Clinical Guidelines for Stroke Management 2017

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.

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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. The Clinical Guidelines can be viewed at www.informme.org.au - Citation: Stroke Foundation. Clinical Guidelines for Stroke Management 2017. Melbourne Australia. © No part of this publication can be reproduced by any process without permission from the Stroke Foundation. August 2017.
Sections

Summary of recommendations..............................................................................................................................................................................4

1 - Introduction ........................................................................................................................................................................................................14

2 - Methodology.......................................................................................................................................................................................................17

3 - Clinical questions ..................................................................................................................................................................................................20

4 - Managing complications - overview .....................................................................................................................................................21

5 - Nutrition and hydration ..............................................................................................................................................................................22

5.1 - Early hydration ................................................................................................................................................................................................22

5.2 - Early feeding..................................................................................................................................................................................................27

6 - Oral hygiene ........................................................................................................................................................................................................41

7 - Spasticity ........................................................................................................................................................................................................51

8 - Contracture ....................................................................................................................................................................................................74

9 - Subluxation ......................................................................................................................................................................................................78

10 - Shoulder pain ..................................................................................................................................................................................................84

11 - Swelling of the extremities .................................................................................................................................................................98

12 - Fatigue ..........................................................................................................................................................................................................99

13 - Incontinence ..............................................................................................................................................................................................100

13.1 - Urinary incontinence .......................................................................................................................................................................100

13.2 - Faecal incontinence ........................................................................................................................................................................110

14 - Mood disturbance ....................................................................................................................................................................................117

14.1 - Mood assessment ..............................................................................................................................................................................117

14.2 - Treatment for Emotional distress ..................................................................................................................................................117

14.3 - Prevention of depression .................................................................................................................................................................119

14.4 - Treatment for depression .................................................................................................................................................................123

14.5 - Treatment for anxiety ........................................................................................................................................................................133

15 - Deep venous thrombosis or pulmonary embolism ...................................................................................................................................134

16 - Falls .................................................................................................................................................................................................................144

17 - Glossary and abbreviations ...............................................................................................................................................................149

References .................................................................................................................................................................................................................155
Summary of recommendations

1 - Introduction
2 - Methodology
3 - Clinical questions
4 - Managing complications - overview
5 - Nutrition and hydration

5.1 - 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])

5.2 - 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 [25])

**Strong Recommendation**
- For stroke patients whose nutrition status is poor or deteriorating, nutrition supplementation should be offered. (Geeganage et al 2012 [18]; Dennis et al 2005 [25])

**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 [18]; Gomes et al 2015 [22]; Dennis et al 2005 [25])
- For stroke patients, there is no preference with regard to continuous pump (meaning using a pump for greater than or equal to 16hrs out of 24hrs for less than or equal to 80ml/hr) feeding versus intermittent bolus feeding (meaning 250-400mls/hr for 4-5times/day) therefore practical issues, cost and patient preferences should guide practice. (Lee et al 2010 [19])
Weak Recommendation AGAINST

For stroke patients who are adequately nourished, routine oral nutrition supplements are not recommended. (Geeganage et al 2012 [18]; Dennis et al 2005 [25])

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.

6 - 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. (Chipps et al 2014 [27]; Lam et al 2013 [28]; Brady et al 2006 [30])

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. (Brady et al 2006 [30])

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 [28])

7 - 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 [32]; Gracies et al 2014 [36])
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 [44]; McIntyre et al 2012 [45]; Olvey et al 2010 [46])

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 [47])

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 [50]; Mills et al 2016 [56]; Santamato et al 2015 [57])

Weak Recommendation AGAINST

For stroke survivors, the routine use of stretch to reduce spasticity is not recommended. (Katalinic et al 2010 [58])

8 - Contracture

Strong Recommendation AGAINST

For stroke survivors at risk of developing contracture, routine use of splints or prolonged positioning of upper or lower limb muscles in a lengthened position (stretch) is not recommended. (Katalinic et al 2010 [58])

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.

9 - 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 [68])
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 [67])

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.

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.

10 - Shoulder pain

Weak Recommendation

For stroke survivors with shoulder pain, shoulder strapping may be used to reduce pain. (Appel et al 2014 [67])

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 [72]; Rah et al 2012 [74])

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 [77])

Weak Recommendation AGAINST

For stroke survivors with shoulder pain, electrical stimulation is not recommended to manage pain. (Vafadar et al 2015 [68])
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.

11 - Swelling of the extremities

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

- dynamic pressure garments;
- electrical stimulation;
- elevation of the limb when resting.

Practice Statement

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

- dynamic pressure garments;
- electrical stimulation;
- continuous passive motion with elevation;
- elevation of the limb when resting.
12 - Fatigue

**Practice Statement**

**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 and education about fatigue.
- Potential modifying factors for fatigue should be considered including avoiding sedating drugs and alcohol, screening for sleep-related breathing disorders and depression.
- While there is insufficient evidence to guide practice, possible interventions could include exercise and improving sleep hygiene.

13 - Incontinence

13.1 - 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 [93])
- For stroke survivors, a portable bladder ultrasound scan should be used to assist in diagnosis and management of urinary incontinence. (Martin et al 2006 [93])

**Weak Recommendation**

- Stroke patients in hospital with confirmed continence difficulties, should have a structured continence management plan formulated, documented, implemented and monitored. (Thomas et al 2008 [89])
- A community continence management plan should be developed with the stroke survivor and family/carer prior to discharge, and should include information on accessing continence resources and appropriate review in the community. (Thomas et al 2008 [89])
- If incontinence persists the stroke survivor should be re-assessed and referred for specialist review. (Thomas et al 2008 [89])

**Weak Recommendation**

For stroke survivors with urge incontinence:
- anticholinergic drugs can be tried (Nabi et al 2006 [92]);
- a prompted or scheduled voiding regime program/ bladder retraining can be trialled (Thomas et al 2015 [88]; Thomas et al 2008 [89]);
- if continence is unachievable, containment aids can assist with social continence.
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.

Practice Statement

**Consensus-based recommendation**

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

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.

13.2 - 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 [98])
- 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 [98])

**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 [99]; Munchiando et al 1993 [100])
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 trialled.
- 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.

14 - Mood disturbance

14.1 - Mood assessment

Info Box

Practice points
- Stroke survivors with suspected altered mood (e.g. depression, anxiety, emotional lability) should be assessed by trained personnel using a standardised and validated scale.
- Diagnosis should only be made following clinical interview.

14.2 - Treatment for Emotional distress

Weak Recommendation
For stroke survivors with emotionalism, antidepressant medication such as selective serotonin reuptake inhibitors (SSRIs) or tricyclic antidepressants may be used. (Hackett et al 2010 [103])

14.3 - Prevention of depression

Weak Recommendation AGAINST
For stroke survivors, routine use of antidepressants to prevent post-stroke depression is not recommended. (Hackett et al 2008 [106])

Weak Recommendation
For stroke survivors, psychological strategies (e.g. problem solving, motivational interviewing) may be used to prevent depression. (Hackett et al 2008 [106])
14.4 - Treatment for depression

**Strong Recommendation**

For stroke survivors with depression or depressive symptoms, 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. (Mead et al 2012 [111]; Hackett et al 2008 [117])

**Weak Recommendation**

For stroke survivors with depression or depressive symptoms, structured exercise programs, particularly those of high intensity, may be used. (Eng et al 2014 [110])

**Weak Recommendation**

For stroke survivors with depression or depressive symptoms, acupuncture may be used. (Zhang et al 2010 [116])

**Weak Recommendation AGAINST**

For stroke survivors with depression, non-invasive brain stimulation (transcranial direct stimulation or repetitive transcranial magnetic stimulation) should not be used in routine practice and only used as part of a research framework. (Tian et al 2011 [112])

14.5 - Treatment for anxiety

15 - 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 [119]; Sherman et al 2007 [126])

**Weak Recommendation**

For acute stroke patients who are immobile, the use of 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 [124])
Antithrombotic stockings are not recommended for the prevention of DVT or PE post stroke. (Naccarato et al 2010)

**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.

**16 - Falls**

**Practice Statement**

**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. (Verheyden et al 2013; Sherrington et al 2016; Dickstein et al 2013; Gillespie et al 2012)

**17 - Glossary and abbreviations**
1 - Introduction

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

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

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

The Stroke Foundation has been developing stroke guidelines since 2002. The existing Clinical Guidelines for Stroke Management 2010 were approved by the National Health and Medical Research Council (NHMRC) in September 2010.

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 5-years. As a result, the Stroke Foundation was contracted by the Australian Government Department of Health to update the Clinical Guidelines for Stroke Management 2010, commencing July 2015.

The Clinical Guidelines for Stroke Management 2017 updates and supersedes the Clinical Guidelines for Stroke Management 2010. 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 (Grading of Recommendations Assessment, Development and Evaluation), and an innovative guideline development and publishing platform, known as MAGICapp (Making Grade the Irresistible Choice). 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 2017 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, secondary prevention, rehabilitation, discharge planning, community participation, and management of TIA. Some issues are dealt with in more detail, particularly where current management is at variance with best management, or where the evidence needs translation into practice.

The Clinical Guidelines do not cover:

- Subarachnoid haemorrhage;
- Stroke in infants, children and youth (i.e. <18 years old); or

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. Refer to documents on InformMe that provide a 2-page summaries of the Clinical Guidelines – one for healthcare professionals, and one for consumers.

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.

Refer to the document on InformMe that summarises all the Clinical Guidelines recommendations.

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 2015 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 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

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

These guidelines 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. 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 5 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. The NHMRC expects that all guidelines will be reviewed no less than once every five years.

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
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Citation

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2 - Methodology

Brief summary of GRADE

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

GRADE methodology includes 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 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)

<table>
<thead>
<tr>
<th>Strong Recommendation</th>
<th>Weak Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>For patients</strong></td>
<td></td>
</tr>
<tr>
<td>Most individuals in this situation would want the recommended course of action and only a small proportion would not.</td>
<td>The majority of individuals in this situation would want the suggested course of action, but many would not.</td>
</tr>
<tr>
<td><strong>For clinicians</strong></td>
<td></td>
</tr>
<tr>
<td>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.</td>
<td>Recognise that different choices will be appropriate for different patients, and that you must help each patient arrive at a management decision consistent with his values and preferences. Decision aids may 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.</td>
</tr>
<tr>
<td><strong>For policy makers</strong></td>
<td></td>
</tr>
<tr>
<td>The recommendation can be adapted as policy in most situations including for the use as performance indicators.</td>
<td>Policy making will require substantial debate and involvement of many stakeholders. Policies are 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.</td>
</tr>
</tbody>
</table>
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 ‘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/NEJMtp1405158#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.
3 - 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 is the best intervention to prevent or treat shoulder pain in stroke survivors?

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

6.9 What interventions to improve cardiovascular fitness improve outcomes for people with stroke?

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

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

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

6.13 What general, non-pharmacological management should be undertaken to reduce emotional distress?

6.14 What interventions prevent depression and/or anxiety?

6.15 What interventions manage depression and/or anxiety?

6.16 What interventions prevent DVT/PE in stroke survivors?

6.17 What interventions are effective in preventing or reducing falls for stroke patients?
4 - 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.
5 - 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 [24]).

5.1 - 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 17% of stroke patients had impaired hydration on admission (Stroke Foundation 2015 [9]).

There is consensus that the hydration status of stroke patients should be routinely assessed, monitored and managed throughout hospital admission. Ninety-five out of 108 hospitals reported having locally agreed management protocols for hydration (Stroke Foundation 2015 [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).

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]).

**Key Info**

**Benefits and harms**

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]).

**Quality of evidence**

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.
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.

### Preference and values

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

#### 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.

<table>
<thead>
<tr>
<th>Outcome Timeframe</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death 3-12 month follow-up</td>
<td>Odds Ratio 1.02 (CI 95% 0.82 - 1.27) Based on data from 2,351</td>
<td><strong>202</strong></td>
<td><strong>205</strong></td>
<td>Moderate Due to serious imprecision</td>
</tr>
</tbody>
</table>

2. Inconsistency: No serious. Indirectness: No serious. Imprecision: Serious. Wide confidence intervals; Publication bias: No serious.


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.


<table>
<thead>
<tr>
<th>Condition</th>
<th>Odds Ratio</th>
<th>Baseline/comparator</th>
<th>Confidence Interval</th>
<th>Statistical Heterogeneity</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Publication Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonia</td>
<td>0.58 (CI 0.17 - 2.01)</td>
<td>Control arm of reference used for intervention.</td>
<td>33 per 1000 (CI 95% 19 - 47)</td>
<td>Serious</td>
<td>No serious</td>
<td>Serious</td>
<td>No serious</td>
</tr>
<tr>
<td>Cerebral Oedema</td>
<td>0.2 (CI 0.02 - 1.74)</td>
<td>Control arm of reference used for intervention.</td>
<td>49 per 1000 (CI 95% 14 - 91)</td>
<td>Serious</td>
<td>No serious</td>
<td>Serious</td>
<td>No serious</td>
</tr>
<tr>
<td>Pulmonary Oedema</td>
<td>2.34 (CI 1.28 - 4.29)</td>
<td>Control arm of reference used for intervention.</td>
<td>45 per 1000 (CI 95% 26 - 81)</td>
<td>Serious</td>
<td>No serious</td>
<td>Serious</td>
<td>No serious</td>
</tr>
</tbody>
</table>

Colloid parenteral fluids may have little or no difference on death or dependence compared to crystalloid fluids.

Colloid parenteral fluids probably have little or no difference on pneumonia compared to crystalloid fluids.

Colloid parenteral fluids may increase risk of pulmonary oedema compared to crystalloid fluids.

Colloid parenteral fluids may have little or no difference on cerebral oedema compared to crystalloid fluids.

Colloid parenteral fluids may have little or no difference on cerebral oedema compared to crystalloid fluids.

Colloid parenteral fluids may have little or no difference on death or dependence compared to crystalloid fluids.
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.
10. **Inconsistency:** No serious. **Indirectness:** No serious. **Imprecision:** Very Serious. Only data from three studies; **Publication bias:** No serious.

**References**


**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.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Timeframe</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>3-12 months</td>
<td>Odds Ratio 0.87 (CI 95% 0.67 - 1.12) Based on data from 1,760 patients in 5 studies. (Randomized controlled) Follow up 3-12 months</td>
<td>210 per 1000 188 per 1000</td>
<td>Low Due to serious inconsistency, Due to serious risk of bias</td>
<td>Parenteral fluid of 0.9% saline may have little or no difference on death</td>
</tr>
<tr>
<td></td>
<td>9 Critical</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death or dependence</td>
<td>3-12 months follow-up</td>
<td>Odds Ratio 1.04 (CI 95% 0.82 - 1.32) Based on data from 1,120 patients in 3 studies.</td>
<td>553 per 1000 563 per 1000</td>
<td>Low Due to serious risk of bias, Due to serious</td>
<td>Parenteral fluid of 0.9% saline may have little or no difference on death or dependence</td>
</tr>
</tbody>
</table>

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.


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.


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.


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.

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**References**

5.2 - Early feeding

Being malnourished is associated with poor outcomes in stroke patients (Martineau et al 2005 [18]). 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 [24]). National Stroke Audits in Australia reported a 19% malnutrition rate on admission to an acute stroke service, 11% to a rehabilitation service, and 9% during admission (Stroke Foundation 2016 [7]; Stroke Foundation 2015 [9]). The differences may be due to criteria used to define malnutrition and protocols to identify malnutrition. The Audit also found that only 61% of patients received malnutrition screening, which means the reported prevalence is likely to have underestimated the true prevalence. On the other hand, once the risk of malnutrition was identified in the screening, over 90% of them were then assessed, monitored and received appropriate nutritional interventions by Accredited Practising Dietitians (Stroke Foundation 2016 [7]).

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 [25])

**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.

**Key Info**

**Benefits and harms**

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 [25]). 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 [20]). 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 [24]).

**Quality of evidence**

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

**Preference and values**

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

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 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
Geeganage et al (2012) [16] conducted a Cochrane review and 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 [23]).

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 [21]). 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.

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.
<table>
<thead>
<tr>
<th>Evidence</th>
<th>Description</th>
<th>Odds Ratio</th>
<th>CI 95%</th>
<th>Difference</th>
<th>PICO Appropriateness</th>
<th>Imprecision</th>
<th>Publication Bias</th>
<th>Criticality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>End of trial</td>
<td>0.58</td>
<td>0.28 - 1.21</td>
<td>49 fewer</td>
<td>Yes</td>
<td>Serious</td>
<td>No</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>9 Critical</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death or dependence</td>
<td>End of trial</td>
<td>1.06</td>
<td>0.94 - 1.2</td>
<td>14 more</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>9 Critical</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Length of stay</td>
<td>At time of hospital discharge</td>
<td>Measured by: Days</td>
<td>Lower better</td>
<td>1.4 more</td>
<td>Yes</td>
<td>Serious</td>
<td>No</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>7 Critical</td>
<td>Based on data from: 4,114 patients in 2 studies. (Randomized controlled)</td>
<td>Follow up: to hospital discharge</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nutritional status</td>
<td>During the study period</td>
<td>Measured by: Energy intake</td>
<td>High better</td>
<td>430.18 more</td>
<td>Yes</td>
<td>Serious</td>
<td>No</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>7 Critical</td>
<td>Based on data from: 174 patients in 3 studies. (Randomized controlled)</td>
<td>Follow up: During the study period</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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**. 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 – 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.
Strong Recommendation

For stroke patients whose nutrition status is poor or deteriorating, nutrition supplementation should be offered. (Geeganage et al 2012 [18]; Dennis et al 2005 [25])

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.

Key Info

Benefits and harms

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 [18]).

Quality of evidence

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

Preference and values

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

Resources and other considerations

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

References


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 [18]; Dennis et al 2005 [25]). 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
Geeganage et al (2012) [16] conducted a Cochrane review and 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 [23]).

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 [21]). 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.

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.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Timeframe</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>End of trial</td>
<td>Odds Ratio 0.58 (CI 95% 0.28 - 1.21) Based on data from 4,343 patients in 7 studies. (Randomized controlled) Follow up Varied - 3 to 12 months</td>
<td>Nutrition support 78 per 1000</td>
<td>Moderate Due to serious imprecision</td>
<td>Nutrition support probably decreases death slightly although this was statistically insignificant</td>
</tr>
</tbody>
</table>

| Difference: | 49 fewer | per 1000 (CI 95% 88 fewer - 23 more) |
## References


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[18]; Gomes et al 2015[22]; Dennis et al 2005 [25])
- For stroke patients, there is no preference with regard to continuous pump (meaning using a pump for greater than or equal to 16hrs out of 24hrs for less than or equal to 80ml/hr) feeding versus intermittent bolus feeding (meaning 250-400mls/hr for 4-5times/day) therefore practical issues, cost and patient preferences should guide practice. (Lee et al 2010 [19])

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.

Key Info

Benefits and harms

There were significantly fewer treatment failures, significantly greater feed delivery (Geeganage et al 2012 [18]) and significantly greater change in mid-arm circumference from baseline (Gomes et al 2015 [22]) 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 [19]).

Quality of evidence

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.

Preference and values

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

Journal

Initially after a stroke, the use of 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 gastrostomy devices have fewer treatment failures, greater feed delivery and preferred aesthetics.

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 [19]). 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 gastrostomy feeding (PEG) compared to nasogastric tube feeding (NG) comes mainly from a Cochrane review by Geeganage et al (2012) [16] comparing percutaneous endoscopic gastrostomy feeding (PEG) and nasogastric tube feeding (NG). A more recent meta-analysis (Gomes et al 2015 [20]) 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).
<table>
<thead>
<tr>
<th>Timeframe</th>
<th>measurements</th>
<th>Nasogastric tube feeding</th>
<th>Percutaneous endoscopic gastrostomy feeding</th>
<th>effect estimates (Quality of evidence)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death or dependence</td>
<td>9 Critical</td>
<td>838 per 1000</td>
<td>805 per 1000</td>
<td>Low Due to serious imprecision, Due to serious inconsistency</td>
</tr>
<tr>
<td>End of trial</td>
<td>Odds Ratio 0.8 (CI 95% 0.12 - 5.55) Based on data from 400 patients in 3 studies. Follow up Varied: discharge to 6 months</td>
<td>Difference: 33 fewer per 1000 (CI 95% 455 fewer - 128 more)</td>
<td>percutaneous endoscopic gastrostomy feeding may have little or no difference on death or dependence</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>9 Critical</td>
<td>449 per 1000</td>
<td>398 per 1000</td>
<td>Low Due to serious inconsistency, Due to serious imprecision</td>
</tr>
<tr>
<td>End of trial</td>
<td>Odds Ratio 0.81 (CI 95% 0.42 - 1.56) Based on data from 455 patients in 5 studies. Follow up Varied: discharge to 6 months</td>
<td>Difference: 51 fewer per 1000 (CI 95% 194 fewer - 111 more)</td>
<td>Percutaneous endoscopic gastrostomy feeding may have little or no difference on death</td>
<td></td>
</tr>
<tr>
<td>Chest infection or pneumonia</td>
<td>8 Critical</td>
<td>378 per 1000</td>
<td>283 per 1000</td>
<td>Low Due to serious inconsistency, Due to serious imprecision</td>
</tr>
<tr>
<td>During study</td>
<td>Odds Ratio 0.65 (CI 95% 0.23 - 1.86) Based on data from 93 patients in 2 studies. Follow up 21 days to 6 weeks</td>
<td>Difference: 95 fewer per 1000 (CI 95% 255 fewer - 153 more)</td>
<td>Percutaneous endoscopic gastrostomy feeding may have little or no difference on chest infection or pneumonia</td>
<td></td>
</tr>
<tr>
<td>Length of stay</td>
<td>7 Critical</td>
<td>Measured by: Days</td>
<td></td>
<td>Low Due to serious inconsistency, Due to serious imprecision</td>
</tr>
<tr>
<td>At time of discharge</td>
<td>Lower better Based on data from: 384 patients in 2 studies. (Randomized controlled) Follow up At discharge</td>
<td>Difference: MD 14.32 more (CI 95% 12.04 fewer - 40.68 more)</td>
<td>Percutaneous endoscopic gastrostomy feeding may have little or no difference on length of stay</td>
<td></td>
</tr>
<tr>
<td>Nutritional status</td>
<td>7 Critical</td>
<td>Measured by: Mid-arm</td>
<td></td>
<td>Low Due to serious inconsistency, Due to serious imprecision</td>
</tr>
<tr>
<td>Last value measured during trial</td>
<td>High better Based on data from: 58 patients in 3 studies. (Randomized controlled) Follow up Last measured value during trial</td>
<td>Difference: MD 2.29 more (CI 95% 0.3 fewer - 4.89 more)</td>
<td>Percutaneous endoscopic gastrostomy feeding may improve nutritional status</td>
<td></td>
</tr>
</tbody>
</table>

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 ;

References


Clinical Question/ PICO

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

Summary

One randomised controlled trial (Lee et al 2010 [17]) has 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.
Weak Recommendation AGAINST

For stroke patients who are adequately nourished, routine oral nutrition supplements are not recommended. (Geeganage et al 2012 [18]; Dennis et al 2005 [25])

Practical Info

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

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### References


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### Study Results and Measurements

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Timeframe</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>up until hospital discharge or 4 weeks</td>
<td>Odds Ratio 0.55 (CI 95% 0.21 - 1.46) Based on data from 178 patients in 1 studies. (Randomized controlled) Follow up discharge from hospital or 4 weeks</td>
<td>140 per 1000</td>
<td>Moderate Due to serious risk of bias ¹</td>
<td>continuous pump feeding probably decreases death</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>4 weeks</td>
<td>Odds Ratio 0.93 (CI 95% 0.4 - 2.14) Based on data from 178 patients in 1 studies. (Randomized controlled) Follow up discharge from hospital or 4 weeks</td>
<td>151 per 1000</td>
<td>Moderate Due to serious risk of bias ²</td>
<td>Continuous pump feeding probably has little or no difference on pneumonia.</td>
</tr>
</tbody>
</table>

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 ;

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### Outcome Timeframe

- **Death**: up until hospital discharge or 4 weeks
- **Pneumonia**: 4 weeks

### Certainty in effect estimates

- ¹ Due to serious risk of bias
- ² Due to serious risk of bias
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.

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

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

Preference and values
The provision of oral nutrition support should be individualised and provided after consultation with an Accredited Practising Dietitian.

Resources and other considerations
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
Geeganage et al (2012) [16] conducted a Cochrane review and 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 [23]).

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 [21]). 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.

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

- **Nutrition support**

- **No nutrition support**

#### Absolute effect estimates

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Timeframe</th>
<th>Study results and measurements</th>
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<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>End of trial</td>
<td>Odds Ratio 0.58 (CI 95% 0.28 - 1.21)</td>
<td><strong>127</strong> per 1000</td>
<td><strong>49 fewer</strong> per 1000 (CI 95% 88 fewer - 23 more)</td>
<td>Moderate Due to serious imprecision 1</td>
</tr>
<tr>
<td></td>
<td>9 Critical</td>
<td>Based on data from 4,343 patients in 7 studies.</td>
<td></td>
<td></td>
<td>Nutrition support probably decreases death slightly although this was statistically insignificant</td>
</tr>
<tr>
<td>Death or dependence</td>
<td>End of trial</td>
<td>Odds Ratio 1.06 (CI 95% 0.94 - 1.2)</td>
<td><strong>457</strong> per 1000</td>
<td><strong>14 more</strong> per 1000 (CI 95% 15 fewer - 45 more)</td>
<td>Moderate Due to serious imprecision 2</td>
</tr>
<tr>
<td></td>
<td>9 Critical</td>
<td>Based on data from 4,023 patients in 1 studies.</td>
<td></td>
<td></td>
<td>Nutrition support may have little or no difference on death or dependence</td>
</tr>
<tr>
<td>Length of stay</td>
<td>At time of hospital discharge</td>
<td>Measured by: Days Lower better Based on data from: 4,114 patients in 2 studies. (Randomized controlled) Follow up to hospital discharge</td>
<td><strong>MD 1.4 more</strong> (CI 95% 0.81 fewer - 3.6 more)</td>
<td></td>
<td>Moderate Due to serious imprecision 3</td>
</tr>
<tr>
<td></td>
<td>7 Critical</td>
<td></td>
<td></td>
<td></td>
<td>Nutrition support probably has little or no difference on length of stay</td>
</tr>
<tr>
<td>Nutritional status</td>
<td>During the study period</td>
<td>Measured by: Energy intake High better Based on data from: 174 patients in 3 studies. (Randomized controlled) Follow up During the study period</td>
<td><strong>MD 430.18 more</strong> (CI 95% 141.61 more - 718.75 more)</td>
<td></td>
<td>Moderate Due to serious inconsistency 4</td>
</tr>
<tr>
<td></td>
<td>7 Critical</td>
<td></td>
<td></td>
<td></td>
<td>Nutrition support may have little or no difference on nutritional status</td>
</tr>
</tbody>
</table>

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 from meta-analysis, good search strategy and 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.;

4. **Publication bias:** **No serious**. Not serious. Good search strategy, awareness of ongoing trials.;
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
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).

References
6 - 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 [6]). It is even more difficult for stroke patients to maintain oral health due to physical weakness, lack of coordination, and impaired cognitive state (Brady et al 2006 [28]). 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 (Brady et al 2006 [28]). 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 [27]).

All stroke patients, particularly those with swallowing difficulties, should have assistance and/or education to maintain good oral and dental (including dentures) hygiene. (Chipps et al 2014 [27]; Lam et al 2013 [28]; Brady et al 2006 [30])

Key Info

Benefits and harms
Evidence of oral hygiene interventions in stroke patients showed no significant differences in functional oral intake and dysphagia between intervention and control groups, and both groups demonstrated significant improvement from baseline (Chipps et al 2014 [27]; Lam et al 2013 [28]; Brady et al 2006 [30]). However, the practice in the control group was unclear. One randomised controlled trial using a decontamination gel showed significant reduction in pneumonia rate. There was no harm reported.

Quality of evidence
The evidence mostly comes from small randomised controlled trials with various methodological quality, and therefore it is uncertain whether oral hygiene interventions assessed in these trials improve or worsen the outcomes.

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

Clinical Question/ PICO

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

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**Summary**

In a small pilot study (n = 42) by Chipps et al (2014) [25], the intervention group received tooth brushing, tongue brushing, flossing, mouth rinse (Listerine) and lip care twice a day. The control group received 'usual care' which was undefined. Patients in both control and intervention groups demonstrated an improvement in oral cavity health, swallowing ability and oral intake but the differences between groups were not statistically significant. This study had serious methodological faults as it was unclear whether participants or personnel were blinded and little detail was given on the reported effects, making the precise nature of the benefit difficult to determine.

In a study by Lam et al (2013) [26], reductions in dental plaque were significantly greater in the two intervention groups that received chlorhexidine and oral hygiene instruction; or chlorhexadine, oral hygiene instruction and assisted brushing when compared to oral hygiene instruction alone. There were no between-group differences in overall physical function (measured using the Barthel Index) or pneumonia.

A home-based oral care training program delivered to family caregivers of stroke survivors was assessed in a randomised trial by Kuo et al (2016) [37], involving 94 caregivers. Caregivers in the intervention group showed significantly improved self-efficacy and oral care behaviour at 1 and 2 month follow-ups, but there was no significant difference in attitudes to oral care practice.

Brady et al (2006) [28] conducted a Cochrane review of staff-led oral care interventions for stroke patients. Results from two studies were included, but data were not pooled due to heterogeneity in interventions. One study is a cluster randomised controlled trial of oral health care education delivered to nursing home care assistants (412 nursing home residents were included, in which 67 had previous stroke). Education training was found to improve staff knowledge and attitude, as well as cleanliness of patients' dentures. The other study is an evaluation of a decontamination gel, which was found to significantly reduce the incidence of pneumonia in a group of 203 stroke patients (OR 0.2, 95%CI 0.05 - 0.84). However, this review did not identify interventions investigating patient-critical outcomes such as functional oral intake and dysphagia.

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<table>
<thead>
<tr>
<th>Outcome</th>
<th>Timeframe</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonia</td>
<td>2-3 weeks</td>
<td>Odds Ratio 0.2 (CI 95% 0.05 - 0.84) Based on data from 203 patients in 1 studies.</td>
<td></td>
<td>Moderate Due to serious imprecision</td>
<td>Oral hygienic care intervention (a decontamination gel) probably decreases pneumonia</td>
</tr>
<tr>
<td></td>
<td>8 Critical</td>
<td>(Randomized controlled) Follow up 2-3 weeks</td>
<td></td>
<td>70 per 1000</td>
<td>15 per 1000</td>
</tr>
<tr>
<td>Difference:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>15 fewer per 1000 ( CI 95% 66 fewer - 11 fewer )</td>
</tr>
</tbody>
</table>

Both the control and intervention group demonstrated improvement in the Functional Oral Intake Scale over time (clinical improvement in oral intake was defined as moving from a non-oral tube feed state - levels 1-3 - to some level of oral intake - levels 4-7). Participants in the intervention group showed more progress in oral intake than those in the control group. However, these differences were not statistically significant.

<table>
<thead>
<tr>
<th>Functional oral intake</th>
<th>Post intervention: 10 days treatment</th>
<th>Based on data from 42 patients in 1 studies.</th>
<th></th>
<th>Very Low Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision</th>
<th>We are uncertain whether oral hygienic care intervention improves or worsens functional oral intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 Critical</td>
<td></td>
<td></td>
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</tbody>
</table>
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.


3. 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. The Functional Oral Intake Scale (FOIS) is used to document the functional level of oral intake of food and liquid. The FOIS has seven levels: 1-3 reflect non-oral feeding/tube feeding abilities, levels 4-6 reflect oral feedings with varying degrees of consistencies, level 7 is a total oral diet with no restrictions.

5. Risk of bias: Serious. Inadequate/lack of blinding: not stated if participants were blinded; not stated whether personnel were blinded, resulting in potential for performance bias; however, did have blinded outcome assessment. As it is a bundled intervention unable to ascertain the impact of each component to overall outcome. No OR/RR/HR data reported only P values reported.; Inconsistency: No serious. We are unable to comment on inconsistency due to lack of data in the Chipps’ paper.; Indirectness: Serious. Time frame was 10 days only. Evidence linking the outcome of decreased functional oral intake with poor oral hygiene is lacking.; Imprecision: Serious. Only data from one study, Low number of patients (n=42); Publication bias: No serious.

6. The Mann Assessment of Swallowing Ability is a 24 item assessment tool that scores a patient’s cognitive, communicative and motor abilities; which impact swallowing. A MASA score of less than 178 out of a possible 200 defines a patient with clinical symptoms associated with dysphagia. A score of less than 170 identifies a patient at risk for aspiration.

7. Risk of bias: Serious. Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; Inconsistency: No serious. Indirectness: Serious. Imprecision: Serious. Only data from one study, Low number of patients (n=42); Publication bias: No serious.

8. A self-administered questionnaire was used to test care assistants' knowledge

9. Systematic review [30].

10. Inconsistency: No serious. Indirectness: No serious. Only a small proportion of the participants were stroke patients but it's expected that the results are transferrable.; Imprecision: Serious. Only data from one study; Publication bias: No serious.
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. (Brady et al 2006 [30])

Practical Info

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

Key Info

Benefits and harms

A Cochrane review (Brady et al 2006 [30]) found education training to improve 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 and dysphagia. There was no harm reported.

Quality of evidence

One randomised controlled trial of high methodological quality provided evidence for the intervention of staff and carer education.

Preference and values

No variation expected

Resources and other considerations

Factors not considered

Rationale

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

References


[28] Lam OL, McMillan AS, Samaranayake LP, Li LS, McGrath C : Randomized clinical trial of oral health promotion interventions among patients following stroke.. Archives of physical medicine and rehabilitation 2013;94(3):435-43 Journal Website


**Clinical Question/ PICO**

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

**Summary**

In a small pilot study (n = 42) by Chipps et al. (2014) [25], the intervention group received tooth brushing, tongue brushing, flossing, mouth rinse (Listerine) and lip care twice a day. The control group received ‘usual care’ which was undefined. Patients in both control and intervention groups demonstrated an improvement in oral cavity health, swallowing ability and oral intake but the differences between groups were not statistically significant. This study had serious methodological faults as it was unclear whether participants or personnel were blinded and little detail was given on the reported effects, making the precise nature of the benefit difficult to determine.

In a study by Lam et al. (2013) [26], 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. There were no between-group differences in overall physical function (measured using the Barthel Index) or pneumonia.

A home-based oral care training program delivered to family caregivers of stroke survivors was assessed in a randomised trial by Kuo et al. (2016) [37], involving 94 caregivers. Caregivers in the intervention group showed significantly improved self-efficacy and oral care behaviour at 1 and 2 month follow-ups, but there was no significant difference in attitudes to oral care practice.

Brady et al. (2006) [28] conducted a Cochrane review of staff-led oral care interventions for stroke patients. Results from two studies were included, but data were not pooled due to heterogeneity in interventions. One study is a cluster randomised controlled trial of oral health care education delivered to nursing home care assistants (412 nursing home residents were included, in which 67 had previous stroke). Education training was found to improve staff knowledge and attitude, as well as cleanliness of patients’ dentures. The other study is an evaluation of a decontamination gel, which was found to significantly reduce the incidence of pneumonia in a group of 203 stroke patients (OR 0.2, 95%CI 0.05 - 0.84). However, this review did not identify interventions investigating patient-critical outcomes such as functional oral intake and dysphagia.

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<td><strong>Pneumonia</strong></td>
<td>Odds Ratio 0.2 (CI 95% 0.05 - 0.84) Based on data from 203 patients in 1 studies. Follow up 2-3 weeks</td>
<td>70 per 1000</td>
<td><strong>Moderate</strong> Due to serious imprecision 3</td>
<td>Oral hygienic care intervention (a decontamination gel) probably decreases pneumonia</td>
</tr>
<tr>
<td>2-3 weeks</td>
<td></td>
<td>15 per 1000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 Critical</td>
<td>Both the control and intervention group demonstrated improvement in the Functional Oral Intake Scale over time (clinical improvement in oral intake was defined as moving from a non-oral tube feed state - levels 1-3 - to some level of oral intake - levels 4-7). Participants in the intervention group</td>
<td></td>
<td>Very Low Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision 5</td>
<td>We are uncertain whether oral hygienic care intervention improves or worsens functional oral intake</td>
</tr>
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</tr>
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</tbody>
</table>
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.


3. 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. The Functional Oral Intake Scale (FOIS) is used to document the functional level of oral intake of food and liquid in stroke patients. The FOIS has seven levels: 1-3 reflect non-oral feeding/tube feeding abilities, levels 4-6 reflect oral feedings with varying degrees of consistencies, level 7 is a total oral diet with no restrictions.

5. Risk of bias: Serious. Inadequate/lack of blinding: not stated if participants were blinded; not stated whether personnel were blinded, resulting in potential for performance bias; however did have blinded outcome assessment. As it is a bundled intervention unable to ascertain the impact of each component to overall outcome. No OR/ RR/ HR data reported only P values reported. Inconsistency: No serious. We are unable to comment on inconsistency due to lack of data in the Chipps' paper. Indirectness: Serious. Time frame was 10 days only. Evidence linking the outcome of decreased functional oral intake with poor oral hygiene is lacking. Imprecision: Serious. Only data from one study, Low number of patients (n=42); Publication bias: No serious.

6. The Mann Assessment of Swallowing Ability is a 24 item assessment tool that scores a patient's cognitive, communicative and motor abilities, which impact swallowing. A MASA score of less than 178 out of a possible 200 defines a patient with clinical symptoms associated with dysphagia. A score of less than 170 identifies a patient at risk for aspiration.

7. Risk of bias: Serious. Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; Inconsistency: No serious. Indirectness: Serious. Imprecision: Serious. Only data from one study, Low number of patients (n=42); Publication bias: No serious.

8. A self-administered questionnaire was used to test care assistants' knowledge

9. Systematic review [30].

10. Inconsistency: No serious. Indirectness: No serious. Only a small proportion of the participants were stroke patients but it's expected that the results are transferrable. Imprecision: Serious. Only data from one study; Publication bias: No serious.
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 [28])

Practical Info

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

Key Info

Benefits and harms

In the study by Lam et al (2013) [28], 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. However, there were no between-group differences in overall physical function (measured using the Barthel Index) or pneumonia. No harm was reported.

Quality of evidence

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

Preference and values

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

Resources and other considerations

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.

References


plaque and gingival bleeding (Lam et al 2013 [28]). Although there was no significant improvement in physical function and pneumonia and the quality of evidence was low, there was no harm associated with this practice. Overall, this practice can be used to improve stroke patients' oral hygiene.

Clinical Question/ PICO

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

**Summary**

In a small pilot study (n = 42) by Chipps et al (2014) [25], the intervention group received tooth brushing, tongue brushing, flossing, mouth rinse (Listerine) and lip care twice a day. The control group received 'usual care' which was undefined. Patients in both control and intervention groups demonstrated an improvement in oral cavity health, swallowing ability and oral intake but the differences between groups were not statistically significant. This study had serious methodological faults as it was unclear whether participants or personnel were blinded and little detail was given on the reported effects, making the precise nature of the benefit difficult to determine.

In a study by Lam et al (2013) [26], reductions in dental plaque were significantly greater in the two intervention groups that received chlorhexidine and oral hygiene instruction; or chlorhexadine, oral hygiene instruction and assisted brushing when compared to oral hygiene instruction alone. There were no between-group differences in overall physical function (measured using the Barthel Index) or pneumonia.

A home-based oral care training program delivered to family caregivers of stroke survivors was assessed in a randomised trial by Kuo et al (2016) [37], involving 94 caregivers. Caregivers in the intervention group showed significantly improved self-efficacy and oral care behaviour at 1 and 2 month follow-ups, but there was no significant difference in attitudes to oral care practice.

Brady et al (2006) [28] conducted a Cochrane review of staff-led oral care interventions for stroke patients. Results from two studies were included, but data were not pooled due to heterogeneity in interventions. One study is a cluster randomised controlled trial of oral health care education delivered to nursing home care assistants (412 nursing home residents were included, in which 67 had previous stroke). Education training was found to improve staff knowledge and attitude, as well as cleanliness of patients’ dentures. The other study is an evaluation of a decontamination gel, which was found to significantly reduce the incidence of pneumonia in a group of 203 stroke patients (OR 0.2, 95%CI 0.05 - 0.84). However, this review did not identify interventions investigating patient-critical outcomes such as functional oral intake and dysphagia.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Timeframe</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates</th>
<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Standard care</td>
<td>Oral hygiene care intervention</td>
<td></td>
</tr>
</tbody>
</table>
| Pneumonia | 2-3 weeks | Odds Ratio 0.2  
(CI 95% 0.05 - 0.84)  
Based on data from 203 patients in 1 studies.  
(Randomized controlled)  
Follow up 2-3 weeks | 70 per 1000  
15 per 1000 | Moderate  
Due to serious imprecision 3  
Oral hygiene care intervention (a decontamination gel) probably decreases pneumonia |                   |
| Functional oral intake | 8 Critical | Based on data from 42 patients in 1 studies. | Both the control and intervention group demonstrated improvement in the Functional Oral Intake Scale over time (clinical | Very Low  
Due to serious risk of bias, Due to |                   |
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 [30]. Baseline/comparator:: Control arm of reference used for intervention.

3. 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. The Functional Oral Intake Scale (FOIS) is used to document the functional level of oral intake of food and liquid in stroke patients. The FOIS has seven levels: 1-3 reflect non-oral feeding/tube feeding abilities, levels 4-6 reflect oral feedings with varying degrees of consistencies, level 7 is a total oral diet with no restrictions.

5. Risk of bias: Serious. Inadequate/lack of blinding: not stated if participants were blinded; not stated whether personnel were blinded, resulting in potential for performance bias; however did have blinded outcome assessment. As it is a bundled intervention unable to ascertain the impact of each component to overall outcome. No OR/RR/HR data reported only P values reported.; Inconsistency: No serious. We are unable to comment on inconsistency due to lack of data in the Chipps' paper.; Indirectness: Serious. Time frame was 10 days only. Evidence linking the outcome of decreased functional oral intake with poor oral hygiene is lacking.; Imprecision: Serious. Only data from one study, Low number of patients (n=42); Publication bias: No serious.

6. The Mann Assessment of Swallowing Ability is a 24 item assessment tool that scores a patient’s cognitive, communicative and motor abilities; which impact swallowing. A MASA score of less than 178 out of a possible 200 defines a patient with clinical symptoms associated with dysphagia. A score of less than 170 identifies a patient at risk for aspiration.

7. Risk of bias: Serious. Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias.; Inconsistency: No serious. Indirectness: Serious. Imprecision: Serious. Only data from one study, Low number of patients (n=42); Publication bias: No serious.

8. A self-administered questionnaire was used to test care assistants’ knowledge

9. Systematic review [30].
10. Inconsistency: No serious. Indirectness: No serious. Only a small proportion of the participants were stroke patients but it's expected that the results are transferrable.; Imprecision: Serious. Only data from one study; Publication bias: No serious.

References


[28] Lam OL, McMillan AS, Samaranayake LP, Li LS, McGrath C: Randomized clinical trial of oral health promotion interventions among patients following stroke.. Archives of physical medicine and rehabilitation 2013;94(3):435-43 Journal Website


7 - 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 [62]).

**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 [32]; Gracies et al 2014 [36])

**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.

**Key Info**

**Benefits and harms**

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 [32]).

**Quality of evidence**

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.

**Preference and values**

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**

It was found that Botulinum toxin A plus upper limb therapy was not cost-effective (given a willingness to pay of £30,000 per QALY gained) compared to upper limb therapy alone, at an additional cost of £93,500 per QALY gained (cost reference year 2007) (Shaw et al 2010 [62]; Shackley et al 2012 [63]).

**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 [32]. 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 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).

<table>
<thead>
<tr>
<th>Outcome Timeframe</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Modifed Ashworth Scale (MAS) 4 weeks</td>
<td>Measured by: Modified Ashworth Scale High better Based on data from: 158 patients in 1 studies. (Randomized controlled) Follow up 4 weeks</td>
<td>3.7 (Mean)</td>
<td>Moderate Due to serious imprecision</td>
<td>abobotulinumtoxina 1000 u probably improves Modified Ashworth Scale (MAS)</td>
</tr>
<tr>
<td>Physician Global Assessment 4 weeks</td>
<td>Measured by: PGA High better Based on data from: 158 patients in 1 studies. (Randomized controlled) Follow up 4 weeks</td>
<td>0.6 (Mean)</td>
<td>Moderate Due to serious imprecision</td>
<td>abobotulinumtoxina 1000 u probably improves physician global assessment</td>
</tr>
<tr>
<td>Disability assessment scale 4 weeks</td>
<td>Measured by: Disability assessment scale Scale: 0-4 Lower better Based on data from: 158 patients in 1 studies. (Randomized controlled) Follow up 4 weeks</td>
<td>2.1 (Mean)</td>
<td>Moderate Due to serious imprecision</td>
<td>abobotulinumtoxina 1000 u probably improves Disability Assessment Scale</td>
</tr>
</tbody>
</table>

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 .
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) [30] 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 [31]). 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 [32]) 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 recent 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 [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.

Other recent 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 [45]; Marciniak et al 2012 [46]; Rosales et al 2012 [47]; Wolf et al 2012 [48]; Kanovsky et al 2011 [49]). 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 [44]).
<table>
<thead>
<tr>
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<th>Certainty in effect estimates (Quality of evidence)</th>
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</tr>
</thead>
</table>
| Disability assessment scale                  | Measured by: Disability Assessment Scale  
Scale: 0-3 Lower better  
Based on data from: 539 patients in 5 studies.  
(Randomized controlled)  
Follow up 2-24 weeks | 0.54 points (Mean)  
CI 95%                                               | Moderate  
Due to serious risk of bias, Due to serious risk of bias | Botulinum toxin A probably improves disability assessment scale                        |
|                                              |                                                                                               |                           |                                                   |                                                                                     |
| Action Research Arm Test                     | Measured by: Action Research Arm Test  
Scale: 0-57 High better  
Based on data from: 383 patients in 2 studies.  
(Randomized controlled)  
Follow up 24-52 weeks | 0.41 points per 4 subscales (Mean)  
CI 95%                                                 | Low  
Due to serious risk of bias, Due to serious imprecision | Botulinum toxin A may improve action research arm test slightly                          |
| Generalised disability                       | Measured by: Barthel Index  
Scale: 0-20 High better  
Based on data from: 112 patients in 2 studies.  
(Randomized controlled)  
Follow up 4 weeks |                                                                                       | Low  
Due to serious risk of bias, Due to serious inconsistency, Due to serious indirectness, Due to serious imprecision | Botulinum toxin A may have little or no difference on generalised disability          |
| Disability - BTX specific                    | Measured by: Disability Assessment Scale, Disability Scale  
High better  
Based on data from: 423 patients in 4 studies.  
(Randomized controlled)  
Follow up 2 to 8 weeks |                                                                                       | Moderate  
Due to serious risk of bias  
Due to serious imprecision  
Due to serious indirectness  
Due to serious inconsistency  | Botulinum toxin A probably improves disability as assessed by BTX specific scales like DAS and Disability Scale |
| Motor function                               | Measured by: Action Research Arm Test, Motor Assessment Scale, Motor Activity Log  
High better  
Based on data from: 500 patients in 4 studies.  
(Randomized controlled)  
Follow up 6 to 12 weeks |                                                                                       | Low  
Due to serious risk of bias, Due to serious imprecision | Botulinum toxin A may improve motor function slightly                                  |

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 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**.

3. Systematic review. **Baseline/comparator**: Control arm of reference used for intervention. **Supporting references**: [32], [33], [34], [35], [36], [37].

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: No serious**. Low number of patients; **Publication bias: No serious**.

5. Systematic review [32]. **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: No 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 [32]. **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**.

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### References


[42] Wolf SL, Milton SB, Reiss A, Easley KA, Shenvi NV, Clark PC: Further assessment to determine the additive effect of botulinum toxin type A on an upper extremity exercise program to enhance function among individuals with chronic stroke but extensor capability.. Archives of physical medicine and rehabilitation 2012;93(4):578-87 Pubmed Journal


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 [42]). 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) [43] 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) [44] 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.
<table>
<thead>
<tr>
<th>Outcome</th>
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<th>Absolute effect estimates</th>
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<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse events</td>
<td>End of follow-up (24 weeks)</td>
<td>Odds Ratio 0.82 (CI 95% 0.5 - 1.34) Based on data from 437 patients in 3 studies. (Randomized controlled) Follow up up to 24 weeks</td>
<td>233 per 1000</td>
<td>199 per 1000</td>
<td>Moderate Due to serious risk of bias. Botulinum toxin A probably has little or no difference on adverse events</td>
</tr>
<tr>
<td>Muscle tone (MAS)</td>
<td>4-12 weeks</td>
<td>Measured by: Modified Ashworth Scale. Scale: 0-4 Lower better Based on data from: 535 patients in 6 studies. (Randomized controlled) Follow up 8-16 weeks</td>
<td>0.51 points (Mean) CI 95%</td>
<td>Very Low Due to serious risk of bias, Due to serious imprecision, Due to serious publication bias, Due to serious inconsistency.</td>
<td>We are uncertain whether Botulinum toxin A increases or decreases muscle tone (mas)</td>
</tr>
<tr>
<td>Muscle tone (CSI)</td>
<td>4-12 weeks</td>
<td>Measured by: Clinical Spasticity Influx. High better Based on data from: 68 patients in 1 studies. (Randomized controlled) Follow up 24 weeks</td>
<td>0.02 (Mean) CI 95%</td>
<td>Very Low Due to serious risk of bias, Due to serious inconsistency, Due to serious imprecision, Due to serious publication bias.</td>
<td>We are uncertain whether Botulinum toxin A improves or worsen muscle tone (csi)</td>
</tr>
<tr>
<td>Gait speed</td>
<td>12 weeks</td>
<td>Measured by: Gait Speed. High better Based on data from: 1,077 patients in 4 studies. (Randomized controlled) Follow up 12 weeks</td>
<td>0 speed (Mean) CI 95%</td>
<td>Moderate Due to serious risk of bias. Botulinum toxin A probably increases gait speed slightly</td>
<td></td>
</tr>
<tr>
<td>Lower limb function</td>
<td>24 weeks</td>
<td>Measured by: Fugl-Meyer score. Scale: 0-226 High better Based on data from: 296 patients in 3 studies. (Randomized controlled) Follow up 24 weeks</td>
<td>3.19 points (Mean) CI 95%</td>
<td>Moderate Due to serious imprecision, Due to serious risk of bias, Due to serious imprecision</td>
<td>Botulinum toxin A probably increases lower limb function</td>
</tr>
<tr>
<td>Adverse events</td>
<td>12 weeks</td>
<td>Measured by: Recording of Adverse events Lower better</td>
<td>0.82 (Mean)</td>
<td>Moderate Due to serious risk of bias. Botulinum toxin A probably increases adverse events slightly</td>
<td></td>
</tr>
</tbody>
</table>

**Notes:**

1. Based on data from 437 patients in 3 studies.
2. Based on data from 535 patients in 6 studies.
3. Based on data from 68 patients in 1 studies.
4. Based on data from: 1,077 patients in 4 studies.
5. Based on data from: 296 patients in 3 studies.
1. “[D]rug-related adverse events included myalgia, injection site and extremity pain, erythema, convulsions and incoordination” (Wu
2. Systematic review [44]. **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;
5. **Risk of bias:** **Serious.** There is no information provided about: inadequate/lack of blinding of participants and personnel, 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);
6. **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;
7. Systematic review [44]. **Baseline/comparator::** Control arm of reference used for intervention.
8. **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 = 55%; **Indirectness:** **No serious.** **Imprecision:** **No serious.** Wide confidence intervals, low number of patients; **Publication bias:** **No serious.** Due to small number of studies;
9. **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.** I^2 = 96%; **Indirectness:** **No serious.** **Imprecision:** **Serious.** Small sample size might be overestimating effect; **Publication bias:** **No serious.** Small number of studies available;
10. **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;
12. **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. **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);
15. Systematic review [44]. **Baseline/comparator::** Control arm of reference used for intervention.
16. **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%;
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 [44]; McIntyre et al 2012 [45]; Olvey et al 2010 [46])

References


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.

Key Info

Benefits and harms

Botulinum toxin A treatment produced improvements in muscle tone that appeared to be maintained up to 12 weeks after treatment (Wu et al 2016 [44]). Botulinum toxin treatment also produced possible improvement in lower limb function, but little apparent effect on gait speed [44]. Adverse effects appeared to be lower overall in patients receiving botulinum toxin treatment compared to controls (Wu et al 2016 [44]).

Quality of evidence

Low

Small net benefit, or little difference between alternatives
The quality of evidence was low overall, with high risk of bias and small sample sizes in the included randomised controlled trials.

### Preference and values

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

**Resources considerations**

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

### Rationale

Botulinum 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 [42]). 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) [43] 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) [44] 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

<table>
<thead>
<tr>
<th>Outcome Timeframe</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse events&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Odds Ratio 0.82 (CI 95% 0.5 - 1.34) Based on data from 437 patients in 3 studies. (Randomized controlled) Follow up Up to 24 weeks</td>
<td>233 per 1000 199 per 1000</td>
<td>Moderate Due to serious risk of bias&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Botulinum toxin A probably has little or no difference on adverse events</td>
</tr>
</tbody>
</table>

<sup>1</sup> End of follow-up (24 weeks)

<sup>3</sup> Botulinum toxin A probably has little or no difference on adverse events
<table>
<thead>
<tr>
<th>Measure</th>
<th>Methodology</th>
<th>Scale</th>
<th>High is Better</th>
<th>Study Population</th>
<th>Follow-up</th>
<th>CI 95%</th>
<th>Quality Rating</th>
<th>Review</th>
<th>Observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle tone (MAS) 4-12 weeks</td>
<td>Measured by: Modified Ashworth Scale</td>
<td>0-4</td>
<td>Lower better</td>
<td>Based on data from: 535 patients in 6 studies.</td>
<td>Follow up 8-16 weeks</td>
<td>0.51 points (Mean)</td>
<td>Very Low</td>
<td>Due to serious risk of bias, Due to serious imprecision, Due to serious publication bias</td>
<td>We are uncertain whether Botulinum toxin A increases or decreases muscle tone (mas)</td>
</tr>
<tr>
<td>Muscle tone (CSI) 4-12 weeks</td>
<td>Measured by: Clinical Spasticity Influx</td>
<td>High</td>
<td>better</td>
<td>Based on data from: 68 patients in 1 studies.</td>
<td>Follow up 24 weeks</td>
<td>0.02 (Mean)</td>
<td>Very Low</td>
<td>Due to serious risk of bias, Due to serious inconsistency</td>
<td>We are uncertain whether Botulinum toxin A improves or worsen muscle tone (csi)</td>
</tr>
<tr>
<td>Gait speed 12 weeks</td>
<td>Measured by: Gait Speed</td>
<td>High</td>
<td>better</td>
<td>Based on data from: 1,077 patients in 4 studies.</td>
<td>Follow up 12 weeks</td>
<td>0 speed (Mean)</td>
<td>Moderate</td>
<td>Due to serious risk of bias</td>
<td>Botulinum toxin A probably increases gait speed slightly</td>
</tr>
<tr>
<td>Lower limb function 24 weeks</td>
<td>Measured by: Fugl-Meyer score</td>
<td>Scale: 0-226</td>
<td>High better</td>
<td>Based on data from: 296 patients in 3 studies.</td>
<td>Follow up 24 weeks</td>
<td>3.19 points (Mean)</td>
<td>Moderate</td>
<td>Due to serious imprecision, Due to serious risk of bias, Due to serious imprecision</td>
<td>Botulinum toxin A probably increases lower limb function</td>
</tr>
<tr>
<td>Adverse events 12 weeks</td>
<td>Measured by: Recording of Adverse events</td>
<td>Lower better</td>
<td>Based on data from: 437 patients in 3 studies.</td>
<td>Follow up 12 weeks</td>
<td>0.82 (Mean)</td>
<td>Moderate</td>
<td>Due to serious risk of bias</td>
<td>Botulinum toxin A probably increases adverse events slightly</td>
<td></td>
</tr>
<tr>
<td>Muscle tone 4 weeks after treatment</td>
<td>Measured by: Modified Ashworth Scale, Clinical Spasticity Influx</td>
<td>Difference: SMD 0.85 more</td>
<td>points (n/a)</td>
<td></td>
<td></td>
<td>Very Low</td>
<td>Due to serious risk of bias, Due to</td>
<td>We are uncertain whether Botulinum toxin A increases or decreases</td>
<td></td>
</tr>
</tbody>
</table>
1. Drug-related adverse events included myalgia, injection site and extremity pain, erythema, convulsions and incoordination (Wu 2016).


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. I² = 13%; Indirectness: No serious. Imprecision: No serious. Small sample size; Publication bias: No serious. Small number of studies;


5. Risk of bias: Serious. There is no information provided about: Inadequate/lack of blinding of participants and personnel, resulting

<table>
<thead>
<tr>
<th>Measure</th>
<th>Outcome</th>
<th>Effect Size</th>
<th>95% CI</th>
<th>P Value</th>
<th>Risk of Bias</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle tone at 4 weeks</td>
<td>SMD</td>
<td>0.42 more</td>
<td>0.07-0.77</td>
<td></td>
<td>Very Low</td>
<td>Due to serious risk of bias, Due to serious imprecision, Due to serious publication bias, Due to serious inconsistency.</td>
</tr>
<tr>
<td>Muscle tone at 12 weeks</td>
<td>SMD</td>
<td>0.02 more</td>
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<td></td>
<td>Very Low</td>
<td>Due to serious risk of bias, Due to serious imprecision, Due to serious publication bias, Due to serious inconsistency.</td>
</tr>
<tr>
<td>Muscle tone at 24 weeks</td>
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<td></td>
<td>Very Low</td>
<td>Due to serious risk of bias, Due to serious imprecision, Due to serious publication bias, Due to serious inconsistency.</td>
</tr>
<tr>
<td>Gait speed at 4 weeks</td>
<td>MD</td>
<td>0.01 more</td>
<td>0.01-0.03</td>
<td></td>
<td>Moderate</td>
<td>Due to serious risk of bias.</td>
</tr>
<tr>
<td>Lower limb function at 4 weeks</td>
<td>MD</td>
<td>3.19 more</td>
<td>0.22-6.16</td>
<td></td>
<td>Moderate</td>
<td>Due to serious imprecision.</td>
</tr>
</tbody>
</table>

---

1. "[D]rug-related adverse events included myalgia, injection site and extremity pain, erythema, convulsions and incoordination" (Wu 2016).
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. I² = 13%; Indirectness: No serious. Imprecision: No serious. Small sample size; Publication bias: No serious. Small number of studies;
5. 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, Indirectness: No serious. Incomplete data and/or large loss to follow up; Inconsistency: Serious. I² = 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);

6. 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. I² = 38%; Indirectness: No serious. Imprecision: Serious. Wide confidence intervals, Low number of patients; Publication bias: Serious. Only 1 study;

7. Systematic review [44]. Baseline/comparator:: Control arm of reference used for intervention.

8. 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;

9. 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;

10. 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;


12. 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 participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; Inconsistency: Serious. I² = 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. 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 participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; Inconsistency: Serious. I² = 81%; Indirectness: No serious. Imprecision: Serious. Low number of patients; Publication bias: Serious. Unable to test due to small number of studies (7 only);

15. Systematic review [44]. Baseline/comparator:: Control arm of reference used for intervention.

16. 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. I² = 81%; Indirectness: No serious. Imprecision: Serious. Low number of patients; Publication bias: Serious. Unable to test due to small number of studies (7 only);

17. Systematic review [44]. Baseline/comparator:: Control arm of reference used for intervention.

18. 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;

19. Risk of bias: No serious. Variability on doses of botulinum toxin and expertise of people performing the injections., Inadequate
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 [47])

Key Info

Benefits and harms
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 [47]). This improvement appeared to be greater for electroacupuncture than for standard acupuncture therapy.

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

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

Resources and other considerations

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

References


Clinical Question/ PICO

**Population:** Adults with stroke with spasticity

**Intervention:** Acupuncture

**Comparator:** Control

Summary

A systematic review by Lim et al (2015) [45] 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 [46]) 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 [47]).

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Timeframe</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spasticity</td>
<td>Post intervention</td>
<td>Measured by: Improvement on Modified Ashworth Scale</td>
<td>Difference: <strong>MD 0.72 more</strong> (CI 95% 0.29 more - 1.14 more)</td>
<td>Very Low Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision</td>
<td>We are uncertain whether acupuncture increases or decreases spasticity</td>
</tr>
</tbody>
</table>

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;
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 [50]; Mills et al 2016 [56]; Santamato et al 2015 [57])

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.

Key Info

Benefits and harms
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.

Quality of evidence
Quality of evidence was very low. Seventeen small randomised controlled trials using 10 different adjunct therapies (Mills et al 2016 [56]). 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 [57]) 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).

Preference and values
Patients are not expected to vary substantially with regard to their desire to reduce spasticity.
Evidence for the benefits of any particular adjunct therapy is very limited. There is only weak evidence for the potential benefit of electrical stimulation, casting and taping and insufficient evidence to draw conclusions about other adjunctive therapies.

### Clinical Question/ PICO

<table>
<thead>
<tr>
<th>Population</th>
<th>Adults with stroke with spasticity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>Neuromuscular electric stimulation</td>
</tr>
<tr>
<td>Comparator</td>
<td>Control</td>
</tr>
</tbody>
</table>

### 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 [48]). 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 [49])
- Repetitive transcranial magnetic stimulation (Etoh et al 2015 [50])
- Transcranial direct current stimulation (Ochi et al 2013 [51]; Wu et al 2013 [52])
- Electrical stimulation combined with passive locomotion-like movement (Yamaguchi et al 2012 [53])

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 Table

<table>
<thead>
<tr>
<th>Outcome Timeframe</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spasticity (MAS)</td>
<td>Post intervention: 3-16 weeks of treatment</td>
<td>Measured by: Modified Ashworth Scale (0-5 Lower better) Based on data from: 383 patients in 14 studies.</td>
<td>Difference: <strong>MD 0.3 fewer</strong> (CI 95% 0.58 fewer - 0.03 fewer)</td>
<td>Very Low We are uncertain whether neuromuscular electric stimulation increases or decreases spasticity</td>
</tr>
<tr>
<td></td>
<td>9 Critical</td>
<td>Follow up 3-16 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range of motion</td>
<td>Post intervention:</td>
<td>Measured by: Goniometer (degrees) High better</td>
<td>Difference: <strong>MD 2.87 more</strong> (CI 95% 1.18 more - 4.56 more)</td>
<td>Low Neurmuscular electric stimulation may have little or no difference on</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
3-16 weeks of treatment

Based on data from: 447 patients in 13 studies. 4 (Randomized controlled) Follow up 3-16 weeks

Due to serious imprecision 5 range of motion

1. Systematic review [50]. 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 studies, Missing intention-to-treat analysis in 10 studies; Inconsistency: No serious; 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 [50]. 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;

References


Clinical Question/ PICO
Population: Adults with stroke with spasticity
Intervention: Adjunct therapies to Botox
**Summary**

Mills et al (2016) [54] 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 [55]) 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.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Spasticity - electrical stimulation</strong>&lt;br&gt;End of treatment</td>
<td>7 Critical</td>
<td>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.</td>
<td>Very Low&lt;br&gt;Due to serious risk of bias, Due to serious inconsistency, Due to serious imprecision</td>
<td>We are uncertain whether electrical stimulation as an adjunct to botox improves or worsens spasticity related outcomes</td>
</tr>
<tr>
<td><strong>Spasticity - taping</strong>&lt;br&gt;End of treatment</td>
<td>3</td>
<td>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.</td>
<td>Low&lt;br&gt;Due to serious imprecision, consistency unknown due to lack of meta-analysis</td>
<td>Taping post-botox injection may improve spasticity related outcomes</td>
</tr>
<tr>
<td><strong>Spasticity - casting</strong>&lt;br&gt;End of treatment</td>
<td>7 Critical</td>
<td>1 small moderate quality RCT found improvements in spasticity (modified Ashworth Scale) following casting, but no improvement on the 10-metre walking test.</td>
<td>Very Low&lt;br&gt;Due to serious risk of bias, Due to serious inconsistency, Due to serious imprecision</td>
<td>We are uncertain whether casting as an adjunct to botox improves or worsens spasticity related outcomes</td>
</tr>
</tbody>
</table>

1. Systematic review [56].
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 [56].
Weak Recommendation AGAINST

For stroke survivors, the routine use of stretch to reduce spasticity is not recommended. (Katalinic et al 2010 [58])

Practical Info

Stretch is defined as any mechanical elongation of soft tissues for varying length of times (Katalinic et al 2010 [58]). 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 [58]). 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).

Key Info

Benefits and harms
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 cumulative 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.

Quality of evidence
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-
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 mobility or spasticity outcomes either immediately post intervention or 24 hours to 1 week later (Katalinic et al 2010 [58]). 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 spasticity) and not statistically significant. There is evidence that neither length of intervention (cumulative 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) [56] 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 spasticity 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) [57] and Jung et al (2011) [58] 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.

<table>
<thead>
<tr>
<th>Outcome Timeframe</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spasticity - immediate effects</td>
<td>Measured by: Various - Tardieu scale, modified Ashworth Lower better Based on data from: 109</td>
<td>Difference: SMD 0.08 more (CI 95% 0.3 fewer - 0.45 more)</td>
<td>Moderate Due to serious imprecision ²</td>
<td>Stretch probably has little or no difference on spasticity immediately after treatment</td>
</tr>
</tbody>
</table>

Preference and values

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

No substantial variability expected

Resources and other considerations

Factors not considered
   - **Inconsistency:** No serious. **Indirectness:** No serious. **Imprecision:** Serious. Wide confidence intervals - covers small to medium effects in both directions; **Publication bias:** No serious.

   - **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.

References


8 - 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 will 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 2016 [7]).

**Strong Recommendation AGAINST**

For stroke survivors at risk of developing contracture, routine use of splints or prolonged positioning of upper or lower limb muscles in a lengthened position (stretch) is not recommended. (Katalinic et al 2010 [58])

Practical Info

There is moderate to strong evidence that stretch interventions including splinting and prolonged positioning has no effect on either preventing or treating contracture. 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 [58]). 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 including splinting and prolonged positioning should not be used routinely 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 the Rehabilitation Chapter).

Key Info

**Benefits and harms**

| Small net benefit, or little difference between alternatives |
| Stretch had little or no effect on immediate or long-term joint mobility and long-term pain (Katalinic et al 2010 [58]). Stretch increased pain immediately post-treatment (Katalinic et al 2010 [58]). |

**Quality of evidence**

| Moderate |
| Effect estimates are rated moderate due to serious imprecision (low number of patients). |

**Preference and values**

| Substantial variability is expected or uncertain |
| Patients reported an increase in pain requiring medication post intervention. |

**Resources and other considerations**

| Factors not considered |

**Rationale**

A Cochrane review of stretch for treatment and prevention of contractures found 24 controlled trials with a total of 782 participants with neurological conditions (Katalinic et al 2010 [58]). The stretch dosage ranged from 20 minutes to 24 hours per day for between 2 days and 7 months in the included studies. The results were pooled in a meta-analysis and the review authors rated the GRADE level of evidence as moderate. They found evidence to indicate that stretch does not have clinically important immediate, short-term or long-term effects on joint mobility. They found moderate quality evidence to suggest that stretch causes immediate increases in pain in people with neurological conditions. There is no clear beneficial effect of stretch on quality of life, activity limitation and participation restriction, however, the effects on these outcomes have not been well investigated. The effects of stretch performed for periods longer than seven months have not been investigated.
Clinical Question/ PICO

- **Population:** Adults with stroke
- **Intervention:** Stretch
- **Comparator:** Usual care

Summary

Katalinic et al (2010) [56] included 35 trials (1391 participants) of stretch interventions for treating people with contractures in a Cochrane review, 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 immediately post-intervention and strong evidence of no effect in the short to long term (24 hours to one week post-intervention). Most trials included people both with and without existing contractures, making interpretation of the relative benefits of stretch for preventing versus treating contracture difficult. However, from the three trials that included only people without existing contracture, there is no evidence that stretch interventions prevent contracture (Katalinic et al 2010 [56]).

<table>
<thead>
<tr>
<th>Outcome Timeframe</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Joint mobility (immediate effects)</strong></td>
<td>Measured by: Passive or active range of motion (degrees) High better Based on data from: 193 patients in 7 studies. [1] (Randomized controlled) Follow up &lt; 24 hours</td>
<td>Difference: <strong>MD 2.17 more</strong> (CI 95% 1.63 fewer - 5.97 more)</td>
<td>Moderate Due to serious imprecision [2]</td>
<td>Stretch probably has little or no difference on joint mobility (immediate effects)</td>
</tr>
<tr>
<td>&lt; 24 hours</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7 Critical</td>
<td></td>
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</tr>
<tr>
<td><strong>Joint mobility (long-term effects)</strong></td>
<td>Measured by: Passive or active range of motion (degrees) High better Based on data from: 134 patients in 4 studies. (Randomized controlled) Follow up &gt; 1 week</td>
<td>Difference: <strong>MD 0.32 fewer</strong> (CI 95% 4.09 fewer - 3.44 more)</td>
<td>Moderate Due to serious imprecision [3]</td>
<td>Stretch may have little or no difference on joint mobility (long-term effects)</td>
</tr>
<tr>
<td>&gt; 1 week after intervention</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7 Critical</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Pain (immediate effects)</strong></td>
<td>Measured by: Various measures e.g. Visual Analogue Scale Lower better Based on data from: 97 patients in 3 studies. (Randomized controlled) Follow up &lt; 24 hours</td>
<td>Difference: <strong>SMD 0.4 more</strong> (CI 95% 0.01 fewer - 0.8 more)</td>
<td>Moderate Due to serious indirectness, Due to serious imprecision [4]</td>
<td>Stretch probably increases pain (immediate effects)</td>
</tr>
<tr>
<td>&lt; 24 hours</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 Critical</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Pain (short-</strong></td>
<td>Measured by: Visual</td>
<td></td>
<td></td>
<td>Moderate</td>
</tr>
<tr>
<td>Term</td>
<td>Description</td>
<td>Baseline/comparator: (Randomized controlled)</td>
<td>Difference:</td>
<td>Due to serious imprecision</td>
</tr>
<tr>
<td>----------------------</td>
<td>-----------------------------------------------------------------------------</td>
<td>----------------------------------------------</td>
<td>-------------</td>
<td>---------------------------</td>
</tr>
<tr>
<td>Pain (long-term)</td>
<td>1 - 7 days</td>
<td>Control arm of reference used for intervention.</td>
<td>MD 0.2 more</td>
<td>CI 95% 0.95 fewer - 1.35 more</td>
</tr>
<tr>
<td></td>
<td>&gt; 1 week</td>
<td></td>
<td>SMD 0.03 more</td>
<td>CI 95% 0.41 fewer - 0.47 more</td>
</tr>
<tr>
<td>Activity limitation</td>
<td>(short-term) 1 - 7 days</td>
<td></td>
<td>MD 1.7 more</td>
<td>CI 95% 0.4 fewer - 3.8 more</td>
</tr>
<tr>
<td></td>
<td>&gt; 1 week</td>
<td></td>
<td>SMD 0.14 more</td>
<td>CI 95% 0.29 fewer - 0.58 more</td>
</tr>
</tbody>
</table>

2. Inconsistency: No serious. Indirectness: No serious. Imprecision: Serious. Low number of patients; Publication bias: No serious.
3. Inconsistency: No serious. Indirectness: No serious. Imprecision: Serious. Low number of patients; Publication bias: No serious.
4. Inconsistency: No serious. Indirectness: No serious. Imprecision: Serious. Low number of patients; Publication bias: No serious.
5. Inconsistency: No serious. Indirectness: No serious. Imprecision: Serious. Low number of patients; Publication bias: No serious.
6. Inconsistency: No serious. Indirectness: No serious. Imprecision: Serious. Low number of patients; Publication bias: No serious.
8. Inconsistency: No serious. Indirectness: No serious. Imprecision: Serious. Low number of patients; Publication bias: No serious.
**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.

**References**

9 - Subluxation

Shoulder subluxation is reported to occur in 3-4% of stroke survivors on admission (Stroke Foundation 2015 [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 [68])

Practical Info

Staff should have training and be familiar with the correct dosages to apply in order to achieve optimal muscle activation. Staff 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 [68]). Once there is return of voluntary movement, interventions should then focus on improving weakness (see the topic Weakness in the Rehabilitation chapter).

Key Info

**Benefits and harms**

Electrical stimulation (ES) decreased shoulder subluxation early after stroke but not late [68]. No effects were seen for reducing pain (Vafadar et al 2015 [68]). No harm is reported (Vafadar et al 2015 [68]).

**Quality of evidence**

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).

**Preference and values**

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

**Resources and other 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. The review authors concluded there was insufficient evidence of efficacy to recommend routine strapping as a treatment for shoulder paralysis.
Summary

Vafadar et al (2015) [66] 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.

<table>
<thead>
<tr>
<th>Outcome Timeframe</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shoulder subluxation (early: &lt; 6 months after stroke)</td>
<td>Measured by: X-ray assessment of subluxation (in mm) Lower better Based on data from: 213 patients in 6 studies. Follow up 4 to 6 weeks of treatment</td>
<td>Difference: <strong>MD 4.9 fewer</strong> (CI 95% 3.3 fewer - 6.6 fewer)</td>
<td>Moderate Due to risk of bias, Due to inconsistency, Due to indirectness, Due to imprecision</td>
<td>Electrical stimulation probably decreases shoulder subluxation early after stroke</td>
</tr>
<tr>
<td>Shoulder subluxation (late: &gt; 6 months after stroke)</td>
<td>Measured by: X-ray assessment of subluxation Lower better Based on data from: 41 patients in 2 studies. Follow up 6 weeks of treatment</td>
<td>Difference: <strong>SMD 0.42 fewer</strong> (CI 95% 1.04 fewer - 0.21 more)</td>
<td>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.</td>
<td>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.</td>
</tr>
<tr>
<td>Motor function (early: &lt; 6 months after stroke)</td>
<td>Measured by: Various - MAS, ARAT, Frenchy, Motricity Index, Chedoke, Brunstrom High better Based on data from: 295 patients in 5 studies.</td>
<td>Difference: <strong>SMD 0.36 more</strong> (CI 95% 0.27 fewer - 0.99 more)</td>
<td>Moderate Due to serious inconsistency, Due to serious indirectness. Note however quality assessment reported in SR</td>
<td>Electrical stimulation is likely to be no more effective for improving motor function than conventional therapy alone.</td>
</tr>
</tbody>
</table>
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 [67])

Key Info

Benefits and harms
There is uncertainty around the benefits of strapping (Appel et al 2014 [67]). There are only minor harms in a small number of patients (5%) such as minor skin irritation (Appel et al 2014 [67]).

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

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

References

1. degree of shoulder subluxation alone is a less important outcome than pain or function
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 .
5. Imprecision: Serious . Low number of patients. n = 32 and 44 for the 2 studies .
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 .
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) [65] 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.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health related quality of life (HRQoL) 13-15 weeks</td>
<td>Measured by: Stroke Specific Quality of Life Scale High better Based on data from: 12 patients in 1 studies. (Randomized controlled) Follow up 13-15 weeks</td>
<td>2.9 points (Mean) 3.44 points (Mean)</td>
<td>Very Low Due to very serious imprecision due to low participant numbers (n=12) (NB: chose to downgrade to very low certainty)</td>
<td>We are uncertain whether strapping improves or worsens health related quality of life (HRQoL)</td>
</tr>
<tr>
<td>Upper Limb Function 3 3 to 6 weeks post intervention</td>
<td>Measured by: Motor Assessment Scale upper limb items Scale: 3-18 High better Based on data from: 117 patients in 3 studies. (Randomized controlled) Follow up 4 to 14 weeks</td>
<td>Difference: MD 0.54 more (CI 95% 1.29 fewer - 2.37 more)</td>
<td>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</td>
<td>We are uncertain whether strapping improves or worsen upper limb function</td>
</tr>
</tbody>
</table>
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.

<table>
<thead>
<tr>
<th>Practical Issues</th>
<th>No strapping</th>
<th>Shoulder strapping</th>
<th>Both</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse effects, interactions and antidote</td>
<td>Minor, fully reversible (on removal of strapping) skin irritations (itching, redness of the skin or rash) experienced by 5% of participants</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. Systematic review [67]. **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 [67]. **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.**

References
Rationale

One small trial reported benefits of prevention and management of shoulder-hand syndrome but there is a high level of uncertainty regarding the treatment effects.

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.
10 - Shoulder pain

The cause of shoulder pain remains unclear but this complication affects 8% of stroke survivors on admission rising to 11% 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 [67])

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.

Key Info

<table>
<thead>
<tr>
<th>Benefits and harms</th>
<th>Small net benefit, or little difference between alternatives</th>
</tr>
</thead>
<tbody>
<tr>
<td>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 [67]). It is unclear whether function of the upper limb can be improved or not from strapping the shoulder.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Quality of evidence</th>
<th>Low</th>
</tr>
</thead>
<tbody>
<tr>
<td>Based on a recent systematic review (Appel et al 2014 [67]), 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</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Preference and values</th>
<th>Substantial variability is expected or uncertain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients' perceptions are likely to vary due to the uncertainty in evidence.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Resources and other considerations</th>
<th>Important issues, or potential issues not investigated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resources considerations</td>
<td></td>
</tr>
<tr>
<td>No literature to understand or describe the potential economic implications of this recommendation was identified.</td>
<td></td>
</tr>
</tbody>
</table>

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 occurring 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) [65] 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 strapping as a treatment for shoulder paralysis.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Health related quality of life</strong>&lt;br&gt; (HRQoL)&lt;br&gt;13-15 weeks</td>
<td>Measured by: Stroke Specific Quality of Life Scale: 49-245 High better Based on data from: 12 patients in 1 studies. (Randomized controlled) Follow up 13-15 weeks</td>
<td>2.9 points (Mean)</td>
<td>7 Critical</td>
<td>We are uncertain whether shoulder strapping improves or worsen health related quality of life (HRQoL)</td>
</tr>
<tr>
<td></td>
<td>Difference: <strong>MD 0.54 more</strong>&lt;br&gt; ( CI 95% 1.29 fewer - 2.37 more )</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Upper Limb Function</strong>&lt;br&gt;3 to 6 weeks post-intervention</td>
<td>Measured by: Motor Assessment Scale upper limb items Scale: 3-18 High better Based on data from: 117 patients in 3 studies. (Randomized controlled) Follow up 4 to 14 weeks</td>
<td>3.44 points (Mean)</td>
<td>7 Critical</td>
<td>We are uncertain whether strapping improves or worsen upper limb function</td>
</tr>
<tr>
<td></td>
<td>Difference: <strong>MD 0.87 more</strong>&lt;br&gt; ( CI 95% 0.07 fewer - 1.81 more )</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Practical issues

<table>
<thead>
<tr>
<th>Risk of bias</th>
<th>No strapping</th>
<th>Shoulder strapping</th>
<th>Both</th>
</tr>
</thead>
<tbody>
<tr>
<td>No serious</td>
<td>Minor, fully reversible (on removal of strapping) skin irritations (itching, redness of the skin or rash) experienced by 5% of participants</td>
<td>Skin irritation</td>
<td>Skin irritation</td>
</tr>
<tr>
<td>Low</td>
<td>on a 5 pt VAS, 9 out of 10 participants rated strapping as (very) comfortable (mean score 4.4, SD 0.59)</td>
<td>Very Low</td>
<td>Very Low</td>
</tr>
</tbody>
</table>

#### Degree of subluxation

- **7 Critical**

Review reports the two trials showed 'benefit' of strapping to reduce subluxation, both from non-randomized case-series studies.

- **Very Low**
  - Due to very serious risk of bias, due to very serious indirectness, due to very serious imprecision

Data poorly expressed in SR. 2 x non-randomised RCTs reported 'showed benefit.' Poor trial quality for both studies. Therefore it is unclear whether strapping reduces subluxation.

#### Pain reduction

- **4-6 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

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. **Risk of bias: Very Serious**. Morin and Bravo: Inadequate sequence generation and allocation concealment Hayner: Unclear sequence generation and allocation concealment reported (although also noted to be a non-randomised case-series design) 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 as well as potential selective reporting of results for Hayner et al.; Indirectness: Very Serious. The outcome time frame in studies were insufficient. 1 study (Morin and Bravo) only implemented the intervention for 5 days.; Imprecision: Very Serious. Low number of patients;
Weak Recommendation

For stroke survivors with shoulder pain, shoulder injections (either subacromial 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 [72]; Rah et al 2012 [74])

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.

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

Key Info

5. **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**.

References

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 [70]). 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.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>measured by VAS Scale: 0-100 lower better</td>
<td>Placebo injection: 7 Critical (Mean) 46.2 mm</td>
<td>Placebo injection: 7 Critical (Mean) 28.14 mm CI 95%</td>
<td>Moderate small number of patients (n=64), only one study Suprascapular nerve block probably improves shoulder pain</td>
</tr>
</tbody>
</table>

Practical issues
- Placebo injection: No adverse effects were seen
- Suprascapular nerve block: No adverse effects were seen
- Emotional well-being: HRQoL as assessed by EuroQol Health Questionnaire- no significant differences
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 [72]). 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.

References

### Practical issues

<table>
<thead>
<tr>
<th>Placebo (lidocaine) injection</th>
<th>Subacromial corticosteroid injection</th>
<th>Both</th>
</tr>
</thead>
<tbody>
<tr>
<td>No important complications noted. 2 patients had facial flushing (days 1-5 post injection)</td>
<td>1 patient had a vasovagal reaction during injection</td>
<td></td>
</tr>
</tbody>
</table>

1. **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 ;
2. **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 ;
3. **Indirectness:** Serious . MBI poor measure of function related to shoulder pain, population highly selected so not applicable to all

#### Daytime Pain

**8 weeks**

**7 Critical**

- **Measured by:** VAS
- **Scale:** 0-10 Lower better
- **Based on data from:** 58 patients in 1 studies.
- **(Randomized controlled)**
- **Follow up 8 weeks**

**Mean:** 4.9 (Mean) CI 95%

**Low**

Due to serious indirectness (highly selected young stroke population with diagnosed rotator cuff pathology), Due to serious imprecision ^1

Subacromial corticosteroid injection may improve daytime pain slightly

#### Pain (Night)

**8 weeks**

**7 Critical**

- **Measured by:** VAS
- **Scale:** 0-10 Lower better
- **Based on data from:** 58 patients in 1 studies.
- **(Randomized controlled)**
- **Follow up 8 weeks**

**Mean:** 5 (Mean) CI 95%

**Low**

Due to highly selected young stroke population with diagnosed rotator cuff pathology, Due to serious imprecision ^2

Subacromial corticosteroid injection may improve pain (night) slightly

#### ADL (modified Barthel Index)

**Measured by:** Modified Barthel Index
**Scale:** 0-100 High better
**Based on data from:** 58 patients in 1 studies.
**(Randomized controlled)**
**Follow up 8 weeks**

**Mean:** 72.7 points (Mean) CI 95%

**Low**

Due to serious indirectness, Due to serious imprecision ^3

Subacromial corticosteroid injection may have little or no difference on ADL functioning as assessed by Modified Barthel Index

#### Shoulder External rotation (ROM)

**Measured by:** Shoulder ROM-External rotation
**High better**
**Based on data from:** 58 patients in 1 studies.
**(Randomized controlled)**
**Follow up 8 weeks**

**Mean:** 40.8 degrees (Mean) CI 95%

**Very Low**

Due to very serious imprecision, Due to serious indirectness ^4

Subacromial corticosteroid injection may make little or no difference on shoulder external rotation (ROM)
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 [77])

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.

Key Info

Benefits and harms

Reduction in pain was noted in medium term but not in short term (Singh et al 2010 [77]).

Quality of evidence

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

Preference and values

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

Resources and other considerations

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 [75]) showed improvements in some disability measures, but no improvement in pain scores at 4 weeks.

References

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

<table>
<thead>
<tr>
<th>Population</th>
<th>Adults with stroke with shoulder pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>Botulinum toxin injection by any route</td>
</tr>
<tr>
<td>Comparator</td>
<td>Placebo injection</td>
</tr>
</tbody>
</table>

### Summary

Singh and Fitzgerald (2010) [75] 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) [73] 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.

### Table: Absolute effect estimates

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Timeframe</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse events</td>
<td>4-24 weeks</td>
<td>Relative risk 1.46 (CI 95% 0.64 - 3.36) Based on data from 65 patients in 3 studies. (Randomized controlled) Follow up 4-24 weeks</td>
<td>Placebo injection: 235 per 1000 Botulinum toxin injection by any route: 343 per 1000 Difference: 108 more per 1000 (CI 95% 85 fewer - 555 more)</td>
<td>Very Low Due to serious risk of bias, Due to serious imprecision, Due to very serious imprecision</td>
<td>We are uncertain whether botulinum toxin injection by any route increases or decreases adverse events</td>
</tr>
<tr>
<td>Pain</td>
<td>4-6 weeks</td>
<td>Measured by VAS Scale: 0-10 Lower better Based on data from: 86 patients in 4 studies. (Randomized controlled) Follow up 4-6 weeks</td>
<td>Difference: MD 1.12 fewer (CI 95% 2.89 fewer - 0.66 more)</td>
<td>Low Due to serious imprecision, Due to serious inconsistency</td>
<td>botulinum toxin injection by any route may reduce shoulder pain slightly</td>
</tr>
<tr>
<td>Pain</td>
<td>12-24 weeks</td>
<td>Measured by VAS Scale: 0-10 Lower better Based on data from: 66 patients in 3 studies.</td>
<td>4.8 (Mean)</td>
<td>Low wide confidence intervals and small numbers of</td>
<td>botulinum toxin injection by any route may decrease shoulder pain slightly</td>
</tr>
</tbody>
</table>

1. We are uncertain whether botulinum toxin injection by any route increases or decreases adverse events.
2. We are uncertain whether botulinum toxin injection by any route increases or decreases adverse events.
3. Due to serious imprecision, Due to serious inconsistency.
4. Due to serious imprecision, Due to serious inconsistency.
5. Due to serious imprecision, Due to serious inconsistency.
6. Due to serious imprecision, Due to serious inconsistency.
**Practical issues**

<table>
<thead>
<tr>
<th></th>
<th>Placebo injection</th>
<th>Botulinum toxin injection by any route</th>
<th>Both</th>
</tr>
</thead>
<tbody>
<tr>
<td>7 Critical (Randomized controlled) Follow up 12-24 weeks</td>
<td>Difference: <strong>MD 1.22 fewer</strong> (CI 95% 2.37 fewer - 0.07 fewer)</td>
<td>patients - results at 12-24 weeks significant yet at 4-6 weeks were not significant</td>
<td></td>
</tr>
</tbody>
</table>

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
7. **Inconsistency: Serious**. Point estimates vary widely; **Imprecision: Serious**. Wide confidence intervals, Low number of patients;

**References**

[75] Marciniak CM, Harvey RL, Gagnon CM, Duraski SA, Denby FA, McCarty S., Bravi LA, Polo KM, Fierstein KM: Does botulinum toxin type A decrease pain and lessen disability in hemiplegic survivors of stroke with shoulder pain and spasticity?: a randomized,
For stroke survivors with shoulder pain, electrical stimulation is not recommended to manage pain. (Vafadar et al 2015 [68])

Key Info

Benefits and harms
Electrical stimulation may prevent or reduce subluxation, but there was no significant effect on pain (Vafadar et al 2015 [68]). Minimal adverse effects (Vafadar et al 2015 [68]).

Quality of evidence
The evidence was low to moderate based on a systematic review and metanalysis of 10 studies (3 for pain measures).

Preference and values
Some patients may have negative perception of electrical stimulation, especially when the benefit is not clear from the evidence.

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 shoulder and increase function. However no significant benefits on pain were seen (in first 6 months), despite improvements in subluxation (Vafadar et al 2015 [68]).

Clinical Question/ PICO

| Population: | Adults with stroke |
| Intervention: | Electrical stimulation |
| Comparator: | Conventional therapy |
Summary
Vafadar et al (2015) [66] 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. Based on this review, it appears that FES does not reduce shoulder pain compared to conventional therapy, although the evidence on FES applied late after stroke was insufficient to draw firm conclusions.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Timeframe</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Plain text summary</th>
</tr>
</thead>
</table>
| Pain (early) <6 months after stroke | Post-treatment (4-8 weeks) | Measured by: Self reported severity of pain | Conventional therapy Electrical stimulation | Difference: **SMD 0.28 fewer**  
( CI 95% 0.67 fewer - 0.11 more ) | Moderate  
Review reports Level 1a and Level 2a quality of evidence, however limited information provided to truly determine quality of these individuals trials. Due to serious inconsistency ²  
FES showed no significant effect on self reported pain severity compared with usual care. |
| Pain (late) | Late (> 6 months) | Measured by: VAS during active rotation of the shoulder | **CI 95%** | **Very Low**  
Due to serious risk of bias, Due to very serious imprecision. SR gave both studies a PEDro score of 3 and Level 3 evidence for quality, Due to serious inconsistency ³  
We are uncertain whether FES applied late after stroke reduces shoulder pain. |
| Motor function (early) | Early (< 6 months) | Measured by: Multiple - MAS, ARAT, Frenchy, Motricity Index, Chedoke, Brunstrom, therefore data converted to percentages | Conventional therapy Electrical stimulation | Difference: **SMD 0.36 more**  
( CI 95% 0.27 fewer - 0.99 fewer ) | **Low**  
Due to serious inconsistency, Due to serious indirectness. Note however quality assessment reported in SR reported 1a evidence for 3  
FES does not appear to improve motor function early after stroke compared to conventional therapy alone |
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.

References


Practice Statement

<table>
<thead>
<tr>
<th>Pain (early) &lt;6 months after stroke</th>
<th>Measured by: Pain free range of movement (lateral rotation)</th>
<th>Difference: SMD 0.31 more (CI 95% 0.13 fewer - 0.75 more)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7 Critical</td>
<td>High better</td>
<td>Good quality RCTs and level 2a evidence from two fair quality RCTs.</td>
</tr>
<tr>
<td></td>
<td>Based on data from: 82 patients in 3 studies.</td>
<td>Moderate Due to serious imprecision</td>
</tr>
<tr>
<td></td>
<td>(Randomized controlled)</td>
<td>FES probably has little or no difference on pain free ROM (early) &lt;6 months after stroke</td>
</tr>
<tr>
<td></td>
<td>Follow up 4-6 weeks</td>
<td></td>
</tr>
</tbody>
</table>

1. as different pain rating scales used, these were pooled using effect sizes only. I have entered these as means and SD with range 0-1, but not sure if this is correct
2. Inconsistency: Serious. The magnitude of statistical heterogeneity was high, with I^2: 34%.; Publication bias: No serious.
3. Risk of bias: Serious. 2 x Quasi-RCTs; Inconsistency: Serious. no statistics reported on whether changes reported significant or not; Imprecision: Very Serious. Low number of patients, n = 17 across the two studies (only 6 participants in the experimental group),
4. Inconsistency: Serious. The magnitude of statistical heterogeneity was high, with I^2: 80%.; Indirectness: Serious. Outcome different for each study and pooled for meta analysis via a percentage calculation.
5. Imprecision: Serious. Low number of patients (82 across 3 studies);

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.
11 - 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.

**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:

- dynamic pressure garments;
- electrical stimulation;
- elevation of the limb when resting.

**Practice Statement**

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

- dynamic pressure garments;
- electrical stimulation;
- continuous passive motion with elevation;
- elevation of the limb when resting.
12 - Fatigue

Fatigue is a common long-term problem after stroke with estimates of prevalence ranging from 16% to 70% (McGeough et al 2009 [100]). A more recent systematic review found a pooled prevalence of 50% (95% CI 43 to 57) (Cumming et al 2016 [103]). 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 [101]). 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 [100]). Recently, diagnostic criteria and an associated structured interview have been developed to identify which stroke patients have clinically significant fatigue (Lynch et al 2007 [102]).

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.

**Practice Statement**

**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 and education about fatigue.
- Potential modifying factors for fatigue should be considered including avoiding sedating drugs and alcohol, screening for sleep-related breathing disorders and depression.
- While there is insufficient evidence to guide practice, possible interventions could include exercise and improving sleep hygiene.
13 - 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).

13.1 - 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 2008 [87]). 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 2008 [87]).

In the most recent National Stroke Audit of Acute Services, patients in Australia, 35% had incontinence within 72 hours of stroke onset (Stroke Foundation 2015 [9]). Among them, only 35% had an incontinence management plan in place, while 60% of hospitals reported having a locally agreed urinary incontinence protocol (Stroke Foundation 2015 [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 [93])
- For stroke survivors, a portable bladder ultrasound scan should be used to assist in diagnosis and management of urinary incontinence. (Martin et al 2006 [93])

**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), rectal and neurological examinations and measurement of body mass index.
4. Simple investigations, including urinalysis, midstream specimen of urine, 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.

**Key Info**

**Benefits and harms**

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 [93]).

**Quality of evidence**

The population investigated was not stroke specific patients, therefore it is uncertain if the results are transferable.
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) [91] 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.

<table>
<thead>
<tr>
<th>Outcome Timeframe</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Plain text summary</th>
</tr>
</thead>
</table>
| Diagnosis of urinary incontinence | 7 Critical | 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) | Simply investigation methods such as urinary diary offer good sensitivity and specificity. When required, multichannel urodynamics provide the most accurate results |
Weak Recommendation

- Stroke patients in hospital with confirmed continence difficulties, should have a structured continence management plan formulated, documented, implemented and monitored. (Thomas et al 2008 [89])
- A community continence management plan should be developed with the stroke survivor and family/carer prior to discharge, and should include information on accessing continence resources and appropriate review in the community. (Thomas et al 2008 [89])
- If incontinence persists the stroke survivor should be re-assessed and referred for specialist review. (Thomas et al 2008 [89])

Key Info

Benefits and harms

Thomas et al (2008) [89] conducted a Cochrane review and found that a Continence Nurse Advisor in the community and a structured functional approach in early rehabilitation may be effective in reducing incontinence (RR 0.26, 95%, CI 0.01 - 4.67). They also showed improvement in quality of life and urinary symptoms.

Quality of evidence

Both studies included in Thomas et al (2008) [89] had serious risk of bias. Moreover, the confidence intervals were very wide due to disparate results reported from the two studies (one was non-significant while the other showed more than 90% risk reduction).

Preference and values

Interviews with carers of stroke survivors with urinary incontinence identified four themes: chaos, hypervigilance, exhaustion, and creating a new life (Tseng et al 2016 [94]). Incontinence is likely to cause burden on both stroke survivors and their carers and they...
Rationale
Evidence has shown potential benefits of structured management plan with professional input for stroke survivors with incontinence in both the community and hospital settings (Thomas et al 2008 [89]). Moreover, stroke survivors and their carers experiencing burden from this condition are likely to want to receive support and appropriate management from health professionals.

Clinical Question/ PICO
Population: Stroke patients with urinary incontinence
Intervention: Specialised professional input
Comparator: Control

Summary
Thomas et al (2008) [87] conducted a Cochrane review of treatment methods for urinary incontinence after stroke. They identified two randomised controlled trials that they categorised as ‘specialised professional input interventions’. One randomised controlled trial (RCT) with 232 participants compared care from a Continence Nurse Advisor to usual care from a GP, while the other (34 participants) used a structured functional approach to assessment and management in early rehabilitation. The primary outcome analysed, the number of people with incontinence after treatment, showed a non-significant reduction (RR 0.85, 95% CI 0.63 to 1.14) in the larger trial and was significant in the smaller trial (RR 0.06, 95% 0.01 to 0.43). Combining these highly disparate estimates led to a pooled estimate that suggested benefit but had very wide confidence intervals (RR 0.26, 95% CI 0.01 to 4.67). Other apparent benefits of the interventions included improvements in quality of life and patient satisfaction. However, the two RCTs generally did not report the same outcomes, meaning pooled analysis was not possible. In the smaller trial, significantly fewer patients were discharged to a setting other than home (RR 0.23, CI 0.07 to 0.72), suggesting decreased cost and service use. Lack of allocation concealment and unblinded assessors in the smaller trial and loss to follow-up in the larger trial meant that both were at risk of bias.

<table>
<thead>
<tr>
<th>Outcome Timeframe</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incontinence After treatment</td>
<td>Relative risk 0.26 (CI 95% 0.01 - 4.67) Based on data from 155 patients in 2 studies. 1 (Randomized controlled Follow up 6 months/)</td>
<td>Control: 672 per 1000 Specialised professional input: 175 per 1000</td>
<td>Low Due to serious imprecision, Due to serious inconsistency 2</td>
<td>Specialised professional input may decrease incontinence</td>
</tr>
</tbody>
</table>

1 Difference: 497 fewer per 1000 (CI 95% 665 fewer - 2,466 more)
1. Systematic review [89]. Baseline/comparator:: Control arm of reference used for intervention.
   2. Risk of bias: No serious. Participants and providers couldn't be blinded., Inadequate/lack of blinding of outcome assessors in one study : Inconsistency: Serious. The magnitude of statistical heterogeneity was high, with I^2: 89%.; Indirectness: No serious. Imprecision: Serious. Very wide confidence intervals ; Publication bias: No serious.
   3. Number of people not cured of all urinary symptoms
   4. Systematic review [89]. 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.
   7. Risk of bias: Serious. 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: No serious. Imprecision: Serious. Only data from one study, Low number of patients ; Publication bias: No serious.

References
Weak Recommendation

For stroke survivors with urge incontinence:
- anticholinergic drugs can be tried (Nabi et al 2006 [92]);
- a prompted or scheduled voiding regime program/bladder retraining can be trialled (Thomas et al 2015 [88]; Thomas et al 2008 [89]);
- if continence is unachievable, containment aids can assist with social continence.

Key Info

Benefits and harms
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 [92]).

A systematic voiding program in a feasibility study (Thomas et al 2015 [88]) 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.

Quality of evidence
Thomas et al (2015) [88] had inadequate sample size and high risk of bias, which may be the reason for insignificant results. Results from Nabi et al (2006) [92] 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.

Preference and values
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
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 trialled. 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) [86] 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) [106] 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 earlier Cochrane review by Thomas et al (2008) [87] had found 3 small trials of behavioural interventions for treating urinary incontinence. Results could not be pooled as the trials generally did not report the same outcomes, so the review authors concluded that there was insufficient evidence to determine the efficacy of these interventions.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continent - 6 weeks</td>
<td>Odds Ratio 0.94 (CI 95% 0.46 - 1.94) Based on data from 160 patients in 1 studies.</td>
<td>280 per 1000</td>
<td>Low Due to serious imprecision (sample size) and serious risk of bias (lack of blinding)</td>
<td>Behavioural intervention may have little or no difference on continence at 6 weeks post stroke</td>
</tr>
<tr>
<td></td>
<td>(Randomized controlled) Follow up 6 weeks</td>
<td>268 per 1000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Continent at discharge</td>
<td>Odds Ratio 1.47 (CI 95% 0.81 - 2.67) Based on data from 288 patients in 1 studies.</td>
<td>310 per 1000</td>
<td>Low Due to serious imprecision (sample size) and serious risk of bias (lack of blinding)</td>
<td>Behavioural intervention may improve continence slightly</td>
</tr>
<tr>
<td></td>
<td>(Randomized controlled) Follow up 6 weeks</td>
<td>398 per 1000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Catheter use</td>
<td>n/a Based on data from 288 patients in 1 studies.</td>
<td>8 per 1000</td>
<td>Very Low Due to serious risk of bias and very serious imprecision</td>
<td>We are uncertain whether behavioural intervention increases or decreases catheter use</td>
</tr>
<tr>
<td>During hospital stay</td>
<td>(Randomized controlled)</td>
<td>24 per 1000</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
1. Dichotomous answer to the question of absence of urinary incontinence on International Consultation on Incontinence Questionnaire.

2. Primary study [88]. **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**: **Very Serious**. Sample size not powered to demonstrate effectiveness, Only data from one study, No relative effect nor confidence intervals; **Publication bias**: **No serious**.

---

### Table: Risk of bias

<table>
<thead>
<tr>
<th>Risk of Bias</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Risk of bias</strong>:</td>
<td><strong>Serious</strong></td>
</tr>
<tr>
<td><strong>Inconsistency</strong>:</td>
<td><strong>No serious</strong></td>
</tr>
<tr>
<td><strong>Indirectness</strong>:</td>
<td><strong>No serious</strong></td>
</tr>
<tr>
<td><strong>Imprecision</strong>:</td>
<td><strong>Serious</strong></td>
</tr>
</tbody>
</table>

1. **UTI During hospital stay**: Follow up To discharge
   - n/a
   - Based on data from 288 patients in 1 studies. (Randomized controlled)
   - **Very Low**. Due to serious risk of bias and very serious imprecision.
   - Behavioural intervention may have little or no difference on UTI

2. **Length of stay**: Follow up To discharge
   - Measured by: Days in stroke unit
   - Lower better
   - Based on data from: 288 patients in 1 studies. (Randomized controlled)
   - **Very Low**. Due to serious risk of bias and very serious imprecision.
   - We are uncertain whether behavioural intervention increases or decreases length of stroke unit stay

3. **HRQoL 6 weeks post stroke**: Follow up To discharge
   - Based on data from 210 patients in 1 studies.
   - 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.
   - Behavioural intervention may worsen HRQoL slightly
**No serious. Imprecision: Serious.** Sample size not powered to demonstrate effectiveness. Only data from one study; **Publication bias: No serious.**

### References


### Clinical Question/ PICO

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

### Summary

Nabi et al (2006) [90] 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.

<table>
<thead>
<tr>
<th>Outcome Timeframe</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Plain text summary</th>
</tr>
</thead>
</table>
| Withdrawal due to adverse events During study | Relative risk 1.11 (CI 95% 0.91 - 1.36) Based on data from 7,576 patients in 20 studies.  
Randomized controlled Follow up 2-12 weeks | 49 per 1000  
**Difference: 5 more** per 1000 (CI 95% 18 more - 4 fewer) | Moderate  
Due to serious indirectness | Anticholinergic drugs probably have little or no difference on withdrawal due to adverse events |

<p>| 7 Critical |</p>
<table>
<thead>
<tr>
<th>Leakage episodes</th>
<th>Measured by: Number of episodes in 24 hours Lower better</th>
<th>Difference: <strong>MD 0.51 fewer</strong> (CI 95% 0.66 fewer - 0.37 fewer)</th>
<th>Low Due to serious risk of bias, Due to serious indirectness</th>
<th>Anticholinergic drugs may decrease the number of leakage episodes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post intervention</td>
<td>Based on data from: 4,582 patients in 12 studies. <em>(Randomized controlled)</em> Follow up 2-12 weeks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Criticality: 7</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Quality of life</th>
<th>Measured by: Number of episodes in 24 hours Lower better</th>
<th>Difference: <strong>MD 0.51 fewer</strong> (CI 95% 0.66 fewer - 0.37 fewer)</th>
<th>Moderate Due to serious indirectness (not stroke specific)</th>
<th>Anticholinergic drugs probably improve quality of life slightly. The reported benefits were of moderate size and may not be clinically significant.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post intervention</td>
<td>Based on data from: 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.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Criticality: 8</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. Systematic review [92]. **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 [92]. **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 [92].
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.**

**References**

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.

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

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.

Key Info

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.

13.2 - Faecal incontinence

Faecal incontinence is one of the most common complications of acute stroke, with reported prevalence ranges from 23-60% in acute stage (Lim et al 2015 [93]). 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 [95]). 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 [98])
- 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 [98])

**Key Info**

**Benefits and harms**

There was an increase of frequency of normal bowel movements (Harari et al 2004 [98]).

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 [98]).

**Quality of evidence**

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

**Preference and values**

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

**Resources and other considerations**

- **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 [98]). 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) 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. 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.

<table>
<thead>
<tr>
<th>Outcome Timeframe</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal bowel movements 6 months</td>
<td>Relative risk</td>
<td>550</td>
<td>750</td>
<td>Low due to serious risk of bias and serious imprecision ¹</td>
</tr>
<tr>
<td></td>
<td>Based on data from 146 patients in 1 studies. (Randomized controlled)</td>
<td>per 1000</td>
<td>per 1000</td>
<td>Nurse-led intervention may improve normal bowel movements</td>
</tr>
</tbody>
</table>

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.

References


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 [99]; Munchiando et al 1993 [100])

Key Info

Benefits and harms
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 [99]; Munchiando et al 1993 [100]). However, it is uncertain if these benefits translate to improvement in quality of life considering potential burden of these treatment.

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

Preference and values
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
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 [99]). Another form of bowel training, digital stimulation of the anus, may also provide some benefit (Munchiando et al 1993 [100]). However, both interventions have low-quality evidence and may not be accepted by patients, therefore potential benefits and issues should be discussed with patients.

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) [95] 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 [98]. 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.

### References


### Clinical Question/ PICO

<table>
<thead>
<tr>
<th>Population:</th>
<th>Stroke patients with constipation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention:</td>
<td>Morning bowel evacuation</td>
</tr>
<tr>
<td>Comparator:</td>
<td>Evening schedule of bowel evacuation</td>
</tr>
</tbody>
</table>
Summary
A systematic review of bowel management strategies by Lim and Childs (2013) [95] 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 [97]. 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.

<table>
<thead>
<tr>
<th>Outcome Timeframe</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to achieve regular bowel movement</td>
<td>Measured by: Efficiency rating. 1 point deducted for every 2 additional days to reach effectiveness High better Based on data from: 58 patients in 1 studies. (Randomized controlled)</td>
<td>7.37 (Mean) Morning bowel evacuation 13.3 (Mean) Evening schedule of bowel evacuation</td>
<td>Low Due to serious risk of bias, Due to serious imprecision 1</td>
<td>morning bowel evacuation may improve time to achieve regular bowel movement</td>
</tr>
</tbody>
</table>

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.

References

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 trialled.
- 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.
14 - 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 [101]). 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 [101]). 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 [101]). 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 [102]). National Stroke Audits report low rates of mood assessment in acute and rehabilitation audits, 28% and 53% respectively (Stroke Foundation 2016; 2015 [7] [9]). This is despite the recognised prevalence of mood impairment in stroke admissions (38% and 47% respectively) (Stroke Foundation 2016; 2015 [7] [9]).

14.1 - Mood assessment

Info Box

Practice points

• Stroke survivors with suspected altered mood (e.g. depression, anxiety, emotional lability) should be assessed by trained personnel using a standardised and validated scale.
• 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. 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 may be more appropriate. Ideally this tool should capture both anxiety and depressive symptoms. A local site champion can be useful in the implementation process.

14.2 - Treatment for Emotional distress

Weak Recommendation

For stroke survivors with emotionalism, antidepressant medication such as selective serotonin reuptake inhibitors (SSRIs) or tricyclic antidepressants may be used. (Hackett et al 2010 [103])

Key Info

Benefits and harms

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 (Hackett et al 2010 [103]). The data on possible adverse events are limited and insufficient to determine possible harms (Hackett et al 2010 [103]).
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 (Hackett et al 2010 [103]).

Quality of evidence

The evidence for the benefits of pharmacological therapy is low, with only a few small RCTs of short duration (Hackett et al 2010 [103]). Trials do not appear to measure emotionalism in a standardised way (Hackett et al 2010 [103]).

Preference and values

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

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

Clinical Question/ PICO

Population: Adults with stroke
Intervention: Pharmaceutical interventions
Comparator: Placebo

Summary

Five trials in the systematic review conducted by Hackett et al (2010) [101] measured 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 but all individual trials showed large effects of treatment. On the other hand, 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 trials with systematic assessment and reporting of adverse events are needed to ensure that these benefits outweigh the risks.

Outcome

<table>
<thead>
<tr>
<th>Outcome Timeframe</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improved emotionalism</td>
<td>Odds Ratio 9.35 (CI 95% 4.26 - 20.54) Based on data from 164 patients in 3 studies. (Randomized controlled)</td>
<td>329 per 1000</td>
<td>Low Due to very serious imprecision</td>
<td>Pharmaceutical interventions may improve emotionalism</td>
</tr>
</tbody>
</table>

| 7 Critical | | 820 per 1000 | | |

Difference: 492 more per 1000 (CI 95% 347 more - 581 more)
14.3 - Prevention of depression

Weak Recommendation AGAINST

For stroke survivors, routine use of antidepressants to prevent post-stroke depression is not recommended. (Hackett et al 2008 [106])

Key Info

Benefits and harms

Trials of antidepressants have shown reductions in the proportion of people with depression but these reductions have generally been non-significant, and the research to date has been too varied to allow a combined estimate of the treatment effects (Hackett et al 2008 [106]). Adverse events were not systematically monitored and reported in most trials, so the potential harms are unclear.

Quality of evidence

The quality of evidence is very low, as existing trials have been too varied to allow a clear treatment effect to be estimated. Lack of blinding for outcome assessors means many of the existing trials have a high risk of bias.

References

**Rationale**

The existing evidence regarding the benefits of antidepressants for preventing depression is insufficient to confirm any benefits or harms.

**Clinical Question/ PICO**

- **Population:** Adults with stroke
- **Intervention:** Pharmacotherapy for the prevention of depression
- **Comparator:** Control

**Summary**

In a Cochrane review, Hackett et al (2008) [104] included 10 pharmaceutical trials investigating interventions for the prevention of depression following stroke. Interventions used in these trials included SSRIs (3 studies), serotonin antagonist and reuptake inhibitors (2 studies), and other treatments with antidepressant effects (e.g. piracetam, maprotiline). 6 trials reported depression outcomes at the end of treatment. The proportion of patients with depression appeared to be lower following pharmacotherapy, but the trials used a variety of criteria (e.g. DSM-III criteria, HADS-D) and meta-analysis was not performed due to the variety of methods and outcomes used in the studies. Only one trial showed a significant reduction in the proportion of people with depression. Similarly, depression scores showed some signs of reduction but meta-analysis was not performed. The review authors concluded that there was insufficient evidence for an effect of pharmacotherapy.

A more recent review by Salter et al (2013) [133] included many of the same trials, but excluded some trials and did not provide details about why individual studies were excluded, so it is unclear why some trials included in the Hackett et al. review were not included. Two newer trials included in the review, published after the Hackett et al. review, had 230 total patients and both showed significant or near-significant reductions in the presence of depression. However, these two newer trials do not appear to provide strong enough evidence to change the conclusions of the earlier review.

Another recent trial by Zhang et al (2012) [138] assessed the effects of duloxetine, a serotonin-norepinephrine reuptake inhibitor, in a single-blind trial with 95 participants. Participants in the intervention group received duloxetine 30-90mg daily for 12 weeks, while the control group received usual care. By 24-week follow-up, the duloxetine group had a significant reduction in minor depression (28.6% in the control group, 12.5% in the intervention), and a significant reduction in major depression (24.5% control vs 8.3% intervention). Significant improvements were also seen in quality of life and activities of daily living. As the trial participants were unblinded there is potential for bias (e.g. placebo effects), although the trial used blinded outcome assessors which should minimise bias in outcome measurement.
Weak Recommendation

For stroke survivors, psychological strategies (e.g. problem solving, motivational interviewing) may be used to prevent depression. (Hackett et al 2008 [106])

Key Info

Benefits and harms
Psychotherapy appears to substantially reduce the risk of developing depression following stroke (81 fewer depression per 1000 patients treated), but may only be effective for patients without cognitive and communication difficulties who can actively participate in treatment (Hackett et al 2008 [106]). There is no indication that psychotherapy increases adverse events such as recurrent stroke, but adverse events were not systematically monitored and reported in all trials.

Quality of evidence
The quality of evidence is moderate, coming from a small number of randomised trials of reasonable quality.

Preference and values
Depending on their level of cognitive or communication impairments, patients may struggle to engage in psychotherapy treatment.
**Rationale**

Psychotherapy interventions such as problem solving and motivational interviewing appear to 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 three published 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
- **Intervention:** Psychotherapy for the prevention of depression
- **Comparator:** Control

**Summary**

A Cochrane review of treatments for preventing depression following stroke included 4 trials of psychotherapy with 902 total participants (Hackett et al 2008 [104]). Psychotherapy interventions 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 odds of depression following psychotherapy (OR 0.64, 95% CI 0.42 to 0.98), and a small but significant reduction in the psychological distress scores on the GHQ-28 (MD -1.37, 95% CI -2.33 to -0.40). There were also fewer reported adverse events in the psychotherapy groups (OR 3.73, 95% CI 1.27 to 10.97). While the risk of bias was generally low due to the use of blinded outcome assessors, 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 psychotherapy, which often requires active patient engagement.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Presence of depression</strong></td>
<td><strong>End of treatment</strong></td>
<td>Odds Ratio 0.64 (CI 95% 0.42 - 0.98)</td>
<td>Based on data from 520 patients in 2 studies.</td>
<td>Moderate</td>
</tr>
<tr>
<td><strong>Depression -</strong></td>
<td><strong>Measured by: Change in</strong></td>
<td>280 per 1000</td>
<td>199 per 1000</td>
<td>Due to serious indirectness</td>
</tr>
</tbody>
</table>
### 14.4 - Treatment for depression

**Strong Recommendation**

For stroke survivors with depression or depressive symptoms, 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. (Mead et al 2012 [111]; Hackett et al 2008 [117])

#### Key Info

**Benefits and harms**

The reported effect sizes for response rates and reduction of depressive symptoms are large, with a meta-analysis suggesting that patients receiving antidepressants show reductions of approximately 2 standard deviations on depression scales (Mead et al 2012 [111]). However, the effects were smaller in trials with a lower risk of bias. Trials have reported larger numbers of seizures among patients taking SSRIs, although no significant difference was found and the risk was low in absolute terms.

**Quality of evidence**

The evidence is of moderate quality, as most trials are small and many appear to have a high risk of bias. Sensitivity analyses restricted to only higher quality trials found smaller effect sizes, suggesting that the true benefits of SSRIs may be smaller than the effect found.
Rationale

SSRIs appear to produce substantial benefit in reducing depression and depressive symptoms, and should therefore be considered for stroke patients exhibiting these symptoms. Patients should be monitored for any adverse events.

There is no evidence currently for the use of stepped care in stroke only in the general population so we have not included it this time.

Clinical Question/ PICO

| Population: | Adults with stroke with depression |
| Intervention: | Selective serotonin reuptake inhibitors |
| Comparator: | Control |

Summary

Mead et al (2012) [111] conducted a Cochrane review of selective serotonin reuptake inhibitors (SSRIs) for stroke recovery, including 52 trials in their meta-analysis. Not all trials required patients to have depression at baseline but subgroup analyses were conducted for the trials where all patients had depression. Meta-analysis of scores on depression measures such as HAMD and BDI showed significantly reduced scores following SSRI treatment for 31 trials where patients had depression at baseline (SMD -2.06, 95% CI -2.54 to -1.58). This effect appeared to be larger than for trials where patients did not have to have depression, but the difference between these subgroups was non-significant. Analysis of dichotomous depression outcomes was only conducted for trials where continuous scores were not available, with data from 2 trials showing a non-significant reduction in the number of patients with depression (OR 0.66, 95% CI 0.30 to 1.46). While this could be interpreted as showing that reductions in symptoms do not translate to reductions in presence of depression, these data were limited compared to the data used for continuous depression scores and had less power to detect a difference.

An earlier systematic review comparing antidepressants to placebo included 10 trials involving people with post-stroke depression where depression was the primary outcome for the trial (Price et al 2011 [113]). Meta-analysis based on 519 participants in 6 trials showed a significant increase in the odds of recovery or remission (OR 2.58, 95% CI 1.56 to 4.26) following antidepressant treatment, while analysis based on 5 trials reporting depression symptoms scores also showed a significant reduction. The improvement in recovery or remission rates suggests that antidepressants do produce clinically significant improvements, and that the negative result seen in the Mead review resulted from low power.

Hackett et al (2008) [117] conducted a Cochrane review of interventions for treating depression after stroke that included all antidepressants, rather than only SSRIs. This included SSRIs, tricyclic antidepressants and other treatments with antidepressant effects such as deanxit. A significant reduction in the number of patients with depression was seen following pharmacotherapy across 7 placebo-controlled trials (OR 0.47, 95% CI 0.22 to 0.98). Patients receiving pharmacotherapy were also significantly less likely to show less than 50% improvement on depression scales (OR 0.22, 95% CI 0.09 to 0.52). However, antidepressants were...
also associated with a significant increase in adverse events such as confusion and constipation. The majority of the included studies used SSRIs and there was insufficient evidence to determine if specific types of antidepressants produced greater benefits.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression - dichotomous outcome</td>
<td>Relative risk 0.66 (CI 95% 0.3 - 1.46) Based on data from 288 patients in 2 studies. (Randomized controlled) Follow up Varied: treatment for 10 days to 12 months</td>
<td>753 per 1000 497 per 1000</td>
<td>Low Due to serious risk of bias: restricting analysis to trials with lower risk of bias yielded smaller effect sizes, Due to serious imprecision 1</td>
<td>SSRIs may have little or no difference on the presence of depression.</td>
</tr>
<tr>
<td>Depression - continuous scores 2</td>
<td>Measured by: Various: HAMD, BDI, MADRS Lower better Based on data from: 2,256 patients in 31 studies. (Randomized controlled) Follow up Varied: treatment for 10 days to 12 months</td>
<td>Difference: SMD 2.06 fewer (CI 95% 2.54 fewer - 1.58 fewer)</td>
<td>Moderate Due to serious risk of bias: restricting analysis to trials with lower risk of bias yielded smaller effect sizes. 3</td>
<td>SSRIs probably decrease depression symptoms.</td>
</tr>
</tbody>
</table>

1. **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. The magnitude of statistical heterogeneity was high, with I^2: 70%.; **Indirectness**: No serious. **Imprecision**: Serious. Wide confidence intervals.; **Publication bias**: No serious.
2. Depression was assessed through various measures, including Hamilton Rating Scale for Depression (HAMD) and the Beck Depression Inventory. Absolute scores at end of treatment were used where possible (rather than change scores), and HAMD was used over BDI if both were reported in a trial
3. **Risk of bias**: Serious. Risk of bias items were not well reported in many trials, with blinding of participants and personnel a particular concern, 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, Selective outcome reporting; **Inconsistency**: No serious. **Imprecision**: No serious. **Publication bias**: No serious. Asymmetrical funnel plot;
Weak Recommendation

For stroke survivors with depression or depressive symptoms, structured exercise programs, particularly those of high intensity, may be used. (Eng et al 2014 [110])

Key Info

Benefits and harms

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.

Quality of evidence

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.

Preference and values

Patients preferences regarding exercise would be similar to that of the general population.

Resources and other considerations

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. It is apparent that these benefits were not maintained in the long term. The effects appear to be greater for high-intensity programs.

References


Clinical Question/ PICO

Population: Adults with stroke
Intervention: Structured exercise
Comparator: Control

Summary

A systematic review by Eng et al (2014) [108] 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 a non-significant 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.

An earlier systematic review of community-based rehabilitation interventions by Graven et al (2011) [151] had suggested much stronger effects of exercise interventions on depression. 10 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 later review should provide less biased results.

Depression scale scores were also assessed in a Cochrane review of physical fitness interventions for stroke survivors (Saunders et al 2016 [156]). Only 2 included trials of cardiorespiratory training reported depression outcomes, with a meta-analysis of data from 80 participants showing a non-significant improvement in depression scores at the end of treatment but a significant improvement at the end of follow-up. Pooled analysis of 2 trials of resistance training showed a significant improvement at the end of treatment, while meta-analysis of 3 trials using mixed cardiorespiratory and resistance training showed no effects at the end of intervention or at follow-up. These trials had depression scales as secondary outcomes and were not restricted to patients with clinical levels of depression, so the results may not reflect the benefits for patients with depression.

<table>
<thead>
<tr>
<th>Outcome Timeframe</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>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 patients in 13 studies. (Randomized controlled)</td>
<td>Difference: <strong>SMD 0.13 fewer</strong> (CI 95% 0.26 fewer - 0.01 fewer)</td>
<td>Low Due to serious risk of bias, Due to serious publication bias¹</td>
<td>Structured exercise may decrease depressive symptoms slightly in the short term. Larger effects were reported for high intensity exercise programs</td>
<td></td>
</tr>
<tr>
<td>Depressive symptoms Measured by: Various - Hospital Anxiety and Depression Scale,</td>
<td>Difference: <strong>SMD 0.04 fewer</strong> (CI 95% 0.17 fewer - 0.09 more)</td>
<td>Low Due to serious risk of bias, Due to</td>
<td>Structured exercise may have little or no difference on depressive symptoms</td>
<td></td>
</tr>
</tbody>
</table>
For stroke survivors with depression or depressive symptoms, acupuncture may be used. (Zhang et al 2010 [116])

References


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**.

**Long term**

**8 Critical**

Geriatric Depression Scale etc. Lower better
Based on data from: 889 patients in 10 studies.
(Randomized controlled) Follow up 10 weeks to 9 months

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.

**Safety**

**During intervention**

**7 Critical**

Based on data from 1,022 patients in 13 studies.

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

We are uncertain whether structured exercise increases or decreases safety

**symptoms in the long term (after exercise programs have stopped)**
Key Info

Benefits and harms
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 [116]). Acupuncture was also reported to produce lower rates of side-effects compared to antidepressants but this analysis was not specific to stroke.

Quality of evidence
The quality of evidence is low, with a lack of blinding and no comparison to sham or placebo acupuncture to rule out placebo effects.

Preference and values
The majority of studies come from Chinese populations. Australian patients may have different preferences regarding acupuncture.

Resources and other considerations
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 [116]). 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.
<table>
<thead>
<tr>
<th>Response rate</th>
<th>Relative risk 1.36 (CI 95% 1.24 - 1.5)</th>
<th>Based on data from 1,572 patients in 13 studies. (Randomized controlled) Follow up 4 to 8 weeks of treatment</th>
<th>431 per 1000</th>
<th>586 per 1000</th>
<th>Low</th>
<th>Due to very serious risk of bias - no blinding/placebo controls</th>
<th>Acupuncture therapy may improve response rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response rate - compared to antidepressants</td>
<td>Relative risk 1.31 (CI 95% 1.19 - 1.44)</td>
<td>Based on data from 1,438 patients in 11 studies. (Randomized controlled) Follow up 4 to 8 weeks of treatment</td>
<td>447 per 1000</td>
<td>586 per 1000</td>
<td>Low</td>
<td>Due to very serious risk of bias - no blinding/placebo controls</td>
<td>Acupuncture therapy may improve response rate compared to antidepressants</td>
</tr>
<tr>
<td>Response rate - compared to waitlist</td>
<td>Relative risk 2.33 (CI 95% 1.44 - 3.78)</td>
<td>Based on data from 134 patients in 2 studies. (Randomized controlled) Follow up 4 to 8 weeks of treatment</td>
<td>447 per 1000</td>
<td>586 per 1000</td>
<td>Low</td>
<td>Due to very serious risk of bias - no blinding/placebo controls</td>
<td>Acupuncture therapy may improve response rate compared to waitlist</td>
</tr>
<tr>
<td>Changes in depression scale</td>
<td>Measured by: Change from baseline on HAMD High better</td>
<td>Based on data from: 1,512 patients in 14 studies. (Randomized controlled) Follow up 4 to 8 weeks of treatment</td>
<td>Difference: MD 2.54 more (CI 95% 1.11 more - 3.97 more)</td>
<td></td>
<td>Low</td>
<td>Due to very serious risk of bias - no blinding/placebo controls</td>
<td>Acupuncture therapy may decrease depression symptoms</td>
</tr>
<tr>
<td>Changes in depression scale - compared to antidepressants</td>
<td>Measured by: Change from baseline on HAMD High better</td>
<td>Based on data from: 1,318 patients in 11 studies. (Randomized controlled) Follow up 4 to 8 weeks of treatment</td>
<td>Difference: MD 1.43 more (CI 95% 0.19 more - 2.68 more)</td>
<td></td>
<td>Low</td>
<td>Due to very serious risk of bias - no blinding/placebo controls</td>
<td>Acupuncture therapy may decrease depressive symptoms compared to antidepressants</td>
</tr>
<tr>
<td>Changes in depression scale - compared to waitlist</td>
<td>Measured by: Change from baseline on HAMD High better</td>
<td>Based on data from: 194 patients in 3 studies.</td>
<td>Difference: MD 7.24 more (CI 95% 5.01 more - 9.46 more)</td>
<td></td>
<td>Low</td>
<td>Due to very serious risk of bias - no blinding/placebo controls</td>
<td>Acupuncture therapy may decrease depressive symptoms compared to waitlist</td>
</tr>
</tbody>
</table>
Weak Recommendation AGAINST

For stroke survivors with depression, non-invasive brain stimulation (transcranial direct stimulation or repetitive transcranial magnetic stimulation) should not be used in routine practice and only used as part of a research framework. (Tian et al 2011[112])

Practical Info

Procedures such as TMS have possible benefits for reducing depression but it is unclear which specific TMS procedures are of most benefit.
Key Info

**Benefits and harms**  
Small net benefit, or little difference between alternatives

Reductions in depressive symptoms have been reported following TMS treatment, but trials have used a variety of parameters and procedures (e.g. high-frequency left prefrontal lobe vs low-frequency right prefrontal lobe) and it is unclear whether particular procedures produce greater benefit. Risks of adverse events (e.g. fainting, seizure) are generally considered to be low but there appears to be little data available for the stroke population specifically.

**Quality of evidence**  
Low

The quality of evidence is low, with only a few small trials and an apparent lack of blinding and placebo control.

**Preference and values**  
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

No literature to understand or describe the potential economic implications of this recommendation was identified. TMS equipment may not be widely available.

Rationale

Although TMS appears to produce benefits in reducing depressive symptoms, the available evidence is of low quality and there does not appear to be enough data to recommend specific TMS procedures.

Clinical Question/ PICO

| Population: | Adults with stroke with depression |
| Intervention: | Non-invasive brain stimulation |
| Comparator: | Control |

Summary

A systematic review by Tian et al (2011) [112] included 7 randomised controlled trials of transcranial magnetic stimulation (TMS) for treating post-stroke dysfunction. The included trials were generally unblinded and had unclear allocation concealment procedures. Meta-analysis showed significant reductions in Hamilton Rating Scale for Depression scores following TMS (MD -6.21, 95% CI -7.55 to -4.87). However, due to the low methodological quality of the trials, there is substantial uncertainty regarding the benefits of TMS treatment.

The Tian et al (2011) [112] review also appears to contain some data errors as the reported number of patients included for the comparison of depression scores differs between the text (N = 191) and the accompanying figure (N = 195). This suggests that the overall quality of the review may be low.
14.5 - 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 [103]).

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 [106]), 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.

References
15 - 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[123]). 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[123]). Those who have significant weakness of legs and who are immobile are at greater risk (Naccarato et al 2010[123]).

National Stroke Audits indicated that only 1% of stroke patients had DVT during admission (Stroke Foundation 2015[7]), compared to 40% reported in the literature (confirmed on magnetic resonance imaging within the first three weeks) (Naccarato et al 2010[123]). 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[119]; Sherman et al 2007[126])

**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[128]) and 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.

**Key Info**

**Benefits and harms**

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[126]) 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)[126] 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)[127]. 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[126] 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).
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 [125]). 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 [124]). However, it is more expensive and patients may not tolerate the compression garments or 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.

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 [125]). 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 [124]). However, it is more expensive and patients may not tolerate the compression garments or 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 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 [117]). 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 [126]). 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 [119]], 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) [121] 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) [120] 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 Absolute effect estimates Control Anticoagulation Certainty in effect estimates (Quality of evidence) Plain text summary

**Deep vein thrombosis**<sup>1</sup>

During treatment (1 week to 1 month)

- Odds Ratio 0.21 (CI 95% 0.15 - 0.29)
- Based on data from 916 patients in 10 studies.
- (Randomized controlled) Follow up 1 week to 1 month of treatment

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Anticoagulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odds</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>per 1000</td>
<td>443</td>
<td>143</td>
</tr>
</tbody>
</table>

**Pulmonary embolism**<sup>4</sup>

During treatment

- Odds Ratio 0.6 (CI 95% 0.44 - 0.81)
- Based on data from 22,544 patients in 14

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Anticoagulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odds</td>
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<td>5</td>
</tr>
<tr>
<td>per 1000</td>
<td>443</td>
<td>143</td>
</tr>
</tbody>
</table>

443 fewer per 1000 (CI 95% 336 fewer - 256 fewer)

**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.**

**Anticoagulation reduces PE risk in this overall analysis of multiple agents and doses.**
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"


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


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.

References


Clinical Question/ PICO

Population: Adults with stroke
Intervention: Low Molecular Weight Heparin
Comparator: Unfractionated heparin

Summary
In a randomised controlled trial (Sherman et al 2007 [126]), 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).

<table>
<thead>
<tr>
<th>Outcome Timeframe</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>All DVT 2 weeks</td>
<td>Relative risk 0.57 (CI 95% 0.43 - 0.75) Based on data from 1,335 patients in 1 studies. (Randomized controlled)</td>
<td>176 per 1000 100 per 1000</td>
<td>Low Due to serious risk of bias, Due to serious publication bias, Due to serious imprecision, Upgraded due to Clear dose-response gradient</td>
<td>LMWH probably decreases all DVT</td>
</tr>
<tr>
<td>8 Critical</td>
<td>Difference: 76 fewer per 1000 ( CI 95% 100 fewer - 44 fewer )</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic ICH (NIHSS score &lt;14)</td>
<td>Relative risk 0.62 (CI 95% 0.43 - 0.81) Based on data from 1,335 patients in 1 studies.</td>
<td>176 per 1000 109 per 1000</td>
<td>Low Due to serious risk of bias, Due to serious</td>
<td>LMWH probably decreases symptomatic ICH (nihss score &lt;14)</td>
</tr>
</tbody>
</table>
Weak Recommendation

For acute stroke patients who are immobile, the use of 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 [124])

Key Info

Benefits and harms
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 [124]). 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.

Quality of evidence
A single high quality randomized trial, underpowered to assess the clinically important outcome of pulmonary embolism.

Preference and values
Substantial variability is expected or uncertain
Interruption 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**

**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 [125]). 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 [124]). However, it is more expensive and patients may not tolerate the compression garments or 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 [122]) 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 [159]) 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) [123] 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.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Timeframe</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Usual care</td>
<td>Intermittent pneumatic compression</td>
<td></td>
</tr>
</tbody>
</table>

140 of 164
<table>
<thead>
<tr>
<th>Condition</th>
<th>Odds Ratio</th>
<th>Confidence Interval</th>
<th>Number of Patients</th>
<th>Follow-up Time</th>
<th>Criticality</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any deep vein thrombosis 6 months</td>
<td>0.72</td>
<td>(0.6 - 0.87)</td>
<td>2,876 patients</td>
<td>6 months</td>
<td>Critical</td>
<td>Moderate due to serious imprecision. Intermittent pneumatic compression probably decreases any deep vein thrombosis at 6 months.</td>
</tr>
<tr>
<td>Proximal deep vein thrombosis 30 days</td>
<td>0.71</td>
<td>(0.6 - 0.86)</td>
<td>2,876 patients</td>
<td>30 days</td>
<td>Critical</td>
<td>Moderate due to serious imprecision. Intermittent pneumatic compression probably decreases proximal deep vein thrombosis at 30 days.</td>
</tr>
<tr>
<td>Pulmonary embolism 30 days</td>
<td>0.83</td>
<td>(0.5 - 1.36)</td>
<td>2,876 patients</td>
<td>30 days</td>
<td>Critical</td>
<td>Low due to very serious imprecision. Intermittent pneumatic compression may decrease pulmonary embolism slightly.</td>
</tr>
</tbody>
</table>

1. any lower limb DVT regardless of death, PE, location of DVT within lower limb, or bilateral leg involvement
2. Primary study [124]. 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.

References
Strong Recommendation AGAINST

Antithrombotic stockings are not recommended for the prevention of DVT or PE post stroke. (Naccarato et al 2010 [125])

Key Info

Benefits and harms
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 [125]). Apart from cost, there were complications with skin ulceration observed.

Quality of evidence
Included studies have high methodological quality but high statistical heterogeneity.

Preference and values
There is no group that is likely to benefit from compression stockings

Resources and other considerations
Factors 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 [125]).

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 [123]). Meta-analysis showed that GCS did not significantly reduce the risk of DVT or death by the end of follow-up.

<table>
<thead>
<tr>
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<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deep vein thrombosis During treatment: 7 days or until</td>
<td>Odds Ratio 0.88 (CI 95% 0.72 - 1.08) Based on data from 2,615 patients in 2 studies.</td>
<td>177 per 1000</td>
<td>Moderate Due to serious inconsistency</td>
<td>Graduated compression stockings probably have little or no difference on deep vein thrombosis</td>
</tr>
</tbody>
</table>

Odds Ratio 0.88 (CI 95% 0.72 - 1.08)
Based on data from 2,615 patients in 2 studies. 1
**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.

**Key Info**

**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.
16 - 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 [127]). 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 [127]). In the most recent clinical audit of rehabilitation services, 15% of stroke patients had a fall during admission (Stroke Foundation 2016 [7]). Incidence figures from studies collecting data between one and six months post-stroke vary from 25 to 37% (Verheyden et al 2013 [127]). 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 [127]).

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.

### Practice Statement

**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 (e.g. cognitive and emotional factors as well as physical factors) should also be considered.

### Key Info

**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. (Verheyden et al 2013 [129]; Sherrington et al 2016 [134]; Dickstein et al 2013 [130]; Gillespie et al 2012 [133])

**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 (Sherrington et al 2016 [134]).

Exercise programs are most effective when they include both strength and balance training (Rimland et al 2016 [135]) include exercise that challenges balance, and include 3 hours or more a week of exercise (Sherrington et al 2016 [134]).
Key Info

Benefits and harms
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 [133]). More recent systematic reviews of fall prevention in stroke survivors (Sherrington et al 2016 [134]; Verheyden et al 2013 [129]) did not find significant between-group differences in falls and quality of life.

Quality of evidence
Insufficient evidence from small trials of high risk of bias.

Preference and values
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
Resources considerations
No literature to understand or describe the potential economic implications of this recommendation was identified.

Rationale
Current evidence shows inconclusive results of interventions in stroke survivors (Verheyden et al 2013 [129]; Sherrington et al 2016 [134]) yet benefits in older community residents (Gillespie et al 2012 [133]). 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 (Verheyden et al 2013 [129]).

Clinical Question/ PICO
Population: Adults with stroke
Intervention: Exercise
Comparator: Control

Summary
In older people living in the community, exercise interventions were found to significantly reduce the risk of falling in a Cochrane review (Gillespie et al 2012 [131]). Effective interventions in the general population of older people living in the community included multicomponent group exercise, home-based exercise, Tai Chi, and multifactorial interventions with individual risk assessment.

However, a Cochrane review by Verheyden et al (2013) [127] could not establish if these interventions are equally effective in stroke survivors, mostly due to the inadequate quality of studies available. Verheyden et al. did not find any significant differences in numbers of fallers and rates of falls in either the acute/subacute stage or chronic stage of stroke, nor in quality of life (QoL). However, the included studies had small sample sizes and high risk of bias and therefore one cannot make a definitive conclusion based on current evidence. A more recently published systematic review included only 3 studies involving stroke survivors and reached similar conclusions (Sherrington et al 2016 [132]). One small RCT study included in the Cochrane review found vitamin D supplements reduced falls in a group of women living in residential care facilities after stroke.
A subsequent randomised trial by Taylor-Piliae et al (2014) [130] compared Tai Chi to strength and range of movement exercises or usual care. The Tai Chi and strength exercise groups attended 3 1-hour exercise sessions per week for 12 weeks. The Tai Chi group had fewer falls than the strength and usual care groups during the intervention period but the difference did not quite reach significance (p = 0.06).

Only one small randomised controlled trial (N = 23) assessing fall efficacy was identified. The motor imagery practice approach employed was reported to significantly improve fall efficacy from baseline within the intervention group but the between-group difference was not significant (Dickstein et al 2013 [128]).

<table>
<thead>
<tr>
<th>Outcome Timeframe</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of fallers - Acute/subacute stage ³ ¹</td>
<td>Relative risk 1.19 (CI 95% 0.83 - 1.71) Based on data from 95 patients in 1 studies. ² (Randomized controlled) Follow up To discharge or independent walking</td>
<td>Control: 510 per 1000</td>
<td>Very Low Due to serious inconsistency, Due to serious indirectness, Due to serious risk of bias, Due to serious imprecision ³</td>
<td>We are uncertain whether exercise increases or decreases the number of fallers in the acute/subacute stage</td>
</tr>
<tr>
<td>Number of fallers - Chronic stage ⁴</td>
<td>Relative risk 1.02 (CI 95% 0.83 - 1.24) Based on data from 616 patients in 6 studies. ⁵ (Randomized controlled) Follow up 6 months to 1 year</td>
<td>Control: 413 per 1000</td>
<td>Low Due to serious risk of bias, Due to serious inconsistency ⁶</td>
<td>Exercise may have little or no difference on the number of fallers in the chronic stage</td>
</tr>
<tr>
<td>Rate of falls - acute/subacute stage (rate ratio) ⁷</td>
<td>Relative risk 0.92 (CI 95% 0.45 - 1.9) Based on data from 95 patients in 1 studies. (Randomized controlled) Follow up To discharge or independent walking</td>
<td>Control: 0.92</td>
<td>Very Low Due to serious risk of bias, Due to serious imprecision, Due to serious indirectness ⁸</td>
<td>We are uncertain whether exercise increases or decreases the rate of falls in acute/subacute stage</td>
</tr>
<tr>
<td>Rate of falls - chronic stage (rate ratio) ⁹</td>
<td>Relative risk 0.75 (CI 95% 0.41 - 1.38) Based on data from 412 patients in 4 studies. (Randomized controlled) Follow up Six months to one year</td>
<td>Control: 0.75</td>
<td>Low Due to serious risk of bias, Due to serious inconsistency ¹⁰</td>
<td>Exercise may have little or no difference on rate of falls in the chronic stage</td>
</tr>
<tr>
<td>Criticality</td>
<td>Measure</td>
<td>Quality of Life (QoL)</td>
<td>Falls Efficacy</td>
<td></td>
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<td>------------</td>
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<td>--------------------------------------------------------------------------------------</td>
<td>-----------------------------------------</td>
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</tr>
<tr>
<td>7</td>
<td>Critical</td>
<td>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 (Verheyden et al 2013). The majority of studies in this review failed to detect a difference in the QoL between stroke survivors receiving and not receiving exercise interventions designed to prevent falls.</td>
<td>A small RCT (N = 23) assessed the effects of a motor imagery practice approach, assessing fall-related self-efficacy using the Falls Efficacy Scale (Swedish version). Significant improvements from baseline were reported within the intervention group following treatment, but the between group difference was non-significant.</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Critical</td>
<td>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 (Verheyden et al 2013). The majority of studies in this review failed to detect a difference in the QoL between stroke survivors receiving and not receiving exercise interventions designed to prevent falls.</td>
<td>A small RCT (N = 23) assessed the effects of a motor imagery practice approach, assessing fall-related self-efficacy using the Falls Efficacy Scale (Swedish version). Significant improvements from baseline were reported within the intervention group following treatment, but the between group difference was non-significant.</td>
<td></td>
</tr>
</tbody>
</table>

1. See Analysis 1.2 of Verheyden (2013) Cochrane SR
3. Risk of bias: Serious . 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, (Outcome assessors were participants.) ; Inconsistency: Serious . NA. Only one study ; Indirectness: No serious . Yes similar population if target population is acute/subacute (rehab) patients. Other issue due to unreliable ascertainment of falls (retrospective recall of six months and three months falls history). ; Imprecision: Serious . Low number of patients (n = 95), Only data from one study ; Publication bias: No serious .
4. See Analysis 1.2 of Verheyden (2013) Cochrane SR
6. Risk of bias: Serious . Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, (Outcome assessors were participants.), Selective outcome reporting, 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. Ticked issues with sequence generation, concealment and selective outcome reporting due to Lau, Holmgren and Marigold. ; Inconsistency: Serious . Point estimates vary widely (for Lau and Holmgren), The direction of the effect is not consistent between the included studies ; Indirectness: No serious . Other issue due to unreliable ascertainment of falls (falls calendar). ; Imprecision: No serious . Wide confidence intervals (for Lau and Holmgren - only 2 out of 6) ; Publication bias: No serious .
7. See Analysis 1.1 of Verheyden (2013) Cochrane SR
8. Risk of bias: Serious . 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 . NA. Only one study ; Indirectness: No serious . Other issue due to unreliable ascertainment of falls (retrospective recall of six months and three months falls history). ; Imprecision: No serious . Only data from one study, Low number of patients ; Publication bias: No serious .
9. See Analysis 1.1 of Verheyden (2013) Cochrane SR
10. **Risk of bias:** Serious. Selective outcome reporting, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Inconsistency:** Serious. Point estimates vary widely, The direction of the effect is not consistent between the included studies, The magnitude of statistical heterogeneity was high, with I^2: 72%; **Indirectness:** No serious. Other issue due to unreliable ascertainment of falls (falls calendar); **Imprecision:** No serious. Wide confidence intervals (Lau 2012 - only 1 out of 4); **Publication bias:** No serious.

11. **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.

12. **Inconsistency:** Serious. Only one study so consistency can't be determined; **Indirectness:** No serious. Imprecision: Very Serious. Low number of patients, Only data from one study, between group differences and confidence intervals not reported; **Publication bias:** No serious.

References


17 - 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 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.

**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.

**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.

**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.

**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:** A 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.

**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.

**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.

**Rehabilitation:** Restoration of the disabled person to optimal physical and psychological functional independence.

**Risk factor:** A characteristic of a person (or people) that is positively associated with a particular disease or condition.

**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.

**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

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>ACE</td>
<td>Angiotensin-converting enzyme</td>
</tr>
<tr>
<td>ADL</td>
<td>Activities of daily living</td>
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<tr>
<td>AF</td>
<td>Atrial fibrillation</td>
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<td>AFO</td>
<td>Ankle foot orthosis</td>
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<td>BAO</td>
<td>Basilar artery occlusion</td>
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<td>BI</td>
<td>Barthel Index</td>
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<tr>
<td>BMI</td>
<td>Body mass index</td>
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<tr>
<td>BP</td>
<td>Blood pressure</td>
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<tr>
<td>CEA</td>
<td>Carotid endarterectomy</td>
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<tr>
<td>CEMRA</td>
<td>Contrast-enhanced magnetic resonance angiography</td>
</tr>
<tr>
<td>CI</td>
<td>Confidence interval</td>
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<tr>
<td>CIMT</td>
<td>Constraint induced movement therapy</td>
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<tr>
<td>CT</td>
<td>Computed tomography</td>
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<tr>
<td>CTA</td>
<td>Computed tomography angiography</td>
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<tr>
<td>CVD</td>
<td>Cardiovascular disease</td>
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<tr>
<td>DALY</td>
<td>Disability-adjusted life years</td>
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<tr>
<td>DBP</td>
<td>Diastolic blood pressure</td>
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<tr>
<td>DOAC</td>
<td>Direct oral anticoagulant</td>
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<td>DSA</td>
<td>Digital subtraction angiography</td>
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<td>DUS</td>
<td>Doppler ultrasonography</td>
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<tr>
<td>DVT</td>
<td>Deep vein thrombosis</td>
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<td>DWI</td>
<td>Diffusion-weighted imaging</td>
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<td>Abbreviation</td>
<td>Description</td>
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<tr>
<td>ECG</td>
<td>Electrocardiography</td>
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<td>ED</td>
<td>Emergency department</td>
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<td>EMG</td>
<td>Electromyographic feedback</td>
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<td>EMS</td>
<td>Emergency medical services</td>
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<td>ESD</td>
<td>Early supported discharge</td>
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<tr>
<td>ESS</td>
<td>European Stroke Scale</td>
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<tr>
<td>FAST</td>
<td>Face, Arm, Speech, Time</td>
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<td>FEES</td>
<td>Fibre-optic endoscopic examination of swallowing</td>
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<td>FeSS</td>
<td>Fever, Sugar, Swallowing</td>
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<tr>
<td>FFP</td>
<td>Fresh frozen plasma</td>
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<tr>
<td>FIM</td>
<td>Functional independence measure</td>
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<td>GP</td>
<td>General practitioner</td>
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<tr>
<td>HR</td>
<td>Hazard ratio</td>
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<td>HRQOL</td>
<td>Health related quality of life</td>
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<td>HRT</td>
<td>Hormone replacement therapy</td>
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<tr>
<td>IA</td>
<td>Intra-arterial</td>
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<td>ICH</td>
<td>Intracerebral haemorrhage</td>
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<tr>
<td>ICU</td>
<td>Intensive care unit</td>
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<tr>
<td>INR</td>
<td>International normalised ratio</td>
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<tr>
<td>IPC</td>
<td>Intermittent pneumatic compression</td>
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<tr>
<td>IV</td>
<td>Intravenous</td>
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<tr>
<td>LMWH</td>
<td>Low molecular weight heparin</td>
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<tr>
<td>LOS</td>
<td>Length of stay</td>
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<td>MCA</td>
<td>Middle cerebral artery</td>
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<td>Abbreviation</td>
<td>Description</td>
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<tr>
<td>MD</td>
<td>Mean difference</td>
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<tr>
<td>MI</td>
<td>Myocardial infarction</td>
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<tr>
<td>MNA</td>
<td>Mini Nutritional Assessment</td>
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<tr>
<td>MR</td>
<td>Magnetic resonance</td>
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<tr>
<td>MRA</td>
<td>Magnetic resonance angiography</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
</tr>
<tr>
<td>mRS</td>
<td>Modified rankin scale</td>
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<tr>
<td>MST</td>
<td>Malnutrition screening tool</td>
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<tr>
<td>MUST</td>
<td>Malnutrition universal screening tool</td>
</tr>
<tr>
<td>N</td>
<td>Number of participants in a trial</td>
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<td>NASCET</td>
<td>North American Symptomatic Carotid Endarterectomy Trial</td>
</tr>
<tr>
<td>NG</td>
<td>Nasogastric</td>
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<td>NHMRC</td>
<td>National Health and Medical Research Council</td>
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<tr>
<td>NIHSS</td>
<td>National Institutes of Health Stroke Scale</td>
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<tr>
<td>NMES</td>
<td>Neuromuscular electrical stimulation</td>
</tr>
<tr>
<td>NNH</td>
<td>Numbers needed to harm</td>
</tr>
<tr>
<td>NNT</td>
<td>Numbers needed to treat</td>
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<tr>
<td>OR</td>
<td>Odds ratio</td>
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<tr>
<td>OT</td>
<td>Occupational therapist</td>
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<tr>
<td>PBS</td>
<td>Pharmaceutical Benefits Scheme</td>
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<tr>
<td>PE</td>
<td>Pulmonary embolism</td>
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<tr>
<td>PEG</td>
<td>Percutaneous endoscopic gastrostomy</td>
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<tr>
<td>PFO</td>
<td>Patent foramen ovale</td>
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<tr>
<td>PPV</td>
<td>Positive predictive value</td>
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<td>Abbreviation</td>
<td>Description</td>
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<tr>
<td>QALYs</td>
<td>Quality-adjusted life years</td>
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<td>QOL</td>
<td>Quality of life</td>
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<tr>
<td>RCT</td>
<td>Randomised controlled trial</td>
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<tr>
<td>rFVIIa</td>
<td>recombinant activated factor VII</td>
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<td>RHS</td>
<td>Right hemisphere syndrome</td>
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<tr>
<td>ROC</td>
<td>Receiver operator curve</td>
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<td>ROM</td>
<td>Range of motion</td>
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<tr>
<td>ROSIER</td>
<td>Recognition of stroke in the emergency room</td>
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<tr>
<td>RR</td>
<td>Relative risk</td>
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<tr>
<td>RRR</td>
<td>Relative risk reduction</td>
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<td>rTMS</td>
<td>repetitive transcranial magnetic stimulation</td>
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<td>rt-PA</td>
<td>Recombinant tissue plasminogen activator</td>
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<td>SBP</td>
<td>Systolic blood pressure</td>
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<td>Subcutaneous</td>
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<td>SD</td>
<td>Standard deviation</td>
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<td>SES</td>
<td>Standardised effect size</td>
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<td>Subjective global assessment</td>
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<td>sICH</td>
<td>symptomatic intracerebral haemorrhage</td>
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<td>SMD</td>
<td>Standardised mean difference</td>
</tr>
<tr>
<td>SSS</td>
<td>Scandinavian stroke scale</td>
</tr>
<tr>
<td>TEE</td>
<td>Transoesophageal echocardiography</td>
</tr>
<tr>
<td>TIA</td>
<td>Transient ischaemic attack</td>
</tr>
<tr>
<td>TOE</td>
<td>Transoesophageal echocardiography</td>
</tr>
<tr>
<td>Acronym</td>
<td>Definition</td>
</tr>
<tr>
<td>-----------</td>
<td>-------------------------------------------</td>
</tr>
<tr>
<td>TOR-BSST</td>
<td>Toronto Bedside Swallowing Screening test</td>
</tr>
<tr>
<td>tPA</td>
<td>Tissue plasmogen activator</td>
</tr>
<tr>
<td>TTE</td>
<td>Transthoracic echocardiography</td>
</tr>
<tr>
<td>UFH</td>
<td>Unfractionated heparin</td>
</tr>
<tr>
<td>UK</td>
<td>United Kingdom</td>
</tr>
<tr>
<td>UL</td>
<td>Upper limb</td>
</tr>
<tr>
<td>VF or VFS</td>
<td>Videofluoroscopy</td>
</tr>
<tr>
<td>VR</td>
<td>Virtual reality</td>
</tr>
<tr>
<td>VTE</td>
<td>Venous thromboembolism</td>
</tr>
<tr>
<td>WMD</td>
<td>Weighted mean difference</td>
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