein 1981, Friedli 1975, Aichner 1998, Bayer 1987, Ginsberg 2011, Gilroy 1969, Rudolf 2002. **Baseline/comparator:** Control arm of reference used for intervention.
2. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Wide confidence intervals. **Publication bias: no serious.**
3. Systematic review [10] with included studies: Matthews 1976, Bayer 1987, Aichner 1998, Ginsberg 2013, Rudolf 2002. **Baseline/comparator:** Control arm of reference used for intervention.
4. **Inconsistency: serious.** The magnitude of statistical heterogeneity was high, with I^2:58 %.. **Indirectness: no serious. Imprecision: serious.** Wide confidence intervals. **Publication bias: no serious.**
5. Systematic review [10] with included studies: Yu 1992, Aichner 1998. **Baseline/comparator:** Control arm of reference used for intervention.
6. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Only data from two studies. **Publication bias:**

no serious.
7. Systematic review [10] with included studies: Aichner 1998. **Baseline/comparator:** Control arm of reference used for intervention.
8. **Inconsistency: no serious. Indirectness: no serious. Imprecision: very serious.** Only data from one study, which did not reach intended number of participants . **Publication bias: no serious.**
9. Systematic review [10] with included studies: Rudolf 2002, Aichner 1998, Ginsberg 2011. **Baseline/comparator:** Control arm of reference used for intervention.
10. **Inconsistency: no serious. Indirectness: no serious. Imprecision: very serious.** Only data from three studies. **Publication bias: no serious.**

Attached Images

Clinical Question/ PICO

Population: Adults with acute stroke
Intervention: Parenteral fluid of 0.9% saline
Comparator: Other parenteral fluid

Summary

A Cochrane Review of trials comparing parenteral fluid regimes (Visvanathan et al 2015 *[10]*) included 5 studies (N = 142) comparing 0.9% saline to another fluid. The odds of death and death or dependence were similar in participants allocated to 0.9% saline or other fluid regimens, with substantial heterogeneity and high risk of bias.

Outcome Timeframe	**Study results and measurements**	**Comparator** Other parenteral fluid	**Intervention** Parenteral fluid of 0.9% saline	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Death 3-12 months 9 Critical	Odds ratio 0.87 (CI 95% 0.67 — 1.12) Based on data from 1,760 participants in 5 studies. [1] (Randomized controlled) Follow up: 3-12 months.	210 per 1000 Difference:	188 per 1000 **22 fewer per 1000** (CI 95% 59 fewer — 19 more)	**Low** Due to serious inconsistency, Due to serious risk of bias [2]	Parenteral fluid of 0.9% saline may have little or no difference on death
Death or dependence 3-12 months follow-up 9 Critical	Odds ratio 1.04 (CI 95% 0.82 — 1.32) Based on data from 1,120 participants in 3 studies. [3] (Randomized controlled) Follow up: 3-12 months.	553 per 1000 Difference:	563 per 1000 **10 more per 1000** (CI 95% 49 fewer — 67 more)	**Low** Due to serious risk of bias, Due to serious inconsistency [4]	Parenteral fluid of 0.9% saline may have little or no difference on death or dependence
Pneumonia 8 Critical	Odds ratio 2 (CI 95% 0.36 — 11.16) Based on data from 216 participants in 1 studies. [5] (Randomized controlled)	19 per 1000 Difference:	37 per 1000 **18 more per 1000** (CI 95% 12 fewer — 159 more)	**Very low** Due to very serious imprecision, Due to very serious risk of bias [6]	We are uncertain whether parenteral fluid of 0.9% saline increases or decreases pneumonia

Outcome Timeframe	**Study results and measurements**	**Comparator** Other parenteral fluid	**Intervention** Parenteral fluid of 0.9% saline	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Pulmonary Oedema 48 hours (mean) 8 Critical	Odds ratio 0.32 (CI 95% 0.14 — 0.69) Based on data from 424 participants in 1 studies. [7] (Randomized controlled) Follow up: 48 hours (mean).	**121** per 1000 Difference:	**42** per 1000 **79 fewer per 1000** (CI 95% 102 fewer — 34 fewer)	**Moderate** Due to serious risk of bias [8]	Parenteral fluid of 0.9% saline probably decreases pulmonary oedema

1. Systematic review [10] with included studies: Bayer 1987, Yu 1992, Rudolf 2002, Ginsberg 2013, Ginsberg 2011. **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of Bias: serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Incomplete data and/or large loss to follow up, Selective outcome reporting. **Inconsistency: serious.** The magnitude of statistical heterogeneity was high, with I^2:53 %.. **Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
3. Systematic review [10] with included studies: Rudolf 2002, Bayer 1987, Ginsberg 2013. **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of Bias: serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Incomplete data and/or large loss to follow up, Selective outcome reporting. **Inconsistency: serious.** The magnitude of statistical heterogeneity was high, with I^2:71 %.. **Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
5. Systematic review [10] with included studies: Yu 1992. **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of Bias: very serious.** Incomplete data and/or large loss to follow up, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Selective outcome reporting. **Inconsistency: no serious. Indirectness: no serious. Imprecision: very serious.** Sample size lower than calculated. **Publication bias: no serious.**
7. Systematic review [10] with included studies: Ginsberg 2011. **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of Bias: serious.** Trials stopping earlier than scheduled, resulting in potential for overestimating benefits. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**

Attached Images

Early feeding

Being malnourished is associated with poor outcomes in stroke patients (Martineau et al 2005 *[21]*). Moreover, malnutrition could persist after a stroke if not effectively managed. Key aspects of nutritional management include malnutrition screening, assessment by an Accredited Practising Dietitian, and nutrition supplementation.

There is some variation of prevalence of malnutrition in the literature, ranging from 6% to 62% on admission and up to 25% in the first weeks after a stroke (Gomes et al 2014 *[27]*). National Stroke Audits in Australia reported a 12% malnutrition rate on admission to a rehabilitation service, and 9% during admission (Stroke Foundation 2020 *[7][9]*). The differences may be due to criteria used to define malnutrition and protocols to identify malnutrition. The Audit also found that only 69% of patients received malnutrition screening, which means the reported prevalence is likely to have underestimated the true prevalence (Stroke Foundation 2019 *[9]*). On the other hand, once the risk of malnutrition was identified in the screening, over 70% of them were then assessed, monitored and received appropriate nutritional interventions by Accredited Practising Dietitians (Stroke Foundation 2019 *[9]*).

This section aims to identify optimal methods and tools to manage malnutrition in stroke patients. For guidelines in general

population, please refer to the *Evidence Based Practice Guidelines for the Nutritional Management of Malnutrition in Adult Patients Across the Continuum of Care* from the Dietitians Association of Australia.

Strong recommendation

All stroke patients should be screened for malnutrition at admission and on an ongoing basis (at least weekly) while in hospital. (Dennis et al 2005 *[26]*)

Practical Info

Routine screening for malnutrition is resource intensive. When considering malnutrition screening; the tool should be validated, simple to use, and able to be performed by support staff (such as nursing staff or allied health assistants). There is no universally accepted gold standard screening tool for use in stroke populations. A number of validated screening tools have been used in the literature such as the Malnutrition Screening Tool (MST), the Malnutrition Universal Screening Tool (MUST), the Mini-Nutritional Assessment (MNS) and MNA-Short Form. There is no one measurement tool recommended over another.

Evidence To Decision

Benefits and harms

Substantial net benefits of the recommended alternative

There are no perceived harms of malnutrition screening, however undetected malnutrition is detrimental.

In a large randomised control trial across 15 countries, a subgroup analysis of acute stroke patients who were undernourished had a non significant but increased mortality rate, compared with those who were well nourished or overweight (Dennis 2005 *[26]*). In a small Australian retrospective audit of 73 acute stroke patients; those who were assessed as malnourished on admission using the Patient Generated Subjective Global Assessment Tool (pgSGA) tool had longer length of stay, increased complications, increased dysphagia and were more likely to require enteral feeding compared with those who were well nourished (Martineau et al 2005 *[21]*). In a metanalysis of studies where patients were undernourished at baseline, there were significantly higher mortality rates, compared to patients who were well nourished (Milne et al 2006 *[25]*)

Certainty of the Evidence

Moderate

The quality of evidence is moderate due to imprecision - wide confidence interval and the majority of data coming from one large trial.

Values and preferences

No substantial variability expected

Given that there are no perceived harms of malnutrition screening, and undetected malnutrition is detrimental, it is expected that screening for malnutrition would be the patient's preference.

Resources and other considerations

No important issues with the recommended alternative

<u>Resources considerations</u>

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

<u>Implementation considerations</u>

There are clinical indicators collected in the National Stroke Audit on the total number of patients with identified malnutrition on admission to acute care and/or rehabilitation, as well as the number of patients with identified malnutrition during their acute and/or rehabilitation admission. There is also a clinical indicator collected to determine if a patient underwent a screening for malnutrition during their admission, as well as an organisational indicator collected on whether hospitals have locally agreed management protocols in place for nutrition.

Rationale

There are no perceived harms of malnutrition screening, however undetected malnutrition in stroke and non stroke populations

is detrimental. The quality of evidence for the detrimental effect of malnutrition in stroke populations is moderate due to imprecision (wide confidence intervals) and the majority of data coming from one large trial. Given this, and that there are no perceived harms, it is expected that screening for malnutrition would be the patient's preference. However routine screening for malnutrition is resource intensive.

Clinical Question/ PICO

Population: Adults with stroke
Intervention: Nutrition support
Comparator: No nutrition support

Summary

A Cochrane review by Geeganage et al (2012) *[19]* compared nutritional supplementation versus no nutritional supplementation in acute stroke patients. There was no significant difference on the outcome of death, death or dependence, and length of hospital stay in the meta-analysis of more than 4000 patients. It should be noted that one study FOOD Trial contributed more than 90% of the patients included in this meta-analysis (Dennis 2005 *[26]*).

In terms of energy and protein intake, three studies totalling 174 patients showed significant improvement with nutritional supplementation. However, it should be noted there is a very high level of statistical heterogeneity (91%) and all three trials reported are very small.

A recent randomised controlled trial of 146 acute stroke patients with dysphagia in China compared nasogastric nutrition and family managed nutrition (Zheng et al 2015 *[24]*). Benefits were shown in improved nutritional status, reduced nosocomial infection and lower mortality rates, whereas no significant differences were found in activities of daily living (measured by Barthel Index) and neurological outcomes (measured by modified Rankin Score). This study had high risk of bias (insufficient reporting of methodology) and limited applicability to an Australian setting.

Liu et al (2022) *[229]* including 16 studies (n = 7,547) comparing nutrition supplement versus no nutrition supplement in patients with stroke. Nutritional supplement intervention resulted in significant reduction in incidence of infection (RR 0.65, 95% CI 0.51 to 0.84) and improvement on activities of daily living (MD 3.26, 95% CI 0.59 to 5.93) compared to the control group. Nutritional supplement composition between included studies varied too widely to provide recommendations of optimal macro and micro nutrient ratios.

Yan et al (2022) *[230]* (n = 173) concluded that individualised nutrition intervention showed a significant improvement in total effect rate of swallowing function (OR 0.278, 95% CI 0.087 to 0.889) in stroke patients with oropharyngeal dysphagia compared to standardised nutritional therapy.

Overall, nutrition support improves nutritional status in adults with stroke but the benefits are less clear in death or dependence. On the other hand, the quality of evidence precludes a definitive conclusion.

Outcome Timeframe	**Study results and measurements**	**Comparator** No nutrition support	**Intervention** Nutrition support	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Death End of trial 9 Critical	Odds ratio 0.58 (CI 95% 0.28 — 1.21) Based on data from 4,343 participants in 7 studies. (Randomized controlled) Follow up: Varied - 3 to 12 months.	127 per 1000 Difference:	78 per 1000 **49 fewer per 1000** (CI 95% 88 fewer — 23 more)	**Moderate** Due to serious imprecision [1]	Nutrition support probably decreases death slightly although this was statistically insignificant
Death or dependence End of trial 9 Critical	Odds ratio 1.06 (CI 95% 0.94 — 1.2) Based on data from 4,023 participants in 1 studies. (Randomized controlled)	457 per 1000 Difference:	471 per 1000 **14 more per 1000** (CI 95% 15 fewer — 45 more)	**Moderate** Due to serious imprecision [2]	Nutrition support may have little or no difference on death or dependence

Outcome Timeframe	**Study results and measurements**	**Comparator** No nutrition support	**Intervention** Nutrition support	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Length of stay At time of hospital discharge 7 Critical	Follow up: 6 months. Measured by: Days Lower better Based on data from 4,114 participants in 2 studies. (Randomized controlled) Follow up: to hospital discharge.	Difference:	**MD 1.4 higher** (CI 95% 0.81 lower — 3.6 higher)	**Moderate** Due to serious imprecision [3]	Nutrition support probably has little or no difference on length of stay
Nutritional status During the study period 7 Critical	Measured by: Energy intake High better Based on data from 174 participants in 3 studies. (Randomized controlled) Follow up: During the study period.	Difference:	**MD 430.18 higher** (CI 95% 141.61 higher — 718.75 higher)	**Moderate** Due to serious inconsistency [4]	Nutrition support may have little or no difference on nutritional status

1. **Inconsistency: no serious.** Not serious, I2 metric is 38%, most studies favouring Nutritional Supplementation or null effect but no overall significant effect. . **Indirectness: no serious.** Not serious – yes PICO is relevant to population in question.. **Imprecision: serious.** Wide confidence intervals. **Publication bias: no serious.** Not serious – no evidence of publication bias from meta-analysis, good search strategy and awareness of future trials.
2. **Inconsistency: no serious. Indirectness: no serious.** Not serious – yes, PICO appropriate. **Imprecision: serious.** Wide confidence intervals; there is only one study included (FOOD Trial) however it is a very large multicentre trial. **Publication bias: no serious.** Not serious – no evidence of publication bias, good search strategy, good awareness of trials in progress..
3. **Inconsistency: no serious.** Not serious – no statistical heterogeneity, both favour control although not significant. Note there are only 2 studies.. **Indirectness: no serious.** Not serious, PICO is appropriate.. **Imprecision: serious.** Wide confidence intervals. **Publication bias: no serious.** Not serious. Good search strategy, awareness of ongoing trials..
4. **Inconsistency: serious.** Whilst the results are consistent across studies (significantly favouring control), I2 is 91% which is very high, and only 3 trials are included, and all are small.. **Indirectness: no serious.** Not serious – yes, PICO is appropriate. **Imprecision: no serious.** Not serious – as the results favour control (significantly), however 3 studies are included and all are small. **Publication bias: no serious.** Not serious – good search strategy, awareness of future trials..

Attached Images

Strong recommendation

For stroke patients whose nutrition status is poor or deteriorating, nutrition supplementation should be offered. (Geeganage et al 2012 *[19]*; Dennis et al 2005 *[26]*)

Practical Info

With a wide variety of supplements available and methods of nutrition support (for example food fortification, small frequent meals and oral sip supplements), individual preference can be catered for to maximise uptake and allow for variability.

Evidence To Decision

Benefits and harms

Substantial net benefits of the recommended alternative

Benefits outweigh harms in terms of reducing infectious complications and mortality when patient is undernourished (a non-significant trend towards less death and dependency) (Geeganage et al 2012 *[19]*).

Certainty of the Evidence

Moderate

Quality of evidence is moderate due to imprecision - wide confidence interval and the majority of data coming from one large trial.

Values and preferences

No substantial variability expected

With a wide variety of supplements available and methods of nutriton support - individual preference can be catered for to maximise uptake and allow for variability.

Resources and other considerations

No important issues with the recommended alternative

Further information may be found in the Practice-based Evidence in Nutrition (PEN) database (http://pennutrition.com/index.aspx).

Implementation considerations

There is a clinical indicator collected in the National Stroke Audit on the type of management that patients with a nutrition impairment receive, this includes the provision of nutritional supplementation.

Rationale

The benefit of nutrition supplementation outweighs harm in terms of reducing infectious complications and mortality when patients are undernourished (Geeganage et al 2012 *[19]*; Dennis et al 2005 *[26]*). The quality of evidence is moderate due to imprecision - a wide confidence interval and the majority of data coming from one large trial.

Clinical Question/ PICO

Population: Adults with stroke
Intervention: Nutrition support
Comparator: No nutrition support

Summary

A Cochrane review by Geeganage et al (2012) *[19]* compared nutritional supplementation versus no nutritional supplementation in acute stroke patients. There was no significant difference on the outcome of death, death or dependence, and length of hospital stay in the meta-analysis of more than 4000 patients. It should be noted that one study FOOD Trial contributed more than 90% of the patients included in this meta-analysis (Dennis 2005 *[26]*).

In terms of energy and protein intake, three studies totalling 174 patients showed significant improvement with nutritional supplementation. However, it should be noted there is a very high level of statistical heterogeneity (91%) and all three trials reported are very small.

A recent randomised controlled trial of 146 acute stroke patients with dysphagia in China compared nasogastric nutrition and family managed nutrition (Zheng et al 2015 *[24]*). Benefits were shown in improved nutritional status, reduced nosocomial infection and lower mortality rates, whereas no significant differences were found in activities of daily living (measured by Barthel Index) and neurological outcomes (measured by modified Rankin Score). This study had high risk of bias (insufficient reporting of methodology) and limited applicability to an Australian setting.

Liu et al (2022) *[229]* including 16 studies (n = 7,547) comparing nutrition supplement versus no nutrition supplement in patients with stroke. Nutritional supplement intervention resulted in significant reduction in incidence of infection (RR

0.65, 95% CI 0.51 to 0.84) and improvement on activities of daily living (MD 3.26, 95% CI 0.59 to 5.93) compared to the control group. Nutritional supplement composition between included studies varied too widely to provide recommendations of optimal macro and micro nutrient ratios.

Yan et al (2022) *[230]* (n = 173) concluded that individualised nutrition intervention showed a significant improvement in total effect rate of swallowing function (OR 0.278, 95% CI 0.087 to 0.889) in stroke patients with oropharyngeal dysphagia compared to standardised nutritional therapy.

Overall, nutrition support improves nutritional status in adults with stroke but the benefits are less clear in death or dependence. On the other hand, the quality of evidence precludes a definitive conclusion.

Outcome Timeframe	**Study results and measurements**	**Comparator** No nutrition support	**Intervention** Nutrition support	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Death End of trial 9 Critical	Odds ratio 0.58 (CI 95% 0.28 — 1.21) Based on data from 4,343 participants in 7 studies. (Randomized controlled) Follow up: Varied - 3 to 12 months.	127 per 1000 Difference:	78 per 1000 **49 fewer per 1000** (CI 95% 88 fewer — 23 more)	**Moderate** Due to serious imprecision [1]	Nutrition support probably decreases death slightly although this was statistically insignificant
Death or dependence End of trial 9 Critical	Odds ratio 1.06 (CI 95% 0.94 — 1.2) Based on data from 4,023 participants in 1 studies. (Randomized controlled) Follow up: 6 months.	457 per 1000 Difference:	471 per 1000 **14 more per 1000** (CI 95% 15 fewer — 45 more)	**Moderate** Due to serious imprecision [2]	Nutrition support may have little or no difference on death or dependence
Length of stay At time of hospital discharge 7 Critical	Measured by: Days Lower better Based on data from 4,114 participants in 2 studies. (Randomized controlled) Follow up: to hospital discharge.	Difference:	**MD 1.4 higher** (CI 95% 0.81 lower — 3.6 higher)	**Moderate** Due to serious imprecision [3]	Nutrition support probably has little or no difference on length of stay
Nutritional status During the study period 7 Critical	Measured by: Energy intake High better Based on data from 174 participants in 3 studies. (Randomized controlled) Follow up: During the study period.	Difference:	**MD 430.18 higher** (CI 95% 141.61 higher — 718.75 higher)	**Moderate** Due to serious inconsistency [4]	Nutrition support may have little or no difference on nutritional status

1. **Inconsistency: no serious.** Not serious, I2 metric is 38%, most studies favouring Nutritional Supplementation or null effect but no overall significant effect. . **Indirectness: no serious.** Not serious – yes PICO is relevant to population in question.. **Imprecision: serious.** Wide confidence intervals. **Publication bias: no serious.** Not serious – no evidence of publication bias from meta-analysis, good search strategy and awareness of future trials.
2. **Inconsistency: no serious. Indirectness: no serious.** Not serious – yes, PICO appropriate. **Imprecision: serious.** Wide confidence intervals; there is only one study included (FOOD Trial) however it is a very large multicentre trial. **Publication bias: no serious.** Not serious – no evidence of publication bias, good search strategy, good awareness of trials in progress..

3. **Inconsistency: no serious.** Not serious – no statistical heterogeneity, both favour control although not significant. Note there are only 2 studies.. **Indirectness: no serious.** Not serious, PICO is appropriate.. **Imprecision: serious.** Wide confidence intervals. **Publication bias: no serious.** Not serious. Good search strategy, awareness of ongoing trials..
4. **Inconsistency: serious.** Whilst the results are consistent across studies (significantly favouring control), I2 is 91% which is very high, and only 3 trials are included, and all are small.. **Indirectness: no serious.** Not serious – yes, PICO is appropriate. **Imprecision: no serious.** Not serious – as the results favour control (significantly), however 3 studies are included and all are small. **Publication bias: no serious.** Not serious – good search strategy, awareness of future trials..

Attached Images

Weak recommendation

- For stroke patients who do not recover a functional swallow, nasogastric tube feeding is the preferred method of feeding in the short term. (Geeganage et al 2012 *[19]*; Gomes et al 2015 *[23]*; Dennis et al 2005 *[26]*)
- For stroke patients, there is no preference with regard to continuous pump (meaning using a pump for greater than or equal to 16 hrs out of 24 hrs for less than or equal to 80 ml/hr) feeding versus intermittent bolus feeding (meaning 250-400 mls/hr for 4-5 times/day) therefore practical issues, cost and patient preferences should guide practice. (Lee et al 2010 *[20]*)

Practical Info

Patients should be considered for a nasal bridle or early placement of a gastrostomy device if unable to tolerate a nasogastric tube. Because there is no significant difference in outcomes when comparing continuous pump feeding versus intermittent bolus feeding; practical issues such as time spent connected to a feeding pump, cost of a feeding pump and tubes, and patient preference (for example feed tolerance and lifestyle) should guide practice.

If mealtime is causing the patient extraordinary anxiety or distress, and the patient is unable to meet their nutritional goals, then a nasogastric tube can be considered for a pre-defined timeframe to aid in a mental health recovery program.

When enteral feeding is administered, supplementation with probiotics may be considered.

Evidence To Decision

Benefits and harms

Substantial net benefits of the recommended alternative

There were significantly fewer treatment failures, significantly greater feed delivery (Geeganage et al 2012 *[19]*) and significantly greater change in mid-arm circumference from baseline (Gomes et al 2015 *[23]*) with the use of percutaneous endoscopic gastronomy feeding, however, all of the studies are small. Continuous pump feeding versus intermittent bolus feeding has little or no impact on death and pneumonia (Lee et al 2010 *[20]*).

Certainty of the Evidence

Low

In relation to continuous pump feeding versus intermittent bolus feeding, the quality of evidence is moderate. Sequence generation, allocation concealment, outcome data completeness, selective reporting were all explicitly reported and well conducted, however, there was inadequate/lack of blinding of outcome assessors, but this was explicitly stated, resulting in potential for detection bias. In relation to NGT vs PEG the quality of evidence is low due to small sample size and heterogeneity.

Values and preferences

Substantial variability is expected or uncertain

Patient preferences and values should be a considered when comparing nasogastric feeding tube and gastrostomy devices.

Initially after a stroke, the use a nasogastric tube feeding is less invasive, uses fewer resources, and is more temporary than a gastrostomy device. Insertion of a gastrostomy is invasive, resource intense and has potential for surgical risk. Therefore, a nasogastric feeding tube suits patients whose swallow recovery is yet to be determined (or who are likely to recover a functional swallow) in the short term and may therefore be the preferred initial method of feeding. When comparing continuous pump feeding versus intermittent bolus feeding practical issues, cost and patient preferences should be considered.

Once there is an established long term need for enteral feeding, the use of a gastrostomy device is preferred because gastrostomy devices have fewer treatment failures, greater feed deliver and preferred asthetics.

Resources and other considerations

Important issues, or potential issues not investigated

Further information may be found in the Practice-based Evidence in Nutrition (PEN) database (http://pennutrition.com/index.aspx).

Resources considerations

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

Implementation considerations

There is a clinical indicator collected in the National Stroke Audit on the type of management that patients with a nutrition impairment receive, this includes the provision of alternative feeding such as NG feeding or PEG.

Rationale

Initially after a stroke, the use a nasogastric tube feeding is less invasive, uses fewer resources, and is more temporary than a gastrostomy device, whereas the insertion of a gastrostomy is invasive, resource intense and has potential for surgical risk. Therefore a nasogastric feeding tube suits patients whose swallow recovery is yet to be determined (or who are likely to recover a functional swallow) in the short term and may therefore be the preferred initial method of feeding. For patients unable to tolerate a nasogastric tube, a nasal bridle or early insertion of a gastrostomy device should be considered. Once there is an established long term need for enteral feeding, the use of a gastrostomy device is preferred because the research has shown significantly fewer treatment failures, significantly greater feed delivery (Geeganage et al 2012 *[19]*) and significantly greater change in mid-arm circumference from baseline (Gomes et al 2015 *[23]*).

In relation to continuous pump feeding versus intermittent bolus feeding, the quality of evidence is moderate and reports little or no difference in death and pneumonia rates (Lee et al 2010 *[20]*). Therefore practical issues, cost and patient preferences should guide practice.

Clinical Question/ PICO

Population: Adults with stroke
Intervention: Percutaneous endoscopic gastrostomy feeding
Comparator: Nasogastric tube feeding

Summary

Evidence on the comparison between percutaneous endoscopic gastronomy feeding (PEG) compared to nasogastric tube feeding (NG) comes mainly from a Cochrane review by Geegagane et al (2012) *[19]* comparing percutaneous endoscopic gastrostomy feeding (PEG) and nasogastric tube feeding (NG). A more recent meta-analysis (Gomes et al 2015 *[23]*) compared PEG and NG but this meta-analysis was not specific to stroke patients and included patients who required tube feeding regardless of whether they had had a stroke or not.

Both meta-analyses showed consistent non-significant differences in critical outcomes of case fatality, death or dependency, length of stay, and chest infection or pneumonia. Indicators of nutritional status such as weight and mid-arm circumferences were also not significantly different. However, the sample sizes in the included trials were generally

small (ranging from 21 to 115).

Juan et al (2020) *[28]* (n=97) tested repeatedly placing and removing oroesophageal tube for bolus feeds (up to 4-6 times/day) compared to NG tube feeding (fed via bolus feeding regime) in patients with dysphagia after stroke. The intervention group had reduced incidence of stroke associated pneumonia, improved comfort, and reduced anxiety and depression. This intervention may not be tolerated for patients (repeated insertion of feeding tube 4-6 times/day) or nursing staff (increased workload) and further large quality studies are needed to confirm the results.

Outcome Timeframe	**Study results and measurements**	**Comparator** Nasogastric tube feeding	**Intervention** Percutaneous endoscopic gastrostomy feeding	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Death or dependence End of trial 9 Critical	Odds ratio 0.8 (CI 95% 0.12 — 5.55) Based on data from 400 participants in 3 studies. (Randomized controlled) Follow up: Varied: discharge to 6 months.	838 per 1000 Difference:	805 per 1000 **33 fewer per 1000** (CI 95% 455 fewer — 128 more)	**Low** Due to serious imprecision, Due to serious inconsistency [1]	percutaneous endoscopic gastrostomy feeding may have little or no difference on death or dependence
Death End of trial 9 Critical	Odds ratio 0.81 (CI 95% 0.42 — 1.56) Based on data from 455 participants in 5 studies. (Randomized controlled) Follow up: Varied: discharge to 6 months.	449 per 1000 Difference:	398 per 1000 **51 fewer per 1000** (CI 95% 194 fewer — 111 more)	**Low** Due to serious inconsistency, Due to serious imprecision [2]	Percutaneous endoscopic gastrostomy feeding may have little or no difference on death
Chest infection or pnuemonia During study 8 Critical	Odds ratio 0.65 (CI 95% 0.23 — 1.86) Based on data from 93 participants in 2 studies. (Randomized controlled) Follow up: 21 days to 6 weeks.	378 per 1000 Difference:	283 per 1000 **95 fewer per 1000** (CI 95% 255 fewer — 153 more)	**Low** Due to serious inconsistency, Due to serious imprecision [3]	Percutaneous endoscopic gastrostomy feeding may have little or no difference on chest infection or pnuemonia
Length of stay At time of discharge 7 Critical	Measured by: Days Lower better Based on data from 384 participants in 2 studies. (Randomized controlled) Follow up: At discharge.	Difference:	**MD 14.32 higher** (CI 95% 12.04 lower — 40.68 higher)	**Low** Due to serious inconsistency, Due to serious imprecision [4]	Percutaneous endoscopic gastrostomy feeding may have little or no difference on length of stay
Nutritional status Last value measured during trial 7 Critical	Measured by: Mid-arm circumference High better Based on data from 58 participants in 3 studies. (Randomized controlled) Follow up: Last measured value during trial.	Difference:	**MD 2.29 higher** (CI 95% 0.3 lower — 4.89 higher)	**Low** Due to serious inconsistency, Due to serious imprecision [5]	Percutaneous endoscopic gastrostomy feeding may improve nutritional status

1. **Inconsistency: serious.** Very serious – 3 trials although one not estimable, heterogeneity is very high (79%), results sit on the side of PEG/NGT but are not significant (P=0.82), . **Indirectness: no serious.** Not serious – yes, PICO is appropriate. **Imprecision: serious.** Note small number of trials (3), one of which is not estimable and high heterogeneity (79%)., Low number of patients. **Publication bias: no serious.** Not serious. Good search strategy and awareness of ongoing trials..
2. **Inconsistency: serious.** Serious – 5 studies included but all are small, totalling 455 patients, however statistical heterogeneity is low (32%). **Indirectness: no serious.** Not serious – yes PICO is appropriate. **Imprecision: serious.** Possibly as the outcome is case fatality and the summary estimate crosses the null. Note small sample size and number of trials with this outcome., Low number of patients. **Publication bias: no serious.** Not serious. Good search strategy and awareness of other trials ongoing..

3. **Inconsistency: serious.** Low level of statistical heterogeneity, two small studies with small number of events, point estimates sitting on side of PEG or null. , The magnitude of statistical heterogeneity was high, with I^2:... %.. **Indirectness: no serious.** Not serious – PICO is appropriate for our needs. **Imprecision: serious.** Serious - Possibly act differently as the outcome is chest infection/pneumonia and both studies cross the null. The two studies are small, and there are a small number of events in both studies. , Low number of patients. **Publication bias: no serious.** Not serious – good search strategy, good awareness of future trials currently recruiting.
4. **Inconsistency: serious.** Serious – only two studies totalling 384 patients, I2 is very high (79%), The magnitude of statistical heterogeneity was high, with I^2:... %.. **Indirectness: no serious. Imprecision: serious.** Low number of patients, possibly act differently although the outcome is LOS. **Publication bias: no serious.** Not serious, good detailed search strategy, good awareness of studies ongoing..
5. **Inconsistency: serious.** Serious – only 3 studies included totally 58 patients, however all three studies have their point estimate favouring NGT (although the overall estimate is non-significant). **Indirectness: no serious.** Not serious – PICO is appropriate. **Imprecision: serious.** Serious – small sample size and only 3 studies, and the outcome is mid arm circumference which clinicians may not value as an important patient oriented outcome. . **Publication bias: no serious.** Not serious – good search strategy, good knowledge of ongoing studies in the area by the authors.

Attached Images

Clinical Question/ PICO

Population: Adults with stroke
Intervention: Continuous pump feeding
Comparator: Intermittent bolus feeding

Summary

Lee et al 2010 *[20]* compared pump feeding undertaken over at least 16 hours of the day to bolus feeding undertaken on at least four to five occasions throughout the day. The study involved 178 patients likely to require nasogastric tube feeding for at least 4 weeks and aged 60 years or older. Most patients were either new or old stroke patients (149/178). Results indicated that compared with bolus feeding, fewer people in the pump feeding group died or developed pneumonia.

Note: Relative effect size, absolute effect size and 95% confidence Intervals were not reported. Therefore, the odds ratio and confidence interval reported here were manually calculated from the raw numbers of events reported.

Outcome Timeframe	**Study results and measurements**	**Comparator** Intermittent bolus feeding	**Intervention** Continuous pump feeding	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Death up until hospital discharge or 4 weeks 9 Critical	Odds ratio 0.55 (CI 95% 0.21 — 1.46) Based on data from 178 participants in 1 studies. (Randomized controlled) Follow up: discharge from hospital or 4 weeks.	140 per 1000 Difference:	82 per 1000 **58 fewer per 1000** (CI 95% 107 fewer — 52 more)	**Moderate** Due to serious risk of bias [1]	continuous pump feeding probably decreases death
Pneumonia 4 weeks 7 Critical	Odds ratio 0.93 (CI 95% 0.4 — 2.14) Based on data from 178 participants in 1 studies. (Randomized controlled)	151 per 1000 Difference:	142 per 1000 **9 fewer per 1000**	**Moderate** Due to serious risk of bias [2]	Continuous pump feeding probably has little or no difference on pneumonia.

Outcome Timeframe	**Study results and measurements**	**Comparator** Intermittent bolus feeding	**Intervention** Continuous pump feeding	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
	Follow up: discharge from hospital or 4 weeks.		(CI 95% 85 fewer — 125 more)		

1. **Risk of Bias: serious.** sequence generation, allocation concealment, outcome data completeness, selective reporting were all explicitly reported and well conducted, however there was inadequate/lack of blinding of outcome assessors, but this was explicitly stated, resulting in potential for detection bias.
2. **Risk of Bias: serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias.

Attached Images

Weak recommendation against

For stroke patients who are adequately nourished, routine oral nutrition supplements are not recommended. (Geeganage et al 2012 *[19]*; Dennis et al 2005 *[26]*)

Practical Info

Oral nutrition supplementation should be individualised and provided in consultation with an Accredited Practising Dietitian.

Evidence To Decision

Benefits and harms

Small net benefit, or little difference between alternatives

There is no clear benefit or harm for oral nutrition supplementation for adequately nourished stroke patients.

Certainty of the Evidence

Moderate

The quality of evidence is low due to imprecision - a wide confidence interval and the majority of data coming from one large trial.

Values and preferences

Substantial variability is expected or uncertain

The provision of oral nutrition support should be individualised and provided after consulation with an Accredited Practising Dietitian

Resources and other considerations

No important issues with the recommended alternative

Further information may be found in the Practice-based Evidence in Nutrition (PEN) database (http://pennutrition.com/index.aspx)

Rationale

The routine provision of oral nutrition supplements is not recommended for people with stroke who are adequately nourished on admission as there is no clear benefit or harm and the quality of evidence is low. Oral nutrition supplementation should be individualised and provided in consultation with an Accredited Practising Dietitian. The cost of providing and monitoring oral

nutrition supplements should be considered.

Clinical Question/ PICO

Population: Adults with stroke
Intervention: Nutrition support
Comparator: No nutrition support

Summary

A Cochrane review by Geeganage et al (2012) *[19]* compared nutritional supplementation versus no nutritional supplementation in acute stroke patients. There was no significant difference on the outcome of death, death or dependence, and length of hospital stay in the meta-analysis of more than 4000 patients. It should be noted that one study FOOD Trial contributed more than 90% of the patients included in this meta-analysis (Dennis 2005 *[26]*).

In terms of energy and protein intake, three studies totalling 174 patients showed significant improvement with nutritional supplementation. However, it should be noted there is a very high level of statistical heterogeneity (91%) and all three trials reported are very small.

A recent randomised controlled trial of 146 acute stroke patients with dysphagia in China compared nasogastric nutrition and family managed nutrition (Zheng et al 2015 *[24]*). Benefits were shown in improved nutritional status, reduced nosocomial infection and lower mortality rates, whereas no significant differences were found in activities of daily living (measured by Barthel Index) and neurological outcomes (measured by modified Rankin Score). This study had high risk of bias (insufficient reporting of methodology) and limited applicability to an Australian setting.

Liu et al (2022) *[229]* including 16 studies (n = 7,547) comparing nutrition supplement versus no nutrition supplement in patients with stroke. Nutritional supplement intervention resulted in significant reduction in incidence of infection (RR 0.65, 95% CI 0.51 to 0.84) and improvement on activities of daily living (MD 3.26, 95% CI 0.59 to 5.93) compared to the control group. Nutritional supplement composition between included studies varied too widely to provide recommendations of optimal macro and micro nutrient ratios.

Yan et al (2022) *[230]* (n = 173) concluded that individualised nutrition intervention showed a significant improvement in total effect rate of swallowing function (OR 0.278, 95% CI 0.087 to 0.889) in stroke patients with oropharyngeal dysphagia compared to standardised nutritional therapy.

Overall, nutrition support improves nutritional status in adults with stroke but the benefits are less clear in death or dependence. On the other hand, the quality of evidence precludes a definitive conclusion.

Outcome Timeframe	**Study results and measurements**	**Comparator** No nutrition support	**Intervention** Nutrition support	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Death End of trial 9 Critical	Odds ratio 0.58 (CI 95% 0.28 — 1.21) Based on data from 4,343 participants in 7 studies. (Randomized controlled) Follow up: Varied - 3 to 12 months.	**127** per 1000 Difference:	**78** per 1000 **49 fewer per 1000** (CI 95% 88 fewer — 23 more)	**Moderate** Due to serious imprecision [1]	Nutrition support probably decreases death slightly although this was statistically insignificant
Death or dependence End of trial 9 Critical	Odds ratio 1.06 (CI 95% 0.94 — 1.2) Based on data from 4,023 participants in 1 studies. (Randomized controlled) Follow up: 6 months.	**457** per 1000 Difference:	**471** per 1000 **14 more per 1000** (CI 95% 15 fewer — 45 more)	**Moderate** Due to serious imprecision [2]	Nutrition support may have little or no difference on death or dependence
Length of stay	Measured by: Days	Difference:	**MD 1.4 higher**	**Moderate**	Nutrition support

Outcome Timeframe	**Study results and measurements**	**Comparator** No nutrition support	**Intervention** Nutrition support	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
At time of hospital discharge 7 Critical	Lower better Based on data from 4,114 participants in 2 studies. (Randomized controlled) Follow up: to hospital discharge.		(CI 95% 0.81 lower — 3.6 higher)	Due to serious imprecision [3]	probably has little or no difference on length of stay
Nutritional status During the study period 7 Critical	Measured by: Energy intake High better Based on data from 174 participants in 3 studies. (Randomized controlled) Follow up: During the study period.	Difference:	**MD 430.18 higher** (CI 95% 141.61 higher — 718.75 higher)	**Moderate** Due to serious inconsistency [4]	Nutrition support may have little or no difference on nutritional status

1. **Inconsistency: no serious.** Not serious, I2 metric is 38%, most studies favouring Nutritional Supplementation or null effect but no overall significant effect. . **Indirectness: no serious.** Not serious – yes PICO is relevant to population in question.. **Imprecision: serious.** Wide confidence intervals. **Publication bias: no serious.** Not serious – no evidence of publication bias from meta-analysis, good search strategy and awareness of future trials.
2. **Inconsistency: no serious. Indirectness: no serious.** Not serious – yes, PICO appropriate. **Imprecision: serious.** Wide confidence intervals; there is only one study included (FOOD Trial) however it is a very large multicentre trial. **Publication bias: no serious.** Not serious – no evidence of publication bias, good search strategy, good awareness of trials in progress..
3. **Inconsistency: no serious.** Not serious – no statistical heterogeneity, both favour control although not significant. Note there are only 2 studies.. **Indirectness: no serious.** Not serious, PICO is appropriate.. **Imprecision: serious.** Wide confidence intervals. **Publication bias: no serious.** Not serious. Good search strategy, awareness of ongoing trials..
4. **Inconsistency: serious.** Whilst the results are consistent across studies (significantly favouring control), I2 is 91% which is very high, and only 3 trials are included, and all are small.. **Indirectness: no serious.** Not serious – yes, PICO is appropriate. **Imprecision: no serious.** Not serious – as the results favour control (significantly), however 3 studies are included and all are small. **Publication bias: no serious.** Not serious – good search strategy, awareness of future trials..

Attached Images

Info Box

Practice points

- For patients with acute stroke food and fluid intake should be monitored.
- Stroke patients who are at risk of malnutrition, including those with dysphagia, should be referred to an Accredited Practising Dietitian for assessment and ongoing management.

Practical Info

Document patient's oral intake prior to stroke.
Patient or family member to document a typical week of eating prior to their stroke.
- When - Day and hour
- What - Day and hour
- List routinely skipped meals by habit/culture

Food charts, fluid balance charts, meal time observation and family involvement can all be utilised to monitor and encourage

adequate food and fluid intake.

Rationale

Patients with acute stroke are more likely to have difficulties maintaining adequate oral intake (e.g. due to dysphagia, hemianopia, hemiplegia, fatigue, and depressed mood). Acute stroke patients may also have problems reporting on their oral intake and/or dietary preferences (e.g. due to dysarthria, dysphasia).

Oral hygiene

Surveys from the Australian Institute of Health and Welfare show that 30-40% of people aged 15 years and over reported adverse oral health impact (AIHW 2014 *[8]*). It is even more difficult for stroke patients to maintain oral health due to physical weakness, lack of coordination, and impaired cognitive state (Campbell et al 2020 *[33]*). Oral health has been found to be significantly poorer after stroke (Zeng et al 2020 *[38]*).

Together with swallowing impairment, all these factors impact on an individual's nutritional intake, which in turn has a negative impact on rehabilitation and other functional outcomes (Campbell et al 2020 *[33]*). Moreover, complications such as chest infection, pneumonia, and heart diseases have been found to be associated with poor oral hygiene and dental diseases (Li et al 2000 *[32]*).

Strong recommendation

All stroke patients, particularly those with swallowing difficulties, should have assistance and/or education to maintain good oral and dental (including dentures) hygiene. (Campbell et al 2020 *[33]*)

Practical Info

Where possible, obtain the dental records of the patient or a summary report from the local dentist, so that a baseline of personal oral health can be taken into consideration.

Evidence To Decision

Benefits and harms

Small net benefit, or little difference between alternatives

Pooling of small number of trials suggest oral hygiene interventions in stroke patients results in a reduction in denture plaque, and improves stroke survivors' and providers knowledge and attitude. There was non significant reductions in dental plaque and gingivitis. (Campbell et al 2020 *[33]*). Several trials used either mouth gel or mouthwash with mixed results. There was no harm reported. Enhanced oral care (nursing education and training, oral care protocols, equipment provision, access to specialist dental services) was no more effective than usual care in reducing pneumonia in a pragmatic, stepped wedge cluster randomised control trial (n=325) (Brady et al 2019 *[36]*).

Certainty of the Evidence

Low

The evidence mostly comes from small randomised controlled trials with various methodological quality, and the overall certainty is very low to low.

Values and preferences

No substantial variability expected

It is expected that all patients would want to receive oral hygiene care for comfort and prevention of complications.

Resources and other considerations

Important issues, or potential issues not investigated

There were no economic evaluations for oral care in stroke. Oral care is not currently an indicator in the National Stroke Audit.

Rationale

Oral care is important after stroke to prevent complications such as xerostomia (dry mouth), pain and discomfort, aid communication and swallowing, maintain good nutrition and general wellbeing. It is essential to continue with daily cleansing routine to reduce the proliferation of pathogenic oral bacteria and prevent dental diseases such as caries, gingivitis and periodontitis (infection and inflammation of the ligaments and bones that support teeth) which if left untreated can lead to serious complications e.g. aspiration pneumonia and cardiovascular disease. In hospitalised dependent patients complications such as chest infection or pneumonia have been associated with poor oral hygiene (Li et al 2000 *[32]*). Post-stroke, oral care can be significantly compromised due to a variety of factors including physical weakness resulting in dental problems.

Oral health care interventions were found to improve knowledge and attitudes of patients and health professionals and appear to

reduce dental plaque. Further studies are needed to clearly demonstrate the impact on oral disease such as gingivitis and reduction of complications such as pneumonia. Although there is no clear evidence on the effective oral hygiene interventions, patients in need would want oral hygiene care maintained for comfort and to prevent potential complications. Moreover, there are no disadvantages of providing oral care. Therefore this practice is recommended, particularly in the group at high risk of developing dental problems.

Clinical Question/ PICO

Population: Adults with stroke
Intervention: Oral hygienic care intervention
Comparator: Standard care

Summary

Campbell et al (2020) *[33]* updated the Cochrane review which compared the effectiveness of specialist oral health care interventions with usual care (often not training) or other treatment options for ensuring oral health in people following stroke. Fifteen studies (n=3631 participants; 1546 with stroke) were included. Seven trials with data for 903 stroke patients investigated oral health care interventions against usual care. Multi-component oral health care interventions showed no evidence of a difference in the mean score (DMS) of dental plaque one month after the intervention (DMS −0.66, 95% CI −1.40 to 0.09). However, the studies were of very low quality. There was no evidence of oral health care intervention effect on gingivitis (DMS −0.60; 95% CI −1.66 to 0.45) or on the incidence of pneumonia (OR 4.17; CI 95% 0.82 to 21.11) among participants receiving the multi-component oral health care protocol compared with usual care one month after the intervention. Oral health care training for stroke survivors and care providers significantly improved their oral health care knowledge at one month after training (SMD 0.70; 95% CI 0.06 to 1.35).

Another study (n=66) by Chen et al (2019)*[35]* provided usual care (twice daily tooth brushing or sponge stick cleaning) plus additional 30 minutes of oral care (brushing, flossing, fluoride toothpaste, use of suction equipment) three times per week prior to swallow therapy for three weeks in patients who had an nasogastric tube. There was no improvement on the functional oral intake scale or removal of nasogastric tube but did find improvements on a modified oral health assessment tool. Rates of dental plaque or pneumonia were not collected.

Yuan et al. (2020) *[37]* in a RCT (n=113) conducted in China, investigated the effects of intensified oral hygiene care on reducing stroke-associated pneumonia incidence. In addition to usual oral self-care the intervention group received mouth wash with 0.12% chlorhexidine digluconate for 5-minutes, 3 times daily for 7 days. The incidence of pneumonia was non-significantly lower in the intervention group than in the control group (OR 0.35, 95% CI 0.12 to 1.03) but the intervention group significantly decreased the prevalence of potential oral pathogens.

The SOCLE II trial by Brady et al (2019) *[36]* with 325 patients and 112 nurses compared enhanced (involving 90 min online training that provided evidence based or best practice information and tutorial on assessment and care) to usual oral healthcare for people in stroke rehabilitation settings. There were no significant difference between enhanced and usual care for pneumonia events (OR 0.61, 95% CI 0.08 to 4.42). Dental plaque, denture plaque and oral health-related quality of life scores were similar between usual and enhanced oral health care. Staff (n=74) demonstrated no changes in their oral health care knowledge or attitudes after training, nor did the registered nurses differ from other nursing staff in their scores. Documentation of oral health care assessment and care plans was poor and increased slightly during the enhanced oral health care phase (3.0% vs 2.5%).

Overall there is a lack of high-quality evidence.

Outcome Timeframe	**Study results and measurements**	**Comparator**	**Intervention**	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Presence of related infection: Pneumonia [1] At 3 month follow-up 8 Critical	Odds ratio 4.17 (CI 95% 0.82 — 21.11) Based on data from 204 participants in 1 studies. [2] (Randomized controlled) Follow up: 3 months.	10 per 1000 Difference:	40 per 1000 **30 more per 1000** (CI 95% 2 fewer — 166 more)	**Low** Due to serious imprecision, Due to serious risk of bias [3]	Oral hygienic care intervention may have little or no difference on presence of related infection: pneumonia

Outcome Timeframe	**Study results and measurements**	**Comparator**	**Intervention**	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
OHC knowledge - carers and survivors 1 month	Measured by: non-validated self-administered questionnaires High better Based on data from 728 participants in 3 studies. [4] (Randomized controlled) Follow up: 1 month.	Difference:	**SMD 0.7 higher** (CI 95% 0.06 higher — 1.35 higher)	**Very low** Due to serious risk of bias, Due to serious imprecision, Due to serious inconsistency, Due to serious indirectness [5]	Oral hygienic care intervention may improve OHC knowledge - carers and survivors
Presence of oral disease: gingivitis 1 month 7 Critical	Based on data from 83 participants in 2 studies. [6] (Randomized controlled) Follow up: 1 month.	Two RCTs that compared oral health care interventions versus usual care were included in the Cochrane review. There was no evidence of a difference in gingivitis among participants receiving the multi-component OHC protocol compared with usual care one month after the intervention (difference in mean score (DMS) – 0.60; 95% CI −1.66 to 0.45; I2 = 93%, p = 0.26)		**Very low** Due to serious risk of bias, Due to serious inconsistency [7]	Oral hygienic care intervention may have little or no difference on presence of oral disease: gingivitis
Dental plaque 1 month 7 Critical	Based on data from 83 participants in 2 studies. [8] (Randomized controlled) Follow up: 1 month.	Two RCTs that compared oral health care (OHC) interventions versus usual care were included in the Cochrane review. There was no evidence of a difference in dental plaque among participants receiving the multi-component OHC protocol compared with usual care one month after the intervention (DMS −0.66; 95% CI −1.40 to 0.09; I2= 83%; p = 0.08)		**Very low** Due to serious risk of bias, Due to serious imprecision, Due to serious inconsistency [9]	Oral hygienic care intervention may have little or no difference on dental plaque

1. A 500mg application of a decontamination gel applied to patients' oral mucous membranes four times daily. Patients with dysphagia (swallowing impairment) were given the intervention over three weeks, while those who did not have dysphagia received the treatment over a two-week period.
2. Systematic review [33] . **Baseline/comparator:** Control arm of reference used for intervention.
3. **Risk of Bias: serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Only data from one study, Low number of patients (no power calculation). **Publication bias: no serious.**
4. Systematic review [33] . **Baseline/comparator:** Control arm of reference used for intervention.
5. **Risk of Bias: serious. Inconsistency: serious. Indirectness: serious.** Differences between the outcomes of interest and those reported (e.g short-term/surrogate,not patient-important). **Imprecision: serious.**
6. Systematic review [33].
7. **Risk of Bias: serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias. **Inconsistency: serious.** The magnitude of statistical heterogeneity was high, with I^2: 93%., The confidence interval of some of the studies do not overlap with those of most included studies/ the point estimate of some of the included studies..
8. Systematic review [33].
9. **Risk of Bias: serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias. **Inconsistency: serious.** The magnitude of statistical heterogeneity was high, with I^2: 83 %.. **Imprecision: serious.**

Attached Images

Strong recommendation

Staff and carers of stroke patients (in hospital, in residential care and home settings) should be trained in assessment and management of oral hygiene. (Campbell et al 2020 *[33]*)

Practical Info

Even an hour-long education session by a trained dental health professional can improve clincians' knowledge and attitude towards administering oral care. The educational benefits are retained and can be successfully transferred to new staff members.

Evidence To Decision

Benefits and harms

Small net benefit, or little difference between alternatives

A Cochrane review (Campbell et al 2020 *[33]*) found education and training improved staff knowledge and attitude, as well as cleanliness of patients' dentures. However, this review did not identify interventions investigating patient-critical outcomes such as functional oral intake. There was no harm reported. One large trial (Brady et al 2019*[36]*) found enhanced oral care (nursing education and training, oral care protocols, equipment provision, access to specialist dental services) was no more effective than usual care in reducing pneumonia.

Certainty of the Evidence

Low

Overall certainty is low.

Values and preferences

No substantial variability expected

No variation expected in patient value and preferences.

Resources and other considerations

Important issues, or potential issues not investigated

Resources considerations

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

Rationale

Evidence suggests that staff and carer education can improve their knowledge and patients' oral hygiene, which may translate to better functional outcomes.

Clinical Question/ PICO

Population: Adults with stroke
Intervention: Oral hygienic care intervention
Comparator: Standard care

Summary

Campbell et al (2020) *[33]* updated the Cochrane review which compared the effectiveness of specialist oral health care interventions with usual care (often not training) or other treatment options for ensuring oral health in people following stroke. Fifteen studies (n=3631 participants; 1546 with stroke) were included. Seven trials with data for 903 stroke patients investigated oral health care interventions against usual care. Multi-component oral health care interventions showed no evidence of a difference in the mean score (DMS) of dental plaque one month after the intervention (DMS −0.66, 95% CI −1.40 to 0.09). However, the studies were of very low quality. There was no evidence of oral health care intervention effect on gingivitis (DMS −0.60; 95% CI −1.66 to 0.45) or on the incidence of pneumonia (OR 4.17; CI 95% 0.82 to 21.11) among participants receiving the multi-component oral health care protocol compared with usual care one month after the intervention. Oral health care training for stroke survivors and care providers significantly improved their oral health care

knowledge at one month after training (SMD 0.70; 95% CI 0.06 to 1.35).

Another study (n=66) by Chen et al (2019)*[35]* provided usual care (twice daily tooth brushing or sponge stick cleaning) plus additional 30 minutes of oral care (brushing, flossing, fluoride toothpaste, use of suction equipment) three times per week prior to swallow therapy for three weeks in patients who had an nasogastric tube. There was no improvement on the functional oral intake scale or removal of nasogastric tube but did find improvements on a modified oral health assessment tool. Rates of dental plaque or pneumonia were not collected.

Yuan et al. (2020) *[37]* in a RCT (n=113) conducted in China, investigated the effects of intensified oral hygiene care on reducing stroke-associated pneumonia incidence. In addition to usual oral self-care the intervention group received mouth wash with 0.12% chlorhexidine digluconate for 5-minutes, 3 times daily for 7 days. The incidence of pneumonia was non-significantly lower in the intervention group than in the control group (OR 0.35, 95% CI 0.12 to 1.03) but the intervention group significantly decreased the prevalence of potential oral pathogens.

The SOCLE II trial by Brady et al (2019) *[36]* with 325 patients and 112 nurses compared enhanced (involving 90 min online training that provided evidence based or best practice information and tutorial on assessment and care) to usual oral healthcare for people in stroke rehabilitation settings. There were no significant difference between enhanced and usual care for pneumonia events (OR 0.61, 95% CI 0.08 to 4.42). Dental plaque, denture plaque and oral health-related quality of life scores were similar between usual and enhanced oral health care. Staff (n=74) demonstrated no changes in their oral health care knowledge or attitudes after training, nor did the registered nurses differ from other nursing staff in their scores. Documentation of oral health care assessment and care plans was poor and increased slightly during the enhanced oral health care phase (3.0% vs 2.5%).

Overall there is a lack of high-quality evidence.

Outcome Timeframe	**Study results and measurements**	**Comparator**	**Intervention**	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Presence of related infection: Pneumonia [1] At 3 month follow-up 8 Critical	Odds ratio 4.17 (CI 95% 0.82 — 21.11) Based on data from 204 participants in 1 studies. [2] (Randomized controlled) Follow up: 3 months.	10 per 1000 Difference:	40 per 1000 **30 more per 1000** (CI 95% 2 fewer — 166 more)	**Low** Due to serious imprecision, Due to serious risk of bias [3]	Oral hygienic care intervention may have little or no difference on presence of related infection: pneumonia
OHC knowledge - carers and survivors 1 month	Measured by: non-validated self-administered questionnaires High better Based on data from 728 participants in 3 studies. [4] (Randomized controlled) Follow up: 1 month.	Difference:	**SMD 0.7 higher** (CI 95% 0.06 higher — 1.35 higher)	**Very low** Due to serious risk of bias, Due to serious imprecision, Due to serious inconsistency, Due to serious indirectness [5]	Oral hygienic care intervention may improve OHC knowledge - carers and survivors
Presence of oral disease: gingivitis 1 month 7 Critical	Based on data from 83 participants in 2 studies. [6] (Randomized controlled) Follow up: 1 month.	Two RCTs that compared oral health care interventions versus usual care were included in the Cochrane review. There was no evidence of a difference in gingivitis among participants receiving the multi-component OHC protocol compared with usual care one month after the intervention (difference in mean score (DMS) – 0.60; 95% CI –1.66 to 0.45; I2 = 93%, p = 0.26)		**Very low** Due to serious risk of bias, Due to serious inconsistency [7]	Oral hygienic care intervention may have little or no difference on presence of oral disease: gingivitis

Outcome Timeframe	Study results and measurements	Comparator	Intervention	Certainty of the Evidence (Quality of evidence)	Plain language summary
Dental plaque 1 month 7 Critical	Based on data from 83 participants in 2 studies. [8] (Randomized controlled) Follow up: 1 month.	Two RCTs that compared oral health care (OHC) interventions versus usual care were included in the Cochrane review. There was no evidence of a difference in dental plaque among participants receiving the multi-component OHC protocol compared with usual care one month after the intervention (DMS −0.66; 95% CI −1.40 to 0.09; I2= 83%; p = 0.08)		Very low Due to serious risk of bias, Due to serious imprecision, Due to serious inconsistency [9]	Oral hygienic care intervention may have little or no difference on dental plaque

1. A 500mg application of a decontamination gel applied to patients' oral mucous membranes four times daily. Patients with dysphagia (swallowing impairment) were given the intervention over three weeks, while those who did not have dysphagia received the treatment over a two-week period.
2. Systematic review [33] . **Baseline/comparator:** Control arm of reference used for intervention.
3. **Risk of Bias: serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Only data from one study, Low number of patients (no power calculation). **Publication bias: no serious.**
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Attached Images

Weak recommendation

For stroke patients, chlorhexidine in combination with oral hygiene instruction, and/or assisted brushing may be used to decrease dental plaque and gingiva bleeding. Caution should be taken, however, for patients with dysphagia. (Lam et al 2013 *[31]*; Yuan et al 2020 *[37]*)

Practical Info

The importance of maintaining good oral hygiene should be emphasised in all stroke units and rehabilitation wards.

A demonstration of how much mouthwash to use, and how and when to use it, would be helpful to those patients who have never used mouthwash before.

Evidence To Decision

Benefits and harms

Small net benefit, or little difference between alternatives

There is some evidence from a small number of studies although the reported benefits are inconsistent. In the study by Lam et al (2013) *[31]*, reductions in dental plaque were significantly greater in the two intervention groups that received chlorhexidine and oral hygiene instruction; or chlorhexidine, oral hygiene instruction and assisted brushing when compared to oral hygiene

instruction alone. Another study by Yuan et al (2020)*[37]* found a decrease in potential oral pathogens with intensified oral care including cholorhexidine mouth wash. No study has found a reduction in pneumonia. No harms were reported.

Certainty of the Evidence

Very low

The evidence comes from a randomised controlled trial of inadequate sample size and high risk of bias, therefore the quality is very low.

Values and preferences

No substantial variability expected

It is expected that patients would want this potentially effective practice with no harm.

Resources and other considerations

Important issues, or potential issues not investigated

Resources considerations

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

Rationale

Use of Chlorhexidine in combination with oral hygiene instruction, and/or assisted brushing was shown to be effective in reducing dental plaque and gingival bleeding (Lam et al 2013 *[31]*) and oral pathogens (Yuan et al 2020 *[37]*). Although there was no significant improvement in physical function and pneumonia and the quality of evidence was very low, there was no harm associated with this practice. Overall, this practice may be used to improve stroke patients' oral hygiene.

Clinical Question/ PICO

Population: Adults with stroke
Intervention: Oral hygienic care intervention
Comparator: Standard care

Summary

Campbell et al (2020) *[33]* updated the Cochrane review which compared the effectiveness of specialist oral health care interventions with usual care (often not training) or other treatment options for ensuring oral health in people following stroke. Fifteen studies (n=3631 participants; 1546 with stroke) were included. Seven trials with data for 903 stroke patients investigated oral health care interventions against usual care. Multi-component oral health care interventions showed no evidence of a difference in the mean score (DMS) of dental plaque one month after the intervention (DMS −0.66, 95% CI −1.40 to 0.09). However, the studies were of very low quality. There was no evidence of oral health care intervention effect on gingivitis (DMS −0.60; 95% CI −1.66 to 0.45) or on the incidence of pneumonia (OR 4.17; CI 95% 0.82 to 21.11) among participants receiving the multi-component oral health care protocol compared with usual care one month after the intervention. Oral health care training for stroke survivors and care providers significantly improved their oral health care knowledge at one month after training (SMD 0.70; 95% CI 0.06 to 1.35).

Another study (n=66) by Chen et al (2019)*[35]* provided usual care (twice daily tooth brushing or sponge stick cleaning) plus additional 30 minutes of oral care (brushing, flossing, fluoride toothpaste, use of suction equipment) three times per week prior to swallow therapy for three weeks in patients who had an nasogastric tube. There was no improvement on the functional oral intake scale or removal of nasogastric tube but did find improvements on a modified oral health assessment tool. Rates of dental plaque or pneumonia were not collected.

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The SOCLE II trial by Brady et al (2019) *[36]* with 325 patients and 112 nurses compared enhanced (involving 90 min

online training that provided evidence based or best practice information and tutorial on assessment and care) to usual oral healthcare for people in stroke rehabilitation settings. There were no significant difference between enhanced and usual care for pneumonia events (OR 0.61, 95% CI 0.08 to 4.42). Dental plaque, denture plaque and oral health-related quality of life scores were similar between usual and enhanced oral health care. Staff (n=74) demonstrated no changes in their oral health care knowledge or attitudes after training, nor did the registered nurses differ from other nursing staff in their scores. Documentation of oral health care assessment and care plans was poor and increased slightly during the enhanced oral health care phase (3.0% vs 2.5%).

Overall there is a lack of high-quality evidence.

Outcome Timeframe	**Study results and measurements**	**Comparator**	**Intervention**	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Presence of related infection: Pneumonia [1] At 3 month follow-up 8 Critical	Odds ratio 4.17 (CI 95% 0.82 — 21.11) Based on data from 204 participants in 1 studies. [2] (Randomized controlled) Follow up: 3 months.	10 per 1000 Difference:	40 per 1000 **30 more per 1000** (CI 95% 2 fewer — 166 more)	**Low** Due to serious imprecision, Due to serious risk of bias [3]	Oral hygienic care intervention may have little or no difference on presence of related infection: pneumonia
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Presence of oral disease: gingivitis 1 month 7 Critical	Based on data from 83 participants in 2 studies. [6] (Randomized controlled) Follow up: 1 month.	Two RCTs that compared oral health care interventions versus usual care were included in the Cochrane review. There was no evidence of a difference in gingivitis among participants receiving the multi-component OHC protocol compared with usual care one month after the intervention (difference in mean score (DMS) – 0.60; 95% CI –1.66 to 0.45; I2 = 93%, p = 0.26)		**Very low** Due to serious risk of bias, Due to serious inconsistency [7]	Oral hygienic care intervention may have little or no difference on presence of oral disease: gingivitis
Dental plaque 1 month 7 Critical	Based on data from 83 participants in 2 studies. [8] (Randomized controlled) Follow up: 1 month.	Two RCTs that compared oral health care (OHC) interventions versus usual care were included in the Cochrane review. There was no evidence of a difference in dental plaque among participants receiving the multi-component OHC protocol compared with usual care one month after the intervention (DMS –0.66; 95% CI –1.40 to 0.09; I2= 83%; p = 0.08)		**Very low** Due to serious risk of bias, Due to serious imprecision, Due to serious inconsistency [9]	Oral hygienic care intervention may have little or no difference on dental plaque

1. A 500mg application of a decontamination gel applied to patients' oral mucous membranes four times daily. Patients with dysphagia (swallowing impairment) were given the intervention over three weeks, while those who did not have dysphagia received the treatment over a two-week period.

2. Systematic review [33] . **Baseline/comparator:** Control arm of reference used for intervention.
3. **Risk of Bias: serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Only data from one study, Low number of patients (no power calculation). **Publication bias: no serious.**
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8. Systematic review [33].
9. **Risk of Bias: serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias. **Inconsistency: serious.** The magnitude of statistical heterogeneity was high, with I^2: 83 %.. **Imprecision: serious.**

Attached Images

Spasticity

Spasticity is defined as a motor disorder characterised by a velocity-dependent increase in tonic stretch reflexes (muscle tone) with exaggerated tendon jerks resulting from hyper-excitability of the stretch reflex as one component of the upper motor neuron syndrome. Spasticity is not a major determinant of activity limitation. Interventions to reduce spasticity should be considered when the level of spasticity interferes with activity or the ability to provide care to the stroke survivor (van Kuijk et al 2002 *[71]*).

Weak recommendation

For stroke survivors with ***upper*** limb spasticity, Botulinum Toxin A in addition to rehabilitation therapy may be used to reduce spasticity, but is unlikely to improve activity or motor function. (Foley et al 2013 *[39]*; Gracies et al 2014 *[43]*)

Practical Info

Use of botulinum toxin A for upper limb spasticity should be combined with concurrent rehabilitation therapy, and be provided in the context of a multidisciplinary team with clear and specific client-centred goals. Greater benefits are seen with improvement on passive function goals compared to active function goals. Outcome measures specifically developed to evaluate spasticity should be used.

Evidence To Decision

Benefits and harms

Substantial net benefits of the recommended alternative

Improvements of small to moderate effect size have been reported for outcomes specific to BTX-A treatment response, motor function outcomes and more generalised disability (Foley et al 2013 *[39]*).

Certainty of the Evidence

Low

The majority of trials included in the systematic review had serious risk of bias. Effect estimates were imprecise and the improvement in generalised disability was non-significant.

Values and preferences

No substantial variability expected

Patients may have varying goals in terms of improving ease of daily activities but are not expected to vary substantially with regard to improving motor function.

Resources and other considerations

Important issues, or potential issues not investigated

<u>Resources considerations</u>

In a multicentre randomised control trial conducted in the UK, the cost-effectiveness of botulinum toxin plus an upper limb therapy program (n=170) compared to upper limb program alone (n=163) was evaluated (Shaw et al 2010 *[69]*; Shackley et al 2012 *[70]*). Data on health services and social services costs were obtained by questionnaire (cost reference year 2007 Pound sterling) and QALYs were estimated using the EQ-5D questionnaire. At 3 months post randomisation, botulinum toxin plus upper limb therapy program was associated with an incremental cost of £374 and an incremental QALY gain of 0.004 (£93,500 per QALY gained), compared to therapy alone. In another study conducted in Germany (n=228), Rychlik et al. (2016) *[72]* reported that treatment with botulinum toxin was cost-effective for the treatment of post stoke spasticity. Patients treated with botulinum toxin plus conventional therapy demonstrated superior results in muscle tone reduction as well as more favourable improvement in functional impairment and quality of life than conventional anti-spastic therapy, over a one year treatment period. Incremental cost-effectiveness ratios for the clinical outcomes evaluated ranged between €768 and €11,549.

There is also some evidence that botulinum toxin treatment may be cost effective in the longer term. A modelled cost-utility analysis was developed to examine the cost effectiveness of extending botulinum toxin treatment beyond four treatment cycles among patients with an adequate response to previous treatment cycles (Makino et al. 2018 *[73]*). Costs to the Australian Healthcare system perspective were estimated (cost reference year 2016 AUD). Data on QALY and response rates to treatment were obtained from previous clinical trials and post hoc analysis. Over a five year time horizon, the incremental cost per QALY

gained of continued use of botulinum toxin beyond the current policy constraint of four treatments was A$59,911 (incremental cost = A$4533; incremental QALYs = 0.076). In multivariable analysis, the probability of the extended treatment regimen being cost-effective.

Rationale

Moderate improvements have been reported with botulinum toxin A, but the quality of the evidence is low due to substantial variation in treatment effect like i.e. different doses of botulinum toxin given, chronicity of spasticity, injection sites, concurrent therapy, outcomes selected, and timing of outcomes . In pooled analysis, botulinum toxin A was associated with a moderate treatment effect size (SMD=0.56+-0.72/95% CI 0.35-0.72/p=<.0001/I^2=38%) with improvements in Disability Assessment Scale, and the Disability Scale scores *[39]* . The Disability Assessment Scale and the Disability Scale were developed purposely to measure the response to Botulinum toxin A treatment. The trials that used one of these scales correlated with the largest effect sizes. Most of the outcome tools used for upper limb measure active rather than passive function, which may respond better to treatment with botulinum toxin A. It is hypothesized that botulinum toxin A impacts on the positive features of upper motor neuron syndrome. It does not impact on the negative features, such as weakness, coordination, fatigability, adaptive soft tissue shortening, which will affect upper limb function , but it may provide a 'window of opportunity' for to address these negative features. The effect of some factors, and how they contribute to the variation in treatment effect is difficult to ascertain. Additional therapy was provided in the majority of the studies, details about the regimes were not specified. It is impossible to isolate the effect of additional therapy when compared to the effect of botulinum toxin A injection per se.

Clinical Question/ PICO

Population: Adults with stroke with lower limb spasticity
Intervention: Botulinum Toxin A
Comparator: Control

Summary

A systematic review of botulinum toxin (BTX) treatments for lower limb spasticity after stroke included 7 randomised trials with 603 total participants (Wu et al 2016 *[51]*). Significant improvements in muscle tone were seen at both 4 week and 12 week follow-ups in meta-analysis (4 weeks: SMD 0.85, 95% CI 0.2 to 1.5, 12 weeks: SMD 0.42, 95% CI 0.07 to 0.77). Participants receiving BTX treatment also had significantly higher Fugl-Meyer scores, however there was no significant difference in gait speed.

A previous systematic review by McIntyre et al (2012) *[52]* included four trials of BTX-A in patients more than 6 months post stroke. No meta-analysis was conducted but the review authors reported that there was good evidence that BTX-A treatment temporarily relieves lower limb spasticity. They noted that the benefits are likely dosage dependent, with larger improvements generally reported in trials using the highest dosages without an increase in adverse events.

An earlier review by Olvey et al (2010) *[53]* included 54 trials of pharmacologic treatments for spasticity, including 23 randomised trials. 38 trials using BTX treatments reported significant reductions in spasticity. Meta-analysis was not conducted due to the lack of a large number of trials reporting the same outcomes.

Outcome Timeframe	**Study results and measurements**	**Comparator** Control	**Intervention** Botulinum Toxin A	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Adverse events [1] End of follow-up (24 weeks) 9 Critical	Odds ratio 0.82 (CI 95% 0.5 — 1.34) Based on data from 437 participants in 3 studies. [2] (Randomized controlled) Follow up: Up to 24 weeks.	233 per 1000 Difference:	199 per 1000 **34 fewer per 1000** (CI 95% 101 fewer — 56 more)	**Moderate** Due to serious risk of bias [3]	Botulinum toxin A probably has little or no difference on adverse events

Outcome Timeframe	**Study results and measurements**	**Comparator** Control	**Intervention** Botulinum Toxin A	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Gait speed 12 weeks 9 Critical	Measured by: Gait Speed High better Based on data from 1,077 participants in 4 studies. [4] (Randomized controlled) Follow up: 12 weeks.	0 speed (Mean)	0.01 speed (Mean) CI 95%	**Moderate** Due to serious risk of bias [5]	Botulinum toxin A probably increases gait speed slightly
Lower limb function 24 weeks 9 Critical	Measured by: Fugl-Meyer score Scale: 0 — 226 High better Based on data from 296 participants in 3 studies. (Randomized controlled) Follow up: 24 weeks.		3.19 points (Mean) CI 95%	**Moderate** Due to serious imprecision, Due to serious risk of bias, Due to serious imprecision [6]	Botulinum toxin A probably increases lower limb function
Adverse events 12 weeks 9 Critical	Measured by: Recording of Adverse events Lower better Based on data from 437 participants in 3 studies. (Randomized controlled) Follow up: 12 weeks.		0.82 (Mean) CI 95%	**Moderate** Due to serious risk of bias [7]	Botulinum toxin A probably increases adverse events slightly
Muscle tone 4 weeks after treatment 9 Critical	Measured by: Modified Ashworth Scale, Clinical Spasticity Influx High better Based on data from 263 participants in 4 studies. [8] (Randomized controlled) Follow up: 4 weeks after treatment.	Difference: points (n/a)	**SMD 0.85 higher** (CI 95% 0.2 higher — 1.5 higher)	**Very low** Due to serious risk of bias, Due to serious imprecision, Due to serious publication bias, Due to serious inconsistency [9]	We are uncertain whether Botulinum toxin A increases or decreases muscle tone at 4 weeks
Muscle tone 12 weeks after treatment 9 Critical	Measured by: Modified Ashworth Scale, Clinical Spasticity Influx High better Based on data from 263 participants in 4 studies. [10] (Randomized controlled) Follow up: 12 weeks after treatment.	Difference: points (n/a)	**SMD 0.42 higher** (CI 95% 0.07 higher — 0.77 higher)	**Very low** Due to serious risk of bias, Due to serious imprecision, Due to serious publication bias, Due to serious inconsistency [11]	We are uncertain whether Botulinum toxin A increases or decreases muscle tone at 12 weeks
Muscle tone 24 weeks after treatment 9 Critical	Measured by: Modified Ashworth Scale, Clinical Spasticity Influx High better Based on data from 68 participants in 1 studies. [12] (Randomized controlled) Follow up: 24 weeks after treatment.	Difference:	**SMD 0.02 higher** (CI 95% 0.46 lower — 0.49 higher)	**Very low** Due to serious risk of bias, Due to serious imprecision, Due to serious publication bias, Due to serious inconsistency [13]	We are uncertain whether Botulinum toxin A increases or decreases muscle tone at 24 weeks
Gait speed	Measured by: Gait Speed (m/s)	Difference:	**MD 0.01 higher** (CI 95% 0.01	**Moderate** Due to serious risk	Botulinum toxin A probably increases gait

Outcome Timeframe	**Study results and measurements**	**Comparator** Control	**Intervention** Botulinum Toxin A	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
4 to 12 weeks after treatment 9 Critical	High better Based on data from 381 participants in 4 studies. [14] (Randomized controlled) Follow up: 4 to 12 weeks.		lower — 0.03 higher)	of bias [15]	speed slightly
Lower limb function 4 to 24 weeks after treatment 9 Critical	Measured by: Fugl-Meyer score High better Based on data from 114 participants in 3 studies. (Randomized controlled) Follow up: 4 to 24 weeks.	Difference:	points (n/a) **MD 3.19 higher** (CI 95% 0.22 higher — 6.16 higher)	**Moderate** Due to serious imprecision [16]	Botulinum toxin A probably increases lower limb function
Muscle tone (MAS) 4-12 weeks 9 Critical	Measured by: Modified Ashworth Scale Scale: 0 — 4 Lower better Based on data from 535 participants in 6 studies. [17] (Randomized controlled) Follow up: 8-16 weeks.		**0.51** points (Mean) CI 95%	**Very low** Due to serious risk of bias, Due to serious imprecision, Due to serious publication bias, Due to serious inconsistency [18]	We are uncertain whether Botulinum toxin A increases or decreases muscle tone (mas)
Muscle tone (CSI) 4-12 weeks 9 Critical	Measured by: Clinical Spasticity Influx High better Based on data from 68 participants in 1 studies. (Randomized controlled) Follow up: 24 weeks.		**0.02** (Mean) CI 95%	**Very low** Due to serious risk of bias, Due to serious inconsistency, Due to serious imprecision, Due to serious publication bias [19]	We are uncertain whether Botulinum toxin A improves or worsen muscle tone (csi)

1. "[D]rug-related adverse events included myalgia, injection site and extremity pain, erythema, convulsions and incoordination" (Wu 2016).
2. Systematic review [51] . **Baseline/comparator:** Control arm of reference used for intervention.
3. **Risk of Bias: serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Incomplete data and/or large loss to follow up. **Inconsistency: no serious.** I^2 = 13%. **Indirectness: no serious. Imprecision: no serious.** Small sample size. **Publication bias: no serious.** Small number of studies.
4. Systematic review [51] . **Baseline/comparator:** Control arm of reference used for intervention.
5. **Risk of Bias: serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Incomplete data and/or large loss to follow up. **Inconsistency: no serious.** I2=55%. **Indirectness: no serious. Imprecision: no serious.** Wide confidence intervals, Low number of patients. **Publication bias: no serious.** Due to small number of studies.
6. **Risk of Bias: no serious.** Variability on doses of botulinum toxin and expertise of people performing the injections., Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Incomplete data and/or large loss to follow up. **Inconsistency: no serious.** I2= 96%. **Indirectness: no serious. Imprecision: serious.** Small sample size might be over estimating effect. **Publication bias: no serious.** Small number of studies available.
7. **Risk of Bias: serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Incomplete data and/or large loss to follow up. **Inconsistency: no serious.** I2= 13%. **Indirectness: no serious. Imprecision: no serious.** Small sample size. **Publication bias: no serious.** Small number of studies.
8. Systematic review [51] . **Baseline/comparator:** Systematic review.
9. **Risk of Bias: serious.** There is no information provided about: Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate sequence generation/ generation of comparable groups, resulting in

potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias. **Inconsistency: serious.** I^2= 81%. **Indirectness: no serious. Imprecision: serious.** Low number of patients. **Publication bias: serious.** Unable to test due to small number of studies (7 only).
10. Systematic review [51] . **Baseline/comparator:** Control arm of reference used for intervention.
11. **Risk of Bias: serious.** There is no information provided about: Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias. **Inconsistency: serious.** I^2= 81%. **Indirectness: no serious. Imprecision: serious.** Low number of patients. **Publication bias: serious.** Unable to test due to small number of studies (7 only).
12. Systematic review [51] . **Baseline/comparator:** Control arm of reference used for intervention.
13. **Risk of Bias: serious.** There is no information provided about: Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias. **Inconsistency: serious.** I^2= 81%. **Indirectness: no serious. Imprecision: serious.** Low number of patients. **Publication bias: serious.** Unable to test due to small number of studies (7 only).
14. Systematic review [51] . **Baseline/comparator:** Control arm of reference used for intervention.
15. **Risk of Bias: serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Incomplete data and/or large loss to follow up. **Inconsistency: no serious.** I2=55%. **Indirectness: no serious. Imprecision: no serious.** Wide confidence intervals, Low number of patients. **Publication bias: no serious.** Due to small number of studies.
16. **Risk of Bias: no serious.** Variability on doses of botulinum toxin and expertise of people performing the injections., Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Incomplete data and/or large loss to follow up. **Inconsistency: no serious.** I2= 96%. **Indirectness: no serious. Imprecision: serious.** Small sample size might be over estimating effect. **Publication bias: no serious.** Small number of studies available.
17. Systematic review [51] . **Baseline/comparator:** Systematic review.
18. **Risk of Bias: serious.** There is no information provided about: Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias. **Inconsistency: serious.** I^2= 52-70%. **Indirectness: no serious. Imprecision: serious.** Low number of patients. **Publication bias: serious.** Unable to test due to small number of studies (7 only).
19. **Risk of Bias: serious.** No information on:, Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/ lack of blinding of outcome assessors, resulting in potential for detection bias, Missing intention-to-treat analysis. **Inconsistency: no serious.** I^2=38%. **Indirectness: no serious. Imprecision: serious.** Wide confidence intervals, Low number of patients. **Publication bias: serious.** Only 1 study.

Attached Images

Clinical Question/ PICO

Population:	Adults with stroke with elbow flexor spasticity
Intervention:	abobotulinumtoxinA 1000 U
Comparator:	Placebo

Summary

This randomised trial (N = 243) compared placebo to BTX-A treatment at both 500 U and 1000 U dosages (Gracies et al 2015 [34]). Both BTX-A groups showed significant improvements on the Modified Ashworth Scale and Physician Global Assessment compared to placebo. The study was not powered to compare the BTX-A dosages but results suggested greater improvements following the higher dose. Data were extracted for the placebo and 1000 U dose groups only (n=158).

Outcome Timeframe	**Study results and measurements**	**Comparator** Placebo	**Intervention** abobotulinumtoxinA 1000 U	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Modified Ashworth Scale (MAS) 4 weeks 7 Critical	Measured by: Modified Ashworth Scale High better Based on data from 158 participants in 1 studies. (Randomized controlled) Follow up: 4weeks.	3.7 (Mean) Difference:	2.6 (Mean) **MD 1.1 lower** (CI 95% 1.4 lower — 0.8 lower)	**Moderate** Due to serious imprecision [1]	abobotulinumtoxina 1000 u probably improves Modified Ashworth Scale (MAS)
Physician Global Assessment 4 weeks 8 Critical	Measured by: PGA High better Based on data from 158 participants in 1 studies. (Randomized controlled) Follow up: 4 weeks.	0.6 (Mean)	1.8 (Mean) n/a	**Moderate** Due to serious imprecision [2]	abobotulinumtoxina 1000 u probably improves physician global assessment
Disability assessment scale 4 weeks 8 Critical	Measured by: Disability assessment scale Scale: 0 — 4 Lower better Based on data from 158 participants in 1 studies. (Randomized controlled) Follow up: 4 weeks.	2.1 (Mean)	1.8 (Mean) n/a	**Moderate** Due to serious imprecision [3]	abobotulinumtoxina 1000 u probably improves Disability Assessment Scale

1. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Only data from one study. **Publication bias: no serious.**
2. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Only data from one study. **Publication bias: no serious.**
3. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Only data from one study. **Publication bias: no serious.**

Attached Images

Clinical Question/ PICO

Population: Adults with stroke with upper limb spasticity
Intervention: Botulinum Toxin A
Comparator: Control

Summary

A systematic review by Foley et al (2013) *[39]* included 16 randomised controlled trials comparing treatment with botulinum toxin type A (BTX-A) to either placebo or a nonpharmacologic treatment. Data from 1000 patients in 10 studies was available for meta-analysis. Meta-analysis showed a small but significant improvement on assessments of motor function such as the Action Research Arm Test, and a large improvement on scales such as the Disability Assessment Scale that have been developed specifically to measure response to BTX-A treatment. Improvement on generalised disability measures (Barthel Index) were small and of borderline significance.
A typographical error in the reported effect on motor function assessments made the confidence interval for this effect unclear and raised some questions about the quality of the meta-analysis.

A subsequent systematic review of BTX-A treatments for upper limb spasticity included 12 trials (Dashtipour et al 2015 *[40]*). No meta-analysis was conducted but the review authors reported that there was strong evidence for the

efficacy of BTX-A in treating spasticity, finding positive results in 9 out of 12 studies using the Modified Ashworth Scale. The included trials largely overlapped with those included by Foley et al. but full details on the excluded studies were not reported so the precise reasons why the included studies differed are unclear.

Another systematic review and meta-analysis of BTX-A treatments for upper limb spasticity (Baker et al 2014 *[41]*) also reported significant improvements in pooled upper limb outcomes that were maintained at up to 6 months. However, although the majority of participants were stroke, this review was not stroke specific so the results may not be as relevant for determining the benefits of BTX-A treatment in stroke patients.

A randomised trial (N = 243) that was not included in the prior systematic reviews compared placebo to BTX-A treatment at both 500 U and 1000 U dosages (Gracies et al 2015 *[43]*). Both BTX-A groups showed significant improvements on the Modified Ashworth Scale and Physician Global Assessment compared to placebo. The study was not powered to compare the BTX-A dosages but results suggested greater improvements following the higher dose.

Other trials that were not included in the earlier systematic reviews have shown similar results, generally showing benefits for measures of muscle spasticity such as the Modified Ashworth Scale but less consistent and smaller benefits on more generalised measures of function and disability (Ward et al 2014 *[46]*; Marciniak et al 2012 *[47]*; Rosales et al 2012 *[48]*; Wolf et al 2012 *[49]*; Kanovsky et al 2011 *[50]*). A randomised trial comparing BTX-A to Neuronox found that Neuronox was not superior for the primary outcome of the Modified Ashworth scale, with no significant differences in adverse events, suggesting equal effectiveness and safety (Seo et al 2015 *[45]*).

Lannin et al (2022) *[232]* studied (n = 140) the long-term effect of 3 months additional upper limb rehabilitation, following botulinum toxin-A injection to a muscle crossing the wrist. There was no significant differences between the intervention and control groups for outcomes measured. When the groups were combined, at 12 month follow up there was a significant improvement in spasticity Tardieu scale (MD = -0.4, 95% CI: -0.7 to -0.2),), contracture (MD = -10 deg, 95% CI: -15 to -5), pain (MD = -0.8, 95% CI: -1.2 to -0.3), and burden of care (MD = -2.3, 95% CI: -3.1 to -1.4), indicating that there was no long term benefit to additional rehabilitation following botulinum toxin-A injection.

Outcome Timeframe	**Study results and measurements**	**Comparator** Control	**Intervention** Botulinum Toxin A	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Disability assessment scale 6 weeks 9 Critical	Measured by: Disability Assessment Scale Scale: 0 — 3 Lower better Based on data from 539 participants in 5 studies. [1] (Randomized controlled) Follow up: 2-24 weeks.	**0.54** points (Mean)	**0.69** points (Mean) CI 95%	**Moderate** Due to serious risk of bias, Due to serious risk of bias [2]	Botulinum toxin A probably improves disability assessment scale
Action Research Arm Test 1 month 9 Critical	Measured by: Action Research Arm Test Scale: 0 — 57 High better Based on data from 383 participants in 2 studies. [3] (Randomized controlled) Follow up: 24-52 weekss.		**0.41** points per 4 subscales (Mean) CI 95%	**Low** Due to serious risk of bias, Due to serious imprecision [4]	Botulinum toxin A may improve action research arm test slightly
Generalised disability 4 weeks 9 Critical	Measured by: Barthel Index Scale: 0 — 20 High better Based on data from 112 participants in 2 studies. [5] (Randomized controlled) Follow up: 4 weeks.	Difference:	**SMD 0.37 higher** (CI 95% 0 lower — 0.75 higher)	**Low** Due to serious risk of bias, Due to serious inconsistency, Due to serious indirectness, Due to serious imprecision [6]	Botulinum toxin A may have little or no difference on generalised disability

Outcome Timeframe	**Study results and measurements**	**Comparator** Control	**Intervention** Botulinum Toxin A	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Disability - BTX specific [7] 2 to 8 weeks 9 Critical	Measured by: Disability Assessment Scale, Disability Scale High better Based on data from 423 participants in 4 studies. [8] (Randomized controlled) Follow up: 2 to 8 weeks.	Difference:	**SMD 0.69 higher** (CI 95% 0.45 higher — 1.01 higher)	**Moderate** Due to serious risk of bias [9]	Botulinum toxin A probably improves disability as assessed by BTX specific scales like DAS and Disability Scale
Motor function 6 to 12 weeks 9 Critical	Measured by: Action Research Arm Test, Motor Assessment Scale, Motor Activity Log High better Based on data from 500 participants in 4 studies. (Randomized controlled) Follow up: 6 to 12 weeks.	Difference:	**SMD 0.41 higher** (CI 95% 0.85 higher — 0.73 higher)	**Low** Due to serious risk of bias, Due to serious imprecision [10]	Botulinum toxin A may improve motor function slightly

1. Systematic review [39] . **Baseline/comparator:** Systematic review.
2. **Risk of Bias: serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Missing intention-to-treat analysis, Incomplete data. The Systematic review and, meta-analysis had inclusion and exclusion criteria for the search. The methodological quality of each RCT was assessed by using the JADED scale . **Inconsistency: no serious.** I^2= 38% (moderate statistical heterogeneity). Substantial variation in treatment effect between studies. Potential sources include chronicity of spasticity, dosing regimes, injection sites, concurrent therapies, outcomes slected, and timing of assessments. **Indirectness: no serious. Imprecision: no serious.** Low number of patients. Not all studies had sdample size calculations, hence some sutdies may have lacked statistical power. **Publication bias: no serious.**
3. Systematic review. **Baseline/comparator:** Control arm of reference used for intervention. **Supporting references:** [39],
4. **Risk of Bias: serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Missing intention-to-treat analysis, Incomplete data. **Inconsistency: no serious.** I^2= 38%. **Indirectness: no serious. Imprecision: serious.** Low number of patients. **Publication bias: no serious.**
5. Systematic review [39] . **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of Bias: serious.** Incomplete data and/or large loss to follow up, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Missing intention-to-treat analysis. **Inconsistency: no serious.** I^2= 38%. **Indirectness: no serious. Imprecision: serious.** Wide confidence intervals. **Publication bias: no serious.**
7. The Disability Assessment scale used in 3/4 studies here measures factors specific to BTX-A treatment and is mostly focused on passive functioning.
8. Systematic review [39] . **Baseline/comparator:** Control arm of reference used for intervention.
9. **Risk of Bias: serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Missing intention-to-treat analysis, Incomplete data. The Systematic review and, meta-analysis had inclusion and exclusion criteria for the search. The methodological quality of each RCT was assessed by using the JADED scale . **Inconsistency: no serious.** I^2= 38% (moderate statistical heterogeneity). Substantial variation in treatment effect between studies. Potential sources include chronicity of spasticity, dosing regimes, injection sites, concurrent therapies, outcomes selected, and timing of assessments. **Indirectness: no serious. Imprecision: no serious.** Low number of patients. Not all studies had sample size calculations, hence some studies may have lacked statistical power. **Publication bias: no serious.**
10. **Risk of Bias: serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Missing intention-to-treat analysis, Incomplete data. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Low number of patients. **Publication bias: no serious.**

Attached Images

Weak recommendation

For stroke survivors with ***lower*** limb spasticity, Botulinum Toxin A in addition to rehabilitation therapy may be used to reduce spasticity but is unlikely to improve motor function or walking. (Wu et al 2016 *[51]*; McIntyre et al 2012 *[52]*; Olvey et al 2010 *[53]*)

Practical Info

Use of botulinum toxin A for lower limb spasticity should be combined with concurrent rehabilitation therapy, and be provided in the context of a multidisciplinary team with clear and specific client-centred goals. Botulinum toxin injection could be a useful and safe strategy for treatment of lower limb spasticity after stroke. The benefits of Botulinum toxin A combined with rehabilitation therapy are enhanced when the treatment goal matches the target muscles injected.

Evidence To Decision

Benefits and harms

Small net benefit, or little difference between alternatives

Botulinum toxin A treatment produced improvements in muscle tone that appeared to be maintained up to 12 weeks after treatment (Wu et al 2016 *[51]*). Botulinum toxin treatment also produced possible improvement in lower limb function, but little apparent effect on gait speed *[51]*. Adverse effects appeared to be lower overall in patients receiving botulinum toxin treatment compared to controls (Wu et al 2016 *[51]*).

Certainty of the Evidence

Low

The quality of evidence was low overall, with high risk of bias and small sample sizes in the included randomised controlled trials .

Values and preferences

No substantial variability expected

Patients may have varying goals in terms of improving ease of daily activities but are not expected to vary substantially with regard to improving motor function.

Resources and other considerations

Important issues, or potential issues not investigated

Resources considerations

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

Rationale

Botilinum toxin treatment appears to have substantial benefit for improving spasticity, but it is unclear whether it also improves walking or motor function more generally.

Clinical Question/ PICO

Population: Adults with stroke with lower limb spasticity
Intervention: Botulinum Toxin A
Comparator: Control

Summary

A systematic review of botulinum toxin (BTX) treatments for lower limb spasticity after stroke included 7 randomised trials with 603 total participants (Wu et al 2016 *[51]*). Significant improvements in muscle tone were seen at both 4 week and 12 week follow-ups in meta-analysis (4 weeks: SMD 0.85, 95% CI 0.2 to 1.5, 12 weeks: SMD 0.42, 95% CI 0.07 to 0.77). Participants receiving BTX treatment also had significantly higher Fugl-Meyer scores, however there was no significant

difference in gait speed.

A previous systematic review by McIntyre et al (2012) *[52]* included four trials of BTX-A in patients more than 6 months post stroke. No meta-analysis was conducted but the review authors reported that there was good evidence that BTX-A treatment temporarily relieves lower limb spasticity. They noted that the benefits are likely dosage dependent, with larger improvements generally reported in trials using the highest dosages without an increase in adverse events.

An earlier review by Olvey et al (2010) *[53]* included 54 trials of pharmacologic treatments for spasticity, including 23 randomised trials. 38 trials using BTX treatments reported significant reductions in spasticity. Meta-analysis was not conducted due to the lack of a large number of trials reporting the same outcomes.

Outcome Timeframe	**Study results and measurements**	**Comparator** Control	**Intervention** Botulinum Toxin A	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Adverse events [1] End of follow-up (24 weeks) 9 Critical	Odds ratio 0.82 (CI 95% 0.5 — 1.34) Based on data from 437 participants in 3 studies. [2] (Randomized controlled) Follow up: Up to 24 weeks.	**233** per 1000 Difference:	**199** per 1000 **34 fewer per 1000** (CI 95% 101 fewer — 56 more)	**Moderate** Due to serious risk of bias [3]	Botulinum toxin A probably has little or no difference on adverse events
Gait speed 12 weeks 9 Critical	Measured by: Gait Speed High better Based on data from 1,077 participants in 4 studies. [4] (Randomized controlled) Follow up: 12 weeks.	**0** speed (Mean)	**0.01** speed (Mean) CI 95%	**Moderate** Due to serious risk of bias [5]	Botulinum toxin A probably increases gait speed slightly
Lower limb function 24 weeks 9 Critical	Measured by: Fugl-Meyer score Scale: 0 — 226 High better Based on data from 296 participants in 3 studies. (Randomized controlled) Follow up: 24 weeks.		**3.19** points (Mean) CI 95%	**Moderate** Due to serious imprecision, Due to serious risk of bias, Due to serious imprecision [6]	Botulinum toxin A probably increases lower limb function
Adverse events 12 weeks 9 Critical	Measured by: Recording of Adverse events Lower better Based on data from 437 participants in 3 studies. (Randomized controlled) Follow up: 12 weeks.		**0.82** (Mean) CI 95%	**Moderate** Due to serious risk of bias [7]	Botulinum toxin A probably increases adverse events slightly
Muscle tone 4 weeks after treatment 9 Critical	Measured by: Modified Ashworth Scale, Clinical Spasticity Influx High better Based on data from 263 participants in 4 studies. [8] (Randomized controlled) Follow up: 4 weeks after treatment.	Difference:	points (n/a) **SMD 0.85 higher** (CI 95% 0.2 higher — 1.5 higher)	**Very low** Due to serious risk of bias, Due to serious imprecision, Due to serious publication bias, Due to serious inconsistency [9]	We are uncertain whether Botulinum toxin A increases or decreases muscle tone at 4 weeks
Muscle tone	Measured by: Modified	Difference:	points (n/a)	**Very low**	We are uncertain

Outcome Timeframe	**Study results and measurements**	**Comparator** Control	**Intervention** Botulinum Toxin A	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
12 weeks after treatment 9 Critical	Ashworth Scale, Clinical Spasticity Influx High better Based on data from 263 participants in 4 studies. [10] (Randomized controlled) Follow up: 12 weeks after treatment.		**SMD 0.42 higher** (CI 95% 0.07 higher — 0.77 higher)	Due to serious risk of bias, Due to serious imprecision, Due to serious publication bias, Due to serious inconsistency [11]	whether Botulinum toxin A increases or decreases muscle tone at 12 weeks
Muscle tone 24 weeks after treatment 9 Critical	Measured by: Modified Ashworth Scale, Clinical Spasticity Influx High better Based on data from 68 participants in 1 studies. [12] (Randomized controlled) Follow up: 24 weeks after treatment.	Difference:	**SMD 0.02 higher** (CI 95% 0.46 lower — 0.49 higher)	**Very low** Due to serious risk of bias, Due to serious imprecision, Due to serious publication bias, Due to serious inconsistency [13]	We are uncertain whether Botulinum toxin A increases or decreases muscle tone at 24 weeks
Gait speed 4 to 12 weeks after treatment 9 Critical	Measured by: Gait Speed (m/s) High better Based on data from 381 participants in 4 studies. [14] (Randomized controlled) Follow up: 4 to 12 weeks.	Difference:	**MD 0.01 higher** (CI 95% 0.01 lower — 0.03 higher)	**Moderate** Due to serious risk of bias [15]	Botulinum toxin A probably increases gait speed slightly
Lower limb function 4 to 24 weeks after treatment 9 Critical	Measured by: Fugl-Meyer score High better Based on data from 114 participants in 3 studies. (Randomized controlled) Follow up: 4 to 24 weeks.	Difference:	points (n/a) **MD 3.19 higher** (CI 95% 0.22 higher — 6.16 higher)	**Moderate** Due to serious imprecision [16]	Botulinum toxin A probably increases lower limb function
Muscle tone (MAS) 4-12 weeks 9 Critical	Measured by: Modified Ashworth Scale Scale: 0 — 4 Lower better Based on data from 535 participants in 6 studies. [17] (Randomized controlled) Follow up: 8-16 weeks.		**0.51** points (Mean) CI 95%	**Very low** Due to serious risk of bias, Due to serious imprecision, Due to serious publication bias, Due to serious inconsistency [18]	We are uncertain whether Botulinum toxin A increases or decreases muscle tone (mas)
Muscle tone (CSI) 4-12 weeks 9 Critical	Measured by: Clinical Spasticity Influx High better Based on data from 68 participants in 1 studies. (Randomized controlled) Follow up: 24 weeks.		**0.02** (Mean) CI 95%	**Very low** Due to serious risk of bias, Due to serious inconsistency, Due to serious imprecision, Due to serious publication bias [19]	We are uncertain whether Botulinum toxin A improves or worsen muscle tone (csi)

1. "[D]rug-related adverse events included myalgia, injection site and extremity pain, erythema, convulsions and incoordination" (Wu 2016).
2. Systematic review [51] . **Baseline/comparator:** Control arm of reference used for intervention.
3. **Risk of Bias: serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Incomplete data and/or large loss to follow up. **Inconsistency: no serious.** I^2 = 13%. **Indirectness: no serious. Imprecision: no serious.** Small sample size. **Publication bias: no serious.** Small number of studies.
4. Systematic review [51] . **Baseline/comparator:** Control arm of reference used for intervention.
5. **Risk of Bias: serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Incomplete data and/or large loss to follow up. **Inconsistency: no serious.** I2=55%. **Indirectness: no serious. Imprecision: no serious.** Wide confidence intervals, Low number of patients. **Publication bias: no serious.** Due to small number of studies.
6. **Risk of Bias: no serious.** Variability on doses of botulinum toxin and expertise of people performing the injections., Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Incomplete data and/or large loss to follow up. **Inconsistency: no serious.** I2= 96%. **Indirectness: no serious. Imprecision: serious.** Small sample size might be over estimating effect. **Publication bias: no serious.** Small number of studies available.
7. **Risk of Bias: serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Incomplete data and/or large loss to follow up. **Inconsistency: no serious.** I2= 13%. **Indirectness: no serious. Imprecision: no serious.** Small sample size. **Publication bias: no serious.** Small number of studies.
8. Systematic review [51] . **Baseline/comparator:** Systematic review.
9. **Risk of Bias: serious.** There is no information provided about: Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias. **Inconsistency: serious.** I^2= 81%. **Indirectness: no serious. Imprecision: serious.** Low number of patients. **Publication bias: serious.** Unable to test due to small number of studies (7 only).
10. Systematic review [51] . **Baseline/comparator:** Control arm of reference used for intervention.
11. **Risk of Bias: serious.** There is no information provided about: Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias. **Inconsistency: serious.** I^2= 81%. **Indirectness: no serious. Imprecision: serious.** Low number of patients. **Publication bias: serious.** Unable to test due to small number of studies (7 only).
12. Systematic review [51] . **Baseline/comparator:** Control arm of reference used for intervention.
13. **Risk of Bias: serious.** There is no information provided about: Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias. **Inconsistency: serious.** I^2= 81%. **Indirectness: no serious. Imprecision: serious.** Low number of patients. **Publication bias: serious.** Unable to test due to small number of studies (7 only).
14. Systematic review [51] . **Baseline/comparator:** Control arm of reference used for intervention.
15. **Risk of Bias: serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Incomplete data and/or large loss to follow up. **Inconsistency: no serious.** I2=55%. **Indirectness: no serious. Imprecision: no serious.** Wide confidence intervals, Low number of patients. **Publication bias: no serious.** Due to small number of studies.
16. **Risk of Bias: no serious.** Variability on doses of botulinum toxin and expertise of people performing the injections., Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Incomplete data and/or large loss to follow up. **Inconsistency: no serious.** I2= 96%. **Indirectness: no serious. Imprecision: serious.** Small sample size might be over estimating effect. **Publication bias: no serious.** Small number of studies available.
17. Systematic review [51] . **Baseline/comparator:** Systematic review.
18. **Risk of Bias: serious.** There is no information provided about: Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias. **Inconsistency: serious.** I^2= 52-70%. **Indirectness: no serious. Imprecision: serious.** Low number of patients. **Publication bias: serious.** Unable to test due to small number of studies (7 only).
19. **Risk of Bias: serious.** No information on:, Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/

lack of blinding of outcome assessors, resulting in potential for detection bias, Missing intention-to-treat analysis. **Inconsistency: no serious.** I^2=38%. **Indirectness: no serious. Imprecision: serious.** Wide confidence intervals, Low number of patients. **Publication bias: serious.** Only 1 study.

Attached Images

Weak recommendation against

For stroke survivors with spasticity, acupuncture should not be used for treatment of spasticity in routine practice other than as part of a research study. (Lim et al 2015 *[54]*)

Evidence To Decision

Benefits and harms

Small net benefit, or little difference between alternatives

Improvements in spasticity were reported following acupuncture and electroacupuncture, but the improvement may not be large enough to be clinically significant (Lim et al 2015 *[54]*). This improvement appeared to be greater for electroacupuncture than for standard acupuncture therapy.

Certainty of the Evidence

Very low

The quality of evidence was very low overall, with high risk of bias due to lack of blinding and allocation concealment.

Values and preferences

Substantial variability is expected or uncertain

The majority of studies were from Asian patient populations. Australian patients may differ with regard to their preferences for acupuncture.

Resources and other considerations

Important issues, or potential issues not investigated

Resources considerations

No literature to understand or describe the potential economic implications of this recommendation was identified. Acupuncture is only available through Medicare if delivered by a registered health care professional, otherwise patients may have to pay for private treatment.

Rationale

While benefits have been reported for acupuncture treatments, the quality of evidence is very low and inlcudes lack of blinding.

Clinical Question/ PICO

Population: Adults with stroke with spasticity
Intervention: Acupuncture
Comparator: Control

Summary

A systematic review by Lim et al (2015) *[54]* included 5 randomised trials of acupuncture or electroacupuncture for treating post-stroke spasticity. Meta-analysis showed significant improvement on the Modified Ashworth Scale, with

electroacupuncture appearing to show greater effects. Most of the included studies were of low quality, with a lack of blinding of participants and personnel representing a particular concern. The total number of trials and participants was also small, suggesting serious imprecision in the effect estimates.

A previous systematic review (Park et al 2014 *[55]*) showed less positive results. 8 randomised trials of acupuncture for treatment of spasticity were included, and while 2 studies overlapped with those in the Lim et al. review it is unclear why the remaining 6 were not included in the Lim review. Meta-analysis showed no significant differences between acupuncture and control groups on the modified Ashworth Scale for either upper or lower extremities. The review authors concluded that the effect of acupuncture was uncertain due to the lack of clear differences on clinical outcomes and the low quality of the included studies.

A subsequent single-blind randomised trial (N = 238) comparing acupuncture with "Deqi" to sham acupuncture reported significant improvements in modified Rankin, Barthel Index, Fugl-Meyer and Modified Ashworth Scale scores following verum acupuncture (Li et al 2014 *[56]*).

Outcome Timeframe	**Study results and measurements**	**Comparator** Control	**Intervention** Acupuncture	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Spasticity Post intervention 9 Critical	Measured by: Improvment on Modified Ashworth Scale High better Based on data from 268 participants in 5 studies. [1] (Randomized controlled) Follow up: Not speficied.	Difference:	**MD 0.72 higher** (CI 95% 0.29 higher — 1.14 higher)	Very low Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision [2]	We are uncertain whether acupuncture increases or decreases spasticity

1. Systematic review [54] . **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of Bias: serious.** Only 2 studies had low risk of bias in regards to sequence generation. Unclear concealment of allocation in 4 studies; 1 study had low risk of bias with concealment of allocation., Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias in 4 studies, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias in 3 studies. **Inconsistency: no serious.** I^2=89%. **Indirectness: serious.** Differences between the population of interest and those studied. **Imprecision: serious.** Low number of patients. **Publication bias: no serious.** Small number of studies.

Attached Images

Weak recommendation

For stroke survivors with spasticity, adjunct therapies to Botulinum Toxin A, such as electrical stimulation, casting and taping, may be used. (Stein et al 2015 *[57]*; Mills et al 2016 *[63]*; Santamato et al 2015 *[64]*)

Practical Info

Therapies such as casting, taping and electrical stimulation, may be used in conjunction with botulinum toxin in the management of spasticity, but the optimum treatment parameters for these interventions are unknown. Careful assessment of the effectiveness of the interventions on outcomes should be included if these therapies are used.

Evidence To Decision

Benefits and harms

Small net benefit, or little difference between alternatives

There is low to very low quality evidence (from a limited number of small trials) that electrical stimulation, taping or casting as adjunct therapies to botulinum toxin may improve spasticity outcomes. The evidence was mixed and these improvements were generally not consistent across trials.

Certainty of the Evidence

Very low

Quality of evidence was very low. Seventeen small randomised controlled trials using 10 different adjunct therapies (Mills et al 2016 *[63]*). Substantial heterogeneity of methods that meant that meta-analysis could not be conducted. Author's claim that using Sackett's level of evidence, there is Level 1 evidence for electrical stimulation and Level 2 evidence for casting improving Modified Ashworth Scale scores. One recent randomised controlled trial (Santamato et al 2015 *[64]*) suggesting significantly greater improvements in spasticity (MAS) and disability (Disability Assessment Scale) scores at 1 month with adhesive taping compared to daily muscle stretching (70 patients only).

Values and preferences

No substantial variability expected

Patients are not expected to vary substantially with regard to their desire to reduce spasticity.

Resources and other considerations

Important issues, or potential issues not investigated

Resources considerations

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

Rationale

Evidence for the benefits of any particular adjunct therapy is very limited. There is only weak evidence for the potential benefit of electical stimulation, casting and taping and insufficient evidence to draw conclusions about other adjunctive therapies.

Clinical Question/ PICO

Population: Adults with stroke with spasticity
Intervention: Neuromuscular electric stimulation
Comparator: Control

Summary

A systematic review of neuromuscular electric stimulation (NMES) trials for patients with spasticity after stroke included 29 randomised trials with 940 total participants (Stein et al 2015 *[57]*). Meta-analysis showed significant reductions in spasticity (Modified Ashworth Scale) following NMES treatment (MD -0.3, 95% CI -0.58 to -0.03), and a small but significant increase in range of motion (MD 2.87, 95% CI 1.18 to 4.56). However, most trials showed a serious risk of bias due to a lack of proper blinding and allocation concealment, creating considerable uncertainty about the expected benefits of the treatment.

Related interventions for treating spasticity investigated in recent randomised controlled trials include:

- Repetitive peripheral magnetic stimulation (Krewer et al 2014 *[58]*)
- Repetitive transcranial magnetic stimulation (Etoh et al 2015 *[59]*)
- Transcranial direct current stimulation (Ochi et al 2013 *[60]*; Wu et al 2013 *[61]*)
- Electrical stimulation combined with passive locomotion-like movement (Yamaguchi et al 2012 *[62]*)

These trials were generally small (N's < 50) and were often not powered to detect differences between intervention and control groups. As such, they provided limited evidence for the benefits of specific treatment methods.

Outcome Timeframe	**Study results and measurements**	**Comparator** Control	**Intervention** Neuromuscular electric stimulation	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Spasticity (MAS) Post intervention: 3-16 weeks of treatment 9 Critical	Measured by: Modified Ashworth Scale Scale: 0 — 5 Lower better Based on data from 383 participants in 14 studies. [1] (Randomized controlled) Follow up: 3-16 weeks.	Difference:	**MD 0.3 lower** (CI 95% 0.58 lower — 0.03 lower)	**Very low** Due to serious risk of bias, Due to serious publication bias, Due to serious imprecision [2]	We are uncertain whether neuromuscular electric stimulation increases or decreases spasticity
Range of motion [3] Post intervention: 3-16 weeks of treatment 9 Critical	Measured by: Gomiometer (degress) High better Based on data from 447 participants in 13 studies. [4] (Randomized controlled) Follow up: 3-16 weeks.	Difference:	**MD 2.87 higher** (CI 95% 1.18 higher — 4.56 higher)	**Low** Due to serious publication bias, Due to serious imprecision [5]	Neuromuscular electric stimulation may have little or no difference on range of motion

1. Systematic review [57] . **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of Bias: serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias in 11 studies, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias in 11 studies, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias in 5 sutdies, Missing intention-to-treat analysis in 10 studies. **Inconsistency: no serious.** I^2= 81%. **Indirectness: no serious. Imprecision: serious.** Low number of patients. **Publication bias: serious.** due to small sample size.
3. Evaluated with use of Goniometer in 13 trials
4. Systematic review [57] . **Baseline/comparator:** Control arm of reference used for intervention.
5. **Inconsistency: no serious.** I^2= 60%. **Indirectness: no serious. Imprecision: serious.** Low number of patients. **Publication bias: serious.** due to small sample size.

Attached Images

Clinical Question/ PICO

Population: Adults with stroke with spasticity
Intervention: Adjunct therapies to Botox
Comparator: Control

Summary

Mills et al (2016) *[63]* assessed adjunct therapies following botulinum toxin injections for limb spasticity in a systematic review. 17 randomised controlled trials were included, using 10 different adjunct therapies including electrical stimulation, taping and casting. Meta-analysis was not performed as treatment methods (e.g. dosage, timing, duration) varied too much for studies to be comparable. There is low to very low quality evidence that electrical stimulation, taping and casting may improve the effects of botulinum toxin on spasticity outcomes.

A recent randomised trial not included in the systematic review (Santamato et al 2015 *[64]*) compared adhesive taping to daily muscle stretching as adjunct therapies following botulinum toxin injection. The adhesive taping group had significantly greater improvements in spasticity (Modified Ashworth) and disability (Disability Assessment Scale) scores at one month.

Outcome Timeframe	**Study results and measurements**	**Comparator** Control	**Intervention** Adjunct therapies to Botox	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Spasticity - electrical stimulation End of treatment 7 Critical	Based on data from participants in 4 studies. [1] (Randomized controlled) Follow up: Up to 12 weeks of treatment.	Out of 4 small RCTs, some significant improvements were reported in spasticity following addition of electrical stimulation to botox treatment. No significant differences were found in activity outcomes. Treatment methods were considered too heterogenous to conduct meta-analysis.		**Very low** Due to serious risk of bias, Due to serious inconsistency, Due to serious imprecision [2]	We are uncertain whether electrical stimulation as an adjunct to botox improves or worsens spasticity related outcomes
Spasticity - taping End of treatment 7 Critical	Based on data from participants in 4 studies. [3] (Randomized controlled) Follow up: 1 to 3 weeks of treatment.	4 small RCTs, of moderate to high quality, found some improvements in spasticity (modified Ashworth) and passive range of motion when compared to sham taping, stretching or botox alone. Gait parameters only showed significant improvement in one trial. No meta-analysis was done due to heterogeneity of treatments.		**Low** Due to serious imprecision, consistency unknown due to lack of meta-analysis [4]	Taping post-botox injection may improve spasticity related outcomes
Spasticity - casting End of treatment 7 Critical	Based on data from participants in 1 studies. (Randomized controlled) Follow up: 4 months of treatment.	1 small moderate quality RCT found improvements in spasticity (modified Ashworth Scale) following casting, but no improvement on the 10-metre walking test.		**Very low** Due to serious risk of bias, Due to serious inconsistency, Due to serious imprecision [5]	We are uncertain whether casting as an adjunct to botox improves or worsens spasticity related outcomes

1. Systematic review [63].
2. **Risk of Bias: serious.** Most studies did not report blinding. **Inconsistency: serious.** Meta-analysis not possible due to heterogeneity of treatments and study methods. **Indirectness: no serious. Imprecision: serious.** Low number of patients, no meta-analysis so range of effects hard to determine. **Publication bias: no serious.**
3. Systematic review [63].
4. **Inconsistency: serious.** Can't determine consistency due to lack of meta-analysis. **Indirectness: no serious. Imprecision: serious.** Low number of patients. **Publication bias: no serious.**
5. **Risk of Bias: serious.** Study described as lower quality/level 2. **Inconsistency: serious.** Consistency unknown due to single study. **Indirectness: no serious. Imprecision: serious.** Only data from one study, Low number of patients. **Publication bias: no serious.**

Attached Images

Weak recommendation against

For stroke survivors, the routine use of stretch to reduce spasticity is not recommended. (Harvey et al 2017 *[76]*)

Practical Info

Stretch is defined as any mechanical elongation of soft tissues for varying length of times (Katalinic et al 2010 *[65]*). There is moderate to strong evidence that stretching interventions (including splinting, prolonged positioning, serial casting and passively applied stretch) have no effect on spasticity or joint mobility. The only uncertainty is in the interpretation of a clinically meaningful effect of joint range of movement. Experts differ as to whether a 5 or 10 degree improvement in joint range is considered clinically meaningful (Katalinic et al 2010 *[65]*). If a 5 degree difference is considered clinically meaningful, there is some uncertainty in the

immediate effects of stretch on joint mobility as the upper limit of the 95% confidence interval crosses this value (mean difference 3 degrees, 95% CI 0 to 7 degrees), but there is no uncertainty in the effect over the short to long term (mean difference 1 degree, 95% CI 0 to 3 degrees). No trials have investigated stretch interventions lasting longer than 7 months. Therefore, stretch interventions should not be routinely used for the treatment of spasticity. Where patients have voluntary movement, interventions should focus on active motor training. In the absence of voluntary movement, interventions such as electrical stimulation should be considered (see Upper Limb Activity section in the ***Rehabilitation Chapter***).

Evidence To Decision

Benefits and harms

Small net benefit, or little difference between alternatives

Stretch interventions including splinting, serial casting, prolonged positioning and sustained passive stretching have no clinically meaningful effect on spasticity immediately post-intervention or in the short to long term (24 hours to 1 week later). There was no evidence that any type of stretch intervention was superior to another, or that the length of time stretch was applied (total cummulative stretch durations ranged from 23 minutes to 1,512 hours) affected results. The maximum amount of time an intervention was applied for was 7 months. There is no evidence about the effectiveness of stretch applied for periods longer than 7 months. There was little evidence that stretching increased pain or caused harm.

Certainty of the Evidence

Low

The evidence for stretch interventions for treating spasticity comes from a small number of studies with small sample sizes, so the effect estimates have high uncertainty.
Not all trials were stroke-specific, however, subgroup analyses were conducted using stroke data. Meta-analysis showed non-significant differences in spasticity and joint mobility outcomes.

Values and preferences

No substantial variability expected

Patients are not expected to differ substantially in their desire to reduce spasticity.

Resources and other considerations

Factor not considered

Rationale

There is moderate to strong evidence that stretch interventions, regardless of type of intervention (therapist applied stretch, prolonged positioning, casting or splinting) has no effect on either joint mobiilty or spasticity outcomes either immediately post intervention or 24 hours to 1 week later (Harvey et al 2017 *[76]*). The estimated effect of stretch on spasticity and joint mobility was too small to be clinically meaningful (eg 1 to 3 degrees of joint range or 0.1 SD difference in measures of spasiticity) and not statistically significant. There is evidence that neither length of intervention (cummulative stretch time provided in the trials ranged from 23 minutes to 1,512 hours) or size of joint (small versus large joints) had any bearing on outcome. The interventions in the trials were applied for between 2 days and 7 months. No trials have investigated the effectiveness of stretch interventions for greater than 7 months.

Clinical Question/ PICO

Population: Adults with stroke with spasticity
Intervention: Stretch
Comparator: Control

Summary

A Cochrane review by Katalinic et al (2010) *[65]* included 35 trials (1391 participants) of stretch interventions for treating people with contractures, 24 trials (782 participants) involving people with neurological conditions. Results of sub-group analyses involving participants with neurological conditions showed moderate evidence of no effect of stretch interventions on joint mobility or spasticity immediately post-intervention and strong evidence of no effect in the short to long term (24 hours to one week post-intervention). With regards to spastiicty specifically, the pooled standard mean difference was 0.1

SD (95% CI -0.3 to 0.5) for immediate effects and -0.3 SD (95% CI -0.9 to 0.4) for long-term effects.

Two subsequent randomised trials by Kim et al (2013) *[66]* and Jung et al (2011) *[67]* assessed the effects of a hand-stretching device (consisting of "a resting hand splint, a finger and thumb stretcher, and a frame") for managing hand spasticity in chronic stroke patients (Ns = 15 and 21 respectively). Modified Ashworth Scale scores were significantly lower in the intervention group after treatment in both trials. However, as small randomised trials from the same research group, the studies provide only limited evidence for the effectiveness of the hand-stretching device.

Outcome Timeframe	**Study results and measurements**	**Comparator** Control	**Intervention** Stretch	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Spasticity - immediate effects Post intervention 9 Critical	Measured by: Various - Tardieu scale, modified Ashworth Lower better Based on data from 109 participants in 4 studies. [1] (Randomized controlled) Follow up: Post-intervention.	Difference:	**SMD 0.08 higher** (CI 95% 0.3 lower — 0.45 higher)	**Moderate** Due to serious imprecision [2]	Stretch probably has little or no difference on spasticity immediately after treatment
Spasticity - long term > 1 week after intervention 9 Critical	Measured by: Various - Tardieu scale, modified Ashworth Lower better Based on data from 42 participants in 1 studies. [3] (Randomized controlled) Follow up: 2 weeks after intervention.	Difference:	**SMD 0.5 lower** (CI 95% 1.12 lower — 0.11 higher)	**Low** Due to very serious imprecision [4]	Stretch may decrease spasticity in the long term

1. Systematic review [65] with included studies: de Jong 2006, Burge 2008, Lannin 2007, Lai 2009. **Baseline/comparator:** Control arm of reference used for intervention.
2. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Wide confidence intervals - covers small to medium effects in both directions. **Publication bias: no serious.**
3. Systematic review [65] with included studies: Lannin 2007, Burge 2008, Lai 2009, de Jong 2006. **Baseline/comparator:** Control arm of reference used for intervention.
4. **Inconsistency: no serious. Indirectness: no serious. Imprecision: very serious.** Low number of patients, Wide confidence intervals, Only data from one study. **Publication bias: no serious.**

Attached Images

Contracture

Contracture is a shortening of soft tissues that results in reduced joint range of motion (ROM) due to impairments (e.g. weakness or spasticity). Particularly common is loss of shoulder external rotation, elbow extension, forearm supination, wrist and finger extension, ankle dorsiflexion and hip internal rotation. People with severe weakness are particularly at risk of developing contractures as any joint or muscle not moved or lengthened regularly is at risk of soft tissue complications which eventually may limit movement and may cause pain. Although it is considered that soft tissues must be lengthened to prevent contracture, the most appropriate intervention to prevent or manage contracture is currently unclear with expert opinion divided. National Stroke Audits report rates of contracture as low as 1% during inpatient rehabilitation (Stroke Foundation 2020 *[7]*).

Strong recommendation against

For stroke survivors at risk of developing contracture who are receiving comprehensive, active therapy the routine use of splints or stretch of the arm or leg muscles is not recommended. (Harvey et al 2017 *[76]*)

Practical Info

The research is sufficiently robust to indicate that stretch or splints should not be used routinely within a rehabilitation program for prevention or treatment of contracture. Where patients have voluntary movement, interventions should focus on active motor training. In the absence of voluntary movement, interventions such as electrical stimulation should be considered (see Upper Limb Activity section in Chapter 5 Rehabilitation). There is insufficient evidence for the use of stretch to address joint mobility impairments in people who are not receiving any other rehabilitation interventions, and for stretch applied >7 months duration. Clinical reasoning is therefore recommended when working in these situations.

Evidence To Decision

Benefits and harms

Small net benefit, or little difference between alternatives

When provided in addition to comprehensive, active therapy, stretch had little or no effect on joint mobility, pain or activity limitation (Harvey et al 2017 *[76]*).

Certainty of the Evidence

High

High certianty for joint mobility when provided to people who are receiving active therapy, but low certainty for pain and activity limitations, or when applied to people who recieve no other interventions.

Values and preferences

No substantial variability expected

As there is little benefit, most patients would not want the discomfort and inconvenience of this treatment.

Resources and other considerations

Important issues, or potential issues not investigated

Stretch can be administered with splints and stretching programs, or with casts, which are changed at regular intervals. Resources for splinting and casting are modest, and very low for stretching programs. However, given the lack of benefit in addition to usual care, resources would be better used for interventions with evidence of benefit.

Rationale

There is moderate to strong evidence that stretch (including splinting and stretching programs) have no effect on either preventing or treating contracture in people with stroke in either the short-term i.e. measured within 1 week after the intervention (MD 1 degree 95%CI -2 to 3 degrees; 11 studies, n=295) or long-term i.e. measured more than 1 week after a period of non-intervention (MD 0 degrees 95%CI -4 to 3 degrees; 4 studies, n=134). The quality of evidence was moderate to high for these outcomes in people who are receiving an active rehabilitation program. There was no difference found for pain, or activity limitations based on low quality evidence. Many studies were conducted in Australia and most compared stretch plus conventional therapy compared to conventional therapy alone. (Harvey et al 2017 *[76]*).

Clinical Question/ PICO

Population: Adults with stroke
Intervention: Stretch plus usual care
Comparator: Usual care

Summary

Harvey et al (2017)*[76]* updated the Cochrane review and included 49 studies (n=2135) of various forms of stretching applied in addition to routine, active therapy. Interventions included passive stretching (self-administered, therapist-administered and device-administered), positioning, splinting and serial casting. The stretch dosage was highly variable, ranging from five minutes to 24 hours per day (median 420 minutes, IQR 38 to 600) for between two days and seven months (median 35 days, IQR 23 to 84). The total cumulative time that stretch was administered ranged from 23 minutes to 1456 hours (median 168 hours, IQR 24 to 672). Data pooled for the subgroup specific to people with stroke (13 studies) was used and is reported here. Many studies were conducted in Australia and most compared stretch plus conventional therapy compared to conventional therapy alone. There is moderate to strong evidence that stretch interventions including splinting and prolonged positioning has no effect on either preventing or treating contracture in either the short-term i.e. measured within 1 week of the end of treatment (MD 1 degree 95%CI -2 to 3; 11 studies, n=295) or long-term i.e. measured more than 1 week after the end of treatment (MD 0 degrees 95%CI -4 to 3; 4 studies, n=134). The quality of evidence was moderate to high for these outcomes. There were no differences found on reported pain or ADL performance based on low quality evidence.

Outcome Timeframe	**Study results and measurements**	**Comparator** Usual care	**Intervention** Stretch	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Joint mobility (short term) measured within 1 week of final treatment 8 Critical	Measured by: ROM (degrees) Scale: 0 — 135 High better Based on data from 295 participants in 11 studies. [1] (Randomized controlled) Follow up: < 1 week.	Difference:	**MD 1 higher** (CI 95% 2 lower — 3 higher)	**High**	Immediately after intervention, stretch probably has little or no difference on joint mobility when added to a comprehensive rehabilitation program
Joint mobility (long term) measured after a period of non-intervention 7 Critical	Measured by: ROM (degrees) High better Based on data from 134 participants in 4 studies. (Randomized controlled) Follow up: > 1 week.	Difference:	**MD 0 lower** (CI 95% 4 lower — 3 higher)	**Moderate** Due to serious imprecision [2]	Beyond the intervention, stretch probably has little or no difference on joint mobility when added to a comprehensive rehabilitation program
Pain (short-term) measured within 1 week of final treatment 8 Critical	Measured by: Visual Analogue Scale Scale: 0 — 10 Lower better Based on data from 135 participants in 4 studies. [3] (Randomized controlled) Follow up: <7 days.	Difference:	**SMD 0.31 higher** (CI 95% 0.03 lower — 0.66 higher)	**Low** Due to serious imprecision, indirectness and risk of bias	Stretch probably has little or no difference on pain (short-term)
Pain (long-term) measured after a period of non-intervention	Measured by: Visual Analogue Scale Lower better Based on data from 132	Difference:	**SMD 0.03 higher** (CI 95% 0.41 lower — 0.47 higher)	**Low** Due to serious imprecision, indirectness and	Stretch probably has little or no difference on pain (long-term)

Outcome Timeframe	**Study results and measurements**	**Comparator** Usual care	**Intervention** Stretch	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
8 Critical	participants in 4 studies. (Randomized controlled) Follow up: > 1 week.			risk of bias	
Activity limitation (short-term) measured within 1 week of final treatment 8 Critical	Measured by: Various measures e.g. Functional Independence Measure 0 — High better Based on data from 170 participants in 5 studies. [4] (Randomized controlled) Follow up: <7 days.	Difference:	**SMD 0.27 higher** (CI 95% 0.09 lower — 0.63 higher)	**Low** Due to serious imprecision, indirectness and risk of bias	Stretch probably has little or no difference on activity limitations
Activity limitation (long-term) [5] measured after a period of non-intervention 8 Critical	Measured by: Various measures High better Based on data from 136 participants in 4 studies. (Randomized controlled) Follow up: > 1 week.	Difference:	**SMD 0.14 higher** (CI 95% 0.29 lower — 0.58 higher)	**Low** Due to serious imprecision, indirectness and risk of bias	Stretch probably has little or no difference on activity limitation

1. Systematic review [77] with included studies: Ada 2005, Horsley 2007, Harvey 2006, Lai 2009, Gustafsson 2006, Dean 2000, De Jong 2006, Turton 2005, Basaran 2012, Lannin 2003a, Lannin 2007a. **Baseline/comparator:** Control arm of reference used for intervention. **Supporting references:** [76],
2. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Low number of patients. **Publication bias: no serious.**
3. Systematic review. **Baseline/comparator:** Control arm of reference used for intervention. **Supporting references:** [76],
4. Systematic review. **Baseline/comparator:** Control arm of reference used for intervention. **Supporting references:** [76],
5. e.g. Functional Independence Measure

Attached Images

Good practice statement

Consensus-based recommendations

- For stroke survivors, serial casting may be trialled to reduce severe, persistent contracture when conventional therapy has failed.
- For stroke survivors at risk of developing contracture or who have developed contracture, active motor training or electrical stimulation to elicit muscle activity should be provided.

Subluxation

Shoulder subluxation is reported to occur in 4% of stroke survivors on admission (Stroke Foundation 2019 *[9]*). Subluxation commonly occurs along with shoulder pain (see Shoulder pain). Management of subluxation consists of strategies to prevent it worsening. Interventions aimed at reducing trauma to the shoulder, such as educating all staff, carers and stroke survivors, should prevent the occurrence of shoulder subluxation and pain resulting from weakness. Such education may include strategies to care for the shoulder during manual handling and transfers and advice regarding positioning. Interventions could include active rehabilitation to elicit muscle activity around the shoulder.

Weak recommendation

For stroke survivors at risk of shoulder subluxation, electrical stimulation may be used in the first six months after stroke to prevent or reduce subluxation. (Vafadar et al 2015 *[80]*; Lee et al 2017 *[83]*)

Practical Info

Health professionals should have training and be familiar with the correct dosages of Electrical Stimulation (ES) to apply in order to achieve optimal muscle activation. Health professionals should consider the patient's capacity to self monitor the device, and ensure appropriate measures are in place to maximize safety whether through training and education of other staff, or patient's family, friends and caregivers.

Beyond the requirement for stimulation parameters to ensure muscular activation, there is currently no consensus on the optimal stimulation parameters to use. Similarly there is uncertainty as to the optimal duration of treatment, and little evidence to guide how long the treatment should be provided for in the absence of return of voluntary muscle activation. Studies have provided intervention between 4 to 6 weeks (Vafadar et al 2015 *[80]*). Once there is return of voluntary movement, interventions should then focus on improving weakness (see the topic Weakness in the ***Rehabilitation chapter***).

Evidence To Decision

Benefits and harms

Small net benefit, or little difference between alternatives

Electrical stimulation (ES) decreased shoulder subluxation early after stroke but not late (Vafadar et al 2015 *[80]*; Lee et al 2017 *[83]*). No harm is reported (Vafadar et al 2015 *[80]*).

Certainty of the Evidence

Moderate

Overall the quality of evidence is rated as moderate, however, there are aspects which are deemed very low (subluxation within 6 months and pain greater than 6 months).

Values and preferences

Substantial variability is expected or uncertain

Some patients may have a negative perception of electrical stimulation, especially when its benefits are not clear.

Resources and other considerations

Important issues, or potential issues not investigated

Resources considerations

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

Rationale

Electrical stimulation (ES) decreased shoulder subluxation early after stroke but not in the later stages (greater than 6 months). There were no benefits from ES in reducing shoulder pain or pain generally. While the evidence is not clear, there were no harms reported. The overall quality of the evidence was moderate to low. The small amount of data available on late treatment means there is considerable uncertainty regarding the possible benefit of ES late after stroke. Most trials also only assessed outcomes up to the end of the treatment period, so it is unclear whether the benefits of ES persist. For other outcomes such as health related

quality of life and pain, meta-analysis was not possible as too few studies reported the outcomes.

Clinical Question/ PICO

Population: Adults with stroke
Intervention: Electrical stimulation
Comparator: Conventional therapy

Summary

Vafadar et al (2015) *[80]* included 10 trials of electrical stimulation (ES) for preventing or improving upper arm impairment following stroke in a systematic review. In all included trials, control groups received conventional physical or occupational therapy, and intervention groups received the same treatment plus ES. Meta-analysis of data from 213 patients in 6 trials showed significant improvements in shoulder subluxation when ES was applied within 6 months of stroke (MD 4.9mm, 95% CI 3.3 to 6.6). However, data from 41 patients in 2 trials where ES was applied more than 6 months after stroke showed no significant improvement in subluxation. The small amount of data available on late treatment means there is considerable uncertainty regarding the possible benefit of ES late after stroke. Most trials also only assessed outcomes up to the end of the treatment period, so it is unclear whether the benefits of ES persist.

Lee at al. (2017) *[83]* evaluated the effectiveness of neuromuscular ES for the management of shoulder subluxation after stroke. The review identified 11 RCTs (n=432). ES significantly reduced subluxation for persons with acute and subacute stroke (SMD−1.11; 95% CI −1.53, to −0.68). However, the effect for patients with chronic stroke was not significant (SMD−1.25; 95% CI −2.60 to 0.11).

A systematic review by Arya et al. (2018) *[82]* assessed the rehabilitation methods for reducing shoulder subluxation in post-stroke hemiparesis. Experimental, quasi-experimental, and single group study designs were considered. The review finally included 22 studies (14 RCTs or controlled trials and 8 pre-post-single group studies). No meta-analysis was conducted and the results were reported narratively. The authors determined that functional functional ES is effective in reducing subluxation in acute stage and had negligible adverse effects based on 11 studies. However, the studies were heterogenious and no uniformity with regard to dosage, frequency, intensity, subject's position, and time duration of the stimulation found.

An additional small study (n=20) by Jeon et al (2017)*[86]* reported electromyography triggered stimulation for 30 minutes, five times a week for four weeks in addition to conventional therapy reduced subluxation and pain more than same dose of functional electrical stimulation and conventional therapy.

Outcome Timeframe	**Study results and measurements**	**Comparator** Conventional therapy	**Intervention** Electrical stimulation	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Shoulder subluxation (early: < 6 months after stroke) [1] 6 weeks of treatment 7 Critical	Measured by: X-ray assessment of subluxation (in mm) Lower better Based on data from 213 participants in 6 studies. [2] (Randomized controlled) Follow up: 4 to 6 weeks of treatment.	Difference:	**MD 4.9 lower** (CI 95% 3.3 lower — 6.6 lower)	**Moderate** Due to risk of bias, Due to inconsistency, Due to indirectness, Due to imprecision [3]	Electrical stimulation probably decreases shoulder subluxation early after stroke
Shoulder subluxation (late: > 6 months after stroke) 6 weeks of treatment 7 Critical	Measured by: X-ray assessment of subluxation Lower better Based on data from 41 participants in 2 studies. [4] (Randomized controlled) Follow up: 6 weeks of treatment.	Difference:	**SMD 0.42 lower** (CI 95% 1.04 lower — 0.21 higher)	**Low** Due to serious imprecision. The systematic review reports the risk of bias as 1a and 2a for the studies included in the meta analysis. [5]	It is uncertain if electrical stimulation reduces subluxation late after stroke, with only 2 trials of small numbers with unclear risk of bias due to insufficient information reported in the systematic review.

Outcome Timeframe	**Study results and measurements**	**Comparator** Conventional therapy	**Intervention** Electrical stimulation	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Motor function (early: < 6 months after stroke) Post treatment: (4-6 weeks) 7 Critical	Measured by: Various - MAS, ARAT, Frenchy, Motricity Index, Chedoke, Brunstromm High better Based on data from 295 participants in 5 studies. [6] (Randomized controlled) Follow up: 4-6 weeks of treatment.	Difference:	**SMD 0.36 higher** (CI 95% 0.27 lower — 0.99 higher)	**Moderate** Due to serious inconsistency, Due to serious indirectness. Note however quality assessment reported in SR reported 1a evidence for 3 good quality RCTs and level 2a evidence from two fair quality RCTs [7]	Electrical stimulation is likely to be no more effective for improving motor function than conventional therapy alone.

1. degree of shoulder subluxation alone is a less important outcome than pain or function
2. Systematic review [80] . **Baseline/comparator:** Control arm of reference used for intervention.
3. **Risk of Bias: serious.** review states evidence comes from 1 good quality RCT and 5 fair quality RCTs. **Inconsistency: no serious.** Point estimates vary widely, The magnitude of statistical heterogeneity was medium to high, with I^2: 46 %.. **Indirectness: no serious. Imprecision: serious.** Wide confidence intervals. **Publication bias: no serious.**
4. Systematic review [80] . **Baseline/comparator:** Control arm of reference used for intervention. Overal p = 0.19 from two fairly good quality RCTs.
5. **Imprecision: serious.** Low number of patients. n = 32 and 44 for the 2 studies..
6. Systematic review [80] . **Baseline/comparator:** Control arm of reference used for intervention.
7. **Inconsistency: no serious.** I^2 = 80%. **Indirectness: serious.** Outcome different for each study and pooled for meta analysis via a percentage calculation.. **Imprecision: no serious. Publication bias: no serious.**

Attached Images

Weak recommendation against

For stroke survivors at risk of shoulder subluxation, shoulder strapping is not recommended to prevent or reduce subluxation. (Appel et al 2014 *[79]*)

Evidence To Decision

Benefits and harms

Small net benefit, or little difference between alternatives

There is uncertainty around the benefits of strapping (Appel et al 2014 *[79]*). There are only minor harms in a small number of patients (5%) such as minor skin irritation (Appel et al 2014 *[79]*).

Certainty of the Evidence

Very low

The overall quality of evidence is very low based on eight studies.

Values and preferences

Substantial variability is expected or uncertain

Cultural values due to accessing skin to apply strapping should be considered.

Resources and other considerations

Factor not considered

Rationale

It is uncertain if strapping is beneficial to prevent or manage shoulder subluxation based on eight trials (N=340 patients). Strapping can lead to minor skin irritation in a small number (5%) of patients. Further robust trials are needed before it can be recommended routinely in clinical practice.

Clinical Question/ PICO

Population: Adults with stroke
Intervention: Shoulder strapping
Comparator: No strapping

Summary

A systematic review by Appel et al (2014) *[79]* included 8 trials of shoulder strapping interventions for reducing stroke-related upper limb impairments. 5 of the trials were randomised or quasi-randomised trials while the remaining 3 were case series or case studies. Meta-analysis of 3 studies reporting Motor Assessment Scale scores showed non-significant improvements in upper limb function in shoulder strapping groups. For other outcomes such as health related quality of life and pain, meta-analysis was not possible as too few studies reported the outcomes. The review authors concluded there was insufficient evidence of efficacy to recommend routine strapping as a treatment for shoulder paralysis.

Ravichandran et al (2019)*[101]* included 8 randomised studies (n=132) of strapping to reduce subluxation or pain. Three small studies included measures of subluxation with 2/3 reporting a reduction in subluxation with strapping.

An additional RCT by Comley-White et al (2018)*[78]* found only a non-significant trend in reduced subluxation with longitudinal strapping.

Outcome Timeframe	**Study results and measurements**	**Comparator**	**Intervention**	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Health related quality of life (HRQoL) 13-15 weeks 7 Critical	Measured by: Stroke Specific Quality of Life Scale High better Based on data from 12 participants in 1 studies. [1] (Randomized controlled) Follow up: 13-15 weeks.	**2.9** points (Mean) Difference:	**3.44** points (Mean) **MD 0.54 higher** (CI 95% 1.29 lower — 2.37 higher)	**Very low** Due to very serious imprecision due to low participant numbers (n=12) (NB:chose to downgrade to very low certainty) [2]	We are uncertain whether strapping improves or worsens health related quality of life (HRQoL)
Upper Limb Function [3] 3 to 6 weeks post intervention 7 Critical	Measured by: Motor Assessment Scale upper limb items Scale: 3 — 18 High better Based on data from 117 participants in 3 studies. [4] (Randomized controlled) Follow up: 4 to 14 weeks.	Difference:	**MD 0.87 higher** (CI 95% 0.07 lower — 1.81 higher)	**Very low** Due to serious indirectness, Due to very serious imprecision. The direct influence of strapping on upper limb function outcome is also questionable. The measured improvements in upper limb function could be due to factors other than	We are uncertain whether strapping improves or worsen upper limb function

Outcome Timeframe	**Study results and measurements**	**Comparator**	**Intervention**	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
				strapping - eg motor rehabilitation provided [5]	

1. Systematic review [79] . **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of Bias: no serious.** The systematic review process included a process by which data was pooled only for studies with adequate review. **Inconsistency: no serious. Indirectness: no serious. Imprecision: very serious.** Low number of patients. **Publication bias: no serious.**
3. Three randomised controlled trials measured upper limb function using the Motor Assessment Scale for Stroke, upper limb items. This outcome was measured at different time points for each of the studies, ranging from one to 14 weeks post-randomisation. A meta-analysis was included in the review, but it is not clear what time points the data were taken from in each study.
4. Systematic review [79] . **Baseline/comparator:** Control arm of reference used for intervention.
5. **Risk of Bias: no serious.** Blinding of providers not possible. Blinding of participants in one of the three studies only. Allocation concealment rated unclear in one of the three studies. **Inconsistency: no serious. Indirectness: serious.** Six different strapping techniques used across studies. Comparison intervention was either no or sham strapping. **Imprecision: very serious.** Wide confidence intervals, Low number of patients, mean improvement in outcome measure (MAS-UL) less than the minimal clinically important difference (NB: CE assumes this - would need to look up published information on MCID for MAS-UL). **Publication bias: no serious.**

Attached Images

Practical issues	**No strapping**	**Shoulder strapping**	**Both**
Adverse effects, interactions and antidote Skin irritation		Minor, fully reversible (on removal of strapping) skin irritations (itching, redness of the skin or rash) experienced by 5% of participants	

Good practice statement

Consensus-based recommendation
For stroke survivors at risk of shoulder subluxation, firm support devices (e.g. devices such as a laptray) may be used. A sling maybe used when standing or walking.

Evidence To Decision

Benefits and harms

Small net benefit, or little difference between alternatives

There is a high level of uncertainty regarding the benefits of supportive devices and orthoses with conflicting results from a limited number of small trials. *[81]* Increased pain was reported in some patients. A previous Cochrane review (Ada et al 2005) found there was insufficient evidence to draw conclusions about the effects of supportive devices to prevent subluxation.

Certainty of the Evidence

Very low

Several small trials with inconsistent results and very low overall certainty of effects.

Values and preferences

Substantial variability is expected or uncertain

Patients' perceptions are likely to vary substantially due to the uncertainty in evidence.

Resources and other considerations

Important issues, or potential issues not investigated

No economic studies were found.

Rationale

Several small trials of different slings or supports have reported conflicting results. The working group suggest it is reasonable to use firm support devices while the patient is sitting and possibly use some type of sling while standing or walking to prevent subluxation or minimise the risk of subluxation worsening.

Clinical Question/ PICO

Population: Adults with stroke
Intervention: Shoulder orthosis / sling / support
Comparator: Conventional treatment

Summary

Hartwig et al (2012) *[81]* included 41 patients with shoulder joint subluxation following ischaemic stroke. The intervention group used a shoulder orthosis (or support), in addition to usual care while the control group received usual care alone. A shoulder-hand syndrome score that assessed the severity of clinical symptoms showed significant reductions in the intervention group. There were also significant reductions in pain and limitation of movement, and a non-significant reduction in subluxation. The trial did not use blinded outcome assessors, so there is a serious risk of bias, and the small number of participants involved in the trial also suggests serious imprecision.

Ada et al (2017)*[85]* included 46 acute patients at risk of subluxation and compared modified lap-tray and a triangular sling with a hemi-sling. No significant difference was found between the two groups in terms of shoulder subluxation (MD -3mm, 95% CI -8 to 3). There were non-significant trends to less pain at rest (MD -0.7 out of 10, 95% CI -8 to 3) and during shoulder external rotation (MD -1.7 out of 10, 95% CI -3.7 to 0.3), and increased shoulder external rotation (MD -10 deg, 95% CI -22 to 2) in favour of the modified lap-tray and triangular sling. There was no significant difference between groups in terms of activity of upper limb and other contactures.

Jung and Choi (2019)*[84]* investigated the effect of active shoulder exercise wit aa sling suspension system on shoulder subluxation, proprioception and upper extremity function in patients with acute stroke (n = 36). Significant differences was observed favouring the intervention group for shoulder subluxation (4.71mm ± 1.72 vs 2.86mm ± 2.16, p = 0.008).

van Bladel et al (2017)*[87]* investigated the effect of two different arm slings (Actimove, Shoulderlift) versus no sling in patients with shoulder weakness (n = 28). There was no significant difference in initial effects of either sling on shoulder subluxation, although the Shoulderlift corrected subluxation by 63% compared to Actimove sling (36% reduction). At six weeks only the control group (no sling) significantly improved compared with baseline in shoulder subluxation (-3.3mm). Additionally, the Actimove group reported more pain at rest (p = 0.036) than the other two groups. There was no difference in arm motor function (Fugl-Meyer assessment).

Outcome Timeframe	**Study results and measurements**	**Comparator** Conventional treatment	**Intervention** Support	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Limitation of movement Post intervention: 28 days of treatment 6 Important	Measured by: SHS limitation of movement (abduction and external rotation) score Lower better Based on data from 41 participants in 1 studies. (Randomized controlled) Follow up: 28 days of treatment.	2.2 (Mean) Difference:	0.9 (Mean) **MD 1.3 lower** (CI 95% 2 lower — 0.7 lower)	**Very low** Due to very serious risk of bias, Due to serious imprecision [1]	Although p value of 0.0002, due to risk of bias, it is unclear whether the use of an orthosis limits freedom of movement.
Subluxation [2] Post intervention: 28 days of treatment 7 Critical	Measured by: Subluxation measurement via "anthropometric measurement" Lower better Based on data from 41 participants in 1 studies. [3] (Randomized controlled) Follow up: 28 days of treatment.	1.6 cm (Mean) Difference:	1.7 cm (Mean) **MD 0.1 higher** (CI 95% 0.4 lower — 0.6 higher)	**Very low** Due to very serious risk of bias, Due to serious imprecision [4]	p value of 0.7634 demonstrated that orthosis did not reduce subluxation significantly, due to the risk of bias in this study, results are unclear.

1. **Risk of Bias: very serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Low number of patients. **Publication bias: no serious.**
2. Subluxation measurement
3. Primary study[81]. **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of Bias: very serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Low number of patients. **Publication bias: no serious.**

Attached Images

Practical issues	**Conventional treatment**	**Shoulder orthosis / sling / support**	**Both**
Procedure and device		3 participants (15%) had occasional severe discomfort, 1 participant (5%) had occasional moderate discomfort and 1 participant (5%) had severe discomfort for the entirety of the trial.	

Good practice statement

Consensus-based recommendation
To prevent complications related to shoulder subluxation, education and training about correct manual handling and positioning should be provided to the stroke survivor, their family/carer and health professionals, and particularly nursing and allied health staff.

Rationale

There is no evidence that subluxation can be reduced after it has developed, hence, prevention is paramount. Trauma to the

shoulder due to incorrect manual handling should be prevented with appropriate education and training.

Pain

Central post-stroke pain

Central post-stroke pain (CPSP) is a neuropathic pain syndrome that can occur after a cerebrovascular accident. This syndrome is characterised by pain and sensory abnormalities in the body parts that correspond to the brain territory that has been injured by the cerebrovascular lesion. (Klit et al. 2009)

Consensus recommendation

New

Consensus-based recommendations

For stroke survivors with central post-stroke pain tricyclic antidepressant or antiepileptic medication may be trialed to reduce pain. Any trial of medications to reduce pain needs to be undertaken with caution with planned follow up to minimise risks. Any non-pharmacological interventions trialed are strongly encouraged to be used within a research framework.

Update approved by NHMRC July 2023.

Practical Info

Any trial of medications or other interventions need to be communicated to the patient with agreed timeframes to review efficacy and monitor for side effects.

- For any chronic pain conditions a multidisciplinary approach should be used, including input from psychology.
- Sensory based approaches could be trialed, ideally within a research framework.
- Medication choice will depend on the individual and other risk factors. For those at risk of seizure an antiepileptic medication such as lyrica could be used. Lamotrigine has also been trialed but there is no evidence it effectively reduces pain. For patients with features of depression, or those at high risk of developing depression, an antidepressant such as duloxetine could be used. Amitriptyline is commonly used, however the impact on pain reduction is unclear.

Evidence To Decision

Benefits and harms

Small net benefit, or little difference between alternatives

Tricyclic antidepressants did not significantly reduce pain intensity based on two small trials (SMD -0.24, 95% CI -0.72 to 0.24)*[224]*. Anticonvulsants, showed no clear benefit with differing results from small trials of different anticonvulsant medications and there was an increase in adverse events (RR 1.61, 95% CI 0.90 to 2.88) like skin rash *[88]*. There is high level of uncertainty regarding the benefits of brain stimulation, opioid antagonists and acupuncture due to the number, size and quality of trials.

Certainty of the Evidence

Very low

The certainty of evidence is very low to low.

Values and preferences

Substantial variability is expected or uncertain

Given the uncertainty in the overall benefit and the presence of side effects, it is expected that some variation in patients' preference may exist.

Resources and other considerations

Important issues, or potential issues not investigated

Post-stroke pain is currently not monitored in any national stroke data collection process. Evidence regarding economic considerations is lacking.

Rationale

Chronic pain after stroke can be debilitating and all efforts should be undertaken to investigate any local causes of pain. Central post-stroke pain (CPSP) is particularly challenging as the evidence to date provides little reliable data to make recommendations for routine practice. It is common for medications such as tricyclic antidepressants or various antiepileptic medication to be trialed. Non-invasive brain stimulation via repetitive transcranial magnetic stimulation may also be trialed ideally in a research framework. Invasive brain stimulation for patients with refractory pain (pain that cannot be adequately controlled despite multidimensional effects) has also been tested but serious side effects limits application broadly. Acupuncture may also be trialed. Further research is needed.

Clinical Question/ PICO

Population: Adults with central post-stroke pain
Intervention: Anticonvulsants
Comparator: Placebo

Summary

A review by Mulla et al (2015)*[88]* investigated the management of central post-stroke pain (CPSP) included eight studies (n=459 participants). Anticonvulsants did not significantly reduce pain intensity (weighted MD -0.75, 95% CI -1.71 to 0.21; 4 studies, n= 307; moderate heterogeneity I^2= 69%; very low certainty evidence) or increase adverse events (RR 1.61, 95% CI 0.90 to 2.88; 4 studies, n= 307; moderate heterogeneity I^2= 80%; very low certainty evidence) compared to placebo.

A review of pharmacotherapies for central post-stroke pain by Bo et al. (2022)*[224]* with 13 studies (n= 529) investigated individual pharmacotherapies and found compared to placebo, levetiracetam (SMD -2.11, 95% CI -2.97 to -1.26; 1 study, n=42), lamotrigine (SMD -1.39, 95% CI -2.21 to -0.58; 1 study, n=27) and pregabalin (SMD -0.46, 95% CI -0.71 to -0.22; 2 studies, n= 259) had significantly better treatment effect. No significant differences were found for carbamazepine (1 study, n=15). For adverse effects, 3 out of the 21 patients receiving levetiracetam withdrew from the trial because of adverse events, 6 of the 14 patients receiving lamotrigine reported mild rash or severe headache. Results are to be interpreted with caution due to small sample sizes and very few studies for each intervention.

Previous Cochrane reviews involving patients with neuropathic pain from a range of conditions (not just stroke) have been undertaken. Wiffen et al (2017)

Wiffen et al (2013) included 12 studies (n=1511) in various patient populations with chronic neuropathic pain (1 study with CPSP, n=30). There was no clear evidence that lamotrigine (at doses 200mg to 400mg daily) reduces pain. Adverse events were common with almost 10% of participants taking lamotrigine reported a skin rash.

Moore et al (2015)PMID: **26146793** included 17 studies (n=1342) of amitriptyline (a tricyclic antidepressant). Studies were small. Only two of seven studies reporting useful efficacy data was amitriptyline significantly better than placebo (very low quality evidence) and adverse events were more common (RR 1.5, 95%CI 1.3 to 1.8; NNH 5.2, 95% CI 3.6 to 9.1 low quality evidence) but serious adverse events were rare. The one small stroke study (Leijon 1989) included reported global improvement occurred in 10 of 15 on amitriptyline, 5 of 15 on carbamazepine, and 1 of 15 on placebo. The authors noted this treatment is common and the evidence indicates there while there are little beneficial effects there is no evidence of a lack of effect.

Derry et al (2019) PMID: 30673120

Duehmke et al (2017) PMID: 28616956

Cooper et al (2017) PMID: 28530786

Outcome Timeframe	**Study results and measurements**	**Comparator** Placebo	**Intervention** Anticonvulsants	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Adverse events 7 Critical	Relative risk 1.61 (CI 95% 0.9 — 2.88) Based on data from 307 participants in 4 studies. [1] (Randomized		CI 95%	**Very low** Due to serious risk of bias, Due to serious inconsistency,	We are uncertain whether anticonvulsants increases or decreases adverse events

Outcome Timeframe	**Study results and measurements**	**Comparator** Placebo	**Intervention** Anticonvulsants	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
	controlled) Follow up: 4 -12 weeks.			Due to serious imprecision [2]	
Pain intensity 7 Critical	Measured by: Visual analog scale Lower better Based on data from 307 participants in 4 studies. [3] (Randomized controlled) Follow up: 4-12 weeks.	Difference:	**MD 0.75 lower** (CI 95% 1.71 lower — 0.21 higher)	**Very low** Due to serious risk of bias, Due to serious inconsistency, Due to serious imprecision [4]	We are uncertain whether anticonvulsants improves or worsen pain intensity

1. Systematic review [88] . **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of Bias: serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Selective outcome reporting. **Inconsistency: serious.** The magnitude of statistical heterogeneity was high, with I^2: 80 %.. **Indirectness: no serious. Imprecision: serious.** Low number of patients.
3. Systematic review [88] . **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of Bias: serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Selective outcome reporting. **Inconsistency: serious.** The magnitude of statistical heterogeneity was high, with I^2: 69%.. **Indirectness: no serious. Imprecision: serious.** Low number of patients.

Attached Images

Clinical Question/ PICO

Population: Adults with central post-stroke pain
Intervention: Tricyclic antidepressants
Comparator: Placebo

Summary

A review by Mulla et al (2015)*[88]* investigated the management of central poststroke pain and included eight studies (n=459 participants). Tricyclic antidepressants, specifically amitriptyline did not significantly reduce pain intensity compared to placebo based on 1 study (n=15; low certainty evidence), but had significantly more adverse events (RR 2.00, 95% CI 1.15 to 3.49; 1 study, n= 15; low quality evidence). This result is the same as reviews by Singer et al (2017)*[90]* and Snedecor et al (2014)*[91]* which includedthe same studies . Another review by Bo et al. (2022)*[224]* with 13 studies (n= 529) identified one additional study for amitriptyline, however the results were similar (SMD -0.24, 95% CI -0.72 to 0.24; 2 studies, n= 54) to the previous reviews.

Outcome Timeframe	**Study results and measurements**	**Comparator** Placebo	**Intervention** Tricyclic antidepressants	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Adverse events	Relative risk 2 (CI 95% 1.15 — 3.49) Based on data from 15		CI 95%	**Very low** Due to serious risk of bias, Due	Tricyclic antidepressants may increase adverse events slightly

Outcome Timeframe	**Study results and measurements**	**Comparator** Placebo	**Intervention** Tricyclic antidepressants	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
7 Critical	participants in 1 studies. [1] (Randomized controlled) Follow up: 4 weeks.			to very serious imprecision [2]	
Pain [3] 7 Critical	Based on data from 15 participants in 1 studies. (Randomized controlled) Follow up: 4 weeks.	10 / 15 patients were reported to have reduced pain during treatment		**Very low** Due to serious risk of bias, Due to very serious imprecision [4]	We are uncertain whether tricyclic antidepressants increases or decreases pain

1. Systematic review [88] . **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of Bias: serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias. **Inconsistency: no serious. Indirectness: no serious. Imprecision: very serious.** Low number of patients, Only data from one study.
3. 10 step verbal scale
4. **Risk of Bias: serious. Inconsistency: no serious. Indirectness: no serious. Imprecision: very serious.**

Attached Images

Clinical Question/ PICO

Population: Adults with central post-stroke pain
Intervention: Opioid antagonists
Comparator: Placebo

Summary

A review by Mulla et al (2015)*[88]* investigated the management of central post-stroke pain and included eight studies (n=459 participants). Opioid antagonists, specifically naloxone had no effect on pain when compared to placebo (1 study, n=20; very low certainty evidence). This finding is the same as review by Singer et al (2017)*[90]* which included the same study .

A review by Scuteri et al. (2020)*[223]* with 8 mixed method studies (n=114) assessed the effect of opioids in post-stroke pain. Meta-analysis was completed with the four RCTs and found no significant difference for opioid agonist and antagonists compared to placebo for analgesic efficacy (RR 1.05, 95% CI 0.57 to 1.92; 3 studies, n= 60; very low quality evidence) and effectiveness on pain-related outcomes (RR 1.00, 95% CI 0.49 to 2.05; 2 studies, n=10; very low quality evidence). Only one included trial involved stroke participants (and has been included in past reviews). The other three studies included patients with neuropathic pain with different etiologies.

Outcome Timeframe	**Study results and measurements**	**Comparator** Placebo	**Intervention** Opioid antagonists	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Pain intensity 7 Critical	Based on data from 20 participants in 1 studies. (Randomized controlled) Follow up: 2 weeks.	Opioid antagonists, specifically naloxone had no effect on pain when compared to placebo (9.35 vs 10.05, p= 0.86; 1 study, n=20)		**Very low** Due to serious risk of bias, Due to very serious	We are uncertain whether opioid antagonists increases or decreases pain

Outcome Timeframe	**Study results and measurements**	**Comparator** Placebo	**Intervention** Opioid antagonists	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
				imprecision [1]	

1. **Risk of Bias: serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias. **Inconsistency: no serious. Indirectness: no serious. Imprecision: very serious.** Low number of patients, Only data from one study, Low number of patients, Only data from one study.

Attached Images

Clinical Question/ PICO

Population: Adults with central post-stroke pain
Intervention: Brain or spinal cord stimulation
Comparator: Sham

Summary

A review by Mulla et al (2015)*[88]* investigated the management of central poststroke pain (CPSP) and included eight studies (n=459 participants). Repetitive transcranial magnetic stimulation (rTMS) was found to have no benefits or harms compared to sham stimulation (1 study, n= 52; low certainty evidence).

Another review by Ojala et al. (2021)*[225]* (n=17) found navigated rTMS (nrTMS) targeted to S2 resulted in a significant long term (baseline to one month follow up) pain intensity reduction (MD -0.9, 95% CI -1.5 to -0.2). All stimulations resulted in a short-term reduction of pain (17-20%), with no significant difference between M1, S2 or sham stimulation, suggesting a strong placebo effect. The cold pressor test for conditioned pain modulation reduced CPSP pain intensity significantly (before mean 5.12, SD 2.15; after mean 4.12, SD 1.69) at baseline and the efficacy did not change after any nrTMS treatment.

Another trial by Zhao et al. (2021)*[226]* (n=40) found navigated rTMS led to significantly lower pain measured using Numeric Rating Scale and Short-form McGill Pain Questionnaire-2 on the seventh day of treatment (Cohen's d=1.302, p<0.001 and d= 0.771, p=0.003 respectively) compared to sham treatment and the effect lasted until the third week (Cohen's d=0.860, p=0.001 and d=0.550, p=0.027). There were no significant differences in mood measured via Hamilton Anxiety Scale and Hamilton Depression Scale between the two groups. No serious adverse effects were observed.

A mixed methods review by Ramger et al (2019)*[89]* explored the effect of non-invasive brain stimulation and included six studies (1 randomised trial, 3 non-randomised trials and 2 case studies) mostly utlising rTMS (one used transcranial direct current stimulation [tDCS]). Five out of the six articles using VAS to measure pain and four of them found a significant decreases in pain (p< 0.05; 4 studies, n=74).

The review by Singer et al (2017)*[90]* included two small non-controlled studies. One study (n= 30) used percutaneous spinal cord stimulation and observed a decreased in pain from VAS score 8 to 6 points(p= 0.001). Another small study (n=11) examined motor cortex stimulation at the pre-central gyrus with 11 participants and found reduced pain in 73% of patients with pre-central stimulation, while 100% reported no pain reduction with post-central stimulation.

A review by Xu et al (2020)*[92]* included 11 studies (n=166) testing nonpharmacological therapies for central poststroke pain. Therapies included implanted electrical brain stimulation (5 studies), rTMS (1 study), tDCS (1 study), caloric vestibular stimulation (1 study), and acupuncture (3 studies). All bar one study was assessed as being at high risk of bias. While invasive electrical stimulation was the most commonly studied therapy, particularly for refractory CPSP (pain that cannot be adequately controlled despite multidimensional effects), some serious adverse events were reported.

Overall there is very limited evidence of a consistent reduction in pain with brain stimulation and further high quality studies are needed.

Clinical Question/ PICO

Population: Adults with central post-stroke pain
Intervention: Acupuncture
Comparator: Sham

Summary

A review by Mulla et al (2015)*[88]* investigated the management of central post-stroke pain (CPSP) included eight studies (n=459 participants). Acipuncture, which is bee venom acupuncture point injection, significantly reduced pain compared to saline acupuncture (36.5 vs 11.50, p= 0.009; 1 study, n= 20; very low quality evidence), however another study found no significant effect of electroacupuncture compared to carbamazepine for the composite of joint pain, dysfunction and tenderness (1 study, n= 60; very low certainty evidence).

The review by Xu et al (2020)*[92]* with 11 studies (n=166) identified one additional trial than the two previously included. Acupuncture (MD 0.22, 95% CI -1.00 to 1.44; 1 study, n=22) had no significant effect for pain compared to oral carbamazepine treatment. All studies have limitations and further studies are needed.

Clinical Question/ PICO

Population: Adults with central post-stroke pain
Intervention: Other pharmacotherapies
Comparator: Placebo

Summary

A review by Bo et al. (2022)*[224]* with 13 studies (n= 529) investigated individual pharmacotherapies and those with significantly better treatment effect than placebo are pamidronate (SMD -2.43, 95% CI -3.54 to -1.31; 1 study, n=21), prednisone (SMD -2.38, 95% CI -3.09 to -1.67; 2 studies, n=79) and etanercept (SMD -0.92, 95% CI -1.8 to -0.03; 1 study, n=26). Lidocaine (1 study, n=16) and ketamin (1 study, n=33) were not effective in reducing pain when compared with placebo.

Shoulder pain

The cause of shoulder pain remains unclear but this complication affects 9% of stroke survivors on admission rising to 12% during admission *[7]*, suggesting activities in-hospital may exacerbate the condition. Shoulder pain often occurs secondarily or with other impairments (see Spasticity, Contracture, and Subluxation).

Interventions aimed at reducing trauma to the shoulder, such as educating all staff, carers and stroke survivors, may also help to minimise shoulder pain. Such education may include strategies to care for the shoulder during manual handling and transfers and advice regarding positioning. As there is no clear evidence for effective interventions once shoulder pain has developed in stroke patients, management should be based on evidence-based interventions for acute musculoskeletal pain.

Weak recommendation

For stroke survivors with shoulder pain, shoulder strapping may be used to reduce pain. (Appel et al 2014 *[79]*)

Practical Info

The main adverse effects are skin reactions which were relatively uncommon (5%). For patients with sensitive skin, the strapping can be applied over a layer of low allergy tape.

Many different strapping protocols exist, with no clear theoretical or practical advantage of any given one technique.

The strapping should be applied firmly to dry, clean skin and maintain adherence despite perspiration and activity. The strapping should be non-stretch tape to provide joint support. The strapping should be replaced every few days when stretched and to check underlying skin.

Evidence To Decision

Benefits and harms

Small net benefit, or little difference between alternatives

Shoulder strapping (in patients with current shoulder pain) was associated with improvements in pain and health-related quality of life, and possibly reduced subluxation of the joint (Appel et al 2014 *[79]*). It is unclear whether function of the upper limb can be improved or not from strapping the shoulder.

Certainty of the Evidence

Low

Based on a recent systematic review (Appel et al 2014 *[79]*), the best evidence is for reduction in pain (low quality evidence) but estimates of benefit for function or subluxation were less clear and based on 1 or 2 trials

Values and preferences

Substantial variability is expected or uncertain

Patients' perceptions are likely to vary due to the uncertainty in evidence.

Resources and other considerations

Important issues, or potential issues not investigated

Resources considerations

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

Rationale

Shoulder strapping is thought to support the shoulder both at rest and during movements and exercise, and unlike external bracing or slings, is in place all the time and does not restrict movement. For patients who have shoulder pain, systematic review evidence suggests a reduction in pain and improvement in HRQOL with strapping, but this is based on a small number of trials. The benefits are modest, but the potential harms from the strapping are very low, thus favouring strapping. The strapping is well tolerated by patients (with minor skin reactions occuring in 5% of patients).

Clinical Question/ PICO

Population: Adults with stroke
Intervention: Shoulder strapping
Comparator: No strapping

Summary

A systematic review by Appel et al (2014) *[79]* included 8 trials of shoulder strapping interventions for reducing stroke-related upper limb impairments. Five of the trials were randomised or quasi-randomised trials while the remaining 3 were case series or case studies. Meta-analysis of 3 studies reporting Motor Assessment Scale scores showed non-significant improvements in upper limb function in shoulder strapping groups. For other outcomes such as health related quality of life and pain, meta-analysis was not possible as too few studies reported the outcomes. The review authors concluded there was insufficient evidence of efficacy to recommend strapping as a treatment for shoulder paralysis.

Ravichandran et al (2019)*[101]* identified 8 RCTs (n=132 participants) and reported overall reduction of shoulder pain but no meta-analysis was conducted. Deng et al (2020)*[106]* included 9 studies (n=424) of kinesio taping to treat shoulder pain. There was a reduction in pain (MD -1.45, 95%CI -1.98 to -0.92 cm) but this is under the threshold for minimal clinically significant difference. Further trials are required to confirm these findings.

Outcome Timeframe	**Study results and measurements**	**Comparator**	**Intervention**	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Health related quality of life (HRQoL) 13-15 weeks 7 Critical	Measured by: Stroke Specific Quality of Life Scale Scale: 49 — 245 High better Based on data from 12 participants in 1 studies. (Randomized controlled) Follow up: 13-15 weeks.	2.9 points (Mean) Difference:	3.44 points (Mean) **MD 0.54 higher** (CI 95% 1.29 lower — 2.37 higher)	**Very low** Due to very serious imprecision due to low participant numbers (n=6) (NB:chose to downgrade to very low certainty) [1]	We are uncertain whether shoulder strapping improves or worsen health related quality of life (HRQoL)
Upper Limb Function [2] 3 to 6 weeks post-intervention 7 Critical	Measured by: Motor Assessment Scale upper limb items Scale: 3 — 18 High better Based on data from 117 participants in 3 studies. (Randomized controlled) Follow up: 4 to 14 weeks.	Difference:	**MD 0.87 higher** (CI 95% 0.07 lower — 1.81 higher)	**Very low** Due to serious indirectness, Due to very serious imprecision. The direct influence of strapping on upper limb function outcome is also questionable. The measured improvements in upper limb function could be due to factors other than strapping - eg motor rehabilitation provided [3]	We are uncertain whether strapping improves or worsen upper limb function
Pain reduction 4-6 weeks post-randomisation 7 Critical	Based on data from 219 participants in 2 studies. (Randomized controlled) Follow up: 4 to 6 weeks post randomisation.	Two RCTs (N = 83 and 136) assessed pain severity following shoulder strapping using the Visual Analogue Scale. Non-significant reductions in pain of -0.7 (95% CI: -1.95, 0.55) and -0.78 points (95% CI: -1.4, 17.0) were reported in the two trials. Meta-analysis could not be performed due to the small number of studies.		**Low** Due to serious indirectness, Due to serious imprecision [4]	Shoulder strapping may have little or no difference on pain reduction

1. **Risk of Bias: no serious.** The systematic review process included a process by which data was pooled only for studies with adequate review. **Inconsistency: no serious. Indirectness: no serious. Imprecision: very serious.** Low number of patients.
2. Three randomised controlled trials measured upper limb function using the Motor Assessment Scale for Stroke, upper limb items. This outcome was measured at different time points for each of the studies, ranging from one to 14 weeks post-randomisation. A meta-analysis was included in the review, but it is not clear what time points the data were taken from in each study.
3. **Risk of Bias: no serious.** Blinding of providers not possible. Blinding of participants in one of the three studies only. Allocation concealment rated unclear in one of the three studies. **Inconsistency: no serious. Indirectness: serious.** Six different strapping techniques used across studies. Comparison intervention was either no or sham strapping. **Imprecision: very serious.** Wide confidence intervals, Low number of patients, mean improvement in outcome measure (MAS-UL) less than the minimal clinically important difference (NB: CE assumes this - would need to look up published information on MCID for MAS-UL). **Publication bias: no serious.**
4. **Inconsistency: no serious. Indirectness: serious.** Six different strapping techniques used across studies. Comparison

intervention was either no or sham strapping. **Imprecision: serious.** Wide confidence intervals. **Publication bias: no serious.**

Attached Images

Practical issues	No strapping	Shoulder strapping	Both
Adverse effects, interactions and antidote Skin irritation		Minor, fully reversible (on removal of strapping) skin irritations (itching, redness of the skin or rash) experienced by 5% of participants	
Physical well-being Comfort of the intervention, as assessed in one case series		on a 5 pt VAS, 9 out of 10 participants rated strapping as (very) comfortable (mean score 4.4, SD 0.59)	

Weak recommendation

For stroke survivors with shoulder pain, electrical stimulation may be used to manage pain. (Qiu et al 2019 *[102]*)

Practical Info

Both TENS (3 trials) and percutaneous stimulation (2 trials) reduced pain with TENS appearing to reduce pain slightly more.

Trials using TENS used a frequency of 30-100 Hz with pulse duration of 200 us and intensity set to elicit muscle contraction. Sessions lasted 15-20 mins.

Trials using percutaneous stimulation used a frequency of 12 Hz, current amplitude of 20mA, pulse duration of 10-200 us with a cycle 20 secs on and 10 secs off.

If equipment is being used outside of therapy time, simple information about the equipment, correct placement of pads, duration and frequency should be written down and provided to person with stroke or family. Photographs of correct placement can assist. Discussion on ongoing need for equipment and options to hire, borrow or puchasing costs (including financial capacity of the person/family) should occur prior to being discharged from hospital services.

Evidence To Decision

Benefits and harms

Small net benefit, or little difference between alternatives

Electrical stimulation leads to a small reduction in reported pain and an increase in motor function (Qiu et al 2019 *[102]*). Minimal adverse effects have been reported (Vafadar et al 2015 *[80]*).

Certainty of the Evidence

Moderate

The evidence was moderate based on a systematic review and meta-analysis of six trials.

Values and preferences

No substantial variability expected

Some patients may have negative perception of electrical stimulation, however, there appears little harms reported and

beneficial reduction in pain.

Resources and other considerations

No important issues with the recommended alternative

Many rehabilitation practices have existing electrical stimulation machines but often patients will need to purchase (or hire) a machine for use in the community. TENS machines are relatively cheap ($100 or less) to buy. Therapists will need to be familiar with electrode placements and educate the person with stroke and their family.

Rationale

Electrical stimulation aims to stimulate the nerves of weakened muscles around the shoulder causing a muscle contraction which might reduce subluxation and pain around the shoulder and increase function. Electrical stimulation, in addition to conventional therapy, leads to a small reduction in reported pain (based on four trials) and an increase in motor function (based on three trials)(Qiu et al 2019*[102]*). Minimal adverse effects have been reported (Vafadar et al 2015*[80]*). This was previously a weak recommendation AGAINST but has been changed due to new evidence.

Clinical Question/ PICO

Population: Adults with stroke
Intervention: Electrical stimulation
Comparator: Conventional therapy

Summary

Vafadar et al (2015) *[80]* included 10 trials of functional electrical stimulation (FES) for preventing or improving upper arm impairment following stroke in a systematic review. In all included trials, control groups received conventional physical or occupational therapy, and intervention groups received the same treatment plus FES. Meta-analysis showed non-significant reductions in pain when FES was applied within 6 months of stroke, both in 3 studies reporting pain-free range of lateral rotation and in 4 studies reporting numeric pain scales. No significant reductions in pain were seen in 2 studies applying FES more than 6 months after stroke. Trials in this review included patients that did not have shoulder pain at baseline and hence based on this review, it appears that FES does not prevent shoulder pain or reduce pain once it occurs compared to conventional therapy.

Qui et al (2019) included six RCTs specifically for patients with existing shoulder pain at baseline. Electrical stimulation, usually in addition to conventional therapy, led to reduction in pain (four studies, n=193; SMD -1.89, 95% CI -3.05 to -0.74) and also improved ADL (Barthel Index) (three studies, n=167; WMD 8.96, 95% CI 5.26-12.66). Subjects ranged from 2 weeks to 2 years post stroke and mean treatment duration was 4.5 wks (range = 3–8 wks). Included studies were rated as moderate to low quality.

Outcome Timeframe	**Study results and measurements**	**Comparator** Conventional therapy	**Intervention** Electrical stimulation	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Pain [1] post-treatment (4-8 weeks) 8 Critical	Measured by: Self reported severity of pain Lower better Based on data from 193 participants in 4 studies. [2] (Randomized controlled)	Difference:	**SMD 1.89 lower** (CI 95% 3.05 lower — 0.74 lower)	**Moderate** Downgraded due to possible risk of bias. Heterogeneity explained by treatment type. [3]	Electrical stimulation probably decreases pain
Motor function	Measured by: Barthel Index Scale: 0 — 100 High better	Difference:	**MD 8.96 higher** (CI 95% 5.26 higher — 12.66	**Moderate** Downgraded due to possible risk of	Electrical stimulation may improve motor function slightly

Outcome Timeframe	**Study results and measurements**	**Comparator** Conventional therapy	**Intervention** Electrical stimulation	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
8 Critical	Based on data from 167 participants in 3 studies. [4] (Randomized controlled)		higher)	bias [5]	

1. as different pain rating scales used, these were pooled using effect sizes only
2. Systematic review. **Baseline/comparator:** Control arm of reference used for intervention. **Supporting references:** [102],
3. **Risk of Bias: serious.** Trials rated as 5-7 on Pedro scale. Unclear from study all ROB items. **Inconsistency: no serious.** The magnitude of statistical heterogeneity was high, with I^2:90% overall but low for TENS (0%) and PNS (0%).. **Indirectness: no serious.** Limited longer term outcomes. **Imprecision: no serious.** Wide confidence intervals, relatively low number of patients.
4. Systematic review. **Baseline/comparator:** Control arm of reference used for intervention. **Supporting references:** [102],
5. **Risk of Bias: serious.** Trials rated as 5-7 on Pedro scale. Unclear from study all ROB items. **Inconsistency: no serious.** Estimates could be narrower. **Indirectness: no serious.** No or limited longer term outcomes. **Imprecision: no serious.** Wide confidence intervals, Low number of patients.

Attached Images

Weak recommendation

For stroke survivors with shoulder pain, shoulder injections (either sub acromial steroid injections for patients with rotator cuff syndrome, or methylprednisolone and bupivacaine for suprascapular nerve block) may be used to reduce pain. (Adey-Wakeling et al. 2013 *[93]*; Rah et al. 2012 *[95]*)

Practical Info

Patients for subacromial corticosteroid injection were highly selected based on clinical and ultrasonic criteria for rotator cuff disorder. The study excluded patients with severe spasticity, shoulder subluxation, primary osteoarthritis of glenohumeral joint and flaccid weakness of deltoid muscle - it is therefore unknown whether these patients would also benefit or not. This study stopped both antiplatelet therapy and anticoagulation for 5 days prior to injection to minimise post injection haemorrhage. Injection was 4ml of 40mg triamcinolone and 1ml 1% lidocaine combined, and was done under ultrasound guidance.

Supraspinatus nerve block was achieved using a single combined injection of 1ml of 40mg/ml methylprednisolone and 10ml 0.5%bupivicaine hydrochloride into supraspinous fossa. This group was general patients with any hemiplegic shoulder pain (ie "all comers")

Evidence To Decision

Benefits and harms

Small net benefit, or little difference between alternatives

There may be a small reduction in shoulder pain after steroid injection (Rah et al 2012 *[95]*). Suprascapular nerve block reduced pain by approximately 1/3, with no adverse effects seen (Adey-Wakeling et al 2013 *[93]*). No improvements in quality of life were seen.

Certainty of the Evidence

Low

Based on one randomised controlled trial each.

Values and preferences

Substantial variability is expected or uncertain

Patients' perceptions are likely to vary due to uncertainty in the evidence.

Resources and other considerations

Important issues, or potential issues not investigated

Resources considerations

No literature to understand or describe the potential economic implications of this recommendation was identified. It requires ultrasound examination to confirm clinical diagnosis of rotator cuff disorder. Subacromial injection technique is easily learnt. Anticoagulants may need to be withheld prior to injection

Rationale

Both suprascapular nerve block and subacromial corticosteroid injection are recognised techniques for managing painful shoulder conditions such as degenerative arthritis and rotator cuff disorders. These conditions frequently coexist in patients with shoulder pain post stroke. Based on one trial each, both injection techniques showed significant reduction in pain scores, with minimal adverse effects. Subacromial injection was useful in patients with painful shoulder and documented rotator cuff disorders (confirmed on ultrasound examination).

Clinical Question/ PICO

Population: Adults with stroke with shoulder pain
Intervention: Suprascapular nerve block
Comparator: Placebo injection

Summary

A placebo-controlled trial of suprascapular nerve block for treating shoulder pain included 64 stroke patients within 1 year of stroke onset (Adey-Wakeling et al 2013 *[93]*). The intervention group showed significantly greater reductions in self-reported pain (Visual Analogue Scale), although there were no significant differences in disability or quality of life. Randomisation, blinding and allocation concealment procedures were clearly described, suggesting a low risk of bias, but the low number of patients included means there is imprecision in the estimated treatment effects.

Yang et al (2020)*[104]* compared pulsed radiofrequency block of suprascapular and axillary nerves to nerve block with lignocaine in a small number of participants (n=20) more than 1 year after stroke. Both treatments reduced pain but there was no between group differences. In a similar study Alanbay et al (2020)*[105]* also compared suprascapular nerve pulsed radiofrequncy treatment compared to suprascapular nerve block with lidocaine in 30 people with shoulder pain more than 3 months after stroke. Both groups received concurrent physiotherapy. Pulsed radiofrequency resulted in reduced pain at 1 and 3 months post treatment compared to nerve block. Further studies are needed.

Outcome Timeframe	**Study results and measurements**	**Comparator** Placebo injection	**Intervention** Suprascapular nerve block	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Pain 12 weeks 7 Critical	Measured by: VAS Scale: 0 — 100 Lower better Based on data from 64 participants in 1 studies. (Randomized controlled) Follow up: 12 weeks.	46.2 mm (Mean)	28.14 mm (Mean) CI 95%	**Moderate** small number of patients (n=64), only one study [1]	Suprascapular nerve block probably improves shoulder pain

1. **Imprecision: serious.** Only data from one study, Low number of patients.

Attached Images

Practical issues	Placebo injection	Suprascapular nerve block	Both
Adverse effects, interactions and antidote No adverse effects were seen			
Emotional well-being HRQoL as assessed by EuroQol Health Questionnaire- no significant differences between intervention and placebo groups			
Physical well-being Disability outcomes as assessed by both Modified Rankin Scale and Croft Disability Scale showed no differences between the two groups			

Clinical Question/ PICO

Population: Adults with stroke with shoulder pain and with diagnosed rotator cuff syndrome (clinically and by ultrasound)

Intervention: Subacromial corticosteroid injection

Comparator: Placebo (lidocaine) injection

Summary

A randomised, multicentre trial with blinded participants, personnel and assessors compared a subacromial corticosteroid injection (triamcinolone 40mg) to placebo (lidocaine) in 58 stroke patients with rotator cuff disorder (Rah et al 2012 *[95]*). The intervention group showed significant improvements in daytime and nighttime pain up to 8 weeks post treatment. The participants included in the trial were generally young (with mean ages ~ 57 in the intervention group and ~ 55 in the placebo) and since only participants with rotator cuff disorder were included they are not representative of the general stroke population.

Outcome Timeframe	**Study results and measurements**	**Comparator** Placebo injection	**Intervention** Subacromial corticosteroid injection	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Shoulder External rotation (ROM)	Measured by: Shoulder ROM-External rotation High better Based on data from 58 participants in 1 studies. (Randomized controlled) Follow up: 8 weeks.	**40.8** degrees (Mean)	**52.6** degrees (Mean) CI 95%	**Very low** Due to very serious imprecision, Due to serious indirectness [1]	Subacromial corticosteroid injection may make little or no difference on shoulder external rotation (ROM)
Daytime Pain 8 weeks 7 Critical	Measured by: VAS Scale: 0 — 10 Lower better Based on data from 58 participants in 1 studies.	**4.9** (Mean)	**3** (Mean) CI 95%	**Low** Due to serious indirectness (highly selected young stroke	Subacromial corticosteroid injection may improve daytime pain slightly

Outcome Timeframe	**Study results and measurements**	**Comparator** Placebo injection	**Intervention** Subacromial corticosteroid injection	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
	(Randomized controlled) Follow up: 8 weeks.			population with diagnosed rotator cuff pathology), Due to serious imprecision [2]	
Pain (Night) 8 weeks 7 Critical	Measured by: VAS Scale: 0 — 10 Lower better Based on data from 58 participants in 1 studies. (Randomized controlled) Follow up: 8 weeks.	5 (Mean)	2.7 (Mean) CI 95%	Low Due to highly selected young stroke population with diagnosed rotator cuff pathology, Due to serious imprecision [3]	Subacromial corticosteroid injection may improve pain (night) slightly

1. **Indirectness: serious.** Highly selected young stroke population with diagnosed rotator cuff pathology. **Imprecision: very serious.** Wide confidence intervals, Only data from one study, Low number of patients.
2. **Indirectness: serious.** population studied young, highly selected with documented rotator cuff issues and differs from most stroke patients. **Imprecision: serious.** Low number of patients, Only data from one study.
3. **Indirectness: serious.** highly selected young stroke population with diagnosed rotator cuff pathology. **Imprecision: serious.** Low number of patients (n=58), Only data from one study.

Attached Images

Practical issues	**Placebo (lidocaine) injection**	**Subacromial corticosteroid injection**	**Both**
Adverse effects, interactions and antidote Safety / Complications	1 patient had a vasovagal reaction during injection	No important complications noted. 2 patients had facial flushing (days 1-5post injection)	

Weak recommendation

For stroke survivors with shoulder pain and upper limb spasticity, Botulinum Toxin A may be used to reduce pain. (Singh et al 2010 *[97]*)

Practical Info

Botulinum toxin injections requires training and some studies used electromyography (EMG) guidance. Botulinum toxin type A was used in all studies and involved either single or multiple site injections. Dose was 500 units of Dysport (manufactured by Ipsen Inc, UK) in three studies and 100 units of Botox (manufactured by Allergan pharmaceuticals, Inc) in three studies and 140-200 units of onabotulinumtoxin A in one study.

Evidence To Decision

Benefits and harms

Small net benefit, or little difference between alternatives

Reduction in pain was noted in medium term but not in short term (Singh et al 2010 *[97]*).

Certainty of the Evidence

Very low

Low quality of evidence from 7 small trials with wide confidence intervals.

Values and preferences

Substantial variability is expected or uncertain

Some patients may not tolerate injections although small incidence of side effects

Resources and other considerations

Important issues, or potential issues not investigated

Resources considerations

No literature to understand or describe the potential economic implications of this recommendation was identified. Use of botulinum toxin requires training and EMG guidance.

Rationale

Six trials provide evidence of benefits regarding reduced pain at 12 weeks, but this benefit on pain was not found early after treatment (4 weeks) although confidence intervals were wide. It is unclear if the benefit of pain relief in post-stroke shoulder pain at three to six months but not at one month is due to limitations of the evidence, which includes small sample sizes with imprecise estimates, or a delayed onset of action. One further study (Marciniak et al 2012 *[96]*) showed improvements in some disability measures, but no improvement in pain scores at 4 weeks.

This therapy is used in selected patients where spasticity is an issue. In these patients, the injections may not only reduce adductor tone but may also reduce pain.

Clinical Question/ PICO

Population: Adults with stroke with shoulder pain
Intervention: Botulinum toxin injection by any route
Comparator: Placebo injection

Summary

Singh and Fitzgerald (2010) *[97]* conducted a Cochrane review of trials of botulinum toxin for treating shoulder pain. The review included 5 RCTs involving people with post-stroke shoulder pain, providing a single intramuscular injection of botulinum toxin A. Meta-analysis showed non-significant reductions in pain at one month, but a significant reduction at 3 to 6-month follow-up. The number of participants included in each comparison was small (< 90), creating serious imprecision in estimating the treatment effects.

A subsequent double-blind, placebo-controlled RCT by Marciniak et al (2012) *[96]* included 21 participants with shoulder pain and spasticity following stroke. Participants needed to have shoulder pain of at least 4/10 and spasticity of shoulder adductors of 3 or 4 (on Ashworth scale). Participants were generally young (mean age 60) and average 2+ years post stroke. Pain was assessed using the weekly mean of daily visual analogue scale (VAS) scores for the best and worst pain as well as pain during upper limb dressing and affecting sleep. The primary outcome was pain assessed at 4 weeks. Pain was also assessed by McGill Pain questionnaire (MPG). Pain (VAS and MPG) and mood were not significantly different between placebo or botulinum toxin at 4 weeks. No significant differences were seen in range of motion at 4 weeks.

Outcome Timeframe	**Study results and measurements**	**Comparator** Placebo injection	**Intervention** Botulinum toxin injection by any route	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Adverse events [1] 4-24 weeks 6 Important	Relative risk 1.46 (CI 95% 0.64 — 3.36) Based on data from 65 participants in 3 studies. (Randomized controlled) Follow up: 4-24 weeks.	235 per 1000 Difference:	343 per 1000 **108 more per 1000** (CI 95% 85 fewer — 555 more)	**Very low** Due to serious risk of bias, Due to serious imprecision, Due to very serious imprecision [2]	We are uncertain whether botulinum toxin injection by any route increases or decreases adverse events
Pain [3] 4-6 weeks 7 Critical	Measured by: VAS Scale: 0 — 10 Lower better Based on data from 86 participants in 4 studies. (Randomized controlled) Follow up: 4-6 weeks.	Difference:	**MD 1.12 lower** (CI 95% 2.89 lower — 0.66 higher)	**Low** Due to serious imprecision, Due to serious inconsistency [4]	botulinum toxin injection by any route may reduce shoulder pain slightly
Pain [5] 12-24 weeks 7 Critical	Measured by: VAS Scale: 0 — 10 Lower better Based on data from 66 participants in 3 studies. [6] (Randomized controlled) Follow up: 12-24 weeks.	4.8 (Mean) Difference:	**MD 1.22 lower** (CI 95% 2.37 lower — 0.07 lower)	**Low** wide confidence intervals and small numbers of patients- results at 12-24 weeks significant yet at 4-6 weeks were not significant [7]	botulinum toxin injection by any route may decrease shoulder pain slightly at 12-24 weeks

1. serious adverse side effects not reported in any of the 3 studies
2. **Risk of Bias: serious.** Serious adverse events not reported in any of the included studies. **Imprecision: very serious.** Low number of patients, Wide confidence intervals.
3. Systematic review of shoulder pain post stroke
4. **Inconsistency: serious.** The direction of the effect is not consistent between the included studies, The magnitude of statistical heterogeneity was high, with I^2:76%.. **Imprecision: serious.** Low number of patients, Wide confidence intervals.
5. Systematic review of 5 RCTs of people with shoulder pain post stroke
6. Systematic review [97] . **Baseline/comparator:** Control arm of reference used for intervention.
7. **Inconsistency: serious.** Point estimates vary widely. **Imprecision: serious.** Wide confidence intervals, Low number of patients.

Attached Images

Practical issues	**Placebo injection**	**Botulinum toxin injection by any route**	**Both**
Physical well-being Surprisingly, the magnitude of the mean difference (MD) between the botulinum toxin and placebo groups on pain at both time points (early @4-6 weeks vs late 12-24 weeks) was similar (MD -1.1, 95% CI -2.9 to 0.7 at 4 to 6 weeks; MD -1.2, 95% CI -2.37 to -0.07 at			

12 to 24 weeks). The I2 statistic was 76% at 4 to 6 weeks, the time point when the difference was not significant; and 0% at the 12 to 24 week end point when the difference was significant.

Weak recommendation

For stroke survivors with shoulder pain, acupuncture in addition to comprehensive rehabilitation may be used to reduce pain. (Liu et al 2019 *[98]*)

Practical Info

The most commonly used acupuncture points were around the shoulder: LI15 Jianyu, LI11 Quchi, TE5 Waiguan, LI4 Hegu, TE14 Jianliao, LI10 Shousanli, HT1 Jiquan, PC6 Neiguan, and SI9 Jianzhen. All studies were carried out in China. Most studies included treatment sessions of 30 mins, provided 5 to 6 times per week for 4 weeks.

Acupuncture for stroke survivors should only be administered by practitioners who are registered with the Chinese Medicine Board (sits under the Australian Health Practitioner registration Agency, AHPRA) and ideally a member of the Australian Acupuncture and Chinese Medicine Association (AACMA).

Evidence To Decision

Benefits and harms

Small net benefit, or little difference between alternatives

Overall acupuncture combined with rehabilitation slightly reduced pain (VAS: 25 studies, MD −1.59, 95%CI −1.86,−1.32). Very few trials report any adverse events. All adverse events reported in one trial were mild (bruising) and did not differ between intervention and control. (Liu et al 2019 *[98]*)

Certainty of the Evidence

Very low

Certainty of the evidence is low to very low due to serious risk of bias (multiple factors) and inconsistency.

Values and preferences

Substantial variability is expected or uncertain

Acupuncture is common practice in Asian communities where all of the existing trials were conducted. Preferences in other populations is uncertain. However, acupuncture may reduce pain and improve motor function with little or no risk of adverse events.

Resources and other considerations

Important issues, or potential issues not investigated

There have been no cost-effectiveness studies identified. Acupuncture requires specific knowledge and experience and may not be available in all locations.

Rationale

Acupuncture in addition to comprehensive rehabilitation appears to reduce ratings of pain (using the visual analogue scale) and increase motor impairment (based on the arm Fugl-Meyer Assessment). Systematic reviews of multiple RCTs and >2000 participants appear consistent, however, there is low certainty of effect due to potential risk of bias and heterogeneity from most of the trials. Few adverse events from acupuncture have been reported. All of the trials were conducted in China where the intervention is commonly applied and further trials in non Asian populations is needed before we are confident in the

generalisability of the treatment effect.

Clinical Question/ PICO

Population: Adults with stroke with shoulder pain
Intervention: Acupuncture
Comparator: Control

Summary

A systematic review of acupuncture for improving shoulder pain after stroke included 38 RCTs or quasi RCTs (N=3184 participants) (Liu et al. 2019 *[98]*). The included studies compared various types of acupuncture combined with rehabilitation and included patients 10 days to 19 months after stroke. 20 studies recruited participants with mild symptoms with remainder being moderate to severe. Twelve of the trials applied electrical stimulation with acupuncture. Overall, acupuncture combined with rehabilitation significantly improved motor impairment (upper-limb Fugl-Meyer Assessment (FMA): 34 studies, MD 8.01, 95% CI 6.69 to 9.33), and reduced pain (visual analogue scale [VAS]: 25 studies, MD −1.59, 95% CI −1.86 to −1.32). It is unclear if this reduction in VAS is a clinically important difference as there is limited evidence in patients specifically with shoulder pain (MCID was 1.4cm in those with rotator cuff injury [Robert et al. 2009] and similarly 1.4cm was noted for people after shoulder arthroplasty [Tashjian et al. 2017]). Acupuncture also improved ADL (modified BI) when compared with rehabilitation alone (11 studies, MD 9.99, 95% CI 5.91 to14.06). The certainty of evidence of all these outcomes was assessed as low by authors but was downgraded to very low due to significant risk of bias and high heterogeneity. The safety of acupuncture was unclear because there is a lack of detailed reporting of adverse events in most studies.

Previous reviews report consistent findings. Peng et al (2018)*[100]* included 20 RCTs and found a reduction in pain (VAS, MD -1.49, 95% CI -1.15 to -1.82). Lee and Lim (2016) *[99]* included 12 trials and reported post-stroke shoulder pain, as assessed by VAS was reduced (weighted MD -1.87, 95% CI -1.20 to -2.54) and increase in FMA (wMD 8.70, 95% CI 6.58 to 10.82).

Outcome Timeframe	**Study results and measurements**	**Comparator** Control	**Intervention** Acupuncture	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Pain (VAS) 2 9 Critical	Measured by: VAS Scale: 0 — 10 Lower better Based on data from 1,896 participants in 25 studies. (Randomized controlled) Follow up: 2-8weeks.	Difference:	**MD 1.59 lower** (CI 95% 1.86 lower — 1.32 lower)	Very low Due to very serious risk of bias, Due to serious inconsistency [1]	Pain may reduced pain (VAS) based on low quality
Motor function [2] 2-8 weeks 7 Critical	Measured by: Fugl-Meyer Assessment Upper Extremity High better Based on data from 2,331 participants in 29 studies. (Randomized controlled) Follow up: 2-8 weeks.	Difference:	**MD 8.01 higher** (CI 95% 6.69 higher — 9.33 higher)	Very low Due to very serious risk of bias, Due to serious inconsistency [3]	Acupuncture may improve motor function based on very low quality evidence.
Adverse events [4]	Based on data from 329 participants in 5 studies. (Randomized controlled) Follow up: 2-8 weeks.			Very low Due to very serious risk of bias, Due to serious inconsistency [5]	Only 5/38 trials reported adverse events. Four reported no events and one reported small but similar numbers in both groups. All adverse events were reported to be mild.

1. **Risk of Bias: very serious.** Overall high risk of bias. Sensitivity analysis for studies with appropriate random allocation resulted in similar results., Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Selective outcome reporting. **Inconsistency: serious.** The magnitude of statistical heterogeneity was high, with I^2:87% although was lower for electro-acupuncture subgroup I^2:43% compared to manual acupuncture I^2%: 90%.. **Indirectness: no serious.** all studies based in China, so unclear effect on other populations, no long term outcomes, intervention in approx 1/3 studies involved electroacupuncture with subgroup analysis reported. **Imprecision: no serious. Publication bias: no serious.**
2. Upper limb Motor function (Fugl-Meyer Assessment).
3. **Risk of Bias: very serious.** Overall high risk of bias. Sensitivity analysis for studies with appropriate random allocation resulted in similar results. **Inconsistency: serious.** The magnitude of statistical heterogeneity was high, with I^2:78% although was lower for electro-acupuncture subgroup I^2:48% compared to manual acupuncture I^2%: 78%.. **Indirectness: no serious.** all studies based in China, so unclear effect on other populations, no long term outcomes, intervention in approx 1/3 studies involved electroacupuncture with subgroup analysis reported. **Imprecision: no serious. Publication bias: no serious.**
4. no data on adverse effects given in systematic review
5. **Risk of Bias: very serious. Inconsistency: serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**

Attached Images

Good practice statement

Consensus-based recommendations
For stroke survivors with severe weakness who are at risk of developing shoulder pain, management may include:

- shoulder strapping;
- education of staff, carers and stroke survivors about preventing trauma;
- active motor training to improve function.

Evidence To Decision

Resources and other considerations

Implementation consideration There is a clinical indicator collected in the National Stroke Audit to determine the total number of patients with shoulder pain on admission to acute care and/or rehabilitation. There is also a clinical indicator collected to determine the number of patients with shoulder pain during their acute care and/or rehabilitation admission.

Rationale

While there is little evidence shoulder strapping prevents pain there are limited other inventions found to be effective and therefore it is deemed to be worth trialling.

Info Box

Practice point
For stroke survivors who develop shoulder pain, management should be based on evidence-based interventions for acute musculoskeletal pain.

Swelling of the extremities

People who are upright (standing or sitting) with their arm or leg hanging and immobile as a result of weakness are at risk of developing swelling of the hand or foot. Limited robust evidence exists for interventions to prevent and treat swelling. Manual edema mobilisation to help reduce subacute and chronic hand oedema has been suggested based on low to moderate quality evidence in mixed populations (Miller et al 2017 *[115]*). This approach involves massage in praximal to distal then distal to proximal direction, exercises, pump point stimulation and low-stretch bandaging. However, conventional therapy including elevation, exercise and compression should be used in most cases. Further trials are needed.

Good practice statement

Consensus-based recommendations
For stroke survivors with severe weakness who are at risk of developing swelling of the extremities, management may include the following

- passive mobilisation;
- elevation of the limb when resting.

Practical Info

Passive mobilisation (or passive range of motion) is time consuming to deliver, with or without a machine. Setting up elevation of the limb and finding a feasible, comfortable position will take time. Photographs or videotape may be helpful to prompt nursing staff and family members who are able to assist with interventions outside of therapy sessions.

Therapists who choose to provide other interventions (such as those reviewed in this guideline) need to think about the time and resources involved. For example, see the extensive Blixembosch protocol described by Kuppens et al (2013)*[107]* which did not result in any significant changes in limb swelling or differences between groups.

If electrical stimulation is already being used to elicit motor recovery in finger or wrist muscles, a reduction in limb swelling may be observed as an additional benefit in individual cases. However there is no trustworthy evidence that electrical stimulation reduces or prevents limb swelling, which is why electrical stimulation is not recommended as an intervention to reduce or prevent swelling.

Early attempts at active task-specific practice by stroke survivors may be important for helping muscles to contract, potentially helping to prevent or reduce limb swelling.

Rationale

Between 14% and 50% of stroke survivors develop swelling of their affected arm (Bell & Muller 2013; Kuppens 2013). Less is known about the incidence of leg swelling post-stroke. When fluid collects in the tissues of the upper limb, joints swell, and finger flexion becomes stiff and painful. Use of the affected hand becomes more impaired, and practice during rehabilitation may be restricted. Therefore, prevention and management of limb swelling is required. Swelling is less common once stroke survivors can actively contract finger and forearm muscles - another reason to encourage active practice early after stroke.

The most widely used intervention to reduce swelling is limb elevation, yet few studies have evaluated the effect of elevation using a randomised controlled trial design. One non-randomised study evaluated a protocol including elevation in a sling along with other interventions for the prevention of upper limb swelling, and management of swelling if and when it occurred (Kuppens et al 2013 *[107]*). That study is one of the few to recruit and intervene prophylactically. Almost all studies recruit stroke survivors with the aim of reducing limb swelling once it arises.

Due to the methodological biases and lack of replication, only consensus-based recommendations can be made about the prevention and management of limb swelling.

Clinical Question/ PICO

Population: Adults with stroke
Intervention: Mixed interventions

Comparator: Usual care

Summary

A systematic review (Giang 2016 *[111]*) identified two RCTs (Burge 2008, Kang 2008), one single-subject cross over trial (Gracies 2000), and one comparative non-randomised trial (Kuppens 2013) which have been classified as 'mixed interventions'.

The effect of a neutral functional realignment orthosis (hand splint) on limb swelling was investigated by Burge and colleagues (2008). Subacute inpatients (n=31) wore the orthosis for at least 6 hours daily in addition to the standard 13-week rehabilitation programme. Control participants received two sessions of physiotherapy per day, and one session of occupational therapy once daily. Experimental group participants wore the orthosis on the palmar surface of the hand. The orthosis did not cover the fingers, allowing participants to hold and manipulate objects. Participants were approximately one month post-stroke at recruitment, with a mean age of 68 (experimental group, n=15) and 64 years (control group, n=16). The primary outcome measure was a visual analogue scale (0 to 10) of pain in the hand at rest. Secondary measures included passive range of motion of the forearm, wrist and fingers, and circumferential measures on both hands, with a tape measure of the index finger at the proximal phalange, the mid-metacarpal line, and the wrist proximal to the metacarpophalangeal joint crease, to evaluate oedema. The presence of oedema was confirmed if the difference at these three anatomical sites was ≥ two standard deviations of the mean difference, between dominant and non-dominant hand (based on differences in a healthy population). Oedema was present only if the difference between limbs was ≥ 0.6. There was no between-group difference in the presence of hand oedema, however, hand and wrist oedema was not common in the sample. At baseline, only one participant in each group presented with oedema. Post-intervention, only 1/15 participant in the experimental group, and 2/16 participants in the control group had measureable oedema. Study methods were classified as moderate quality (PEDro score 6/10).

The effect of an upper limb lycra garment (hand and arm orthotic) was investigated in a small single subject crossover trial by Gracies et al (2000)*[109]*. They recruited 16 stroke participants with hemiparesis and upper limb spasticity who had sustained their stroke more than 3 weeks before the study commenced (inpatients and outpatients). Experimental participants wore the garments for 3 hours, and changes in limb swelling over the 3 hour period were compared to a 3 hour period without the garment. Significant reduction in swelling of the middle digit and the forearm was reported after use of the garment, among 6 experimental participants with a swollen paretic arm. Study methods were classified as low quality (PEDro 4/10).

A multi-component best-practice protocol (the 'Blixembosch protocol') for preventing and treating hand oedema was compared with usual care (Kuppens et al 2013*[107]*). This prospective, non-randomized 2-group study recruited 206 participants 5-7 weeks post stroke at two different rehabilitation centres. Between 35% and 50% had oedema at the initial measurement. Usual care included elevation in a sling, compression using tape on the fingers and hand, and splinting. The experimental protocol included five steps, each step taking at least two weeks with re-assessment weekly (or bi-weekly if no oedema) until discharge, which was usually at three months. The five steps included a prevention phase (checking for oedema and range of motion, ensuring elevation at rest, encouraging active movement and hand exercises), then treatment (hand splint at night initially, cryotherapy three times daily, elastic glove during the day, compression taping). The primary outcome was the presence (or absence) of oedema (Y/N), but no measures of limb oedema were provided. The secondary outcome was mean duration of oedema. There was a small positive effect of the intervention protocol on hand oedema compared with usual care (16% of the intervention group developed oedema, compared with 21% of the control group, post admission). Change scores were not reported. The intervention group also experienced oedema for a longer duration (6.5 weeks v 3.1 weeks) but more of the experimental group had oedema at the time of the first measure, 5-7 weeks poststroke (50% v 33% for the control group). Study methods were classified as low quality (PEDro score 5/10), with unblinded outcome assessors, and a high loss to follow-up (only 49% of the experimental group)

The effect of meridian acupressure on poststroke hand oedema (n56) was investigated by Kang et al (2009), and summarised in a review by Giang et al (2016). The intervention group received acupressure for 10 minutes daily after general physical therapy over a 2-week period, and the control group received routine care and physical therapy. Participants were 14 to 56 weeks post stroke, with an age range 50 to 71 years. Meridian acupressure is a finger acupressure technique pressing on the 14 meridian points in the Qi flow. The outcome measure was index finger circumference measured in millimetres by a blinded assessor using a jeweller's ring measurement device, before and after two weeks. The results showed a statistically significant reduction in index finger oedema in both groups, greater in the experimental group. However the amount of actual change (-0.25mm for experimental group and -0.06mm for controls) was small, and the between-group difference in finger oedema after two weeks was small (0.19mm). The study methods were rated as high quality (PEDro score of 7/10).

Outcome Timeframe	**Study results and measurements**	**Comparator** Usual care	**Intervention** Mixed interventions	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Hand oedema 7 Critical	(Randomized controlled)	One study by Burge et al (2008)(n=31) involved wearing a hand splint at least 6 hours daily during subacute inpatient care. There were too few patients with hand oedema for meaningful comparison. Gracies et al (2000) assessed the use of a lycra arm sleeve in 16 patients and reported reduction in swelling. Kuppens et al (2013) involved a step wise, multicomponent treatment in 206 post-acute stroke patients. No formal measure of oedmea was used but there was a small overall reduction in reported presence of hand oedema. Kang et al (2009) investigated acupressure treatment in 56 patients. Significant reduction in hand oedema using ring measurement device was found.		Very low Generally low to moderate quality studies testing different interventions in different population groups. 1	The use of various interventions to reduce hand eodema is unclear based on range of small trials.

1. **Risk of Bias: serious. Inconsistency: no serious. Indirectness: serious. Imprecision: serious. Publication bias: no serious.**

Attached Images

Clinical Question/ PICO

Population: Adults with stroke
Intervention: Compression therapy
Comparator: Standard therapy

Summary

One systematic review identified two RCTs and one cross over controlled trial (Giang 2016 *[111]*) regarding compression therapy. In a small underpowered randomised controlled trial with 17 acute stroke patients compared kinesio tape to standard therapy (Bell et al 2013). The between-group difference seen in limb circumference was small and clinically insignificant. At the end of 6 days of treatment, there was only 0.5 cm difference in metacarpophalangeal circumference and 0.1 cm difference in wrist circumference between groups and neither difference was significant. The trial was moderate quality (PEDro score 6/10). The other RCT (Roper et al 1999) included 37 participants in subacute phase (3-6 weeks after stroke). Intermittent pneumatic compression was applied with 30 second inflation and 20 second deflation cycles for two hours per day for one month. No difference in outcomes between groups. The trial was moderate quality (PEDro score 5/10).

Another cross over trial (N=8, Gustafsson et al 2014) included in the review compared high and low stretch compression bandages. Hand oedema was reduced only during the 1-week intervention but increased again afterwards. No difference was found between high and low compression groups. This study was low quality (PEDro score 4/10).

Outcome Timeframe	**Study results and measurements**	**Comparator** Standard therapy	**Intervention** Compression therapy	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Wrist circumference After 6 days of treatment 7 Critical	Measured by: Gulick measuring tape Lower better Based on data from 17 participants in 1 studies. (Randomized controlled) Follow up: 6 days.	17.7 centimetres (Median) Difference:	17.8 centimetres (Median) **MD 0.1 higher**	Low The difference between groups was non-significant (p = 0.189). Due to serious risk of bias, Due to serious imprecision [1]	Kinesio tape plus standard therapy may have little or no difference on wrist circumference
MCP circumference After 6 days of treatment 7 Critical	Measured by: Gulick measuring tape Lower better Based on data from 17 participants in 1 studies. (Randomized controlled) Follow up: 6 days.	20.4 centimetres (Median) Difference:	20.9 centimetres (Median) **MD 0.5 higher** CI 95%	Low The difference between groups was non-significant (p = 0.111). Due to serious risk of bias, Due to serious imprecision [2]	Kinesio tape plus standard therapy may have little or no difference on MCP circumference

1. **Risk of Bias: serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data and/or large loss to follow up, Missing intention-to-treat analysis, Selective outcome reporting. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Low number of patients, Only data from one study, no confidence intervals reported so range of possible treatment effects can't be determined. **Publication bias: no serious.**
2. **Risk of Bias: serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data and/or large loss to follow up, Selective outcome reporting, Missing intention-to-treat analysis. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Low number of patients, Only data from one study, no confidence intervals reported so range of possible treatment effects can't be determined. **Publication bias: no serious.**

Attached Images

Clinical Question/ PICO

Population: Adults with stroke
Intervention: Passive mobilisation
Comparator: Control

Summary

An RCT comparing continuous passive motion (CPM) of the fingers plus limb elevation was conducted to treat hand oedema using a within-subjects design, with 16 participants (Giudice et al. 1990 *[110]*). The trial was not stroke-specific but included 11 participants who had visible hand oedema after four weeks due to arm injury or surgery or arm paresis. Changes in hand volume and finger circumference were measured after two consecutive days. The timeframe was therefore very short. One group received CPM alone on Day 1, with limb elevation added on Day 2. The second group received CPM plus limb elevation on Day 1, then CPM alone on Day 2. Both groups received the intervention for 30 minutes on each occasion. Hand volume and finger circumference showed significant reductions following CPM plus elevation, compared to elevation alone. Mean change in *hand volume* was 14.5 ml (SD 8.4) compared with 6.1 ml (SD 9.5) following elevation alone. Mean change in finger circumference was 1.4 mm (SD 0.9) compared to 0.6 mm (SD 0.6) following elevation alone. However, the quality of evidence is very low due to risk of bias and imprecision (PEDro score 3/10) and very limited participants. Allocation to groups was not randomised, and blinded assessors were not used.

An additional RCT (n=37) compared bilateral passive range of motion exercise performed twice daily for 4 weeks with a control group receiving the same protocol but only for 2 weeks (Kim et al. 2014). The RCT was summarised in the systematic review by Giang et al. (2016) *[111]*. Participants were recruited within 72 hours post-stroke from three hospitals in South Korea, mostly from neuroscience intensive care units. The stroke survivors were shown how to complete passive range of motion exercises first of the unaffected arm then the affected arm. The intervention occurred for about 15 minutes morning and evening, five days a week for 4 weeks. The control group received usual care for the first two weeks, then 2 weeks of the passive range of motion exercises. Measures of finger, wrist and elbow circumference were obtained with a tape measure pre-test, at 2 weeks and 4 weeks by a blinded assessor. Significant differences in oedema were reported between intervention and control at 2 and 4 weeks post intervention. The experimental group had reduced oedema at the finger, wrist and elbow, while the control group showed increased circumference and oedema at all three points, even after introduction of the passive range of motion exercises at 2 weeks. For example, finger circumference reduced in the experimental group from a mean of 73.3 mm at baseline, to 69.2mm after 2 weeks and 65.9mm after 4 weeks. Finger circumference in the control group increased from a mean of 73.7mm at baseline, to 77.6mmm after 2 weeks, and 77.9mmm after 4 weeks. Between-group differences in finger oedema were clinically and statistically significant after 4 weeks (7.4mm decrease in finger circumference for the experimental group vs 4.2mm increase for the control group, p=0.002). This study was rated as high (PEDro score 8/10)

Outcome Timeframe	**Study results and measurements**	**Comparator** Control	**Intervention** Mobilisation	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Wrist circumference [1] 2 weeks 7 Critical	Measured by: Tape measure Lower better Based on data from 37 participants in 1 studies. (Randomized controlled) Follow up: 4 weeks.	6.1 mm (Mean) Difference:	14.5 mm (Mean) **MD 8.4 higher**	Very low The treatment effect was significant (p < 0.01), Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision [2]	We are uncertain whether continuous passive motion improves or worsens hand volume
Finger circumference After 30 minutes of treatment 7 Critical	Measured by: Reduction in finger circumference (mm) High better Based on data from 16 participants in 1 studies. [3] (Observational (non-randomized)) Follow up: 30 minutes.	0.6 mm (Mean) Difference:	1.4 mm (Mean) **MD 0.8 higher**	Very low The treatment effect was significant (p < 0.02), Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision [4]	We are uncertain whether continuous passive motion increases or decreases finger circumference

1. measured by tape measure
2. **Risk of Bias: serious.** Non-randomised trial. Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias. **Inconsistency: no serious. Indirectness: serious.** Differences between the population of interest and those studied: not stroke-specific, 11/16 included participants had CVA. **Imprecision: serious.** Low number of patients, Only data from one study, Confidence intervals for effect not reported. **Publication bias: no serious.**
3. Primary study[110]. **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of Bias: serious.** Non-randomised trial. Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias. **Inconsistency: no serious. Indirectness: serious.** Differences between the population of interest and those studied: not stroke-specific, 11/16 included participants had CVA.

Imprecision: serious. Low number of patients, Only data from one study, Confidence intervals for effect not reported.
Publication bias: no serious.

Attached Images

Clinical Question/ PICO

Population: Adults with stroke with complex regional pain syndrome
Intervention: Heat therapy (various means)
Comparator: Usual care

Summary

Sezgin Ozcan et al (2019)*[112]* reported the effectiveness of fluidotherapy in 32 participants with poststroke complex regional pain syndrome in the upper limb. All subjects were in the subacute period and received usual physiotherapy and occupational therapy (positioning, ROM, stretching, strengthening exercises, postural control, weight-shifting, gait training, endurance training, orthosis [if required], education and conventional TENS). Treatment occured 5 days a week over 3 weeks. The intervention group recieived additional treatment of fluidotherapy which provides heat therapy while also encouraging active ROM. Treatment occured 5 times per week at 40 degrees for 20mins. Intervention resulted in reduced oedema volume compared to usual care ($p<0.05$). Assessment occurred after the 3 week treatment and no long term outcomes are known. Study methods were rated as being of moderate quality (PEDro score 6/10). Further trials are needed to confirm these findings.

Outcome Timeframe	**Study results and measurements**	**Comparator** Usual care	**Intervention** Heat therapy	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Distal arm volume post intervention 7 Critical	Based on data from 32 participants in 1 studies. (Randomized controlled)	The intervention group who had usual care plus active movement in warm (40 degree) fluidotherapy device. A total of 15 sessions over 3 weeks was provided. Intervention lead to a significantly greater reduction in volume (p=0.001) than the usual care alone.		**Low** Due to serious risk of bias, Due to serious imprecision [1]	Fluidotherapy plus routine therpay may reduce oedema volume in distal arm compared to routine therapy alone.

1. **Risk of Bias: serious. Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.**

Attached Images

Clinical Question/ PICO

Population: Adults with stroke with hand swelling
Intervention: Electrical stimulation
Comparator: Usual care

Summary

One non-randomised trial evaluated the effect of electrical stimulation compared to elevation on upper limb swelling (Faghri et al 1997*[114]*). A small sample of stroke survivors was recruited (n=8), < 6 months post stroke, with visible oedema and a flaccid limb. Four participants received electrical stimulation on Day 1 and elevation on Day 2. Another four participants received elevation on Day 1, and electrical stimulation on Day 2. Elevation was provided in supine, 30° shoulder forward

flexion, 30° abduction, 70° elbow flexion. Electrical stimulation was also provided in supine, with the affected hand by the side. Reciprocal stimulation was provided alternately to wrist flexors and extensors, with a duty cycle of 10:10:10s flexion: extension: off, using a frequency of 35 Hz. Both groups also received 'usual oedema therapy' (not stated). Both groups received the treatment for 30 minutes for two consecutive days. The primary outcome was limb size, measured using a volumeter and displaced water (two successive measures taken), and circumferential measures of the upper and lower arm with a flexible tape measure, before and immediately after 30 minutes of treatment. Limb circumference decreased more after 30 mins of electrical stimulation compared to 30 mins of limb elevation. The benefits were not maintained beyond 24 hours. Electrical stimulation may be more beneficial than elevation, but study replication is needed with blinding of assessors and a randomised control group. Despite the many trials that have investigated electrical stimulation, few have measured the effect on limb circumference and swelling.

Outcome Timeframe	**Study results and measurements**	**Comparator** Usual care	**Intervention** Electrical stimulation	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Volume after 2 days of treatment 7 Critical	(Observational (non-randomized))	Hand volume and arm volume were reduced with electrical stimulation compared to elevation of the arm (hand: -13.38 ml vs 1.88 ml; arm: -32.63 ml vs 26.5ml).		Very low Due to serious risk of bias, Due to very serious imprecision [1]	Electrical stimulation may reduce swelling more than simple elevation.

1. **Risk of Bias: serious. Imprecision: very serious.** Only data from one study (n=8).

Attached Images

Good practice statement

Consensus-based recommendations
For stroke survivors who developed swelling of the hands or feet, management may include the following:

- passive mobilisation;
- elevation of the limb when resting.

Practical Info

Premorbid swelling and risk factors needs to be assessed.

Passive mobilisation (or passive range of motion) is time consuming to deliver, with or without a machine. Setting up elevation of the limb and finding a feasible, comfortable position will take time. Photographs or videotape may be helpful to prompt nursing staff and family members who are able to assist with interventions outside of therapy sessions.

Therapists who choose to provide other interventions (such as those reviewed in this guideline) need to think about the time and resources involved.

If electrical stimulation is already being used to elicit motor recovery in finger or wrist muscles, a reduction in limb swelling may be observed as an additional benefit in individual cases. However there is no trustworthy evidence that electrical stimulation reduces or prevents limb swelling, which is why electrical stimulation is not recommended.

If mirror therapy is already being used to elicit motor recovery in finger or wrist muscles, a reduction in limb swelling may be observed as an additional benefit in individual cases (Saha, 2020). However, there is no trustworthy evidence that mirror therapy reduces or prevents limb swelling, which is why mirror therapy is not recommended.

Early attempts at active task-specific practice by stroke survivors may be important for helping muscles to contract, potentially helping to prevent or reduce limb swelling.

Rationale

Several studies have evaluated interventions to reduce swelling, often using small underpowered samples and methods that involve methodological biases. Single studies reviewed in this section evaluated the effect on limb swelling of a hand orthosis (Burge et al 2008), lycra garment (Gracies et al 2000), acupressure (Kang et al 2009), compression therapy using kinesio tape (Bell & Muller 2013), intermittent pneumatic compression via machine (Roper et al 1999), compression bandaging (Gustafsson et al 2014), passive joint mobilisation with or without elevation (Guidice et al 1990 and Kim et al 2014 respectively), heat therapy (Sezgin Ozcan et al 2019) and electrical stimulation (Faghri et al 1997). No studies have replicated an intervention or protocol, therefore comparisons are not possible.

Due to the methodological biases and lack of replication, only consensus-based recommendations can be made about the prevention and management of limb swelling.

Clinical Question/ PICO

Population: Adults with stroke
Intervention: Mixed interventions
Comparator: Usual care

Summary

A systematic review (Giang 2016 *[111]*) identified two RCTs (Burge 2008, Kang 2008), one single-subject cross over trial (Gracies 2000), and one comparative non-randomised trial (Kuppens 2013) which have been classified as 'mixed interventions'.

The effect of a neutral functional realignment orthosis (hand splint) on limb swelling was investigated by Burge and colleagues (2008). Subacute inpatients (n=31) wore the orthosis for at least 6 hours daily in addition to the standard 13-week rehabilitation programme. Control participants received two sessions of physiotherapy per day, and one session of occupational therapy once daily. Experimental group participants wore the orthosis on the palmar surface of the hand. The orthosis did not cover the fingers, allowing participants to hold and manipulate objects. Participants were approximately one month post-stroke at recruitment, with a mean age of 68 (experimental group, n=15) and 64 years (control group, n=16). The primary outcome measure was a visual analogue scale (0 to 10) of pain in the hand at rest. Secondary measures included passive range of motion of the forearm, wrist and fingers, and circumferential measures on both hands, with a tape measure of the index finger at the proximal phalange, the mid-metacarpal line, and the wrist proximal to the metacarpophalangeal joint crease, to evaluate oedema. The presence of oedema was confirmed if the difference at these three anatomical sites was ≥ two standard deviations of the mean difference, between dominant and non-dominant hand (based on differences in a healthy population). Oedema was present only if the difference between limbs was ≥ 0.6. There was no between-group difference in the presence of hand oedema, however, hand and wrist oedema was not common in the sample. At baseline, only one participant in each group presented with oedema. Post-intervention, only 1/15 participant in the experimental group, and 2/16 participants in the control group had measureable oedema. Study methods were classified as moderate quality (PEDro score 6/10).

The effect of an upper limb lycra garment (hand and arm orthotic) was investigated in a small single subject crossover trial by Gracies et al (2000)*[109]*. They recruited 16 stroke participants with hemiparesis and upper limb spasticity who had sustained their stroke more than 3 weeks before the study commenced (inpatients and outpatients). Experimental participants wore the garments for 3 hours, and changes in limb swelling over the 3 hour period were compared to a 3 hour period without the garment. Significant reduction in swelling of the middle digit and the forearm was reported after use of the garment, among 6 experimental participants with a swollen paretic arm. Study methods were classified as low quality (PEDro 4/10).

A multi-component best-practice protocol (the 'Blixembosch protocol') for preventing and treating hand oedema was compared with usual care (Kuppens et al 2013*[107]*). This prospective, non-randomized 2-group study recruited 206 participants 5-7 weeks post stroke at two different rehabilitation centres. Between 35% and 50% had oedema at the initial measurement. Usual care included elevation in a sling, compression using tape on the fingers and hand, and splinting. The experimental protocol included five steps, each step taking at least two weeks with re-assessment weekly (or bi-weekly if no oedema) until discharge, which was usually at three months. The five steps included a prevention phase (checking for oedema and range of motion, ensuring elevation at rest, encouraging active movement and hand exercises), then treatment (hand splint at night initially, cryotherapy three times daily, elastic glove during the day, compression taping). The primary outcome was the presence (or absence) of oedema (Y/N), but no measures of limb oedema were provided. The secondary outcome was mean duration of oedema. There was a small positive effect of the intervention protocol on hand oedema compared with usual care (16% of the intervention group developed oedema, compared with 21% of the control group, post

admission). Change scores were not reported. The intervention group also experienced oedema for a longer duration (6.5 weeks v 3.1 weeks) but more of the experimental group had oedema at the time of the first measure, 5-7 weeks poststroke (50% v 33% for the control group). Study methods were classified as low quality (PEDro score 5/10), with unblinded outcome assessors, and a high loss to follow-up (only 49% of the experimental group)

The effect of meridian acupressure on poststroke hand oedema (n56) was investigated by Kang et al (2009), and summarised in a review by Giang et al (2016). The intervention group received acupressure for 10 minutes daily after general physical therapy over a 2-week period, and the control group received routine care and physical therapy. Participants were 14 to 56 weeks post stroke, with an age range 50 to 71 years. Meridian acupressure is a finger acupressure technique pressing on the 14 meridian points in the Qi flow. The outcome measure was index finger circumference measured in millimetres by a blinded assessor using a jeweller's ring measurement device, before and after two weeks. The results showed a statistically significant reduction in index finger oedema in both groups, greater in the experimental group. However the amount of actual change (-0.25mm for experimental group and -0.06mm for controls) was small, and the between-group difference in finger oedema after two weeks was small (0.19mm). The study methods were rated as high quality (PEDro score of 7/10).

Outcome Timeframe	**Study results and measurements**	**Comparator** Usual care	**Intervention** Mixed interventions	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Hand oedema 7 Critical	(Randomized controlled)	One study by Burge et al (2008)(n=31) involved wearing a hand splint at least 6 hours daily during subacute inpatient care. There were too few patients with hand oedema for meaningful comparison. Gracies et al (2000) assessed the use of a lycra arm sleeve in 16 patients and reported reduction in swelling. Kuppens et al (2013) involved a step wise, multicomponent treatment in 206 post-acute stroke patients. No formal measure of oedmea was used but there was a small overall reduction in reported presence of hand oedema. Kang et al (2009) investigated acupressure treatment in 56 patients. Significant reduction in hand oedema using ring measurement device was found.		Very low Generally low to moderate quality studies testing different interventions in different population groups. 1	The use of various interventions to reduce hand eodema is unclear based on range of small trials.

1. **Risk of Bias: serious. Inconsistency: no serious. Indirectness: serious. Imprecision: serious. Publication bias: no serious.**

Attached Images

Clinical Question/ PICO

Population: Adults with stroke
Intervention: Compression therapy
Comparator: Standard therapy

Summary

One systematic review identified two RCTs and one cross over controlled trial (Giang 2016 *[111]*) regarding compression therapy. In a small underpowered randomised controlled trial with 17 acute stroke patients compared kinesio tape to standard therapy (Bell et al 2013). The between-group difference seen in limb circumference was small and clinically insignificant. At the end of 6 days of treatment, there was only 0.5 cm difference in metacarpophalangeal circumference and 0.1 cm difference in wrist circumference between groups and neither difference was significant. The trial was moderate

quality (PEDro score 6/10). The other RCT (Roper et al 1999) included 37 participants in subacute phase (3-6 weeks after stroke). Intermittent pneumatic compression was applied with 30 second inflation and 20 second deflation cycles for two hours per day for one month. No difference in outcomes between groups. The trial was moderate quality (PEDro score 5/10).

Another cross over trial (N=8, Gustafsson et al 2014) included in the review compared high and low stretch compression bandages. Hand oedema was reduced only during the 1-week intervention but increased again afterwards. No difference was found between high and low compression groups. This study was low quality (PEDro score 4/10).

Outcome Timeframe	**Study results and measurements**	**Comparator** Standard therapy	**Intervention** Compression therapy	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Wrist circumference After 6 days of treatment 7 Critical	Measured by: Gulick measuring tape Lower better Based on data from 17 participants in 1 studies. (Randomized controlled) Follow up: 6 days.	17.7 centimetres (Median) Difference:	17.8 centimetres (Median) **MD 0.1 higher**	Low The difference between groups was non-significant (p = 0.189). Due to serious risk of bias, Due to serious imprecision [1]	Kinesio tape plus standard therapy may have little or no difference on wrist circumference
MCP circumference After 6 days of treatment 7 Critical	Measured by: Gulick measuring tape Lower better Based on data from 17 participants in 1 studies. (Randomized controlled) Follow up: 6 days.	20.4 centimetres (Median) Difference:	20.9 centimetres (Median) **MD 0.5 higher** CI 95%	Low The difference between groups was non-significant (p = 0.111). Due to serious risk of bias, Due to serious imprecision [2]	Kinesio tape plus standard therapy may have little or no difference on MCP circumference

1. **Risk of Bias: serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data and/or large loss to follow up, Missing intention-to-treat analysis, Selective outcome reporting. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Low number of patients, Only data from one study, no confidence intervals reported so range of possible treatment effects can't be determined. **Publication bias: no serious.**
2. **Risk of Bias: serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data and/or large loss to follow up, Selective outcome reporting, Missing intention-to-treat analysis. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Low number of patients, Only data from one study, no confidence intervals reported so range of possible treatment effects can't be determined. **Publication bias: no serious.**

Attached Images

Clinical Question/ PICO

Population: Adults with stroke
Intervention: Passive mobilisation
Comparator: Control

Summary

An RCT comparing continuous passive motion (CPM) of the fingers plus limb elevation was conducted to treat hand oedema using a within-subjects design, with 16 participants (Giudice et al. 1990 *[110]*). The trial was not stroke-specific but included 11 participants who had visible hand oedema after four weeks due to arm injury or surgery or arm paresis. Changes in hand volume and finger circumference were measured after two consecutive days. The timeframe was therefore very short. One group received CPM alone on Day 1, with limb elevation added on Day 2. The second group received CPM plus limb elevation on Day 1, then CPM alone on Day 2. Both groups received the intervention for 30 minutes on each occasion. Hand volume and finger circumference showed significant reductions following CPM plus elevation, compared to elevation alone. Mean change in *hand volume* was 14.5 ml (SD 8.4) compared with 6.1 ml (SD 9.5) following elevation alone. Mean change in finger circumference was 1.4 mm (SD 0.9) compared to 0.6 mm (SD 0.6) following elevation alone. However, the quality of evidence is very low due to risk of bias and imprecision (PEDro score 3/10) and very limited participants. Allocation to groups was not randomised, and blinded assessors were not used.

An additional RCT (n=37) compared bilateral passive range of motion exercise performed twice daily for 4 weeks with a control group receiving the same protocol but only for 2 weeks (Kim et al. 2014). The RCT was summarised in the systematic review by Giang et al. (2016) *[111]*. Participants were recruited within 72 hours post-stroke from three hospitals in South Korea, mostly from neuroscience intensive care units. The stroke survivors were shown how to complete passive range of motion exercises first of the unaffected arm then the affected arm. The intervention occurred for about 15 minutes morning and evening, five days a week for 4 weeks. The control group received usual care for the first two weeks, then 2 weeks of the passive range of motion exercises. Measures of finger, wrist and elbow circumference were obtained with a tape measure pre-test, at 2 weeks and 4 weeks by a blinded assessor. Significant differences in oedema were reported between intervention and control at 2 and 4 weeks post intervention. The experimental group had reduced oedema at the finger, wrist and elbow, while the control group showed increased circumference and oedema at all three points, even after introduction of the passive range of motion exercises at 2 weeks. For example, finger circumference reduced in the experimental group from a mean of 73.3 mm at baseline, to 69.2mm after 2 weeks and 65.9mm after 4 weeks. Finger circumference in the control group increased from a mean of 73.7mm at baseline, to 77.6mmm after 2 weeks, and 77.9mmm after 4 weeks. Between-group differences in finger oedema were clinically and statistically significant after 4 weeks (7.4mm decrease in finger circumference for the experimental group vs 4.2mm increase for the control group, p=0.002). This study was rated as high (PEDro score 8/10)

Outcome Timeframe	**Study results and measurements**	**Comparator** Control	**Intervention** Mobilisation	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Wrist circumference [1] 2 weeks 7 Critical	Measured by: Tape measure Lower better Based on data from 37 participants in 1 studies. (Randomized controlled) Follow up: 4 weeks.	6.1 mm (Mean) Difference:	14.5 mm (Mean) **MD 8.4 higher**	Very low The treatment effect was significant (p < 0.01), Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision [2]	We are uncertain whether continuous passive motion improves or worsens hand volume
Finger circumference After 30 minutes of treatment 7 Critical	Measured by: Reduction in finger circumference (mm) High better Based on data from 16 participants in 1 studies. [3] (Observational (non-randomized)) Follow up: 30 minutes.	0.6 mm (Mean) Difference:	1.4 mm (Mean) **MD 0.8 higher**	Very low The treatment effect was significant (p < 0.02), Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision [4]	We are uncertain whether continuous passive motion increases or decreases finger circumference

1. measured by tape measure
2. **Risk of Bias: serious.** Non-randomised trial. Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for

selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/ lack of blinding of outcome assessors, resulting in potential for detection bias. **Inconsistency: no serious. Indirectness: serious.** Differences between the population of interest and those studied: not stroke-specific, 11/16 included participants had CVA. **Imprecision: serious.** Low number of patients, Only data from one study, Confidence intervals for effect not reported. **Publication bias: no serious.**

3. Primary study[110]. **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of Bias: serious.** Non-randomised trial. Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/ lack of blinding of outcome assessors, resulting in potential for detection bias. **Inconsistency: no serious. Indirectness: serious.** Differences between the population of interest and those studied: not stroke-specific, 11/16 included participants had CVA. **Imprecision: serious.** Low number of patients, Only data from one study, Confidence intervals for effect not reported. **Publication bias: no serious.**

Attached Images

Clinical Question/ PICO

Population: Adults with stroke with complex regional pain syndrome
Intervention: Heat therapy (various means)
Comparator: Usual care

Summary

Sezgin Ozcan et al (2019)*[112]* reported the effectiveness of fluidotherapy in 32 participants with poststroke complex regional pain syndrome in the upper limb. All subjects were in the subacute period and received usual physiotherapy and occupational therapy (positioning, ROM, stretching, strengthening exercises, postural control, weight-shifting, gait training, endurance training, orthosis [if required], education and conventional TENS). Treatment occured 5 days a week over 3 weeks. The intervention group recieived additional treatment of fluidotherapy which provides heat therapy while also encouraging active ROM. Treatment occured 5 times per week at 40 degrees for 20mins. Intervention resulted in reduced oedema volume compared to usual care ($p<0.05$). Assessment occurred after the 3 week treatment and no long term outcomes are known. Study methods were rated as being of moderate quality (PEDro score 6/10). Further trials are needed to confirm these findings.

Outcome Timeframe	**Study results and measurements**	**Comparator** Usual care	**Intervention** Heat therapy	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Distal arm volume post intervention 7 Critical	Based on data from 32 participants in 1 studies. (Randomized controlled)	The intervention group who had usual care plus active movement in warm (40 degree) fluidotherapy device. A total of 15 sessions over 3 weeks was provided. Intervention lead to a significantly greater reduction in volume (p=0.001) than the usual care alone.		**Low** Due to serious risk of bias, Due to serious imprecision [1]	Fluidotherapy plus routine therpay may reduce oedema volume in distal arm compared to routine therapy alone.

1. **Risk of Bias: serious. Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.**

Attached Images

Clinical Question/ PICO

Population: Adults with stroke with hand swelling
Intervention: Electrical stimulation
Comparator: Usual care

Summary

One non-randomised trial evaluated the effect of electrical stimulation compared to elevation on upper limb swelling (Faghri et al 1997*[114]*). A small sample of stroke survivors was recruited (n=8), < 6 months post stroke, with visible oedema and a flaccid limb. Four participants received electrical stimulation on Day 1 and elevation on Day 2. Another four participants received elevation on Day 1, and electrical stimulation on Day 2. Elevation was provided in supine, 30° shoulder forward flexion, 30° abduction, 70° elbow flexion. Electrical stimulation was also provided in supine, with the affected hand by the side. Reciprocal stimulation was provided alternately to wrist flexors and extensors, with a duty cycle of 10:10:10s flexion: extension: off, using a frequency of 35 Hz. Both groups also received 'usual oedema therapy' (not stated). Both groups received the treatment for 30 minutes for two consecutive days. The primary outcome was limb size, measured using a volumeter and displaced water (two successive measures taken), and circumferential measures of the upper and lower arm with a flexible tape measure, before and immediately after 30 minutes of treatment. Limb circumference decreased more after 30 mins of electrical stimulation compared to 30 mins of limb elevation. The benefits were not maintained beyond 24 hours. Electrical stimulation may be more beneficial than elevation, but study replication is needed with blinding of assessors and a randomised control group. Despite the many trials that have investigated electrical stimulation, few have measured the effect on limb circumference and swelling.

Outcome Timeframe	**Study results and measurements**	**Comparator** Usual care	**Intervention** Electrical stimulation	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Volume after 2 days of treatment 7 Critical	(Observational (non-randomized))	Hand volume and arm volume were reduced with electrical stimulation compared to elevation of the arm (hand: -13.38 ml vs 1.88 ml; arm: -32.63 ml vs 26.5ml).		Very low Due to serious risk of bias, Due to very serious imprecision [1]	Electrical stimulation may reduce swelling more than simple elevation.

1. **Risk of Bias: serious. Imprecision: very serious.** Only data from one study (n=8).

Attached Images

Fatigue

Fatigue is a common long-term problem after stroke with estimates of prevalence ranging from 16% to 70% (McGeough et al 2009 *[118]*). A more recent systematic review found a pooled prevalence of 50% (95% CI 43 to 57) (Cumming et al 2016 *[121]*). Fatigue is defined here as abnormal (or pathological) fatigue which is characterised by weariness unrelated to previous exertion levels and is usually not ameliorated by rest (de Groot et al 2003 *[119]*). Exertional fatigue, which is a general state of tiredness, can be improved with rest. The aetiology of fatigue after stroke is uncertain (McGeough et al 2009 *[118]*). Recently, diagnostic criteria and an associated structured interview have been developed to identify which stroke patients have clinically significant fatigue (Lynch et al 2007 *[120]*).

Healthcare professionals should recognise patients with excess levels of fatigue and provide information and practical strategies such as negotiating therapy times and times for rest on a case-by-case basis. Enforced rest periods should not be used.

Consensus recommendation

Consensus-based recommendations

- Therapy for stroke survivors with fatigue should be organised for periods of the day when they are most alert.
- Stroke survivors and their families/carers should be provided with information, education and strategies to assist in managing fatigue.
- Potential modifying factors for fatigue should be considered, including avoiding sedating drugs and alcohol, and screening for sleep-related breathing disorders and depression.
- While there is insufficient evidence to guide practice, possible interventions could include cognitive behavioural therapy (focusing on fatigue and sleep with advice on regular exercise), exercise and improving sleep hygiene.

Practical Info

The cognitive behavioural therapy intervention was psychologist delivered – 8 once-weekly sessions composed of 6 modules addressing fatigue and sleep, and a one-off review by an exercise physiologist to prescribe target heart rate zones and advice regarding exercising for 30 minutes of moderate exercise, 3–5 times/week.

Clinical Question/ PICO

Population: Adults with stroke
Intervention: Interventions to treat fatigue
Comparator: Control

Summary

A Cochrane review by Wu et al (2015) *[116]* investigating interventions for preventing or treating post-stroke fatigue included 12 trials with 703 participants. Interventions used in the trials included pharmacological interventions (e.g. fluoxetine, enerion) and non-pharmacological therapy (a fatigue education program and a mindfulness-based stress reduction program). A meta-analysis comparing the overall fatigue severity between intervention and control groups showed a significant reduction in fatigue, but there was significant heterogeneity between trials (I^2 = 87%). The effect was non-significant when restricting analysis to trials with adequate allocation concealment, suggesting biased results. Overall, there is currently insufficient evidence to recommend for or against specific pharmacologic or non-pharmacologic interventions to treat fatigue in stroke survivors.

Pacheco et al (2019)*[117]* included two trials (n=77) of modafinil in post stroke fatigue. One trial (Bivard et al 2017) used 200mg vs placebo and the other (Polsen et al 2015) used 400mg for those under 65 years of age or 200mg over 65 years. Both trials reported reduction in Fatigue Severity Scale. Other outcomes varied between studies which varied in quality, and overall certainty of effect was rated as very low. Further data is required. *[117]*

A very small (n=15) pilot parallel two-group randomised controlled trial by Nguyen et al (2019)*[122]* assessed the impact of a psychologist-delivered cognitive behavioural therapy (CBT) intervention delivered weekly for 8 weeks. The intervention involved 6 modules addressing fatigue and sleep, and a one-off review by an exercise physiologist to prescribe target heart rate zones and advice regarding exercising for 30 minutes of moderate exercise 3–5 times/week. The intervention group (n=9) compared to control (n=6) at 4 months from baseline had significantly lower self-reported fatigue (Fatigue Severity Scale mean difference: 1.92, 95%CI 0.24 to 3.6), improved sleep quality (Pittsburgh Sleep Quality index mean difference: 2.46 95%CI 0.29 to 4.64) and less depression (Hospital Anxiety and Depression Scale score mean difference: 4.67 95%CI 1.35 to 7.99) than the control group (n=6). This pilot trial provides evidence for the potential value for CBT in managing

post-stroke fatigue, but further data are needed.

Outcome Timeframe	**Study results and measurements**	**Comparator** Control	**Intervention** Interventions to treat fatigue	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Fatigue - self-reported presence of fatigue End of 3 months treatment 7 Critical	Relative risk 0.89 (CI 95% 0.75 — 1.05) Based on data from 83 participants in 1 studies. [1] (Randomized controlled) Follow up: 3 months of treatment.	930 per 1000 Difference:	828 per 1000 **102 fewer per 1000** (CI 95% 232 fewer — 47 more)	**Low** Single small RCT [2]	Fluoxetine 20 mg daily for 3 months may have little or no effect on post stroke fatigue
Fatigue severity - Pharmacological interventions [3] End of treatment (1-3 months) 7 Critical	Measured by: Various - FSS, MFS, MFI-20, CIS-f, SSQOL-energy Lower better Based on data from 209 participants in 5 studies. [4] (Randomized controlled) Follow up: 1-3 months of treatment.	Difference:	**SMD 1.23 lower** (CI 95% 2.4 lower — 0.06 lower)	**Very low** The beneficial effect was not seen in trials using the adequate strategies for allocation concealment or those using adequate blinding of outcome assessors (risk of bias). In addition, there is substantial heterogeneity between the trials, but the available data were insufficient to identify the source of heterogeneity (inconsistency). Furthermore, this result did not provide information for the efficacy of any specific intervention (indirectness). [5]	Pharmacological interventions may decrease post stroke fatigue, however the result is of borderline significance and the quality of evidence is very low.
Fatigue severity - non-pharmacological interventions [6] End of treatment (4-6 weeks) 7 Critical	Measured by: Various - FSS, MFS, MFI-20, CIS-f, SSQOL-energy Lower better Based on data from 35 participants in 2 studies. [7] (Randomized controlled) Follow up: 4-6 weeks of treatment.	Difference:	**SMD 0.68 lower** (CI 95% 1.37 lower — 0.02 higher)	**Very low** Only two small trials (each with fewer than 20 participants) were identified, thus it is possible that these trials did not have adequate power to detect clinical difference, rather than these interventions had no effect on fatigue (imprecision). In	We are uncertain whether non-pharmacological interventions improve or worsen post stroke fatigue

Outcome Timeframe	**Study results and measurements**	**Comparator** Control	**Intervention** Interventions to treat fatigue	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
				addition, neither trial used adequate allocation concealment or intention-to-treat analysis (risk of biases). [8]	

1. Systematic review [116] with included studies: Choi-Kwon 2007. **Baseline/comparator:** Control arm of reference used for intervention.
2. **Inconsistency: no serious.** Only one study for the dichotomous outcome. **Indirectness: serious.** Generalisability of Korean data uncertain. **Imprecision: serious.** Only data from one study. **Publication bias: no serious.**
3. 4 trials with a range of different pharmacological interventions and follow up periods (1-3 months)
4. Systematic review [116] with included studies: Guo 2012, Guo 2012, Johansson 2012a, Choi-Kwon 2007, Gurak 2005. **Baseline/comparator:** Control arm of reference used for intervention.
5. **Risk of Bias: serious.** Missing intention-to-treat analysis, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias. **Inconsistency: serious.** substantial heterogeneity between the trials, but the available data were insufficient to identify the source of heterogeneity . **Indirectness: serious.** Differences between the population of interest and those studied. **Imprecision: serious.** Low number of patients. **Publication bias: no serious.**
6. Two trials with different follow up (4-6 weeks)
7. Systematic review [116] with included studies: Clarke 2012, Johansson 2012b. **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of Bias: serious.** Both trial had ROB related to allocation and missing intention-to-treat analysis. **Inconsistency: no serious. Indirectness: no serious. Imprecision: very serious.** Low number of patients, Wide confidence intervals. **Publication bias: no serious.**

Attached Images

Incontinence

Dysfunction of the bladder and/or bowel may be caused by a combination of stroke-related impairments (e.g. weakness, cognitive or perceptual impairments).

Urinary incontinence

Urinary incontinence is defined as the complaint of any involuntary leakage of urine. The most likely pattern of incontinence is urinary frequency, urgency (a sudden compelling desire to pass urine which is difficult to defer) and urge incontinence (involuntary leakage) (Thomas et al 2019 *[125]*). This is generally the result of detrusor overactivity although this may depend on the site of the stroke lesion, with damage to the frontal lobe being considered to be associated with urinary dysfunction after stroke. Functional incontinence can also occur, which is associated with normal bladder function, and may be related to cognitive and language deficits and/or physical immobility post stroke. Urinary incontinence is not only a predictor of poor functional outcomes but also a source of distress for both stroke survivors and their caregivers (Thomas et al 2019 *[125]*).

In the most recent National Stroke Audit of Acute Services, patients in Australia, 32% had incontinence within 72 hours of stroke onset (Stroke Foundation 2019 *[9]*). Among them, only 37% had an incontinence management plan in place, while 64% of hospitals reported having a locally agreed urinary incontinence protocol (Stroke Foundation 2019 *[9]*).

Weak recommendation

- All stroke survivors with suspected urinary continence difficulties should be assessed by trained personnel using a structured functional assessment. (Martin et al 2006 *[129]*)
- For stroke survivors, a portable bladder ultrasound scan should be used to assist in diagnosis and management of urinary incontinence. (Martin et al 2006 *[129]*)

Practical Info

Several types of urinary incontinence occur after stroke and hence assessment is important to identify the distinct aetiology in order to begin targeted interventions. Diagnostic assessment has been described as a five-step sequential process.

1. Clinical history-taking, including history of incontinence before the stroke, nature, duration and reported severity of symptoms, and exacerbating factors including diet, fluid and medications.
2. Validated scales that measure the severity of symptoms and impact of symptoms on QOL.
3. Physical examination, including abdominal, perineal (pelvic floor strength, vaginitis, vaginal prolapse), rectal and neurological examinations and measurement of body mass index.
4. Simple investigations, including urinalysis, midstream specimen of urine if clinically indicated, measurement of post-void residual volume, provocation stress test, frequency–volume charts and pad tests.
5. Advanced investigations, including urodynamics tests such as cystometry, urethral pressure measurement, pressure–flow studies, video-urodynamics and ambulatory monitoring.

Assessment for urinary incontinence should be preceded and accompanied by psychological support and full information (ideally in verbal, written and diagrammatic forms). The patient's dignity, privacy and emotional wellbeing should be protected throughout. It is also important that the health practitioner keeps in mind the statistics of sexual assault for women and men, when conducting their assessment.

For more information on the assessment of urinary incontinence in general, see the guidelines from the 6th International Consultation on Incontinence (Abrams et al 2017*[222]*).

Evidence To Decision

Benefits and harms

Small net benefit, or little difference between alternatives

A systematic review of diagnostic methods for urinary incontinence showed reasonable diagnostic performance from clinical history to diagnose urodynamic stress incontinence in women, question 3 of the Urogenital Distress Inventory,

and urinary diary, with ultrasound imaging being the optimal method - sensitivity 0.94, specificity 0.83 (Martin et al 2006 *[129]*).

Certainty of the Evidence

Moderate

The population investigated was not stroke specific patients, therefore it is uncertain if the results are transferable.

Values and preferences

No substantial variability expected

Patients would want to be appropriately diagnosed to allow for subsequent treatment to be planned.

Resources and other considerations

Important issues, or potential issues not investigated

Resources considerations

In economic modelling, keeping a diary of urinary incontinence was found to be the most cost-effective method of assessing urinary incontinence at £35 to £77 more per case diagnosed compared to standard care (cost reference year 2002) (Martin et al 2006 *[129]*).

Implementation considerations

There are clinical indicators collected in the National Stroke Audit on the total number of patients with incontinence present within the first 72 hours of stroke onset and the total number assessed for urinary incontinence during their admission. There is also a clinical indicator collected, for patients in rehabilitation, on whether an assessment for urinary incontinence was carried out within 72 hours of admission.

Rationale

Structured functional assessment is a cost-effective diagnosis method for urinary incontinence. Ultrasound imaging is the most accurate method and should be used if resources are available.

Clinical Question/ PICO

Population: Adults with suspected urinary incontinence
Intervention: Diagnostic assessment of urinary incontinence
Comparator: Multichannel urodynamics

Summary

Martin et al (2006) *[129]* conducted a systematic review of diagnostic methods for urinary incontinence. Across 121 studies, there was considerable variety in the methods used, meaning results could only be combined in some cases. Sensitivity and specificity of different methods were analysed using multichannel urodynamics as the gold standard. Using clinical history to diagnose urodynamic stress incontinence in women had sensitivity of 0.92, specificity 0.56. Question 3 of the Urogenital Distress Inventory had sensitivity 0.88, specificity 0.60. Results for urinary diary could only be extracted from 1 study, with sensitivity 0.88 and 0.83. Diagnosis by ultrasound imaging had sensitivity 0.94, specificity 0.83. In economic modelling, urinary diary methods were found to be the most cost-effective method, offering a cost-effectiveness ratio of £35 to £77 per case diagnosed.

Outcome Timeframe	**Study results and measurements**	**Comparator** Multichannel urodynamics	**Intervention** Diagnostic assessment	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Diagnosis of urinary incontinence 7 Critical	Based on data from participants in 121 studies. [1] (Observational (non-randomized))	A systematic review of diagnostic methods for urinary incontinence analysed the sensitivity and specificity of different methods, using multichannel urodynamics as the gold standard. Using clinical history to diagnose urodynamic stress incontinence in women had sensitivity of 0.92, specificity 0.56. Question 3 of the Urogenital Distress Inventory had sensitivity 0.88, specificity 0.60. Results for urinary diary could only be extracted from 1 study, with sensitivity 0.88 and 0.83. Diagnosis by ultrasound imaging had sensitivity 0.94, specificity 0.83.		**Moderate** Due to serious indirectness (not stroke specific) [2]	Simply investigation methods such as urinary diary offer good sensitivity and specificity. When required, multichannel urodynamics provide the most accurate results

1. Systematic review [129].
2. **Risk of Bias: no serious.** The study design quality was reported to be high in the majority of studies. **Inconsistency: no serious. Indirectness: serious.** Differences between the population of interest and those studied: not stroke specific. **Imprecision: no serious. Publication bias: no serious.**

Attached Images

Weak recommendation

Updated

- Stroke patients in hospital with confirmed continence difficulties, should have a structured continence management plan formulated, documented, implemented and monitored. (Wikander et al 1998 *[202]*)
- If incontinence persists the stroke survivor should be re-assessed and referred for specialist review once in the community. (Thomas et al 2019 *[125]*)

Update approved by NHMRC December 2022.

Practical Info

A bladder management plan should incorporate the type of urinary incontinence, the patient's goal/s (or goal/s of treatment) and strategies for achieving the goal/s.

While incontinence tends to resolve over time a significant number of people leave hospital with incontinence. It is recommended that the management plan be reviewed towards the end of any in-hospital rehabilitation. A new plan focused on community care should include information on accessing continence information and resources and who to follow up with in the community.

For more information on urinary incontinence in general, the 6th International Consultation on Incontinence (Abrams et al 2017 *[222]*) has provided further advice.

Evidence To Decision

Benefits and harms

Small net benefit, or little difference between alternatives

In-hospital rehabilitation using a structured approach reduced incontinence and improved quality of life in one study (Wikander et al 1998 *[202]*). In another community-based study included in the review by Thomas et al (2008) *[125]*, a Continence Nurse Advisor using a structured and comprehensive approach compared to usual care by a general practitioner reduced overall urinary symptoms and had greater satisfaction but did not change the number of people incontinent three or six months after intervention.

Certainty of the Evidence

Low

One study was moderate quality whereas the other study (Wikander et al 1998) was deemed low quality.

Values and preferences

No substantial variability expected

Interviews with carers of stroke survivors with urinary incontinence identified four themes: chaos, hypervigilance, exhaustion, and creating a new life (Tseng et al 2016 *[130]*). Incontinence is likely to cause burden on both stroke survivors and their carers and they would want to be provided with appropriate management options and support.

Resources and other considerations

Important issues, or potential issues not investigated

Resources considerations

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

Implementation considerations

There are clinical indicators collected in the National Stroke Audit to determine whether patients with identified continence impairments had a continence management plan in place.

Rationale

One study found a structured management plan within a multidisciplinary rehabilitation team to significantly reduce incontinence by discharge and reduce the need for high levels of care. Specialised professional input using a structured approach by continence nurse practitioners in the community, compared to usual care by a GP, may reduce overall symptoms of incontinence but it is unclear if there is any difference in the number of patients incontinent 3-6 months after intervention. There was higher satisfaction with the specialist nurse intervention. Moreover, stroke survivors and their carers experiencing burden from this complication are likely to want to receive support and appropriate management from specialist health professionals.

Clinical Question/ PICO

Population: Stroke patients with urinary incontinence
Intervention: Specialised professional input
Comparator: Control

Summary

Thomas et al (2019) *[125]* conducted a Cochrane review of treatment methods for urinary incontinence after stroke. They identified one moderate-quality randomised controlled trial (n = 232) that they categorised as 'specialised professional input interventions'. Assessment and management by a continence nurse practitioner in the community compared to usual care provided by a GP made little or no difference to the number of people continent three months after treatment (RR 1.28, 95% CI 0.81 to 2.02) or after six months (RR 0.96, 95% CI 0.83 to 1.1, n = 146). There was a larger proportion of people without any of the four urinary symptoms in the treatment group compared to controls (46.1% vs 29.6%; RR 1.55, 95% CI 0.97 to 2.48). However, there was no impact on urinary frequency (RR 0.94; 0.83-1.11) or nocturia (RR 1.00, 0.87-1.14) alone. The study reported the intervention improved the daytime severity of

leakage at three months (P = 0.038) but there was no data presented for further analysis. There was significantly greater satisfaction with the continence nurse intervention (RR 0.32, 95%CI 0.17 to 0.59).

Wikander et al 1998 *[202]* (n=34) enrolled patients during inpatient rehabilitation (11-19 days after stroke). A structured assessment and management approach based on the Functional Impairment Measure (FIM) led to a significantly reduced incidence of incontinence compared to usual rehabilitation care (1/21 vs 10/13, RR 0.06; 95% CI 0.01 to 0.43). There was also significant improvement in reported quality of life (Psychological General Well-being Index, WMD -39.00, 95%CI -51.19 to - 26.81). The intervention also resulted in significantly more people discharged home (18/21 vs 5/13, RR 0.23, 95%CI 0.07 to 0.72). The overall quality is rated low.

Outcome Timeframe	**Study results and measurements**	**Comparator** Control	**Intervention** Specialised professional input	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Incontinence After treatment 7 Critical	Relative risk 1.28 (CI 95% 0.81 — 2.02) Based on data from 121 participants in 1 studies. [1] (Randomized controlled) Follow up: 3 months.	354 per 1000 Difference:	453 per 1000 **99 more per 1000** (CI 95% 67 fewer — 361 more)	**Moderate** Due to serious risk of bias, Due to serious imprecision [2]	Specialised professional input probably has little or no difference for incontinence
Urinary symptoms [3] After treatment 7 Critical	Relative risk 1.55 (CI 95% 0.97 — 2.48) Based on data from 143 participants in 1 studies. [4] (Randomized controlled) Follow up: 6 months.	296 per 1000 Difference:	459 per 1000 **163 more per 1000** (CI 95% 9 fewer — 438 more)	**Low** Due to serious risk of bias, Due to serious imprecision [5]	Specialised professional input may decrease urinary symptoms

1. Systematic review [125] . **Baseline/comparator:** Control arm of reference used for intervention. **Supporting references:** [125],
2. **Risk of Bias: serious.** Participants and providers couldn't be blinded, concealment of allocation during randomisation process was unclear, resulting in potential for selection bias, Incomplete data and/or large loss to follow up. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious.** Only data from one study. **Publication bias: no serious.**
3. Number of people not cured of all urinary symptoms
4. Systematic review [125] . **Baseline/comparator:** Control arm of reference used for intervention.
5. **Risk of Bias: serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data and/or large loss to follow up. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Only data from one study, Low number of patients. **Publication bias: no serious.**

Attached Images

Weak recommendation

For stroke survivors with urge incontinence:

- anticholinergic drugs can be tried (Nabi et al 2006 *[128]*; Abrams et al 2017 *[222]*);
- a prompted or scheduled voiding regime program/ bladder retraining can be trialled (Thomas et al 2015 *[124]*; Thomas et al 2019 *[125]*; Abrams et al 2017 *[222]*);
- if continence is unachievable, containment aids can assist with social continence.

Practical Info

The option of anticholinergics should be considered by the medical team/pharmacist and discussed with the patient taking into considering individual patient factors such as cognitive impairment. Assess patient's current bladder pattern by using a bladder chart such as Continence Foundation Bladder chart, and establish with the patient, a realistic goal for increasing time between voids. Educate the patient regarding distraction techniques and good bladder habits, eg. reducing caffeine intake, etc. Consider delay strategies as well as prompted voiding in relation to a patient's voiding pattern (using a 72 hours bladder diary). Tools for this include SCAMP (as seen on Stroke Foundation InformMe website), which gives clinicians a standardised, evidence-based protocol to improve continence for people after stroke. The Continence Foundation of Australia also have a link to a bladder diary.

Evidence To Decision

Benefits and harms

Small net benefit, or little difference between alternatives

For people with urge incontinence, anticholinergic drugs have been shown to improve the incontinence and quality of life with little side effects in a systematic review of 61 randomised controlled trials (Nabi et al 2006 *[128]*).

A systematic voiding program in a feasibility study (Thomas et al 2015 *[124]*) did not find significant benefits in stroke patients with urinary incontinence. However, the patients with urge incontinence had a higher rate of being continent at discharge, though the difference was non-significant.

Certainty of the Evidence

Low

Thomas et al (2015) *[124]* had inadequate sample size and high risk of bias, which may be the reason for insignificant results. Results from Nabi et al (2006) *[128]* may not be transferrable to stroke patients as the population was all adults with overactive bladder syndrome, and they included a number of studies of low methodological quality. Overall, the quality of evidence is low and future studies are needed to support or refute these practices.

Values and preferences

No substantial variability expected

Patients with urge incontinence would want their symptoms to be managed and treated. From current evidence, there is no particularly effective intervention. The options of anticholinergic drugs and bladder retraining can be trialled. However, if continence cannot be achieved, containments can be used in assisting social continence.

Resources and other considerations

Important issues, or potential issues not investigated

Resources considerations

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

Rationale

Current evidence is insufficient to support a particular intervention. However, patients with urge incontinence would want their symptoms to be managed and treated. The options of anticholinergic drugs and bladder retraining can be trialed. If continence cannot be achieved, containments can then be used in assisting social continence.

Clinical Question/ PICO

Population: Stroke patients with urinary incontinence
Intervention: Behavioural intervention
Comparator: Control

Summary

An exploratory cluster randomised trial by Thomas et al (2015) *[124]* included 413 stroke patients. The primary

intervention was a systematic voiding program, comprised of assessment, bladder training (including education, individualised voiding regimens, and patient-held voiding diaries), and review. For patients with cognitive impairment, prompted voiding instead of bladder training was used. There were no clear benefits but this is a feasibility study not powered to demonstrate effectiveness. Patients with urge incontinence and stress incontinence had a higher chance of being free of incontinence at discharge, however the differences were not significant.

Moon et al (2012) *[126]* studied effects of bladder reconditioning using indwelling urethral catheter (IUC) clamping before IUC removal. 60 patients admitted to a rehabilitation unit in South Korea between April 2010 and 2011 were randomised to 0, 1 and 3 day IUC clamping groups (20 patients in each group). IUC's were clamped in the 1 and 3 day clamping groups for 4 hours followed by 5 mins of unclamping to allow the bladder to drain. Time to full volume (FV), FV-vol, residual urine volume after FV, voiding method, mean voided volume and residual volume on the 3rd day after IUC removal showed no significant differences between the 0 day and other 2 clamping groups. This study has a few limitations: a small sample size; a lack of analysis according to stroke lesion; subjects had IUC for a relatively long time, hence clamping commenced on insertion of IUC may be more effective; participants in this study had fluid and food intake controlled at 3000mls; which is unusually high in the clinical setting and may result in a higher rate of UTI's and urinary leakage. In conclusion, IUC clamping may have no effect in stroke patients and may induce additional problems.

An updated Cochrane review by Thomas et al (2019) [125] had found 3 small trials of behavioural interventions for treating urinary incontinence in the post-acute period. A low quality trial (n = 18) that suggested that behaviour interventions may have little to no difference to the mean number of incontinent episodes in 24 hrs (MD -1.00, 95% CI -2.74 to 0.74). Low quality evidence was also found suggesting it makes little to no difference to quality of life (SMD -0.99, 95% CI -2.83 to 0.86; 2 studies, n = 55).

The 6th International Consultation on Incontinence (Abrams et al, 2017 *[222]*) recommended that urinary incontinence in stroke/white matter disease (WMD) should be divided into two types with differing management. Those with functional urinary incontinence (immobility and loss of initiative/cognition) are suggested behavioural therapy primarily based on the narrative review of the Thomas et al (2005) Cochrane review, a review of behavioural therapies by Dumoulin et al (2007) and a RCT by Tibaek et al (2005).

Outcome Timeframe	**Study results and measurements**	**Comparator** Control	**Intervention** Behavioural intervention	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Continent - 6 weeks [1] 6 weeks post stroke 7 Critical	Odds ratio 0.94 (CI 95% 0.46 — 1.94) Based on data from 160 participants in 1 studies. [2] (Randomized controlled) Follow up: 6 weeks.	280 per 1000 Difference:	268 per 1000 **12 fewer per 1000** (CI 95% 128 fewer — 150 more)	**Low** Due to serious imprecision (sample size) and serious risk of bias (lack of blinding) [3]	Behavioural intervention may have little or no difference on continence at 6 weeks post stroke
Continent at discharge [4] At discharge 7 Critical	Odds ratio 1.47 (CI 95% 0.81 — 2.67) Based on data from 288 participants in 1 studies. (Randomized controlled)	310 per 1000 Difference:	398 per 1000 **88 more per 1000** (CI 95% 43 fewer — 235 more)	**Low** Due to serious imprecision (sample size) and serious risk of bias (lack of blinding) [5]	Behavioural intervention may improve continence at discharge slightly
Catheter use During hospital stay 7 Critical	n/a Based on data from 288 participants in 1 studies. (Randomized controlled) Follow up: To discharge.	8 per 1000	24 per 1000	**Very low** Due to serious risk of bias and very serious imprecision [6]	We are uncertain whether behavioural intervention increases or decreases catheter use

Outcome Timeframe	**Study results and measurements**	**Comparator** Control	**Intervention** Behavioural intervention	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
UTI During hospital stay 7 Critical	n/a Based on data from 288 participants in 1 studies. (Randomized controlled)	105 per 1000	110 per 1000	**Very low** Due to serious risk of bias and very serious imprecision [7]	Behavioural intervention may have little or no difference on UTI
Length of stay 7 Critical	Measured by: Days in stroke unit Lower better Based on data from 288 participants in 1 studies. (Randomized controlled)	43 Days (Median) Difference:	52.5 Days (Median) **9.5 higher** CI 95%	**Very low** Due to serious risk of bias and very serious imprecision [8]	We are uncertain whether behavioural intervention increases or decreases length of stroke unit stay
HRQoL [9] 6 weeks post stroke 8 Critical	Based on data from 210 participants in 1 studies. (Randomized controlled)	Across the five domains of EQ5D, the estimated effects were in favour of the control group for all domains except mobility. Only two differences were significant: the anxiety or depression and usual activity domains showed significant effects in favour of the usual care group		**Low** Due to serious imprecision and serious risk of bias [10]	Behavioural intervention may worsen HRQoL slightly

1. Dichotomous answer to the question of absence of urinary incontinence on International Consultation on Incontinence Questionnaire.
2. Primary study[124]. **Baseline/comparator:** Control arm of reference used for intervention.
3. **Risk of Bias: serious.** All outcomes were self-reported - no objective measurement; . **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Sample size not powered to demonstrate effectiveness, Only data from one study, Wide confidence intervals. **Publication bias: no serious.**
4. Dichotomous answer to the question of absence of urinary incontinence on International Consultation on Incontinence Questionnaire.
5. **Risk of Bias: serious.** All outcomes were self-reported - no objective measurement; . **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Sample size not powered to demonstrate effectiveness, Only data from one study, Wide confidence intervals. **Publication bias: no serious.**
6. **Risk of Bias: serious.** All outcomes were self-reported - no objective measurement; . **Inconsistency: no serious. Indirectness: no serious. Imprecision: very serious.** Sample size not powered to demonstrate effectiveness, Only data from one study, No relative effect nor confidence intervals. **Publication bias: no serious.**
7. **Risk of Bias: serious.** All outcomes were self-reported - no objective measurement; . **Inconsistency: no serious. Indirectness: no serious. Imprecision: very serious.** Sample size not powered to demonstrate effectiveness, Only data from one study, No relative effect nor confidence intervals. **Publication bias: no serious.**
8. **Risk of Bias: serious.** All outcomes were self-reported - no objective measurement; . **Inconsistency: no serious. Indirectness: no serious. Imprecision: very serious.** Sample size not powered to demonstrate effectiveness, Only data from one study, No relative effect nor confidence intervals. **Publication bias: no serious.**
9. Self-reported results of EQ5D
10. **Risk of Bias: serious.** All outcomes were self-reported - no objective measurement; . **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Sample size not powered to demonstrate effectiveness, Only data from one study. **Publication bias: no serious.**

Attached Images

Clinical Question/ PICO

Population: Adults with overactive bladder syndrome
Intervention: Anticholinergic drugs
Comparator: Placebo

Summary

Nabi et al (2006) *[128]* conducted a Cochrane review of anticholinergic drugs for treatment of overactive bladder symptoms. The review was not specific to stroke populations. 61 randomised controlled trials were included, with 11,956 total patients. Most were of high quality but there were issues with reporting of allocation concealment and dropouts. The meta-analysis showed significant improvements in the number of patients reporting cure or improvement (RR 1.39, 95% CI 1.28 to 1.51) and number of leakage episodes (MD -0.51, 95% CI -0.67 to -0.41). The more recent trials included in the review reported quality of life outcomes, with most reporting statistically significant but modest improvements. There was little long-term follow-up in the included studies, meaning long-term benefits are unclear.

The 6th International Consultation on Incontinence (Abrams et al, 2017 *[222]*) recommended that urinary incontinence in stroke/white matter disease (WMD) should be divided into two types with differing management. Those with neurogenic urinary incontinence (overactive bladder wet) are suggested to have anticholinergic drugs that do not penetrate the blood brain barrier easily based on the narrative review of five studies for different anticholingeric drugs in patients following brain disease.

Outcome Timeframe	**Study results and measurements**	**Comparator** Placebo	**Intervention** Anticholinergic drugs	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Withdrawal due to adverse events During study 7 Critical	Relative risk 1.11 (CI 95% 0.91 — 1.36) Based on data from 7,576 participants in 20 studies. [1] (Randomized controlled) Follow up: 2-12 weeks.	49 per 1000 Difference:	54 per 1000 **5 more per 1000** (CI 95% 18 more — 4 fewer)	**Moderate** Due to serious indirectness [2]	Anticholinergic drugs probably have little or no difference on withdrawal due to adverse events
Leakage episodes Post intervention 7 Critical	Measured by: Number of episodes in 24 hours Lower better Based on data from 4,582 participants in 12 studies. [3] (Randomized controlled) Follow up: 2-12 weeks.	Difference:	**MD 0.51 lower** (CI 95% 0.66 lower — 0.37 lower)	**Low** Due to serious risk of bias, Due to serious indirectness [4]	Anticholinergic drugs may decrease the number of leakage episodes
Quality of life Post intervention 8 Critical	Based on data from participants in 7 studies. [5] (Randomized controlled) Follow up: 2-12 weeks.	7 RCTs reporting quality of life were found in a systematic review. Pooled results from 3 RCTs reporting the King's Health Questionnaire found significant results on all domains. Combined results from two RCTs reporting IIQ-7 found significant improvements in the travel domain, with one of these RCTs also reporting significant improvements in social life, physical activity and emotional health.		**Moderate** Due to serious indirectness (not stroke specific) [6]	Anticholinergic drugs probably improve quality of life slightly. The reported benefits were of moderate size and may not be clinically significant.

1. Systematic review [128] . **Baseline/comparator:** Control arm of reference used for intervention.
2. **Inconsistency: no serious. Indirectness: serious.** Differences between the population of interest and those studied. **Imprecision: no serious. Publication bias: no serious.**
3. Systematic review [128] . **Baseline/comparator:** Control arm of reference used for intervention.

4. **Risk of Bias: serious.** The systematic review noted that reporting of allocation concealment and dropouts was poor in the majority of trials. **Inconsistency: no serious. Indirectness: serious.** Differences between the population of interest and those studied. **Imprecision: no serious. Publication bias: no serious.**
5. Systematic review [128].
6. **Risk of Bias: no serious.** The systematic review reported that the included RCTs were mostly of moderate to high quality. **Inconsistency: no serious.** Different quality of life measures across trials so results not pooled across all studies. **Indirectness: serious.** Differences between the population of interest and those studied: not stroke specific populations. **Imprecision: no serious. Publication bias: no serious.**

Attached Images

Good practice statement

Consensus-based recommendations
For stroke patients with urinary retention:

- The routine use of indwelling catheters is not recommended. However if urinary retention is severe, intermittent catheterisation should be used to assist bladder emptying during hospitalisation. If retention continues, intermittent catheterisation is preferable to indwelling catheterisation.
- If using intermittent catheterisation, a closed sterile catheterisation technique should be used in hospital.
- Where management of chronic retention requires catheterisation, consideration should be given to the choice of appropriate route, urethral or suprapubic.
- If a stroke survivor is discharged with either intermittent or indwelling catheterisation, they and their family/carer will require education about management, where to access supplies and who to contact in case of problems.

Practical Info

Assessment and treatment for urinary retention should be preceded and accompanied by psychological support and full information (in verbal, written and diagrammatic form). The patient's dignity, privacy and emotional well-being should be protected throughout. It is also important that the health practitioner keeps in mind the statistics of sexual assault for women and men, when conducting their treatment.

Good practice statement

Consensus-based recommendation
For stroke survivors with functional incontinence, a whole-team approach is recommended.

Good practice statement

Consensus-based recommendation
For stroke survivors, the use of indwelling catheters should be avoided as an initial management strategy except in acute urinary retention.

Practical Info

Where necessary, intermittent catheterisation is preferred over indwelling catheters for people requiring intervention in hospital. Closed (sterile) catheterisation should be carried out by health professionals to reduce the risk of infection. If intermittent catheterisation is still required after discharge from hospital, a clean self-catheterisation technique can be used. Refer to continence practitioners on discharge if catheterization is still required.

Evidence To Decision

Resources and other considerations

Implementation consideration

There are clinical indicator collected in the National Stroke Audit to determine whether urinary catherisation was used for urinary retention, urinary incontinence, for critical skin care, and for accurate fluid balance monitoring.

Faecal incontinence

Faecal incontinence is one of the most common complications of acute stroke, with reported prevalence ranging from 23-60% in acute stage (Lim et al 2015 *[132]*). Symptoms of bowel dysfunction include constipation and diarrhoea. Toilet access and constipating drugs are two modifiable risk factors after stroke. It has a negative effect on the both the patients' and their caregivers' quality of life and may limit social activities (Lim et al 2013 *[134]*). However, management is typically based on experience, and evidence on this topic is very limited.

Weak recommendation

- All stroke survivors with suspected faecal continence difficulties should be assessed by trained personnel using a structured functional assessment. (Harari et al 2004 *[135]*)
- For stroke survivors with constipation or faecal incontinence, a full assessment (including a rectal examination) should be carried out and appropriate management of constipation, faecal overflow or bowel incontinence established and targeted education provided. (Harari et al 2004 *[135]*)

Practical Info

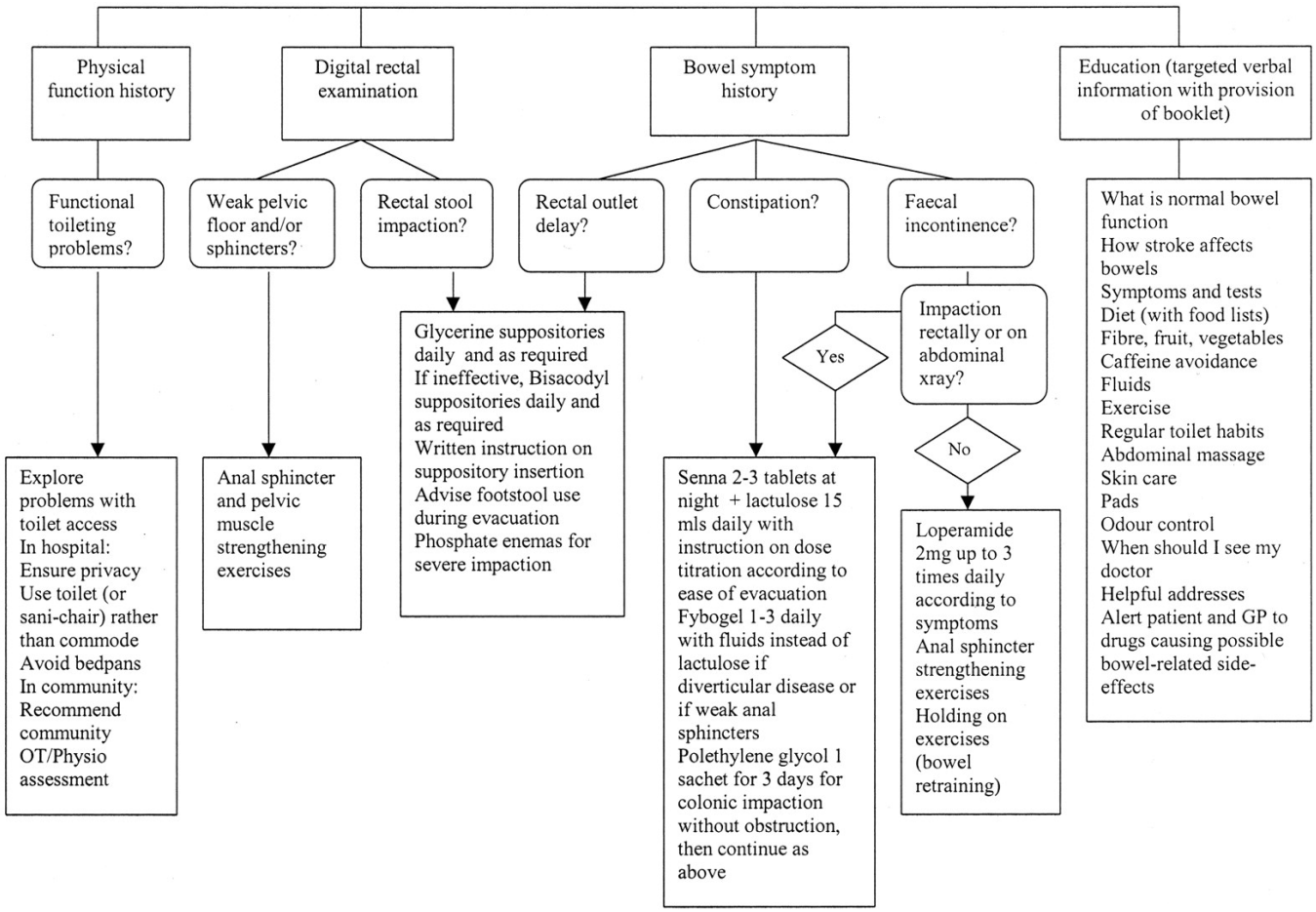
Individualised stroke survivor and carer education about the causes, treatment options and prognosis in relation to faecal incontinence should be provided in written, pictorial and culturally appropriate ways.

The psychological, physical, cultural/gender and other diversity implications of treatment options should be discussed thoroughly before implementation, ensuring informed consent is obtained.

Trauma informed practice and adherence to legislated Privacy Principles should be a pre-condition for any treatment.

Refer also to the recommendations for stroke from the Continence Foundation of Australia.

Also refer to the Assessment and treatment protocol from original trial publication: Harari et al. 2004. Figure 2 Assessment and treatment protocol Other published assessment tools may also be useful (e.g. see Norton 2000 *[139]*).



Evidence To Decision

Benefits and harms

Substantial net benefits of the recommended alternative

Bowel habits were improved, for up to 12 months, in patients who received intervention (Harari et al 2004 *[135]*).

One-fifth of all patients involved in this study (including half of all those who had faecal incontinence) were found to have faecal loading/impaction, emphasising the importance of a rectal examination in the evaluation of bowel problems or faecal incontinence (Harari et al 2004 *[135]*).

Certainty of the Evidence

Low

One single randomised controlled trial with high risk of bias, and small sample size make the quality of evidence low.

Values and preferences

No substantial variability expected

Patient preferences include return to normal activities of daily living, privacy being a necessity.

Resources and other considerations

Important issues, or potential issues not investigated

Resources considerations

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

Implementation consideration

There is an organisational indicator collected in the National Stroke Audit to determine whether hospitals have locally agreed assessment protocols in place for incontinence of faeces.

Rationale

One randomised controlled trial of nurse-led intervention showed some benefit of appropriate assessment and target education (Harari et al 2004 *[135]*). However, this single study with high risk of bias and small sample size does not warrant a strong recommendation.

Clinical Question/ PICO

Population: Stroke patients with constipation
Intervention: Nurse-led intervention
Comparator: Routine care

Summary

A systematic review of bowel management strategies by Lim and Childs (2013) *[134]* included 3 trials, all delivering different interventions. A randomised trial by Harari et al (2004) with 146 participants investigated a nurse-led intervention including assessment, provision of information and delivery of treatment recommendations to the patient's general practitioner or ward physician *[135]*. The intervention group showed significantly greater proportions of normal bowel movements (self-reported) compared to the usual care control group.

The study by Harari et al (2004) has good methodological qualities of randomisation (computer generated numbers), allocation concealment (closed envelopes) and intention to treat analysis. In addition, power analysis was used to calculate the sample size in the study. Baseline comparison between groups was clearly presented. The study described clearly the inclusion criteria of a defined term of constipation. Risk of bias in this study included: (1) the treatment recommendations were based on an unvalidated protocol and the targeted education programme was not fully described; (2) the subjects' adherence to treatment recommendations was not assessed therefore it was difficult to determine that the positive effects were due to the treatment recommendations; (3) the outcome measure of using a grading system of bowel movement rated as normal by the subjects was not described; and (4) this nurse-led intervention has a multicomponent intervention whereby it was difficult to define which single action had most effect on the positive outcomes.

Outcome Timeframe	**Study results and measurements**	**Comparator** Routine care	**Intervention** Nurse-led intervention	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Normal bowel movements 6 months	Relative risk Based on data from 146 participants in 1 studies. (Randomized controlled)	550 per 1000 Difference:	750 per 1000 **200 more per 1000** CI 95%	Low Due to serious risk of bias and serious imprecision [1]	nurse-led intervention may improve normal bowel movements

1. **Risk of Bias: serious.** Selective outcome reporting, Use of unvalidated and/or subjective outcome measures. **Inconsistency: no serious. Indirectness: no serious.** Multiple factors involved, difficult to ascertain if treatment was cause of positive outcome. **Imprecision: serious.** Only data from one study, Low number of patients. **Publication bias: no serious.**

Attached Images

Weak recommendation

For stroke survivors with bowel dysfunction, bowel habit retraining using type and timing of diet and exploiting the gastro-colic reflex should be used. (Venn et al 1992 *[136]*; Munchiando et al 1993 *[137]*)

Evidence To Decision

Benefits and harms

Small net benefit, or little difference between alternatives

There was benefit on the outcome of regular bowel movement shown in bowel habit retraining and digital stimulation of the anus (Venn et al 1992 *[136]*; Munchiando et al 1993 *[137]*). However, it is uncertain if these benefits translate to improvement in quality of life considering potential burden of these treatment.

Certainty of the Evidence

Low

The evidence has low quality due to high risk of bias and small sample size in included randomised controlled trials.

Values and preferences

Substantial variability is expected or uncertain

Patient preferences include return to normal activities of daily living, privacy being a necessity. The use of digital anal stimulation is invasive and may not be accepted by patients.

Resources and other considerations

Important issues, or potential issues not investigated

Resources considerations

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

Rationale

One trial found a bowel regime (time of day plus suppository) that replicates pre-stroke function to be effective (Venn et al 1992 *[136]*). Another form of bowel training, digital stimulation of the anus, may also provide some benefit (Munchiando et al 1993 *[137]*) . However, both interventions have low-quality evidence and may not be accepted by patients, therefore potential benefits and issues should be discussed with patients. A further study in the use of transcutaneous electrical acustimulation in the prevention of stroke induced constipation requires replication to confirm the benefits but may provide a novel therapy option. (Liu et al 2018 [102])

Clinical Question/ PICO

Population: Stroke patients with constipation
Intervention: Daily digital stimulation
Comparator: Digital stimulation every other day

Summary

A systematic review of bowel management strategies by Lim and Childs (2013) *[134]* included 3 trials, all delivering different interventions. A single quasi-experimental trial by Munchiando and Kendall (1993) with 48 participants compared daily digital stimulation to digital stimulation every other day *[137]*. Participants receiving daily stimulation were more likely to establish bowel regularity, but patients in the control group who achieved regularity achieved it in less time.

The digital stimulation study by Munchiando and Kendall (1993) has several risks of bias. Firstly, loss of subjects was acknowledged as one of the study's limitations but the drop-out rates were not reported. Although there was some baseline comparability between the groups which found no statistical significance, there was no description of the study subjects' race and stroke characteristics or severity. There was no description of the statistical analysis method used. Another variable which could have an influence on the study outcome was the subjects' pre-existing bowel dysfunctions, which were not determined prior to the interventions. Lastly, the criteria of the established bowel programme were devised by the researchers and not validated thus making the results difficult to be interpreted.

Outcome Timeframe	**Study results and measurements**	**Comparator** Digital stimulation every other day	**Intervention** Daily digital stimulation	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Bowel regularity [1]	n/a Based on data from 48 participants in 1 studies. (Randomized controlled) Follow up: n/a.	696 per 1000 Difference:	960 per 1000 **264 more per 1000** CI 95%	Low Due to serious risk of bias, Due to serious imprecision [2]	daily digital stimulation may improve bowel regularity

1. A series of four consecutive timed defecations, whether spontaneous or assisted, that occur at least every other day
2. **Risk of Bias: serious.** Incomplete data and/or large loss to follow up, Use of unvalidated and/or subjective outcome measures, due to [reason] adherance not assessed. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Low number of patients, Only data from one study. **Publication bias: no serious.**

Attached Images

Clinical Question/ PICO

Population: Stroke patients with constipation
Intervention: Morning bowel evacuation
Comparator: Evening schedule of bowel evacuation

Summary

A systematic review of bowel management strategies by Lim and Childs (2013) *[134]* included 3 trials, all delivering different interventions. A 4 arm randomised trial by Venn et al (1992) with 58 participants compared morning to evening bowel training, with either mandatory or optional suppositories *[136]*. The morning training groups showed more effective bowel movement patterns than evening training groups. No significant difference was seen between mandatory and optional suppository groups.

The risk of bias in the randomised controlled trial of comparing four bowel programmes by Venn et al (1992) included: firstly, the lack of description of its randomisation process. The study also did not indicate details of the subjects' characteristics (sex, onset and severity of stroke, concomitant treatments, etc.) and did not report baseline comparison of the study groups to determine that the effect difference was truly due to the intervention alone. Assessment was based on several staff members' clinical observations which could affect the reliability of the measurements. The efficiency rating used to assess the subjects' bowel function was devised by the researchers and not validated. Lastly, there was no description of the numbers and types of suppository used by the mandatory suppository group and whether the groups assigned to the optional suppository have received any suppositories.

Outcome Timeframe	**Study results and measurements**	**Comparator** Evening schedule of bowel evacuation	**Intervention** Morning bowel evacuation	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Time to achieve regular bowel movement	Measured by: Efficiency rating. 1 point deducted for every 2 additional days to reach effectiveness High better	7.37 (Mean) Difference:	13.3 (Mean) **MD 5.93 higher** CI 95%	Low Due to serious risk of bias, Due to serious imprecision [1]	morning bowel evacuation may improve time to achieve regular bowel movement

Outcome Timeframe	**Study results and measurements**	**Comparator** Evening schedule of bowel evacuation	**Intervention** Morning bowel evacuation	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
	Based on data from 58 participants in 1 studies. (Randomized controlled)				

1. **Risk of Bias: serious.** Incomplete data and/or large loss to follow up, Selective outcome reporting, Use of unvalidated and/or subjective outcome measures. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Only data from one study, Low number of patients. **Publication bias: no serious.**

Attached Images

Clinical Question/ PICO

Population: Stroke patients with constipation
Intervention: Transcutaneous electrical acustimulation
Comparator: Sham treatment

Summary

Liu et al (2018) *[138]* conducted a RCT involving 86 ischeamic stroke patients. Stroke-inducted constipation was reported in 68% of cases in acute stroke. Transcutaneious electrical acustimulation reduced constipation (42.9 vs. 68.2%, P = 0.029), increased frequency of bowel movements (4.5 vs. 5.5, P = 0.001) and increased spontaneous bowel movements (3.0 vs. 4.5, P = 0.003) per week. The effects were thought to be mediated via the autonomic function.

A previous RCT by Guo et al (2014) *[127]* involved electrical stimulation for incontinence (n= 61). The study observed patients with urinary incontinence who were randomly allocated to receive TENS experienced significantly greater improvement in the bowel function component of the Barthel Index (intervention: median 6.72, SD 3.01 vs control: median 2.93, SD 3.41, p< 0.05). However, this study was focused on patients with urinary incontinence and further studies specifically focused on bowel incontinence are needed.

Outcome Timeframe	**Study results and measurements**	**Comparator**	**Intervention**	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Avoidance of stroke-induced constipation [1] 2 weeks	Relative risk 0.63 (CI 95% 0.42 — 0.94) Based on data from 86 participants in 1 studies. (Randomized controlled)	682 per 1000 Difference:	430 per 1000 **252 fewer per 1000** (CI 95% 396 fewer — 41 fewer)	**Low** Due to serious indirectness, Due to serious imprecision [2]	Transcutaneous electrical acustimulation may decrease stroke-induced constipation

1. Avoided constipation vs constipation during 2 weeks of trial period in intervention vs sham groups.
2. **Inconsistency: no serious. Indirectness: serious.** The outcome time frame in studies were insufficient. Study only included ischemic stroke patients at the acute stage.. **Imprecision: serious.** Low number of patients, Only data from one study. **Publication bias: no serious.**

Attached Images

Good practice statement

Consensus-based recommendations

For stroke survivors with bowel dysfunction:

- Education and careful discharge planning should be provided.
- Use of short-term laxatives may be trialed.
- Increase frequency of mobilisation (walking and out of bed activity) to reduce constipation.
- Use of the bathroom rather than use of bed pans should be encouraged.
- Use of containment aids to assist with social continence where continence is unachievable.

Mood disturbance

Mood is frequently affected following a stroke. Depression is the most common mood disturbance with a meta-analysis of 61 observational studies finding almost one-third of patients with depression after stroke (Hackett et al 2014 *[140]*). Anxiety is also common after stroke (19-24%)(Knapp et al 2020*[142]*). Despite increased evidence describing validated depression screening tools and effective treatment and prevention strategies for depression after stroke, there has not been a significant reduction in the proportion of people experiencing depression after stroke (Hackett et al 2014 *[140]*). The consistently high proportion of stroke survivors with depression and other mood disorders emphasises the importance of screening and assessment for mood disturbance following stroke and specifically depression (Hackett et al 2014 *[140]*). However, there is a lack of evidence about whether *routine* screening for depression outweighs the potential harms, or is cost effective, therefore specific recommendations about *who* should be screened and *when* cannot be made. However, where mood disturbances are suspected, screening and assessment should occur by trained staff who are aware of scoring thresholds and provide a programme of treatment that is monitored with clear stopping rules (Gilbody et al 2008 *[141]*). Health professionals working with people with aphasia should have competencies specifically needed to work with people with aphasia, including supported communication training. National Stroke Audits report low rates of mood assessment in acute and rehabilitation audits, 27% and 63% respectively (Stroke Foundation 2019 *[9]*; Stroke Foundation 2020 *[7]*). This is despite the recognised prevalence of mood impairment in stroke admissions (34% and 44% respectively) (Stroke Foundation 2019 *[9]* ; Stroke Foundation 2020*[7]*).

Mood assessment

Practice points

- Stroke survivors with suspected altered mood (e.g. depression, anxiety, emotionalism) should be assessed by trained personnel using a standardised and validated scale for use in people with stroke.
- Diagnosis should only be made following clinical interview.

Practical Info

There is some evidence that clinicians find it difficult to detect symptoms of mood disorders. Therefore, specific training in recognising signs and symptoms of mood disorders is advised. It is also important to note several factors have been found to be associated with the development of depression after stroke. These include history of depression (strongest risk factor), previous stroke, more severe stroke/disability and those with aphasia. (Perrain et al 2020 *[219]* ; Kutlubaev 2014 *[220]*) Post-stroke anxiety is also correlated with post-stroke depression. (Wright et al 2017 *[221]*).

Where altered mood is suspected, formal screening should occur using a validated tool that is agreed upon within the local team. For people with communication and cognitive impairments, an observational tool (e.g., The Stroke Aphasia Depression Questionnaire; The Behavioural Outcomes of Anxiety) may be more appropriate (Eccles et al 2017 *[216]* ; Van Dijk et al 2016 *[217]*). Ideally this tool should capture anxiety and depressive symptoms. Supported communication techniques may also be used to discuss symptoms with the person and self-report using appropriate tools (e.g., Depression Intensity Scale Circles). A local site champion can be useful in the implementation process.

People with aphasia with possible depression or anxiety should have further assessment of mood through a clinical interview by specialist health professionals (medical practitioner and/or psychologist) who are competent in communicating with people with aphasia, and health professionals should liaise or work with speech pathologists, if needed. Communication supports and strategies should be used in the clinical interview (e.g, effective communication partner; pictorial supports; input from speech pathologist as needed). ~~A local site champion can be useful in the implementation process.~~

Treatment for Emotionalism

Weak recommendation

For stroke survivors with emotionalism, antidepressant medication such as selective serotonin reuptake inhibitors (SSRIs) or tricyclic antidepressants may be used. (Allida et al 2022 *[143]*)

Evidence To Decision

Benefits and harms

Substantial net benefits of the recommended alternative

Substantial decreases in emotionalism have been reported in a small number of trials, with meta-analysis of diminished tearfulness outcomes suggesting a NNT benefit of 2 (Allida et al 2022 *[143]*). The data on possible adverse events are limited and insufficient to determine possible harms (Allida et al 2022 *[143]*).

Certainty of the Evidence

Low

The evidence for the benefits of pharmacological therapy is low, with only a few small RCTs of short duration (Allida et al 2022 *[143]*). Trials do not measure emotionalism in a standardised way.

Values and preferences

Substantial variability is expected or uncertain

There will be significant variability in patient preferences regarding consumption of antidepressant medications.

Resources and other considerations

Important issues, or potential issues not investigated

Resources considerations

No literature on the potential economic implications was identified.

Rationale

Evidence for the use of antidepressants in reducing emotionalism is limited but the existing trials have reported substantial reductions in symptoms such as pathological laughter and crying (Allida et al 2022 *[143]*).

Clinical Question/ PICO

Population: Adults with stroke with emotionalism
Intervention: Pharmacotherapy
Comparator: Placebo

Summary

Five trials (N=213) in the systematic review conducted by Allida et al (2022) *[143]* were included (two of the seven total studies were cross-over trials and data not used). These five trials categorised the outcome of emotionalism in different ways: 50% reduction in emotionalism, diminished tearfulness, improvements (reduction) in lability, tearfulness and scores on the Pathological Laughter and Crying Scale. Meta-analysis was conducted for the outcome measuring diminished tearfulness based on three studies with a large effect of treatment found. However, confidence intervals were wide indicating that treatment may have had only a small positive effect. Only two included studies systematically recorded and reported adverse events, providing limited data on adverse events such as confusion, constipation or dysuria. Analysis of the number of dropouts and withdrawals across all trials showed no significant differences between treatment and control groups. More large trials with systematic assessment and reporting of adverse events are needed to ensure that these benefits outweigh the risks.

Outcome Timeframe	**Study results and measurements**	**Comparator** Placebo	**Intervention** Pharmacotherapy	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Diminished tearfulness [1]	Relative risk 2.18 (CI 95% 1.29 — 3.71) Based on data from 164	292 per 1000	636 per 1000	**Moderate** One study had high risk of	Pharmacological interventions may reduce tearfulness

Outcome Timeframe	**Study results and measurements**	**Comparator** Placebo	**Intervention** Pharmacotherapy	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
7 Critical	participants in 3 studies. [2] (Randomized controlled)	Difference:	**344 more per 1000** (CI 95% 133 more — 708 more)	attrition bias [3]	
Adverse events 7 Critical	Based on data from 213 participants in 5 studies. [4] (Randomized controlled) Follow up: During study period.	Only two included studies systematically recorded adverse events. Results could not be pooled due the heterogeneity of reporting.		**Very low** Due to serious inconsistency, Due to serious imprecision, Due to serious risk of bias [5]	We are uncertain whether pharmaceutical interventions increase or decrease the risk of adverse events

1. Measured by diminished tearfulness
2. Systematic review [143] with included studies: Choi-Kwon 2006, Murray 2005, Burns 1999. **Baseline/comparator:** Control arm of reference used for intervention.
3. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Low number of patients, Wide confidence intervals. **Publication bias: no serious.**
4. Systematic review [143].
5. **Risk of Bias: serious.** Some included trials may not have systematically recorded adverse events. **Inconsistency: serious.** Adverse events not reported consistently/systematically across trials. **Indirectness: no serious. Imprecision: serious.** Available data could not be pooled to give an effect estimate and range. **Publication bias: no serious.**

Attached Images

Prevention of depression

Weak recommendation

Updated

For stroke survivors, antidepressant medication may be used to prevent depression. (Allida et al 2020 *[145]*)

Update approved by NHMRC August 2022.

Evidence To Decision

Benefits and harms

Small net benefit, or little difference between alternatives

Trials of antidepressants have shown reductions in the proportion of people with depression (125 fewer with depression per 1000 patients treated) but adverse event data are limited and insufficient to determine possible harms. (Allida et al 2020 *[145]*) Another meta-analysis of generally large trials of SSRIs (Legg et al 2021 *[215]*) found a small reduction in average depression scores (SMD -0.14, 95% CI 0.19 lower to 0.08 lower) and reduced the proportion with depression (RR 0.75, 95% CI 0.65 to 0.86). But SSRIs increased the risk of seizure (RR 1.40) and a bone fracture (RR 2.35).

Certainty of the Evidence

Very low

The quality of evidence is very low, because of inadequate reporting in existing trials and the use of multiple measures for depression within trials. Lack of blinding for outcome assessors means many of the existing trials have a high risk of bias. Certainty of evidence was moderate to high for the meta-analysis of SSRIs which included six trials of low risk of bias across all domains.

Values and preferences

Substantial variability is expected or uncertain

There will be significant variability in patient preferences regarding consumption of antidepressant medications.

Resources and other considerations

Important issues, or potential issues not investigated

Resources considerations

No literature on the potential economic implications was identified.

Rationale

There is accumulating evidence that there is a small reduction in incidence of depression with antidepressants. However, there is also a risk of harm, specifically for SSRIs, and careful consideration of individual patient factors and values and preferences should be considered. Specific factors that should be considered include history of depression (strongest risk factor), previous stroke, more severe stroke/disability and those with aphasia. (Perrain et al 2020 *[219]*; Kutlubaev 2014*[220]*)

This recommendation should not be considered to be for routine use of antidepressants to prevent depression given the quality of evidence and possible harms. However, antidepressants may be useful in some circumstances given the negative impact on depression for stroke recovery.

Clinical Question/ PICO

Population: Adults with stroke
Intervention: Pharmacotherapy for the prevention of depression
Comparator: Placebo

Summary

In a Cochrane review, Allida et al (2020) *[145]* included 12 pharmaceutical trials (14 interventions) investigating interventions for the prevention of depression following stroke. Interventions used in these trials included SSRIs (6 trials), serotonin antagonist and reuptake inhibitors (1 trial), and other treatments with antidepressant effects (e.g. piracetam, maprotiline). 8 trials (9 interventions) reported depression outcomes at the end of treatment. The proportion of patients with depression was lower following pharmacotherapy, despite the trials using a variety of criteria (e.g. DSM-III criteria, DAM-IV criteria, HADS-D etc). The review authors concluded that more trials are needed.

Gu et al (2020)*[148]* included 12 studies (n=1257) of pharmacotherapy. Compared to control group, pharmacotherapy reduced the risk of depression (RR 0.33, 95%CI 0.25 to 0.43). No difference was found between different types of antidepressants.

Legg et al (2021)*[215]* updated a Cochrane review and included 76 studies (n=13,029) with half (38) studies not requiring participants have depression on enrollment. Meta-analysis of studies with low risk of bias across all domains (N=6, non of which used depression as an inclusion criteria) identified a small reduction in average depression scores (SMD -0.14, 95% CI 0.19 lower to 0.08 lower; 4 studies; 5356 participants, high-quality evidence) and reduced the proportion with depression (RR 0.75, 95% CI 0.65 to 0.86; 3 studies, 5907 participants, high-quality evidence). SSRIs increased the risk of seizure (RR 1.40, 95% CI 1.00 to 1.98; 6 studies, 6080 participants, moderate-quality evidence) and a bone fracture (RR 2.35, 95% CI 1.62 to 3.41; 6 studies, 6080 participants, high-quality evidence). Additional trials generally had low numbers (<10%) of people depressed on enrollment but depression was often a secondary outcome.

Outcome Timeframe	**Study results and measurements**	**Comparator** Placebo	**Intervention** Pharmacotherapy for the prevention of depression	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Presence of depression At end of treatment	Relative risk 0.5 (CI 95% 0.37 — 0.68) Based on data from 734 participants in 9 studies. [1] (Randomized controlled) Follow up: 2 weeks to 12 months.	250 per 1000 Difference:	125 per 1000 **125 fewer per 1000** (CI 95% 157 fewer — 80 fewer)	**Very low** Due to serious risk of bias, Due to serious imprecision [2]	The available evidence suggests that pharmacological therapy might reduce the risk of developing depression in stroke patients.
Depression - mean score HDRS [3] Varied-from end of treatment up to 15 months 7 Critical	Measured by: Hamilton Depression Rating Scale (HDRS) Lower better Based on data from 100 participants in 4 studies. [4] (Randomized controlled)	Difference:	**MD 0.59 higher** (CI 95% 1.46 lower — 2.63 higher)	**Very low** High risk of bias, wide confidence intervals	We are uncertain whether antidepressants improves or worsen depression

1. Systematic review [145] . **Baseline/comparator:** Systematic review [145] .
2. **Risk of Bias: very serious.** Incomplete data and/or large loss to follow up, Selective outcome reporting. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Wide confidence intervals.
3. Hamilton Depression Rating Scale
4. Systematic review [145] . **Baseline/comparator:** Control arm of reference used for intervention.

Attached Images

Weak recommendation

For stroke survivors, psychological therapies (e.g. problem solving, motivational interviewing) may be used to prevent depression. (Allida et al 2020 *[145]*)

Practical Info

Therapies and approaches can be modified and are feasible to deliver for people with cognitive and communication disabilities such as aphasia (Baker et al. 2018; Hilari et al. 2021; Holland et al 2018; Northcott et al. 2021) but further information about their effectiveness is needed. Communication partner training and goal setting can enhance mood and wellbeing for people with aphasia.

Evidence To Decision

Benefits and harms

Small net benefit, or little difference between alternatives

Psychological therapies appear to substantially reduce the risk of developing depression following stroke (95 fewer with depression per 1000 patients treated), but may only be effective for patients without cognitive and communication difficulties who can actively participate in treatment (Allida et al 2020 *[145]*). There is no indication that psychological therapies increase adverse events such as recurrent stroke, but adverse events were not systematically monitored and reported in all trials.

Certainty of the Evidence

Very low

The quality of evidence is very low, coming from a small number of randomised trials with a serious risk of bias and imprecision.

Values and preferences

Substantial variability is expected or uncertain

Depending on their level of cognitive or communication impairments, patients may struggle to engage in psychological therapies.

Resources and other considerations

Important issues, or potential issues not investigated

Resources considerations

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

Implementation consideration

There is a clinical indicator collected in the National Stroke Audit to determine the type of management used for a patient with an identified mood impairment in acute care and/or rehabilitation. This includes psychological interventions such as cognitive behavioural therapy.

Rationale

Psychological therapies such as problem solving and motivational interviewing may be effective in preventing depression but may only be suitable for stroke patients without cognitive and communication impairment. There is no evidence for one form of psychological therapy being better than another. Each of the publlshed trials used a different therapy and the estimate of effectiveness was based on the pooled results across these trials.

Clinical Question/ PICO

Population: Adults with stroke without depression
Intervention: Psychological therapy
Comparator: Control or attention control

Summary

A Cochrane review of therapies for preventing depression following stroke included 7 trials of psychological therapies with 1046 total participants (Allida et al 2020 *[145]*). Psychological therapies used in the trials included problem-solving therapy, home-based therapy and motivational interviewing. Meta-analysis of 2 studies reporting the presence of depression at the end of treatment showed a significant reduction in the risk of depression following psychotherapy (RR 0.68, 95% CI 0.49 to 0.94), and a small but significant reduction in the psychological distress scores on the GHQ-28 (MD -1.37, 95% CI -2.27 to -0.48). There was high risk of bias due to high loss to follow-up or dropouts and most trials excluded patients with communication difficulties and cognitive impairments. These exclusion criteria would exclude a large proportion of stroke survivors, meaning the findings may not be applicable to the broader stroke population. However, these kinds of exclusion criteria may also be necessary for psychological therapies, which often require active patient engagement.

Outcome Timeframe	**Study results and measurements**	**Comparator** Control or attention control	**Intervention** Psychological therapy	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Presence of depression At end of treatment	Relative risk 0.68 (CI 95% 0.49 — 0.94) Based on data from 607 participants in 2 studies.	296 per 1000 Difference:	201 per 1000 **95 fewer per**	**Very low** Due to very serious risk of bias, Due to	Psychological therapy may reduce the risk of depression slightly.

Outcome Timeframe	**Study results and measurements**	**Comparator** Control or attention control	**Intervention** Psychological therapy	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
8 Critical	[1] (Randomized controlled) Follow up: Not reported.		**1000** (CI 95% 151 fewer — 18 fewer)	serious imprecision, Due to serious indirectness [2]	

1. Systematic review [145] . **Baseline/comparator:** Systematic review [145] .
2. **Risk of Bias: very serious. Imprecision: serious.** Wide confidence intervals.

Attached Images

Treatment for depression

Weak recommendation

Updated

For stroke survivors with depression, antidepressants, which includes SSRIs should be considered. There is no clear evidence that particular antidepressants produce greater effects than others and will vary according to the benefit and risk profile of the individual. (Allida et al 2020 *[155]*)

Update approved by NHMRC August 2022.

Practical Info

Individual factors (such as medical condition; age) and potential adverse events; withdrawal and side effects of medications must be considered in clinical decision-making with the stroke survivor (Legg et al 2021*[215]*; Taylor, 2018 *[218]*). Before prescribing antidepressants it is important to know how their effectiveness will be assessed to determine if and when the type and dose should be changed, tapered gradually or stopped.

Evidence To Decision

Benefits and harms

Small net benefit, or little difference between alternatives

Meta-analysis suggests pharmacotherapy reduces depression by 30%, however, there are increased central nervous system and gastrointestinal adverse events. (Allida et al 2020 *[155]*) A separate meta-analysis specific to SSRIs found a very small decrease in depression (SMD -0.14; 95%CI -0.19 to -0.08) and higher risk of seizures and bone fractures. (Legg et al 2021 *[215]*) However, this was based on high quality studies with mix of participants most of who did not have depression on enrollment.

Certainty of the Evidence

Very low

The evidence is of very low quality.

Values and preferences

Substantial variability is expected or uncertain

Patient preferences may vary due to uncertain benefits and harms.

Resources and other considerations

No important issues with the recommended alternative

Implementation consideration

There is a clinical indicator collected in the National Stroke Audit to determine the type of management used for a patient an identified mood impairment in acute care and/or rehabilitation. This includes antidepressants and psychological interventions such as cognitive behavioural therapy.

Rationale

Antidepressants (most commonly SSRIs) appear to reduce depression and depressive symptoms, and should therefore be considered for stroke patients with depression. However, patients should be monitored for any adverse events.

Clinical Question/ PICO

Population: Adults with stroke with depression
Intervention: pharmacological interventions
Comparator: Placebo

Summary

The Cochrane review by Allida et al (2020)*[155]* included 49 trials (n=3342); 20 comparisions of pharmacotherapy vs placebo. Antidepressants decreased the number of people diagnosed with depression (RR 0.70, 95%CI 0.55 to 0.88; 8 trials, n=1025 participants; very low-certainty evidence) and decreased the number of people with less than 50% reduction in depression scale scores at end of treatment (RR 0.47, 95%CI 0.32 to 0.69; six trials, n=511 participants; very low-certainty evidence). Adverse events related to the central nervous system were higher with pharmacotherapy (RR 1.55, 95%CI 1.12 to 2.15; 5 trials, n=488 participants; very low-certainty evidence) as were gastrointestinal adverse events (RR 1.62, 95% CI1.19 to 2.19; 4 trials, n=473 participants; very low-certainty evidence). The majority of the included comparisons (12/20) used SSRIs and there was insufficient evidence to determine if specific types of antidepressants produced greater benefits or the longer term effects of treatment.

Another Cochrane review by Legg et al (2021)*[215]* included 76 studies (n=13,029) with 38 studies requiring participants have depression on enrollment. Meta-analysis of studies with low risk of bias across all domains (N=6, non of which used depression as an inclusion criteria) identified a small reduction in average depression scores (SMD -0.14, 95% CI 0.19 lower to 0.08 lower; 4 studies; 5356 participants, high-quality evidence) and reduced the proportion with depression (RR 0.75, 95% CI 0.65 to 0.86; 3 studies, 5907 participants, high-quality evidence). SSRIs increased the risk of seizure (RR 1.40, 95% CI 1.00 to 1.98; 6 studies, 6080 participants, moderate-quality evidence) and a bone fracture (RR 2.35, 95% CI 1.62 to 3.41; 6 studies, 6080 participants, high-quality evidence).

Outcome Timeframe	**Study results and measurements**	**Comparator** Placebo	**Intervention** pharmacological interventions	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Depression - dichotomous outcome End of treatment 9 Critical	Relative risk 0.7 (CI 95% 0.55 — 0.88) Based on data from 1,025 participants in 8 studies. [1] (Randomized controlled) Follow up: Varied: treatment for 10 days to 12 months.	708 per 1000 Difference:	499 per 1000 **209 fewer per 1000** (CI 95% 360 fewer — 66 fewer)	**Very low** Due to serious imprecision, Due to serious inconsistency, Due to serious risk of bias [2]	Pharmacological interventions may decrease depression
Depression - <50% reduction in scale scores End of treatment	Relative risk 0.47 (CI 95% 0.32 — 0.69) Based on data from 511 participants in 6 studies. [3] (Randomized controlled)	821 per 1000 Difference:	563 per 1000 **258 fewer per 1000** (CI 95% 447	**Very low** Due to serious risk of bias, Due to serious inconsistency, Due to serious	Pharmacological interventions may decrease depression - <50% reduction in scale scores slightly

Outcome Timeframe	**Study results and measurements**	**Comparator** Placebo	**Intervention** pharmacological interventions	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
9 Critical	Follow up: Varied: treatment for 10 days to 12 months.		fewer — 94 fewer)	imprecision [4]	
Death end of follow up 7 Critical	Relative risk 0.64 (CI 95% 0.2 — 2.07) Based on data from 848 participants in 9 studies. [5] (Randomized controlled)	**19** per 1000 Difference:	**11** per 1000 **8 fewer per 1000** (CI 95% 15 fewer — 15 more)	**Very low** Due to serious risk of bias, Due to serious imprecision [6]	We are uncertain whether pharmacological interventions improves or worsen death

1. Systematic review [155] . **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of Bias: serious.** Risk of bias items were not well reported in many trials, with blinding of participants and personnel a particular concern. **Inconsistency: serious.** The magnitude of statistical heterogeneity was high, with I^2: 68%.. **Indirectness: no serious. Imprecision: serious.** Wide confidence intervals. **Publication bias: no serious.**
3. Systematic review [155] . **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of Bias: serious.** Risk of bias items were not well reported in many trials, with blinding of participants and personnel a particular concern. **Inconsistency: serious.** The magnitude of statistical heterogeneity was moderate (30%-49%). **Indirectness: no serious. Imprecision: serious.** Wide confidence intervals. **Publication bias: no serious.**
5. Systematic review [155] . **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of Bias: serious.** Risk of bias items were not well reported in many trials, with blinding of participants and personnel a particular concern. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Wide confidence intervals. **Publication bias: no serious.**

Attached Images

Weak recommendation

New

For stroke survivors with depression or depressive symptoms, psychological therapy may be provided. (Allida et al 2020 *[155]*)

Update approved by NHMRC August 2022.

Practical Info

Psychological therapy involves direct person-professional interaction which could vary from counselling to specific psychological therapy, provided it is directed at helping people develop their coping skills and adjust to the emotional impact of stroke. Interventions include motivational interviewing, cognitive behavioural therapy and broadly labelled ‘psychological therapy’ delivered by *trained* psychologists, nurses, counsellors or other health professionals.

Adaptations to therapy to ensure its suitability for people with cognitive and communication disabilities such as aphasia are required (e.g., additional structure, reminders, communication supports, communication partner training for health professionals facilitating therapy) (Baker et al. 2018; Kneebone 2016; Thomas et al. 2013).

The exact duration, timing and number of sessions needed is unclear.

Evidence To Decision

Benefits and harms

Small net benefit, or little difference between alternatives

Psychological therapy appears to reduce depression (Allida et al 2020 *[155]*). There were no reported adverse events with therapy.

Certainty of the Evidence

Very low

The certainty of the evidence is very low.

Values and preferences

No substantial variability expected

People with depression after stroke are likely to consider psychological therapy given the potential benefits without known harms.

Resources and other considerations

Important issues, or potential issues not investigated

Implementation consideration

There is a clinical indicator collected in the National Stroke Audit to determine the type of management used for a patient with an identified mood impairment in acute care and/or rehabilitation. This includes antidepressants and psychological interventions such as cognitive behavioural therapy.

There was no economic literature identified regarding pyschological therapy.

Rationale

Psychological therapy was found to reduce the number of people with depression by 23% without evidence of harms (Allida et al 2020 *[155]*). People with mild to moderate depression after stroke may prefer to be offered psychological therapy before pharmacological therapy due to lower risk of harms. This is a new recommendation as new evidence in the updated Cochrane Review provided more certainty of benefits vs harms.

Clinical Question/ PICO

Population: Adults with stroke with depression
Intervention: Psychological therapy
Comparator: Usual care / attention control

Summary

The Cochrane review by Allida et al (2020)[146] included 49 trials (n=3342); 16 comparisons of psychological therapy vs usual care/attention control were included. Psychological therapy decreased the number of people diagnosed with depression at the end of the intervention (RR 0.77, 95%CI 0.62 to 0.95; six trials, 521 participants; very low-certainty evidence). The average score between baseline and end of treatment was lower with psychological therapy than usual care (MD 6.20 lower; 95%CI 8.24 lower to 4.16 lower). But there was no difference in the number of people meeting criteria for depression at the end of follow-up (RR 0.85, 95%CI 0.59 to 1.21; 3 trials, n=201; very low-certainty evidence). There was no difference in deaths or adverse events between groups but the certainty of evidence was very low.

Combined psychological therapy plus antidepressants compared to antidepressants alone was found to reduce mean scores on the Hamilton Depression Rating Scale at the end of treatment (MD -1.53, 95%CI -2.10 to -0.96; 2 trials, n=198; very low-certainty evidence).

Baker et al (2018)*[156]* included three studies (n=265) of psychological therapy in people with post-stroke aphasia. There was evidence for improved mood for people with aphasia following behavioural therapy from one study. There was limited evidence of benefit for web-based support for people with aphasia in another, however, carers mood

improved.

Outcome Timeframe	Study results and measurements	Comparator Usual care / attention control	Intervention Psychological therapy	Certainty of the Evidence (Quality of evidence)	Plain language summary
Depression End of treatment 8 Critical	Relative risk 0.77 (CI 95% 0.62 — 0.95) Based on data from 521 participants in 6 studies. [1] (Randomized controlled)	750 per 1000 Difference:	585 per 1000 **165 fewer per 1000** (CI 95% 293 fewer — 42 fewer)	**Very low** Due to serious risk of bias, Due to serious imprecision [2]	Psychological therapy may improve depression.
Change in depression scores [3] end of treatment 7 Critical	Measured by: Hamilton depression scale Lower better Based on data from 189 participants in 3 studies. [4] (Randomized controlled)	Difference:	**MD 6.2 lower** (CI 95% 8.24 lower — 4.16 lower)	**Very low** Risk of bias, wide confidence intervals	Psychological therapy may improve reduction in depression scores

1. Systematic review [155] . **Baseline/comparator:** Systematic review.
2. **Risk of Bias: serious. Inconsistency: no serious. Indirectness: no serious. Imprecision: serious. Publication bias: no serious.**
3. Average change between baseline and end of treatment
4. Systematic review [155] . **Baseline/comparator:** Control arm of reference used for intervention.

Attached Images

Weak recommendation

Updated

For stroke survivors with depression or depressive symptoms, structured exercise programs, particularly resistance training or programs of high intensity, may be used. (Eng et al 2014 *[151]*; Saunders et al 2020 *[154]*)

Update approved by NHMRC August 2022.

Practical Info

People with aphasia should be offered communicatively accessible psychological therapies. They may benefit from a range of psychological therapies with communication supports (e.g., behavioural therapy) (Baker et al, 2018; Thomas et al. 2013).

Evidence To Decision

Benefits and harms

Small net benefit, or little difference between alternatives

The reported effect sizes for improvements in depressive symptoms were small. Effects were larger for high-intensity

programs. There was little evidence about safety and possible adverse events.

Certainty of the Evidence

Low

Lack of assessor blinding was an issue in many trials, as was a lack of an intention to treat analysis. There was some suggestion of publication bias.

Values and preferences

Substantial variability is expected or uncertain

Patients' preferences regarding exercise would be similar to that of the general population.

Resources and other considerations

Important issues, or potential issues not investigated

Resources considerations

Lower intensity exercise programs may not produce significant improvements. Interventions may need to be high-intensity to be successful, e.g. 3 times a week over 12 weeks and then maintained for the longer term for any benefits to continue. This treatment regime will increase the required resources.

Rationale

There is evidence that structured exercise programs reduce depressive symptoms in stroke patients but the quality of evidence is low and the effect is small (Eng et al 2014*[151]*). It is apparent that these benefits were not maintained in the long term. The effects appear to be greater for high-intensity programs. In addition, only resistance training was found to reduce depression in another review (Saunders et al 2020 *[154]*) but overall the evidence on depression is unclear. Given there are other benefits of exercise and few adverse events we suggest trialing exercise to manage depression and depressive symptoms.

Clinical Question/ PICO

Population: Adults with stroke
Intervention: Structured exercise
Comparator: Control

Summary

A systematic review by Eng et al (2014) *[151]* included 13 randomised trials of structured exercise with 1022 participants, investigating the effect on depressive symptoms. Meta-analysis showed a small but significant overall reduction in depressive symptoms immediately after the end of treatment (SMD -0.13, 95% CI -0.26 to -0.01), but no difference at longer-term follow-up. A subgroup analysis that included only high-intensity programs (of at least 3 sessions per week for >= 4 weeks) showed a greater but still small treatment effect (SMD -0.24, 95% CI -0.46 to -0.02). The corresponding analysis for low-intensity programs showed no significant difference. Sensitivity analyses that only included trials using an intention to treat analysis showed non-significant effects, and funnel plots suggested that trials with non-significant results were underrepresented. Both of these factors suggest a high risk of bias. It is also unclear if participants had depression at the start of the studies or if there was concomitant use of antidepressants.

An earlier systematic review of community-based rehabilitation interventions by Graven et al (2011)*[152]* had suggested much stronger effects of exercise interventions on depression. Ten trials of exercise interventions were included, and meta-analysis based on 2 of these trials showed a large reduction in depression symptoms (SMD -2.03, 95% CI -3.22 to -0.85). However, as this analysis was only based on 2 small trials, there is substantial risk of bias and the more comprehensive analysis in the more recentreview should provide less biased results.

The Cochrane review on fitness training (Saunders et al 2020 *[154]*) reported the effect of different types of training on mood. Cardiorespiratory training had no effect on depression based on two small studies (n=56). Resistance training did have a small to moderate effect on depression (SMD -0.36, 95%CI -0.64 to -0.09; three studies, n=209; very low certainty evidence). Mixed training had no effects on mood based on three studies (n=391). Studies were a mix of those with and without depression at the start of the intervention.

Another review (Lyu et al 2020 *[159]*) included 11 trials (n=723). Meta-analysis of six trials found those who received Tai Chi training showed greater reduction in depression scores/symptoms than conventional therapy (SMD = 0.36, 95%CI 0.10 to 0.61; very low certainty evidence).

Outcome Timeframe	**Study results and measurements**	**Comparator** Control	**Intervention** Structured exercise	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Depressive symptoms Post-intervention 8 Critical	Measured by: Various - Hospital Anxiety and Depression Scale, Geriatric Depression Scale etc. Lower better Based on data from 1,022 participants in 13 studies. (Randomized controlled)	Difference:	**SMD 0.13 lower** (CI 95% 0.26 lower — 0.01 lower)	**Low** Due to serious risk of bias, Due to serious publication bias [1]	Structured exercise may decrease depressive symptoms slightly in the short term. Larger effects were reported for high intensity exercise programs
Depressive symptoms Long term 8 Critical	Measured by: Various - Hospital Anxiety and Depression Scale, Geriatric Depression Scale etc. Lower better Based on data from 889 participants in 10 studies. (Randomized controlled) Follow up: 10 weeks to 9 months.	Difference:	**SMD 0.04 lower** (CI 95% 0.17 lower — 0.09 higher)	**Low** Due to serious risk of bias, Due to serious publication bias [2]	Structured exercise may have little or no difference on depressive symptoms in the long term (after exercise programs have stopped)
Safety During intervention 7 Critical	Based on data from 1,022 participants in 13 studies. (Randomized controlled)	Out of 13 studies, only 2 reported adverse event data. One RCT reported no adverse events. In another, 8/32 patients in the exercise group reported falls compared to 4/34 in the control group, with all falls occurring outside exercise sessions.		**Very low** Adverse event data not well reported in most trials [3]	We are uncertain whether structured exercise increases or decreases safety

1. **Risk of Bias: serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Restricting analysis to ITT trials only produced similar results but a non-significant effect. **Inconsistency: no serious. Indirectness: no serious.** Differences between the population of interest and those studied: most patients in trials not above clinical thresholds for depressive symptoms. **Imprecision: no serious. Publication bias: serious.** Asymmetrical funnel plot reported.
2. **Risk of Bias: serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: serious.** Asymmetrical funnel plot.
3. **Risk of Bias: very serious.** Incomplete data and/or large loss to follow up, lack of reporting. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Low number of patients. **Publication bias: no serious.**

Attached Images

Weak recommendation

Updated

For stroke survivors with depression, non-invasive brain stimulation (repetitive transcranial magnetic stimulation [rTMS]) may be used. (Allida et al 2020 *[155]*)

Update approved by NHMRC August 2022.

Practical Info

rTMS is usually delivered in clinic settings and the treatment regimen may require multiple visits to the clinic each week. There is little information on the best treatment montage (where and how electrodes are placed) for the treatment of post-stroke depression. While 'at home' delivery under supervision has been trialed in other populations, effectiveness and safety data are not available for people with stroke.

Evidence To Decision

Benefits and harms

Small net benefit, or little difference between alternatives

Reductions in depressive symptoms have been reported following rTMS treatment (Allida et al 2020 *[155]*).

Certainty of the Evidence

Very low

The quality of evidence is very low.

Values and preferences

Substantial variability is expected or uncertain

TMS is unfamiliar for many people, and patients may be anxious about undergoing the procedure. Some patients may find the procedure uncomfortable.

Resources and other considerations

Important issues, or potential issues not investigated

Resources considerations

No literature to understand or describe the potential economic implications of this recommendation was identified. TMS equipment may not be widely available. Treatment may require travel to a central location for treatments multiple times each week. Clinicians will also need training in the use of TMS.

Rationale

Although rTMS appears to produce benefits in reducing depressive symptoms, the available evidence is of very low quality. Equipment may not be widely available and patient preferences and values should be considered before trialing.

Clinical Question/ PICO

Population: Adults with stroke with depression
Intervention: Non-invasive brain stimulation
Comparator: Sham stimulation or usual care

Summary

The Cochrane review by Allida et al (2020)*[155]* included 49 trials (n=3342); 8 comparisons of various forms of non-invasive brain stimulation compared to sham stimulation or usual care were included. Brain stimulation (repetitive transcranial magnetic stimulation) decreased mean scores on the Hamilton Depression Rating Scale at the end of the

intervention (MD -6.63, 95%CI -9.71 to -3.55; 8 trials, n=495; very low-certainty evidence) as well as at the end of follow-up (MD -2.60, 95%CI -3.33 to -1.87; 3 trials, n=170; very low-certainty evidence).

Non-invasive brain stimulation plus antidepressants compared to antidepressants alone was found to reduce mean scores on the Hamilton Depression Rating Scale at the end of treatment (MD -4.09, 95%CI -5.61 to -2.57; 9 trials, n=665; very low-certainty evidence).

Another review by Liu et al (2018)*[157]* included 17 studies (n=1171) and assessed high frequency repetitive transcranial magnetic stimulation. Most of the trials (14/17) were conducted in China, three studies were published in English journals and 5 studies used a sham control stimulation as the comparison. Treatment ranged from 2-12 weeks. Brain stimulation led to a significant reduction in depression scores (using Hamilton Depression Scale v17 or v24: SMD -1.01, 95%CI -1.36 to -0.66; 15 studies, n=1053; high heterogeneity I^2=85%). Total length of treatment was found to lead to the high heterogeneity with effectiveness reduced with treatment longer than 6 weeks. Brain stimulation increased the number of people with a reduction of 50% or more on scores (OR 3.31, 95%CI 2.25 to 4.88; n=529) and who reported remission of depression (OR 2.72, 95%CI 1.69 to 4.38; n=529). There was higher rate of adverse events (most commonly headaches) with active intervention (OR 3.53; 95%CI, 1.85 to 8.55). The authors reported good quality of included studies (mean 7.35/10 on PEDro scale) but all studies did not report allocation concealment and only 4/17 studies had blinded assessors.

Outcome Timeframe	**Study results and measurements**	**Comparator** Sham stimulation or usual care	**Intervention** Non-invasive brain stimulation	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Depression -mean scores End of treatment 8 Critical	Measured by: Hamilton Depression Rating Scale (HDRS) Lower better Based on data from 495 participants in 8 studies. [1] (Randomized controlled)	Difference:	**MD 6.63 lower** (CI 95% 9.71 lower — 3.55 lower)	**Very low** Due to very serious risk of bias, serious imprecision and very serious inconsistency [2]	Non-invasive brain stimulation may decrease depression symptoms
Depression - mean scores at end of follow up 8 Critical	Measured by: Hamilton Depression Rating Scale (HDRS) Based on data from 170 participants in 3 studies. (Randomized controlled)	Difference:	**MD 2.6 lower** (CI 95% 3.33 lower — 1.87 lower)	**Very low** Due to very serious risk of bias, and very serious inconsistency [3]	Non-invasive brain stimulation may decrease depression symptom

1. Systematic review [155] . **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of Bias: serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias. **Inconsistency: serious.** The magnitude of statistical heterogeneity was high, with I^2:... %.. **Indirectness: serious. Imprecision: serious.** Wide confidence intervals. **Publication bias: no serious.**
3. **Risk of Bias: serious. Inconsistency: no serious. Imprecision: serious.** Wide confidence intervals.

Attached Images

Weak recommendation

Updated evidence, no change in recommendation

For stroke survivors with depression or depressive symptoms, acupuncture may be used. (Zhang et al 2010 *[153]*)

Evidence To Decision

Benefits and harms

Substantial net benefits of the recommended alternative

Substantial differences in response rate (>=50% reduction in scores on depression scales) have been reported when comparing acupuncture to antidepressants and waitlist controls (Zhang et al 2010 *[153]*). Acupuncture was also reported to produce lower rates of side-effects compared to antidepressants but this analysis was not specific to stroke.

Certainty of the Evidence

Low

The quality of evidence is low, with a lack of blinding and no comparison to sham or placebo acupuncture to rule out placebo effects.

Values and preferences

Substantial variability is expected or uncertain

The majority of studies come from Chinese populations. Australian patients may have different preferences regarding acupuncture.

Resources and other considerations

Important issues, or potential issues not investigated

Resources considerations

No literature to understand or describe the potential economic implications of this recommendation was identified. Acupuncture is only available through Medicare if delivered by a medical professional, otherwise patients may have to pay for private treatment.

Rationale

Acupuncture appears to reduce depression and depressive symptoms but the low quality of the research means substantial bias is possible.

Clinical Question/ PICO

Population: Adults with stroke with depression
Intervention: Acupuncture therapy
Comparator: Control

Summary

A systematic review included 15 trials of acupuncture for post-stroke depression, involving 1680 participants (Zhang et al 2010 *[153]*). The included trials compared acupuncture monotherapy to either antidepressants or to waitlisted control groups. Meta-analysis showed significant improvements in response rate when acupuncture was compared to antidepressants and waitlisted controls, as well as significant improvements on measurements of depression symptoms (HAMD) for both comparisons. The lack of sham acupuncture controls suggests that trials had serious risk of bias. Investigation of acupuncture in properly-blinded controlled trials is required to confirm any potential benefits for people with post-stroke depression.

Li et al (2018)*[160]* included 18 trials (n=1536). There was no difference in severity of depression with electroacupuncture compared to antidepressants after 4, 6 or 8 weeks after treatment. However, the was lower adverse events (RR 0.21, 95%CI 0.14 to 0.33).

Outcome Timeframe	**Study results and measurements**	**Comparator** Control	**Intervention** Acupuncture therapy	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Response rate [1] End of treatment 9 Critical	Relative risk 1.36 (CI 95% 1.24 — 1.5) Based on data from 1,572 participants in 13 studies. (Randomized controlled) Follow up: 4 to 8 weeks of treatment.	431 per 1000 Difference:	586 per 1000 **155 more per 1000** (CI 95% 103 more — 216 more)	**Low** Due to very serious risk of bias - no blinding/ placebo controls [2]	Acupuncture therapy may improve response rate
Response rate - compared to antidepressants [3] End of treatment 9 Critical	Relative risk 1.31 (CI 95% 1.19 — 1.44) Based on data from 1,438 participants in 11 studies. (Randomized controlled) Follow up: 4 to 8 weeks of treatment.	447 per 1000 Difference:	586 per 1000 **139 more per 1000** (CI 95% 197 more — 85 more)	**Low** Due to very serious risk of bias - no blinding/ placebo controls [4]	Acupuncture therapy may improve response rate compared to antidepressants
Response rate - compared to waitlist [5] End of treatment 9 Critical	Relative risk 2.33 (CI 95% 1.44 — 3.78) Based on data from 134 participants in 2 studies. (Randomized controlled) Follow up: 4 to 8 weeks of treatment.	447 per 1000 Difference:	586 per 1000 **139 more per 1000** (CI 95% 197 more — 85 more)	**Low** Due to very serious risk of bias - no blinding/ placebo controls [6]	Acupuncture therapy may improve response rate compared to waitlist
Changes in depression scale End of treatment 8 Critical	Measured by: Change from baseline on HAMD High better Based on data from 1,512 participants in 14 studies. (Randomized controlled) Follow up: 4 to 8 weeks of treatment.	Difference:	**MD 2.54 higher** (CI 95% 1.11 higher — 3.97 higher)	**Low** Due to very serious risk of bias - no blinding/ placebo controls [7]	Acupuncture therapy may decrease depression symptoms
Changes in depression scale - compared to antidepressants End of treatment 8 Critical	Measured by: Change from baseline on HAMD High better Based on data from 1,318 participants in 11 studies. (Randomized controlled) Follow up: 4 to 8 weeks of treatment.	Difference:	**MD 1.43 higher** (CI 95% 0.19 higher — 2.68 higher)	**Low** Due to very serious risk of bias - no blinding/ placebo controls [8]	Acupuncture therapy may decrease depressive symptoms compared to antidepressants
Changes in depression scale - compared to waitlist End of treatment 8 Critical	Measured by: Change from baseline on HAMD High better Based on data from 194 participants in 3 studies. (Randomized controlled) Follow up: 4 to 8 weeks of treatment.	Difference:	**MD 7.24 higher** (CI 95% 5.01 higher — 9.46 higher)	**Low** Due to very serious risk of bias - no blinding/ placebo controls [9]	Acupuncture therapy may decrease depressive symptoms compared to waitlist

1. Response rates were generally defined as >= 50% reduction in scores on depression scales
2. **Risk of Bias: very serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias. **Inconsistency: no serious. Indirectness: no serious.** Differences between the population of interest and those studied: mostly Chinese studies. **Imprecision: no serious. Publication bias: no serious.**
3. Response rates were generally defined as >= 50% reduction in scores on depression scales
4. **Risk of Bias: very serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias. **Inconsistency: no serious. Indirectness: no serious.** Differences between the population of interest and those studied. **Imprecision: no serious. Publication bias: no serious.**
5. Response rates were generally defined as >= 50% reduction in scores on depression scales
6. **Risk of Bias: very serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias. **Inconsistency: no serious. Indirectness: no serious.** Differences between the population of interest and those studied. **Imprecision: no serious. Publication bias: no serious.**
7. **Risk of Bias: very serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias. **Inconsistency: no serious. Indirectness: no serious.** Differences between the population of interest and those studied: mostly Chinese studies. **Imprecision: no serious. Publication bias: no serious.**
8. **Risk of Bias: very serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias. **Inconsistency: no serious. Indirectness: no serious.** Differences between the population of interest and those studied. **Imprecision: no serious. Publication bias: no serious.**
9. **Risk of Bias: very serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias. **Inconsistency: no serious. Indirectness: no serious.** Differences between the population of interest and those studied. **Imprecision: no serious. Publication bias: no serious.**

Attached Images

Treatment for anxiety

The Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) classifies anxiety disorders as a collection of individual syndromes that include generalized anxiety disorder (GAD), panic disorder (with or without agoraphobia), agoraphobia (with or without panic), specific phobia, social phobia, obsessive-compulsive disorder (OCD), posttraumatic stress disorder (PTSD), acute stress disorder, anxiety disorder due to a general medical condition, substance-induced anxiety disorder, and anxiety disorder not otherwise specified. Each disorder has certain distinct features, yet they all share similar hallmark characteristics of excessive and irrational fear, feeling apprehensive and tense, and difficulty and distress in managing daily tasks. Certain physiological symptoms such as palpitations, dizziness, or trembling may also be present. Anxiety after stroke occurs frequently however can be misdiagnosed due to commonalities in symptomology with other post-stroke complications such as sleep disturbance and fatigue (Campbell Burton et al 2013 *[?]*).

Interventions include pharmacological (e.g. antidepressants) and psychological strategies (e.g. problem solving or motivational interviewing). No recommendation has been made specifically for mindfulness-based interventions. A systematic review of mindfulness-based interventions following TIA and stroke including 4 trials, 1 randomised trial, 2 case series and 1 case control study (Lawrence et al 2013 *[149]*), was identified in the literature review. The randomised trial was small (N = 12) and showed no significant between-group differences in mental fatigue or depression and anxiety. Significant effects on depression and anxiety were seen in the non-randomised trials but this represents low-quality evidence. Overall there is insufficient evidence to confirm any benefits or harms of mindfulness-based interventions and further research is required. Further research is also required for treatment of anxiety post-stroke.

Consensus recommendation

New

Consensus-based recommendations

For people with anxiety after stroke, psychological therapy and/or relaxation strategies, such as yoga may be trialed to reduce levels of anxiety. The addition of pharmacotherapy should be very carefully considered taking into account higher risk of harms.

Approved by NHMRC August 2022.

Practical Info

People with aphasia should be offered communicatively accessible therapies.

Rationale

There is very little high quality evidence to guide practice therefore a consensus-based recommendation has been provided. Pyschological therapy or mindfulness therapy such as yoga have been reported to have beneficial effects on anxiety but have little or no side effects and it is reasonable to trial these interventions first. The addition of SSRI pharmacotherapy should be very carefully considered taking into account the increase in harms (seizures and bone fractures). Pharmacotherapy (e.g. paroxetine) may lead to lower rates of anxiety but were reported to have high rates of adverse events.

Clinical Question/ PICO

Population: Adults with stroke with anxiety
Intervention: Pharmacological and/or psychological interventions
Comparator: No control group

Summary

A Cochrane review by Knapp et al (2017) *[161]* included 3 trials (four interventions; n=196). One pilot study (n=21) found lower anxiety listening to a relaxation CD over four weeks in community-dwelling stroke survivors compared to wait list control. Scores on the Hospital Anxiety and Depression Scale at three months were lower (p=0.001). The other two trials that were included both involved participants with co-morbid anxiety and depression (total n=81 and n=94). Intervention groups received paroxetine, paroxetine plus psychotherapy or buspirone hydrochloride, while the control groups received usual care. All intervention groups had significantly lower anxiety levels than controls at follow-up. However, the trials were not placebo controlled, and it is unclear whether the results would apply to patients who only had anxiety. Adverse events were also a concern, particularly for paroxetine where half of the participants receiving paroxetine reported events such as nausea, vomiting and dizziness. The quality of the evidence was very low.

Another review by Chun et al (2018)*[165]* included 14 studies (12 stroke; one stroke & TBI; one TBI; n=928 total). Overall pharmacotherapy favoured intervention over control (SMD: -2.12, 95%CI -3.05 to -1.18; very high heterogeneity: I^2=89%). One comparison of mixed pharmacotherapy and psychotherapy favoured intervention over usual care (SMD: -4.79, 95%CI -5.87 to -3.71). Psychotherapy improved intervention over control (SMD: -0.41, 95%CI -0.79 to -0.03). All studies were noted as having high risk of bias and sample sizes were small in studies. Studies that commenced in the post-acute phase appear more positive, however, no follow measures were undertaken. Further studies are needed.

A Cochrane review by Legg et al (2021) *[215]* included 76 studies (n=13,029) with 38 studies requiring participants have depression on enrollment. Meta-analysis of studies with low risk of bias across all domains (N=6, non of which used depression or anxiety as an inclusion criteria) identified a small reduction in average depression scores (S MD -0.14, 95% CI 0.19 lower to 0.08 lower; 4 studies; 5356 participants, high-quality evidence) and reduced the proportion with depression (RR 0.75, 95% CI 0.65 to 0.86; 3 studies, 5907 participants, high-quality evidence). SSRIs increased the risk of seizure (RR 1.40, 95% CI 1.00 to 1.98; 6 studies, 6080 participants, moderate-quality evidence) and a bone fracture (RR 2.35, 95% CI 1.62 to 3.41; 6 studies, 6080 participants, high-quality evidence).

Outcome Timeframe	**Study results and measurements**	**Comparator** No control group	**Intervention** Interventions	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Anxiety (HAM-A)	Based on data from 196 participants in 3 studies. [1] (Randomized controlled)	A systematic review found two RCTs of patients with comorbid depression and anxiety comparing paroxetine (an SSRI) and buspirone (an anxiolytic) to standard care. Both reported significant effects for anxiety symptoms as measured by HAM-A. The quality of evidence was judged to be too low to conduct meta-analysis		Very low Due to very serious risk of bias: low quality trials and lack of placebo control, Due to serious indirectness: only patients with comorbid depression and anxiety included [2]	We are uncertain whether pharmacological interventions improve or worsen anxiety symptoms

1. Systematic review [161].
2. **Risk of Bias: very serious.** Quality indices were not clearly described so bias could not be assessed properly. No comparison to placebo, just standard care. **Indirectness: serious.** Differences between the population of interest and those studied: only patients with comorbid depression and anxiety were included, so patients with anxiety only would have been excluded.

Attached Images

Practical issues	**No control group**	**Pharmacological and/or psychological interventions**	**Both**
Adverse effects, interactions and antidote Adverse effects of pharmacological treatments		In the paroxetine trial, half the patients receiving paroxetine experienced adverse events including nausea, vomiting or dizziness. 14% of patients receiving buspirone experienced nausea or palpitations	

Clinical Question/ PICO

Population: Adults with stroke and axiety
Intervention: Yoga
Comparator: Control

Summary

Lawrence et al (2017)*[163]* conducted a Cochrane review with two studies. Anxiety and depression were measured in one study. Three measures were used: the Geriatric Depression Scale-Short Form (GCDS15), and two forms of State Trait Anxiety Inventory (STAI, Form Y) to measure state anxiety (i.e. anxiety experienced in response to stressful situations) and trait anxiety (i.e. anxiety associated with chronic psychological disorders). No significant effect was found for depression (GDS15, MD -2.10, 95% CI -4.70 to 0.50, P = 0.11) or for trait anxiety (STAI-Y2, MD -6.70, 95% CI -15.35 to 1.95, P = 0.13), based on very low-grade evidence. However, a significant effect was found for state anxiety: STAI-Y1 (MD -8.40, 95% CI -16.74 to -0.06, P = 0.05); the evidence for this finding was very low grade. No adverse events were reported.

Another review by Thayabaranathan et al (2017)*[164]* included four RCTs with small sample sizes (n = 17–47). Yoga was

found to reduce state anxiety symptoms in the intervention group compared to the control group (MD 6.05, 95% CI −0.02 to 12.12; p = 0.05; low quality evidence). Further large and well conducted studies are needed.

Outcome Timeframe	**Study results and measurements**	**Comparator** Control	**Intervention** Yoga	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Anxiety 7 Critical	Based on data from 22 participants in 1 studies. (Randomized controlled) Follow up: End of 10 week intervention.	One small study reported a significant effect on state anxiety (MD -8.40, 95% CI -16.74 to -0.06, P = 0.05). No adverse events were reported.		**Very low** Small sample size, incomplete data, and the small number of studies	We are uncertain whether yoga improves or worsen anxiety

Attached Images

Personality and behaviour

Personality and behaviour changes can happen after stroke and can include irritability, aggression, emotional lability, apathy or adynamia, perseveration, impulsivity and disinhibition, lack of awareness or insight, socially or sexually inappropriate behaviour. These may make maintaining relationships, community participation and reintegration challenging (Kelly et al 2008*[211]*, Murray et al 2007*[212]*, Hochstenbach et al 2005*[210]*, Stone et al 2004*[213]*) Personality and behaviour changes in a person after stroke can also pose difficulties for family, friends and carers, and can contribute to carer stress. (Murray et al 2007*[212]*, Stone et al 2004*[213]*) There is limited stroke research on assessment and rehabilitation of behaviour changes, but there is useful research in other groups of people after acquired brain injuries.

Providing information and education about behaviour changes is important for both the survivor of stroke and their family/carer.(Fisher et al 2015*[206]*) (see 7.1 Information and education)

Consensus recommendation

New

Consensus-based recommendations

a. Behavioural changes after stroke can impact on a person's ability to engage in meaningful activities and also their quality of life. Therefore, the impact of any behavioural changes on relationships, employment and leisure should be assessed and addressed across the lifespan.
b. Stroke survivors and their families/carers should be given access to individually tailored interventions for personality and behavioural changes. This may include positive behaviour support programs, anger-management therapy and rehabilitation training and support in management of complex and challenging behaviour.

Approved by NHMRC August 2022.

Practical Info

Where a Positive Behavioural Support approach is used, aim to follow the approach used in the trials. For example, the trial by Ponsford et al 2022 *[204]* involved setting collaborative goals with the individual and addressing barriers to achieving the goals, including behaviours of concern. In addition four fundamental principles were used including 'Person driven, Learning together,

Uniting supports, and Skill building'. These underpineed the focus on supporting the person to achieve a better life rather than focusing on managing the challenging behaviour. The frequency and location of treatment was negotiated. Goal Attainment Scaling was used to set goals and monitor progress. Strategies included behavioural self-regulation, increasing social support, environmental changes and addressing cognitive, emotional and communication and physical barriers. Additional strategies included executive control scripts, developing theory of mind, or learning how to consider other people's perspective, and creating identity maps. Therapists trained to deliver the intervention included neuropsychologists, occupational therapists or speech pathologists. Training involved written and group learning (approximately 8 hours).

Information related to other approaches can be found in acquired brain injury resources such as the Canadian Evidence-Based Review of moderate to severe Acquired Brain Injury (https://erabi.ca/).

Rationale

When a survivor of stroke demonstrates behaviour which causes distress to themselves or to others, they should be assessed by an appropriately trained healthcare professional to assess the behaviours, determine the underlying cause/s and advise on management. A psychologist, neuropsychologist, occupational therapist, social worker or speech pathologist trained in assessing behaviours of concern would usually undertake such an assessment. The person with the stroke and their family and team should be actively included in the assessment.

Assessment and rehabilitation approaches in this area of practice vary, and we acknowledge that there is more research in the field of traumatic brain injury. Research which has been conducted with adults who've experienced a stroke is limited, and primarily uses small numbers or single-case studies. This research suggests that there may be benefit in using neurobehavioural approaches to decreasing the frequency, intensity and duration of behaviours of concern (e.g. functional behaviour assessment and non-aversive interventions, antecedent control, verbal feedback, establishing a therapeutic relationship, and altering staff attributions). (Alderman et al 1994*[205]*, Yody et al 2000*[214]*, Giles et al 2006*[209]*). There are high quality randomised controlled trials in the traumatic brain injury populations which provide useful research to support approaches in stroke. For example, a randomised-controlled trial found that using Positive Behaviour Support with adults with traumatic brain injury and stroke can improve self-regulation of otherwise challenging behaviours, and improved the level of confidence to manage behaviours by family and close others (Gould et al 2021a*[207]*, Gould et al 2021b*[208]*, Ponsford et al 2022*[204]*).

Recognising the limited direct evidence in a stroke population and the potential overlapping issues of cognitive decline or dementia in older patients, consensus-based recommendations have been provided.

Clinical Question/ PICO

Population: Adults with acquired brain injury
Intervention: Positive behaviour support
Comparator: Usual care

Summary

A study by Ponsford et al. (2022)*[204]* with 49 individuals with acquired brain injury (61%, n=30 traumatic brain injury; 27%, n= 13 stroke) compared positive behaviour support (PBS) with waitlist treatment-as-usual. PBS+PLUS involved setting collaborative goals with the individual and addressing barriers to achieving the goals, including challenging behaviour. The waitlist treatment-as-usual group was not denied an intervention from other providers during the intervention period. For the Overt Behaviour Scale, both groups showed a significant reduction in challenging behaviour over the 12 month intervention and up to 8 months post-intervention. For the close-others' confidence in addressing challenging behaviours assessed by the Challenging Behaviour Self-Efficacy Scale (CBSES), the PBS+PLUS intervention group had significantly greater gains than the waitlist treat-as-usual group at the end of intervention period (p=0.02).

Deep venous thrombosis or pulmonary embolism

Venous thromboembolism is one of the most important, potentially preventable, causes of death and morbidity in patients in hospital (Naccarato et al 2010 *[172]*). Stroke patients are at high risk of deep venous thrombosis (DVT) and pulmonary embolism (PE) due to an increase in thrombin formation and platelet hyperactivity (Naccarato et al 2010 *[172]*). Those who have significant weakness of legs and who are immobile are at greater risk (Naccarato et al 2010 *[172]*).

National Stroke Audits indicated that only 2% of stroke patients had DVT during admission (Stroke Foundation 2020 *[7]*), compared to 40% reported in the literature (confirmed on magnetic resonance imaging within the first three weeks) (Naccarato et al 2010 *[172]*). This may be because clinically apparent DVT is less common or because current management strategies have improved. Importantly, asymptomatic DVTs may cause important complications related to post-phlebitic venous hypertension including swelling and skin ulceration.

The risk of DVT and PE can be reduced through the use of low dose anticoagulation or intermittent pneumatic compression and there is debate surrounding the optimal approach.

Weak recommendation

For acute ischaemic stroke patients who are immobile, low molecular weight heparin in prophylactic doses may be used in the absence of contraindications. (Sandercock et al 2015 *[166]*; Sherman et al 2007 *[173]*)

Practical Info

The American Heart Association and Canadian Heart and Stroke Foundation guidelines recommend low molecular weight heparin for immobilized ischaemic stroke patients. The European Stroke Organization 2016 recommendations state that low molecular weight heparin "should be considered in immobile patients with ischaemic stroke in whom the benefits of reducing the risk of venous thromboembolism is high enough to offset the increased risks of intracranial and extracranial bleeding associated with their use" (Dennis et al 2016 *[175]*). The UK 2016 guidelines state that low molecular weight heparin should not be used due to the perceived bleeding risk.

Even though pulmonary embolism appears relatively rare, post-thrombotic syndrome resulting from venous valvular incompetence causes pain, swelling, and skin changes, including varicose eczema and ulceration. This may affect over 20% of those with symptomatic DVT within 2 years and can also occur after asymptomatic DVT.

Evidence To Decision

Benefits and harms

Substantial net benefits of the recommended alternative

Immobilised stroke patients are at high risk of venous thromboembolism. Unfractionated heparin substantially reduces the risk of deep vein thrombosis (DVT) and pulmonary embolism (PE) in ischaemic stroke. Low molecular weight heparin was demonstrated in one randomised trial PREVAIL (Sherman et al 2007 *[173]*) to be more effective than unfractionated heparin, has a lower rate of heparin-induced thrombocytopenia and is more cost effective due to once daily administration.

There have been concerns about haemorrhagic transformation of the infarct, largely based on the International Stroke Trial (IST) *[173]* which tested both low and high dose heparin. However, the risk of symptomatic haemorrhagic transformation with prophylactic dose heparin was low in IST (an increase of 3 per 1000 versus no antithrombotic compared to an increase of 1 per 1000 if aspirin was administered) *[174]*. It should be noted that standards of care have evolved since IST when CT brain prior to anticoagulation was not standard and some patients with intracerebral haemorrhage were randomized.

In the PREVAIL trial *[173]* which compared unfractionated versus low molecular weight heparin, there was no difference in symptomatic intracerebral haemorrhage between groups. Overall, 10/1792 (0.6%) patients developed symptomatic haemorrhagic transformation which is similar to spontaneous rates of symptomatic haemorrhage in control patients in the alteplase trials but there was no untreated control group in PREVAIL to allow direct comparison. The low absolute rate of bleeding adverse events appears to be offset by reduced pulmonary embolism and probably reduced recurrent ischemic stroke (in IST low dose heparin was associated with a net reduction in all cause stroke versus control and to a lesser degree versus aspirin).

Certainty of the Evidence

Moderate

Multiple high-quality randomized controlled trials, although doses and agents used was variable

Values and preferences

Substantial variability is expected or uncertain

There is marked variation in international guidelines on pharmacological DVT prophylaxis due to varying interpretation of the risk of symptomatic intracerebral haemorrhage. Whilst intermittent pneumatic compression does not have this risk, the data is predominantly based on one trial which did not demonstrate a significant reduction in the clinically important outcome of pulmonary embolism and there are greater cost and adherence issues compared to low molecular weight heparin.

Resources and other considerations

Important issues, or potential issues not investigated

Resources considerations

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

Implementation considerations

There is a clinical indicator collected in the National Stroke Audit on the provision of heparin for patients with deep venous thrombosis prophylaxis.

Rationale

The best method for venous thromboembolism prevention in stroke patients has been controversial. Compression stockings have convincingly been shown to be ineffective (Naccarato et al 2010 *[172]*). Intermittent pneumatic compression is effective for DVT prevention (reduction in PE did not reach significance) and does not carry potential bleeding complications associated with pharmacological prophylaxis (Dennis et al 2013 *[171]*). However, it is more expensive and patients may not tolerate the compression garments or may wear them for an insufficient proportion of the day. If pharmacological prophylaxis is used then low molecular weight heparin (enoxaparin) reduces deep vein thrombosis (DVT) compared with unfractionated heparin with similar bleeding risk but reduced heparin-induced thrombocytopenia. International guidelines vary markedly in their recommendations on pharmacological prophylaxis and we have therefore made a weak recommendation, although the working party assessment of the evidence was that the absolute risk of bleeding complications with low molecular weight heparin was low and offset by important benefits. There are also resource implications of intermittent pneumatic compression. Either treatment is acceptable for most patients with intermittent pneumatic compression particularly suitable in those with relative contraindications to pharmacological prophylaxis.

Clinical Question/ PICO

Population: Adult with ischaemic stroke
Intervention: Anticoagulation
Comparator: Control

Summary

A Cochrane review of early anticoagulant therapy in people with ischaemic stroke included 24 randomised trials with 23,748 participants (Sandercock et al 2015 *[166]*). Anticoagulants used in the trials included subcutaneous and intravenous heparin, low-molecular-weight heparin, heparinoids and oral vitamin K antagonists at both prophylactic and therapeutic doses which confounds interpretation. Meta-analyses showed significant reductions in deep vein thrombosis and pulmonary embolism following anticoagulant treatments. The review also found that early anticoagulant therapy (combining all types and doses) significantly increased rates of symptomatic intracranial haemorrhage (OR 2.55; 95% CI 1.95 to 3.33), with the absolute increase offset by a reduction in recurrent ischaemic stroke leading to no significant differences in odds of death or dependency at follow-up.

The European Stroke Organization published a guideline in 2016 that included a revised meta-analysis only including low dose anticoagulation (Dennis et al 2016 *[175]*). Again, a number of agents and doses that are not used in local clinical practice were included. These data have formed the basis of data extraction for symptomatic ICH.

Notably, on the question of symptomatic intracerebral haemorrhage, 85% of the overall data and 99.5% of the data on subcutaneous unfractionated heparin came from the IST trial which used both 5000 units BD (as practiced for prophylaxis)

as well as a high dose of 12500 units BD. When only the low dose of heparin in IST is considered, the excess risk of symptomatic intracerebral haemorrhage versus control reported in the IST publication was 0.3% (or 0.2% versus aspirin alone). This needs to be weighed against the net reduction in PE which was of similar magnitude and the reduction in all cause stroke (including haemorrhages) which was significant (0.9%) versus control and probably greater than with aspirin alone. The true rate of symptomatic intracerebral haemorrhage in ischaemic stroke patients given low dose unfractionated heparin may be lower than reported in IST as CT brain scans were not routinely performed prior to randomisation in IST and the final diagnosis included intracerebral haemorrhage in a proportion of patients.

An individual patient data meta-analysis of heparin treatments (Whiteley et al 2013 *[168]*), again combining multiple agents and doses, examined whether anticoagulation could be targeted to individuals at higher risk of thrombotic events or lower risk of haemorrhagic complications. They were unable to define a population with favourable risk benefit.

A meta-analysis by Geeganage et al (2013) *[170]* focussing on prophylactic or low-dose anticoagulation treatments compared the rates of symptomatic intracranial haemorrhage versus pulmonary embolism. Overall, SICH rates were higher than PE rates. However, despite the paper's conclusion, this provides no information about whether PE was reduced more than SICH was increased. PE and SICH rates were identical in trials examining low dose unfractionated heparin (OR 0.99 95%CI 0.65-1.52).

Turpie et al (2013) *[169]* reported data from 389 patients involved in the EXCLAIM trial (total N = 5963) who had ischaemic stroke, and who were receiving either extended-duration prophylaxis with enoxaparin or placebo for 4 weeks after their initial 10 day treatment period with enoxaparin. Venous thromboembolism was significantly reduced by 5.6% (mostly asymptomatic DVT) but major bleeding events were significantly increased by 1.5%.

No new significant variant data has been published compared to previous guidelines. However, in this edition, interpretation has been based on studies that used agents and doses of relevance to current practice (ie 5000 units BD subcutaneous unfractionated heparin and 40mg daily subcutaneous enoxaparin). As a result we have found that the risk of symptomatic haemorrhage is low and offset by a reduction in pulmonary embolism and recurrent ischaemic stroke, in addition to the sizeable benefits in reduction in symptomatic and asymptomatic DVT. Nonetheless we acknowledge the local and international variation in interpretation of the available data, hence the weak recommendation.

Outcome Timeframe	**Study results and measurements**	**Comparator** Control	**Intervention** Anticoagulation	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Deep vein thrombosis [1] During treatment (1 week to 1 month) 7 Critical	Odds ratio 0.21 (CI 95% 0.15 — 0.29) Based on data from 916 participants in 10 studies. [2] (Randomized controlled) Follow up: 1 week to 1 month of treatment.	443 per 1000 Difference:	143 per 1000 **300 fewer per 1000** (CI 95% 336 fewer — 256 fewer)	**High** [3]	Anticoagulation reduces DVT risk in this overall analysis of multiple agents and doses. The unfractionated heparin and low molecular weight heparin subgroups also showed significant reductions although heterogeneity was noted.
Pulmonary embolism [4] During treatment (1 week to 1 month) 8 Critical	Odds ratio 0.6 (CI 95% 0.44 — 0.81) Based on data from 22,544 participants in 14 studies. [5] (Randomized controlled) Follow up: 1 week to 1 month of treatment.	9 per 1000 Difference:	5 per 1000 **4 fewer per 1000** (CI 95% 5 fewer — 2 fewer)	**High** [6]	Anticoagulation reduces PE risk in this overall analysis of multiple agents and doses although the magnitude of effect may vary depending on the dose and agent used.
Symptomatic intracerebral haemorrhage [7] During treatment (1 week to 1 month)	Odds ratio 1.68 (CI 95% 1.11 — 2.55) Based on data from 15,688 participants in 9 studies. (Randomized controlled)	5 per 1000 Difference:	9 per 1000 **4 more per 1000** (CI 95% 1 more — 7 more)	**High** [8]	anticoagulation increases symptomatic intracerebral haemorrhage risk

Outcome Timeframe	**Study results and measurements**	**Comparator** Control	**Intervention** Anticoagulation	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
9 Critical	Follow up: treatment period (mostly 14 days).				

1. From Sandercock (2015): "objective evidence of deep vein thrombosis detected by the systematic use of imaging techniques such as iodine 125 fibrinogen scanning (I-125 scan), ultrasound of the leg, plethysmography, or X-ray contrast venography in all participants during the scheduled treatment period and during scheduled follow up. These methods therefore detected clinically silent deep vein thrombosis as well as confirming or refuting the diagnosis in participants with clinical features suggestive of deep vein thrombosis"
2. Systematic review [166] . **Baseline/comparator:** Control arm of reference used for intervention.
3. **Inconsistency: no serious.** The magnitude of statistical heterogeneity was high, with I^2:72 %. However, all trials were consistent with a reduction in DVT.. **Indirectness: no serious.** Differences between the dose and agent used in clinical practice and some of the doses and agents included in meta-analysis. **Imprecision: no serious. Publication bias: no serious.**
4. Symptomatic pulmonary embolism post ischaemic stroke
5. Systematic review [166] . **Baseline/comparator:** Systematic review.
6. **Risk of Bias: no serious.** Possible incomplete data - some trials (eg IST) reported that PE may have been incompletely ascertained. **Inconsistency: no serious.** Point estimates vary widely. Some classes of anticoagulants seem to be more effective than others. However the effect in the unfractionated heparin and LMW heparin subgroups was significant.. **Indirectness: no serious.** Differences between the dose and agent of interest and some of the doses and agents among the trials included in the meta-analysis. **Imprecision: no serious.**
7. Symptomatic intracerebral haemorrhage (bleeding into the brain)
8. **Inconsistency: no serious. Indirectness: no serious.** The majority of data is from the IST study which did not have universal CT brain prior to treatment leading to potential inclusion of patients with intracerebral haemorrhage. Some of the included trials used agents and doses that are not those in current clinical use.. **Imprecision: no serious. Publication bias: no serious.**

Attached Images

Clinical Question/ PICO

Population: Adults with ischaemic stroke
Intervention: Low Molecular Weight Heparin
Comparator: Unfractionated heparin

Summary

In a randomised controlled trial (Sherman et al 2007 *[173]*),1762 acute ischaemic stroke patients, within 48 h of the onset of stroke symptoms, received either enoxaparin 40 mg subcutaneously once daily or unfractionated heparin 5000 U subcutaneously every 12 h for 10 days (range 6–14). Study treatment was not blinded. The primary efficacy endpoint was the cumulative occurrence of confirmed venous thromboembolism, defined as the composite of symptomatic or asymptomatic deep vein thrombosis, or symptomatic or fatal pulmonary embolism during the study treatment phase (up to day 14). The primary safety endpoints were symptomatic intracranial haemorrhage, major extracranial haemorrhage, and all-cause mortality up to 48 h after treatment. Enoxaparin significantly reduced the frequency of venous thromboembolism in the efficacy population at day 14 compared with unfractionated heparin (relative risk [RR] reduction 43%; difference −7·9%, 95% CI −11·6 to −4·2).

Outcome Timeframe	**Study results and measurements**	**Comparator** Unfractionated heparin	**Intervention** LMWH	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
All DVT 2 weeks 8 Critical	Relative risk 0.57 (CI 95% 0.43 — 0.75) Based on data from 1,335 participants in 1 studies. (Randomized controlled)	176 per 1000 Difference:	100 per 1000 **76 fewer per 1000** (CI 95% 100 fewer — 44 fewer)	Low Due to serious risk of bias, Due to serious publication bias, Due to serious imprecision, Upgraded due to Clear dose-response gradient [1]	LMWH probably decreases all DVT
Symptomatic ICH (NIHSS score <14) 48 hrs post treatment 8 Critical	Relative risk 0.62 (CI 95% 0.43 — 0.81) Based on data from 1,335 participants in 1 studies. (Randomized controlled)	176 per 1000 Difference:	109 per 1000 **67 fewer per 1000** (CI 95% 100 fewer — 33 fewer)	Low Due to serious risk of bias, Due to serious imprecision, Due to serious publication bias, , Upgraded due to Large magnitude of effect [2]	LMWH probably decreases symptomatic ICH (nihss score <14)

1. **Risk of Bias: serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Only data from one study, Only data from one study. **Publication bias: serious.** Sanofi-Aventis funded the study., Mostly commercially funded studies. **Upgrade: clear dose-response gradient.**
2. **Risk of Bias: serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Only data from one study. **Publication bias: serious.** Funded by Sanofi-aventis. **Upgrade: large magnitude of effect.**

Attached Images

Weak recommendation

For acute stroke patients who are immobile, intermittent pneumatic compression may be used, either as an alternative to low molecular weight heparin or in those with a contraindication to pharmacological DVT prophylaxis (including patients with intracerebral haemorrhage or within 24 hours of thrombolysis). (Dennis et al 2013 *[171]*)

Evidence To Decision

Benefits and harms

Substantial net benefits of the recommended alternative

Intermittent pneumatic compression was shown to reduce DVT (52 fewer cases per 1000 patients treated) in the CLOTS 3 randomised trial (Dennis et al 2013 *[171]*). Reduction in pulmonary embolism did not reach statistical significance. Background use of prophylactic enoxaparin or unfractionated heparin was relatively low (17% with an additional 14% receiving therapeutic anticoagulation). There was no interaction detected between anticoagulant/thrombolysis use and the treatment effect of compression. Other than cost, modest patient adherence with wearing the compression garments and potential for skin breaks, there are no harms of intermittent pneumatic compression. The biological plausibility and clinical relevance of a statistically significant but small magnitude reduction in mortality (which occurred in the more severely disabled patients) is uncertain.

Certainty of the Evidence

Moderate

A single high quality randomized trial, underpowered to assess the clinically important outcome of pulmonary embolism.

Values and preferences

Substantial variability is expected or uncertain

Intermittent pneumatic compression is universally recommended in guidelines although some patients may find the compressions uncomfortable. Compression garments are also more expensive than low molecular weight heparin.

Resources and other considerations

Important issues, or potential issues not investigated

Resources considerations

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

Rationale

The best method for venous thromboembolism prevention in stroke patients has been controversial. Compression stockings have convincingly been shown to be ineffective (Naccarato et al 2010 *[172]*). Intermittent pneumatic compression is effective for DVT prevention (reduction in PE did not reach significance) and does not carry potential bleeding complications associated with pharmacological prophylaxis (Dennis et al 2013 *[171]*). However, it is more expensive and patients may not tolerate the compression garments or may wear them for an insufficient proportion of the day. If pharmacological prophylaxis is used then low molecular weight heparin (enoxaparin) reduces deep vein thrombosis (DVT) compared with unfractionated heparin with similar bleeding risk but reduced heparin-induced thrombocytopenia. International guidelines vary markedly in their recommendations on pharmacological prophylaxis and we have therefore made a weak recommendation, although the working party assessment of the evidence was that the absolute risk of bleeding complications with low molecular weight heparin was low and offset by important benefits. There are also resource implications of intermittent pneumatic compression. Either treatment is acceptable for most patients with intermittent pneumatic compression particularly suitable in those with relative contraindications to pharmacological prophylaxis.

Clinical Question/ PICO

Population: Adults with stroke
Intervention: Intermittent pneumatic compression
Comparator: Usual care

Summary

A multicentre randomised trial (Dennis et al 2013 *[171]*) involving 2,876 participants assessed the effectiveness of intermittent pneumatic compression (IPC) on the prevention of deep vein thrombosis (DVT). The CLOTS3 trial is the largest randomised controlled trial of IPC to date. IPC was shown to significantly reduce proximal DVT (32 per 1000) and all DVTs (52 per 1000). There was a trend towards reduced pulmonary embolism at 30 days in the intervention group but the difference was not statistically significant (OR 0.83, 95% CI 0.60 - 1.36) and the investigators did not screen systematically for pulmonary embolism. The main risk of IPC is of skin breaks which were present to a small degree (3% in the treatment arm vs 1% in the control arm) but showed a statistically significant difference. This risk did not seem to lead to poorer outcomes overall. There also appears to be a reduction of death by 6 months (OR 0.85, 95%CI 0.70 - 1.01) which in sub-analyses seems to occur in the most disabled group of patients.

Economic analyses of the CLOTS3 data (Dennis et al 2015 *[167]*) showed that the direct cost of preventing DVT using IPC was £1282 (95% CI £785 to £3077)

A previous Cochrane review by Naccarato et al (2010) *[172]* had found a non-significant reduction in DVTs from IPC (OR 0.45, 95% CI 0.19 to 1.10). However, this was based on two small trials with only 177 participants. The CLOTS3 trial had much greater power to detect an effect.

Yogendrakumar et al (2020)*[176]* identified four RCTs (n=607) including pharmacological and physical thromboprophylaxis. In a network meta-analysis pneumatic compression devices (PCD) were associated with a significant decrease in venous thromboembolism compared to control (OR: 0.43, 95% Credible limits 0.23 to 0.80; three studies, n=532). There was no difference between PCD and pharmacological thromboprophylaxis (OR: 0.47, 95% Credible limits 0.09 to 2.54; one study, n=75).

Outcome Timeframe	**Study results and measurements**	**Comparator** Usual care	**Intervention** Intermittent pneumatic compression	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Any deep vein thrombosis [1] 6 months 7 Critical	Odds ratio 0.72 (CI 95% 0.6 — 0.87) Based on data from 2,876 participants in 1 studies. [2] (Randomized controlled) Follow up: 6 months.	217 per 1000 Difference:	166 per 1000 **51 fewer per 1000** (CI 95% 74 fewer — 23 fewer)	**Moderate** Due to serious imprecision [3]	intermittent pneumatic compression probably decreases any deep vein thrombosis at 6 months
Proximal deep vein thrombosis [4] 30 days 7 Critical	Odds ratio 0.71 (CI 95% 0.6 — 0.86) Based on data from 2,876 participants in 1 studies. (Randomized controlled) Follow up: 6 months.	121 per 1000 Difference:	89 per 1000 **32 fewer per 1000** (CI 95% 45 fewer — 15 fewer)	**Moderate** Due to serious imprecision [5]	intermittent pneumatic compression probably decreases proximal deep vein thrombosis at 30 days
Pulmonary embolism [6] 30 days 9 Critical	Odds ratio 0.83 (CI 95% 0.5 — 1.36) Based on data from 2,876 participants in 1 studies. (Randomized controlled) Follow up: 30 days.	24 per 1000 Difference:	20 per 1000 **4 fewer per 1000** (CI 95% 12 fewer — 8 more)	**Low** Due to very serious imprecision [7]	intermittent pneumatic compression may decrease pulmonary embolism slightly

1. any lower limb DVT regardless of death, PE, location of DVT within lower limb, or bilateral leg involvement
2. Primary study[171]. **Baseline/comparator:** Control arm of reference used for intervention.
3. **Inconsistency: no serious. Indirectness: no serious.** There may be differences between the population of interest and that studied in the background use of pharmacological prophylaxis.. **Imprecision: serious.** Data from only one study.. **Publication bias: no serious.**
4. DVT in the proximal veins detected on a screening CDU or any symptomatic DVT in the proximal veins confirmed on imaging
5. **Risk of Bias: no serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, but it's unlikely to have caused bias due to the subjective nature of assessment. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Only data from one study. **Publication bias: no serious.**
6. All confirmed pulmonary embolism (imaging or autopsy) within 30 days of randomization
7. **Inconsistency: no serious. Indirectness: no serious. Imprecision: very serious.** Wide confidence intervals for the clinically important outcome of reduction in pulmonary embolism which did not reach statistical significance, data from only one study. . **Publication bias: no serious.**

Attached Images

Strong recommendation against

Antithrombotic stockings are not recommended for the prevention of DVT or PE post stroke. (Naccarato et al 2010 *[172]*)

Evidence To Decision

Benefits and harms

Small net benefit, or little difference between alternatives

Both thigh length and knee length compression stockings have been demonstrated to be ineffective in stroke patients in the CLOTs 1 and 2 randomized trials (Naccarato et al 2010 *[172]*). Apart from cost, there were complications with skin ulceration observed.

Certainty of the Evidence

Moderate

Included studies have high methodological quality but high statistical heterogeneity.

Values and preferences

No substantial variability expected

There is no group that is likely to benefit from compression stockings

Resources and other considerations

Factor not considered

Rationale

Compressions stockings (both thigh and knee length) are ineffective in preventing deep vein thrombosis in stroke patients and may cause skin ulceration (Naccarato et al 2010 *[172]*).

Clinical Question/ PICO

Population: Adults with stroke
Intervention: Graduated compression stockings
Comparator: Usual care

Summary

A Cochrane review of physical methods for preventing deep vein thrombosis (DVT) after stroke included two randomised trials of graduated compression stockings (GCS), involving 2615 participants (Naccarato et al 2010 *[172]*). Meta-analysis showed that GCS did not significantly reduce the risk of DVT or death by the end of follow-up.

Outcome Timeframe	**Study results and measurements**	**Comparator** Usual care	**Intervention** Graduated compression stockings	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Deep vein thrombosis During treatment: 7 days or until discharge 6 Important	Odds ratio 0.88 (CI 95% 0.72 — 1.08) Based on data from 2,615 participants in 2 studies. [1] (Randomized controlled) Follow up: Treatment for 7 days or until discharge.	177 per 1000 Difference:	159 per 1000 **18 fewer per 1000** (CI 95% 43 fewer — 11 more)	**Moderate** Due to serious inconsistency [2]	Graduated compression stockings probably have little or no difference on deep vein thrombosis
Symptomatic pulmonary embolism During treatment (until discharge)	Odds ratio 0.65 (CI 95% 0.33 — 1.3) Based on data from 2,518 participants in 1 studies. (Randomized controlled)	16 per 1000 Difference:	10 per 1000 **6 fewer per 1000** (CI 95% 11 fewer	**Moderate** Due to serious imprecision - only one study [3]	Graduated compression stockings probably have little or no difference on symptomatic pulmonary embolism

Outcome Timeframe	**Study results and measurements**	**Comparator** Usual care	**Intervention** Graduated compression stockings	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
7 Critical	Follow up: During treatment (until discharge).		— 5 more)		

1. Systematic review [172] . **Baseline/comparator:** Control arm of reference used for intervention.
2. **Inconsistency: serious.** The magnitude of statistical heterogeneity was high, with I^2:65 %.. **Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
3. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Only data from one study. **Publication bias: no serious.**

Attached Images

Info Box

Practice points

- For stroke patients, pharmacological prophylaxis should not be used in the first 24 hours after thrombolysis until brain imaging has excluded significant haemorrhagic transformation.
- For acute stroke patients, early mobilisation and adequate hydration should be encouraged to help prevent DVT and PE.
- For stroke patients receiving intermittent pneumatic compression, skin integrity should be assessed daily.
- For patients with intracerebral haemorrhage, pharmacological prophylaxis may be considered after 48-72 hours and once haematoma growth has stabilised, although evidence is limited.

Evidence To Decision

Resources and other considerations

Implementation consideration

There is a clinical indicator collected in the National Stroke Audit to determine the total number of patients with deep venous thrombosis on admission to acute care and/or rehabilitation. There is also a clinical indicator collected to determine the number of patients with deep venous thrombosis during their acute care and/or rehabilitation admission.

Rationale

Meta-analysis of small patient numbers (n=194) found no increase in haematoma enlargement in patients with intracerebral haemorrhage with anticoagulant therapy but there were no significant benefits of treatment. However, favourable trends were noted in reduced venous thromboembolism.(Paciaroni et al 2020*[177]*). Further studies are needed to clarify the role and optimal timing of pharmacological prophylaxis.

Clinical Question/ PICO

Population: Adults with stroke
Intervention: Intermittent pneumatic compression
Comparator: Usual care

Summary

A multicentre randomised trial (Dennis et al 2013 *[171]*) involving 2,876 participants assessed the effectiveness of intermittent pneumatic compression (IPC) on the prevention of deep vein thrombosis (DVT). The CLOTS3 trial is the largest randomised controlled trial of IPC to date. IPC was shown to significantly reduce proximal DVT (32 per 1000) and all DVTs (52 per 1000). There was a trend towards reduced pulmonary embolism at 30 days in the intervention group but the difference was not statistically significant (OR 0.83, 95% CI 0.60 - 1.36) and the investigators did not screen systematically for pulmonary embolism. The main risk of IPC is of skin breaks which were present to a small degree (3% in the treatment arm vs 1% in the control arm) but showed a statistically significant difference. This risk did not seem to lead to poorer outcomes overall. There also appears to be a reduction of death by 6 months (OR 0.85, 95%CI 0.70 - 1.01) which in sub-analyses seems to occur in the most disabled group of patients.

Economic analyses of the CLOTS3 data (Dennis et al 2015 *[167]*) showed that the direct cost of preventing DVT using IPC was £1282 (95% CI £785 to £3077)

A previous Cochrane review by Naccarato et al (2010) *[172]* had found a non-significant reduction in DVTs from IPC (OR 0.45, 95% CI 0.19 to 1.10). However, this was based on two small trials with only 177 participants. The CLOTS3 trial had much greater power to detect an effect.

Yogendrakumar et al (2020)*[176]* identified four RCTs (n=607) including pharmacological and physical thromboprophylaxis. In a network meta-analysis pneumatic compression devices (PCD) were associated with a significant decrease in venous thromboembolism compared to control (OR: 0.43, 95% Credible limits 0.23 to 0.80; three studies, n=532). There was no difference between PCD and pharmacological thromboprophylaxis (OR: 0.47, 95% Credible limits 0.09 to 2.54; one study, n=75).

Outcome Timeframe	**Study results and measurements**	**Comparator** Usual care	**Intervention** Intermittent pneumatic compression	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Any deep vein thrombosis [1] 6 months 7 Critical	Odds ratio 0.72 (CI 95% 0.6 — 0.87) Based on data from 2,876 participants in 1 studies. [2] (Randomized controlled) Follow up: 6 months.	217 per 1000 Difference:	166 per 1000 **51 fewer per 1000** (CI 95% 74 fewer — 23 fewer)	**Moderate** Due to serious imprecision [3]	intermittent pneumatic compression probably decreases any deep vein thrombosis at 6 months
Proximal deep vein thrombosis [4] 30 days 7 Critical	Odds ratio 0.71 (CI 95% 0.6 — 0.86) Based on data from 2,876 participants in 1 studies. (Randomized controlled) Follow up: 6 months.	121 per 1000 Difference:	89 per 1000 **32 fewer per 1000** (CI 95% 45 fewer — 15 fewer)	**Moderate** Due to serious imprecision [5]	intermittent pneumatic compression probably decreases proximal deep vein thrombosis at 30 days
Pulmonary embolism [6] 30 days 9 Critical	Odds ratio 0.83 (CI 95% 0.5 — 1.36) Based on data from 2,876 participants in 1 studies. (Randomized controlled) Follow up: 30 days.	24 per 1000 Difference:	20 per 1000 **4 fewer per 1000** (CI 95% 12 fewer — 8 more)	**Low** Due to very serious imprecision [7]	intermittent pneumatic compression may decrease pulmonary embolism slightly

1. any lower limb DVT regardless of death, PE, location of DVT within lower limb, or bilateral leg involvement
2. Primary study[171]. **Baseline/comparator:** Control arm of reference used for intervention.
3. **Inconsistency: no serious. Indirectness: no serious.** There may be differences between the population of interest and that studied in the background use of pharmacological prophylaxis.. **Imprecision: serious.** Data from only one study.. **Publication bias: no serious.**

4. DVT in the proximal veins detected on a screening CDU or any symptomatic DVT in the proximal veins confirmed on imaging
5. **Risk of Bias: no serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, but it's unlikely to have caused bias due to the subjective nature of assessment. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Only data from one study. **Publication bias: no serious.**
6. All confirmed pulmonary embolism (imaging or autopsy) within 30 days of randomization
7. **Inconsistency: no serious. Indirectness: no serious. Imprecision: very serious.** Wide confidence intervals for the clinically important outcome of reduction in pulmonary embolism which did not reach statistical significance, data from only one study. . **Publication bias: no serious.**

Attached Images

Clinical Question/ PICO

Population: Adults with haemorrhagic stroke
Intervention: Pharmacotherapy
Comparator: Usual care

Summary

Paciaroni et al (2020)*[177]* conducted a trial of enoxaparin to prevent venous thromboembolism (VTE) for people within 72 hours after intracerebral hemorrhage (ICH). The trial was stopped prematurely due to slow recruitment with only 73 participants recruited. rate. Enoxaparin may have reduced the prevalence of any VTE at 10 days (15.8% vs 20.0%; RR 0.79, 95%CI 0.29 to 2.12] although numbers were small. The authors then combined the data with previous studies (9 studies, n=4,609) and found anticoagulatants did not reduce VTE, pulmonary embolism or mortality. There was no hematoma enlargement (OR 0.97). Most analysis had moderate to high heterogenity. Results confined to just results of RCTs (n=194) was similar (non significant benefits or harms).

Yogendrakumar et al (2020)*[176]* identified four RCTs (n=607) including pharmacological and physical thromboprophylaxis. In a network meta-analysis pneumatic compression devices (PCD) were associated with a significant decrease in venous thromboembolism compared to control (OR: 0.43, 95% Credible limits 0.23 to 0.80). There was no differences between pharmacological thromboprophylaxis and control (OR: 0.93, 95% Credible limits 0.19 to 4.37) or between PCD and pharmacological thromboprophylaxis (OR: 0.47, 95% Credible limits 0.09 to 2.54).

Cochrane review of antithrombotic treatment for haemorrhagic stroke included two randomised trials (n=121) (Perry et al 2017*[178]*). Anticoagulation (heparin in one trial and enoxaparin in the other) did not reduce deep vein thrombosis (RR 0.99, 95% CI 0.49 to 1.96; low quality evidence).

Outcome Timeframe	**Study results and measurements**	**Comparator** Usual care	**Intervention** Pharmacotherapy	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Deep vein thrombosis During treatment: 7 days or until discharge 7 Critical	Odds ratio 0.88 (CI 95% 0.72 — 1.08) Based on data from 2,615 participants in 2 studies. [1] (Randomized controlled) Follow up: Treatment for 7 days or until discharge.	**177** per 1000 Difference:	**159** per 1000 **18 fewer per 1000** (CI 95% 43 fewer — 11 more)	**Moderate** Due to serious inconsistency [2]	Graduated compression stockings probably have little or no effect on deep vein thrombosis
Symptomatic pulmonary embolism During treatment	Odds ratio 0.65 (CI 95% 0.33 — 1.3) Based on data from 2,518 participants in 1 studies.	**16** per 1000	**10** per 1000	**Moderate** Due to serious imprecision - only one study [3]	Graduated compression stockings probably have little or no effect on symptomatic pulmonary

Outcome Timeframe	**Study results and measurements**	**Comparator** Usual care	**Intervention** Pharmacotherapy	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
(until discharge) 7 Critical	(Randomized controlled) Follow up: During treatment (until discharge).	Difference:	**6 fewer per 1000** (CI 95% 11 fewer — 5 more)		embolism

1. Systematic review [172] . **Baseline/comparator:** Control arm of reference used for intervention.
2. **Inconsistency: serious.** The magnitude of statistical heterogeneity was high, with I^2:65 %.. **Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
3. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Only data from one study. **Publication bias: no serious.**

Attached Images

Falls

Many stroke-related impairments (e.g. muscle weakness, sensory loss, reduced attention, and vision and spatial abnormalities) contribute to deficits of balance and therefore falls (Verheyden et al 2013 *[148]*). With these ongoing impairments, and with decreased mobility, people who have had a stroke are likely to be at increased risk of falling (Verheyden et al 2013 *[148]*). In the most recent clinical audit of rehabilitation services, 165% of stroke patients had a fall during admission (Stroke Foundation 202016 *[7]*). Incidence figures from studies collecting data between one and six months post-stroke vary from 25 to 37% (Verheyden et al 2013 *[148]*). Not all falls are serious enough to require medical attention, but they can lead to fear of falling, restrict a person's activities of daily living, and be a predictor for a future fall (Verheyden et al 2013 *[148]*).

Evidence for effective interventions to prevent falls in stroke survivors is limited, but principles for preventing falls in the general elderly can be applied to the stroke population.

Consensus recommendation

Consensus-based recommendations

- For stroke patients, a falls risk assessment, including fear of falling, should be undertaken on admission to hospital. A management plan should be initiated for all patients identified as at risk of falls.
- For stroke survivors at high risk of falls, a comprehensive home assessment for the purposes of reducing falling hazards should be carried out by a qualified health professional. Appropriate home modifications (as determined by a health professional) for example installation of grab rails and ramps may further reduce falls risk.

Practical Info

Assessment of falls needs to consider the specific underlying cause. Balance (e.g. using Berg Balance Scale) or mobility do not predict falls. Where problems are stroke-specific (e.g. difficulty standing), interventions should target these difficulties. Fear of falling, visual impairment, cognitive and emotional factors as well as physical factors should also be considered.

Specific contributors to fears surrounding balance can include:
- medical staff being smaller than the stroke survivor in height and weight, leading to a fear that if the need arose, the medical staff would not manage to support or 'catch' the patient
- depression medication side effects such as sleepiness, impacting on balance
- the patient not eating enough to sustain consistent energy levels, and thus strength, to maintain balance

Evidence To Decision

Resources and other considerations

Implementation consideration

There is a clinical indicator collected in the National Stroke Audit to determine the total number of patients who suffered a fall on or before admission to acute care and/or rehabilitation. There is also a clinical indicator collected to determine the number of patients who have fallen during their acute care and/or rehabilitation admission.

Weak recommendation

For stroke survivors who are at risk of falling, multifactorial interventions in the community, including an individually prescribed exercise program and advice on safety, should be provided. (Denissen et al 2019 *[179]*; Gillespie et al 2012 *[181]*)

Practical Info

Multifactorial interventions typically include individually prescribed exercise, as well as comprehensive assessment of falls risk and the home environment as well as prescribed exercise time*[182]*.

Exercise programs are most effective when they include both strength and balance training (Rimland et al 2016 *[183]*), include exercise that challenges balance, and include 3 hours or more a week of exercise (Sherrington et al 2016 *[182]*).

When prescribing exercise for strength and balance, consider issues such as:
- the availability and suitability of a dedicated, or semi-dedicated space in the home to conduct exercises
- the patient's potentially limited memory of exactly how to do the prescribed exercises

Evidence To Decision

Benefits and harms — Small net benefit, or little difference between alternatives

Previous evidence found multifactorial interventions with individual risk assessment and exercise was effective in reducing falls in older people living in the community (Gillespie et al 2012 *[181]*). More recent systematic reviews of fall prevention in stroke survivors (Sherrington et al 2016 *[182]*; Denissen et al 2018 *[179]*) did not find significant between-group differences in falls and quality of life.

Certainty of the Evidence — Very low

Insufficient evidence from small trials of high risk of bias.

Values and preferences — Substantial variability is expected or uncertain

Patients are likely to want to receive treatments that reduce their risk of falling. However, they may be uncertain about which treatments are adequately effective and safe.

Resources and other considerations — Important issues, or potential issues not investigated

Resources considerations

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

Rationale

Current evidence shows exercise may reduce the rate of falls but not number of people with stroke who fall (Denissen et al 2019 *[179]*) yet interventions including exercise appear to benefit older community residents (Gillespie et al 2012 *[181]*). Most clinical trials have included individually prescribed exercise programs, and some have also included other interventions including environmental assessments, comprehensive falls risk assessment, single vision glasses or medications (Denissen et al 2019 *[179]*).

Clinical Question/ PICO

Population: Adults with stroke
Intervention: Exercise
Comparator: Control

Summary

A Cochrane review by Denissen et al (2019) [149] included 14 studies (n=1358). Based on pooled data from 8 studies (n=765), exercise decreased the rate of falls for people with stroke (RR 0.72 95%CI 0.54 to 0.94, low-quality evidence). Sensitivity analysis with only high quality studies resulted in little or no difference in rate of falls (RR 0.88 95% CI 0.65 to 1.20, n=462). Exercise did not reduce the number of fallers (RR 1.03 95% CI 0.90 to 1.10; 10 studies, n=969, low quality evidence). There was no difference in effects from sensitivity analyes of single vs multifactorial interventions, time post stroke and higher quality studies. Overall there is little evidence to demonstrate the effectivenss of exercising in reducing falls post stroke.

Yang et al. (2021)*[203]* conducted a review that included 13 studies (n= 1352) investigating interventions for preventing falls. Meta-analyses of the 15 interventions showed no intervention was significantly more effective in preventing falls than placebo training (OR 0.88, 95% CI 0.64 to 1.21; 13 studies, n= 1352). All interventions showed little effect in improving the fall risk factors (SMD − 0.01 to 0.06). The most promising group involved walking-based interventions (OR 0.44, 95%CI 0.17

to 1.10; 3 studies, n=167).

Correia et al (2020)*[192]* explored the effect of oculomotor and gaze stability exercises in addition to usual care rehabilitation program (n= 68). Patients all were over 60 yrs and had positive Romberg test. During the intervention, falls were recorded for 3/35 of those in the control group and no falls occurred in those who completed the oculomotor and gaze stability exercises (p= 0.064).

Handelzalts et al (2019)*[187]* completed a study exploring perturbation-based balance training (PBBT) compared to weight shifting and gait training (n= 34) and found no significant difference in fall-threshold between groups post intervention and at follow up (ES 0.36, p= 0.182 and ES 0.22, p= 0.439). A similar study conducted by Mansfield et al (2018)*[190]* (n= 83) found no significant difference between groups for the odds of falls (OR 0.71, 95% CI 0.30 to 1.70) and rate of falls (rate ratio 0.85, 95% CI 0.42 to 1.69).

Winser et al (2018)*[186]* reviewed the effect of Tai Chi exercise on falls and included 3 studies (n= 303). The review found Tai Chi exercises significantly reduced falls incidence (OR 0.21, 95% CI 0.09 to 0.48; 1 study, n= 145, moderatequality evidence). Tai Chi compared to active therapies was non-significant for balance (Timed up and go test) at 12 weeks (WMD -0.45, 95% CI -3.43 to 2.54; 2 studies, n=158) and at 18 weeks (WMD 1.81, 95% CI -5.39 to 9.02; 2 studies, n= 158; low quality evidence).

Pang et al (2018)*[184]* included 84 participants in the chronic phase of recovery. Three, 60 minute sessions for 8 weeks involving dual-task balance/mobility training reduced the risk of falls by 25%. This intervention is only possible for those without cognitive impairments.

Liu et al (2019)*[189]* explored decreasing the fear of falling through cognitive behaviour therapy and task-oriented training (n= 89) and found a greater reduction in the fear of falling in the intervention group at end intervention (MD 1.77, p= 0.04) and up to 12 months (MD 2.94, p= 0.01).

Lee et al (2019)*[191]* evaluated the effects of a community-based walking training compared to treadmill walking and control (n= 45). The fall-related self-efficacy increased significantly after treatments in all groups and was significantly better in the community-based walking training igroup compared to the other groups (p < 0.01)

Outcome Timeframe	**Study results and measurements**	**Comparator** Control	**Intervention** Exercise	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Number of fallers Two months to one year 7 Critical	Relative risk 1.03 (CI 95% 0.9 — 1.19) Based on data from 969 participants in 10 studies. [1] (Randomized controlled) Follow up: From 2 months -12 months.	411 per 1000 Difference:	424 per 1000 **13 more per 1000** (CI 95% 36 fewer — 84 more)	**Very low** Due to serious risk of bias, Due to serious indirectness, due to imprecision [2]	Exercise may have little or no difference on the number of fallers
Rate of falls 7 Critical	Measured by: Rate of falls Lower better Based on data from 765 participants in 8 studies. [3] (Randomized controlled)	Difference:	**MD 0.72 lower** (CI 95% 0.54 lower — 0.94 lower)	**Low** Due to high risk of bias, Due to imprecision	Exercise may decrease rate of falls
QOL 8 Critical	Based on data from participants in 14 studies. (Randomized controlled) Follow up: Up to 1 year.	Quality of life (QoL) is a commonly reported outcome measure in studies investigating the effects of exercise on falls prevention but heterogeneity of outcome measures used in such studies prevented pooling of data in the most recent Cochrane review (Denissen et al 2019). The majority of studies in this review failed to detect a difference in the QoL between stroke survivors		**Low** Due to serious risk of bias, Due to serious imprecision [4]	Falls prevention exercises may have little or no effect on QoL (which encompasses quality of life, fear of falling and community activity participation).

Outcome Timeframe	**Study results and measurements**	**Comparator** Control	**Intervention** Exercise	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
		receiving and not receiving exercise interventions designed to prevent falls.			

1. Systematic review [179] . **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of Bias: serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias.

Indirectness: serious. Differences between the intervention/comparator of interest and those studied.

3. Systematic review [179] . **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of Bias: serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Missing intention-to-treat analysis, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias. **Inconsistency: no serious.** Heterogeneity in outcome measures. **Indirectness: no serious.** Direct comparisons not available. **Imprecision: serious.** No pooling of data due to heterogeneity. **Publication bias: no serious.**

Attached Images

Pressure injury

Pressure injuries (previously referred to as pressure ulcers or pressure sores) are areas of localised damage to the skin or underlying soft tissue, or both, caused by unrelieved pressure, shear or friction. (Shi et al. 2021 *[200]*) One large multicentre trial reported 1% of patients developed pressure injuries following acute stroke admission. (Dennis 2005 *[197]*) Age, stroke severity, immobility, incontinence, nutritional status and diabetes are contributing risk factors. Pressure area care policies are a common characteristic of stroke unit care.(Langhorne 2002 *[196]*) Risk assessment scales, such as the Braden, Norton or Waterlow Risk Assessment scales, have only modest sensitivity and specificity but may be more useful than clinical judgement alone to identify stroke survivors at high risk of developing pressure injuries.(Pancorbo-Hidalgo 2006 *[199]*) It is unclear if the use of risk assessment scales reduces the actual incidence of pressure injuries.(Moore 2019 *[198]*)

New

Info Box

Practice point

Staff and carers of patients with stroke at risk of pressure injuries (in hospital, in residential care and home settings) should be trained to assess skin, provide appropriate pressure area care, and treat pressure injuries consistent with existing guidelines such as the International Guidelines for the Prevention and Treatment of Pressure Ulcers/Injuries. (EPUAP, NPIAP and PPPIA 2019 *[201]*)

Approved by NHMRC August 2022.

Glossary and abbreviations

Glossary

Activities of daily living: The basic elements of personal care such as eating, washing and showering, grooming, walking, standing up from a chair and using the toilet.
Activity: The execution of a task or action by an individual. Activity limitations are difficulties an individual may have in executing activities.
Agnosia: The inability to recognise sounds, smells, objects or body parts (other people's or one's own) despite having no primary sensory deficits.
Aphasia: Impairment of language, affecting the production or comprehension of speech and the ability to read and write.
Apraxia: Impaired planning and sequencing of movement that is not due to weakness, incoordination or sensory loss.
Apraxia of speech: Inability to produce clear speech due to impaired planning and sequencing of movement in the muscles used for speech.
Atrial fibrillation: Rapid, irregular beating of the heart.
Augmentative and alternative communication: Non-verbal communication, e.g. through gestures or by using computerised devices.
Central register: collection of large dataset related to patients' diagnoses, treatments and outcomes
Cochrane: Cochrane is a worldwide, not-for-profit organisation that produces systematic reviews of medical research. Systematic reviews summarise all the research that has been done on a given topic, so that health professionals, patients and policy-makers can make evidence-based decisions.
Cochrane are partnering with the Stroke Foundation on the Living Stroke Guidelines project.
Cochrane review: a comprehensive systematic review and meta-analysis published online in Cochrane library, internationally recognized as the highest standard in evidence-based health care resources
Conflict of Interest (COI) form: A conflict of interest form is signed by all working group members (including all members of the consumer panel). It highlights whether there is any risk of the person's professional judgement (eg. their assessment of research) being influenced by a secondary interest they may have, such as financial gain or career advancement.
Covidence: Covidence is computer software that Cochrane uses to help identify research for systematic reviews. It reduces the workload by allowing the person using it to quickly scan-read and screen scientific papers for relevance, make a summary of their main findings, and assess how well the research was done and whether there is a risk of bias.
Covidence will be used to screen all stroke-related research articles so that only the most accurate ones go into the Living Stroke Guidelines.
Deep vein thrombosis: Thrombosis (a clot of blood) in the deep veins of the leg, arm, or abdomen.
Disability: A defect in performing a normal activity or action (e.g. inability to dress or walk).
Drip and ship: A model of thrombolysis service provision that involves assessment of patients at a non-specialist centres with telemedicine support by stroke specialists, commencing thrombolysis (if deemed appropriate) and subsequent transfer to the stroke specialist centre.
Dyad: involvement of both patients and their caregivers
Dysarthria: Impaired ability to produce clear speech due to the impaired function of the speech muscles.
Dysphagia: Difficulty swallowing.
Dysphasia: Reduced ability to communicate using language (spoken, written or gesture).
Emotionalism: An increase in emotional behaviour—usually crying, but sometimes laughing that is outside normal control and may be unpredictable as a result of the stroke.
Endovascular thrombectomy (also called mechanical thrombectomy or endovascular clot retrieval): a minimally invasive procedure performed via angiogram, in which a catheter passes up into the brain to remove the clot in the blocked blood vessel.
Enteral tube feeding: Delivery of nutrients directly into the intestine via a tube.
Evaluation (of project): An evaluation is an assessment of a project. The aim of an evaluation is to determine the project's effectiveness, efficiency, impact and sustainability.
Evidence-based decision-making: Evidence-based decision-making is a process for making decisions about an intervention, practice etc, that is grounded in the best available research evidence.
Evidence summary: An evidence summary is a short summary of the best available evidence for a particular (guidelines') question. It aims to help clinicians use the best available evidence in their decision-making about particular interventions.
Executive function: Cognitive functions usually associated with the frontal lobes including planning, reasoning, time perception, complex goal-directed behaviour, decision making and working memory.
Family support / liaison worker: A person who assists stroke survivors and their families to achieve improved quality of life by providing psychosocial support, information and referrals to other stroke service providers.
GRADE: The GRADE approach (Grading of Recommendations Assessment, Development and Evaluation) is a standardised way of assessing research (also known as the *quality of evidence*) and determining the strength of recommendations. It was designed to be transparent and rigorous and has become the leading method used for guideline development.
GRADE will be applied to the Living Stroke Guidelines to ensure that their recommendations are accurate and robust.
Impairment: A problem in the structure of the body (e.g. loss of a limb) or the way the body or a body part functions (e.g. hemiplegia).

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

Stroke: Sudden and unexpected damage to brain cells that causes symptoms that last for more than 24 hours in the parts of the body controlled by those cells. Stroke happens when the blood supply to part of the brain is suddenly disrupted, either by blockage of an artery or by bleeding within the brain.
Systematic review: Systematic reviews summarise all the research that has been done on a given topic, so that health professionals, patients and policy-makers can make evidence-based decisions.
Task-specific training: Training that involves repetition of a functional task or part of the task.
Transient ischaemic attack: Stroke-like symptoms that last less than 24 hours. While TIA is not actually a stroke, it has the same cause. A TIA may be the precursor to a stroke, and people who have had a TIA require urgent assessment and intervention to prevent stroke.

Abbreviations

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

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

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

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

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