Stroke FOUNDATION

Clinical Guidelines for Stroke Management 2017

Chapter 2 of 8:
Early assessment and diagnosis

Main editor

Stroke Foundation

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This is the second in a series of eight Clinical Guideline chapters that provide evidence-based recommendations for recovery from stroke and TIA.

Contact

Stroke Foundation
Melbourne, Victoria, Australia
guidelines@strokefoundation.org.au
+61396701000

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Summary of recommendations

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Transient ischaemic attack

Strong Recommendation

- All patients with suspected transient ischaemic attack (TIA), i.e. focal neurological symptoms due to focal ischaemia that have fully resolved, should have urgent clinical assessment. (Lavallee et al. 2007 *[25]*; Rothwell et al. 2007 *[26]*) *(Refer to the 'Practical Information' section for further useful information)*
- Patients with symptoms that are present or fluctuating at time of initial assessment should be treated as having a stroke and be immediately referred for emergency department and stroke specialist assessment, investigation and reperfusion therapy where appropriate. (Lavallee et al 2007 *[25]*; Rothwell et al. 2007 *[26]*)
- In pre-hospital settings, high risk indicators (e.g. crescendo TIA, current or suspected AF, current use of anticoagulants, carotid stenosis or high $ABCD^2$ score) can be used to identify patients for urgent specialist assessment. (Lavallee et al. 2007 *[25]*; Rothwell et al. 2007 *[26]*)

Strong Recommendation

When TIA patients present to primary care, the use of TIA electronic decision support, when available, is recommended to improve diagnostic and triage decisions. (Ranta et al. 2015 *[15]*)

Weak Recommendation Against

In TIA patients, use of the $ABCD^2$ risk score in isolation to determine the urgency of investigation may delay recognition of atrial fibrillation and symptomatic carotid stenosis in some patients and should be avoided. (Wardlaw et al. 2015 *[8]*)

Strong Recommendation

All TIA patients with anterior circulation symptoms should undergo early carotid imaging with CT angiography (aortic arch to cerebral vertex), carotid Doppler ultrasound or MR angiography. Carotid imaging should preferably be done during the initial assessment but should not be delayed more than 2 days (see Imaging).

Weak Recommendation

Patients with TIA should routinely undergo brain imaging to exclude stroke mimics and intracranial haemorrhage. MRI, when available, is recommended to improve diagnostic accuracy (see Imaging).

Strong Recommendation

Patients with suspected TIA should commence secondary prevention therapy urgently (see Secondary Prevention).

Strong Recommendation

- All patients with TIA should be investigated for atrial fibrillation with ECG during initial assessment and referred for possible prolonged cardiac monitoring as required (see Cardiac Investigations).
- TIA patients with atrial fibrillation should commence anticoagulation therapy early after brain imaging has excluded haemorrhage, unless contraindicated (see Anticoagulant therapy in Secondary Prevention).

Practice Statement

Consensus-based recommendations

- All patients and their family/carers should receive information about TIA, screening for diabetes, tailored advice on lifestyle modification strategies (smoking cessation, exercise, diabetes optimisation if relevant – see Secondary prevention), return to driving (see Driving in Community participation and long-term care) and the recognition of signs of stroke and when to seek emergency care.
- All health services should develop and use a local TIA pathway covering primary care, emergency and stroke specialist teams to ensure patients with suspected TIA are managed as rapidly and comprehensively as possible within locally available resources.

Rapid assessment in the emergency department

Strong Recommendation

All suspected stroke patients who have been pre-notified to the stroke or ED team, and who may be candidates for reperfusion therapy, should be met at arrival and assessed by the stroke team or other experienced personnel. (Meretoja et al. 2012 *[40]*; Meretoja et al. 2013 *[39]*)

Weak Recommendation

The use of clinical screening tools to identify stroke by ED staff is recommended where an expert stroke team is unable to immediately assess a patient. (Jiang et al. 2014 *[33]*; Whiteley et al. 2011 *[34]*)

Recommendation Strength Not Set

Practice points

- Initial diagnosis should be reviewed by a clinician experienced in the evaluation of stroke.
- Stroke severity should be assessed and recorded on admission by a trained clinician using a validated tool (e.g. NIHSS).
- A blood glucose reading should be taken to improve specificity (hypoglycaemia can present as a 'stroke mimic').

Investigations

Imaging

Brain imaging

Strong Recommendation

All patients with suspected stroke who are candidates for reperfusion therapies should undergo brain imaging immediately. All other suspected stroke patients should have an urgent brain CT or MRI ('urgent' being immediately where facilities are available and preferably within 60 minutes). (Brazzelli et al. 2009 *[41]*)

Weak Recommendation

In patients with suspected stroke and TIA, MRI is more sensitive and specific than non-contrast CT and is the preferred modality when diagnostic confirmation is required. (Brazzelli et al. 2009 *[41]*)

Practice Statement

Consensus-based recommendation
Either CT or MRI are acceptable acute imaging options but these need to be immediately accessible to avoid delaying reperfusion therapies.

Strong Recommendation

If using CT to identify hyperdense thrombus, thin slice (< 2 mm) non-contrast CT should be used rather than the standard 5 mm slices to improve diagnostic sensitivity for vessel occlusion. (Mair et al. 2015 *[46]*)

Weak Recommendation

CT perfusion imaging may be used in addition to routine imaging to improve diagnostic and prognostic accuracy. (Biesbroek et al. 2012 *[49]*)

Recommendation Strength Not Set

Practice points

- If a patient with stroke develops neurological deterioration, immediate clinical assessment and further brain imaging (CT or MRI) should be considered.
- Routine brain imaging approximately 24 hours after reperfusion therapies have been administered is recommended to identify haemorrhagic transformation and delineate the extent of infarction, both of which are important when making decisions about antithrombotic therapy and DVT prophylaxis.

Vascular imaging

Strong Recommendation

- All patients who would potentially be candidates for endovascular thrombectomy should have vascular imaging from aortic arch to cerebral vertex (CTA or MRA) to establish the presence of vascular occlusion as a target for thrombectomy and to assess proximal vascular access. (Goyal et al. 2016 *[52]*; Broderick et al. 2013 *[58]*)
- All other patients with carotid territory symptoms who would potentially be candidates for carotid re-vascularisation should have early vascular imaging to identify stenosis in the ipsilateral carotid artery. CT angiography (if not already performed as part of assessment for reperfusion therapies), Doppler ultrasound or contrast-enhanced MR angiography are all reasonable options depending on local experience and availability. (Netuka et al. 2016 *[42]*; Chappell et al. 2009 *[43]*; Nonent et al. 2011 *[44]*; Anzidei et al. 2012 *[69]*)

Recommendation Strength Not Set

Practice points

- In ischaemic stroke and TIA patients, routinely imaging the entire vasculature from aortic arch to cerebral vertex with CTA or MRA is encouraged to improve diagnosis, recognition of stroke aetiology and assessment of prognosis.
- The administration of intravenous iodinated contrast for CT angiography/perfusion, when clinically indicated, should not be delayed by concerns regarding renal function. Post-hydration with intravenous 0.9% saline is advisable. (RANZCR guidelines 2016 *[64]*; Ang et al. 2015 *[63]*).

Recommendation Strength Not Set

Practice point

Vascular imaging should not be performed for syncope or other non-focal neurological presentations.

Cardiac investigations

Weak Recommendation

Initial ECG monitoring should be undertaken for all patients with stroke. The duration and mode of monitoring should be guided by individual patient factors but would generally be recommended for at least the first 24 hours. (Kurka et al. 2015 *[66]*)

Strong Recommendation

For patients with embolic stroke of uncertain source, longer term ECG monitoring (external or implantable) should be used. (Afzal et al. 2015 *[67]*)

Weak Recommendation

Further cardiac investigations should be performed where clarification of stroke aetiology is required after initial investigations. In patients with ischaemic stroke, echocardiography should be considered based on individual patient factors. Transoesophageal echocardiography is more sensitive for suspected valvular, left atrial and aortic arch pathology. (Holmes et al. 2014 *[68]*)

Glossary and abbreviations

Introduction

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

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

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

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

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

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

Purpose
The *Clinical Guidelines for Stroke Management 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 management, secondary prevention, rehabilitation, discharge planning, community participation, and management of TIA. Some issues are dealt with in more detail, particularly where current management is at variance with best practice, or where the evidence needs translation into practice.

The Clinical Guidelines do not cover:

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

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

Development
The Guidelines are published in eight separate chapters:
Pre-hospital care
Early assessment and diagnosis

Acute medical and surgical management
Secondary prevention
Rehabilitation
Managing complications
Discharge planning and transfer of care
Community participation and long-term care

The Clinical Guidelines have been developed according to processes prescribed by the National Health and Medical Research Council (NHMRC) under the direction of an interdisciplinary working group. Refer to the document on InformMe that details the Interdisciplinary Working Group Membership and Terms of Reference.

Use
The primary goal of the Clinical Guidelines is to help healthcare professionals improve the quality of the stroke care they provide. Refer to documents on InformMe that provide 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 (based on the 2017 version) by a number of organisations and associations. Refer to the document on InformMe that details the organisations formally endorsing the Clinical Guidelines.

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

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

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

Publication Approval

Australian Government
National Health and Medical Research Council

These guideline recommendations were approved by the Chief Executive Officer of the National Health and Medical Research Council (NHMRC) on 25 July 2017, with subsequent amendments approved on 22 November 2017, 9 July 2018 (updated recommendations for Neurointervention), and 7 November 2019 (updated recommendations for Thrombolysis, Acute antiplatelet therapy, and Patent foramen ovale management) 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 five years.

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

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

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

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

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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 may only be used in the context of research. We have done this because these are guidelines for clinical practice, and while the intervention cannot be recommended as standard practice at the current time, we recognise there is good rationale to continue further research.

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

	Strong Recommendation	Weak Recommendation
For patients	Most individuals in this situation would want the recommended course of action and only a small proportion would not.	The majority of individuals in this situat the suggested course of action, but ma
For clinicians	Most individuals should receive the recommended course of action. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.	Recognise that different choices will be different patients, and that you must he arrive at a management decision consis his values and preferences. Decision aid useful helping individuals making decisi with their values and preferences. Clini expect to spend more time with patien towards a decision.
For policy makers	The recommendation can be adapted as policy in most situations including for the use as performance indicators.	Policy making will require substantial d involvement of many stakeholders. Poli more likely to vary between regions. Pe indicators would have to focus on the f adequate deliberation about the manag has taken place.

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

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

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

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

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

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

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

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

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

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

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

Clinical questions

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

2.2 Do clinical assessment tools improve diagnostic accuracy in the emergency department?

2.3 What is the optimal modality for brain imaging for suspected acute stroke?

2.4 What is the optimal modality for cardiac investigations for possible atrial fibrillation?

2.5 What is the optimal modality for carotid/vascular imaging?

Early assessment and diagnosis - overview

The aim of assessment of a patient with suspected stroke or TIA is to:

- Confirm the diagnosis,
- Identify and treat the cause,
- Guide early rehabilitation, and
- Guide relevant early secondary prevention to prevent complications or stroke reccurrence.

Appropriate diagnosis and immediate referral to a stroke team is particularly important given advances in reperfusion therapies. Strong working relationships are required between emergency department staff and the stroke team to improve timely assessment and early management.

This chapter will discuss transient ischaemic attack, rapid assessment in the emergency department, and investigations (brain and vascular imaging and cardiac investigations).

Transient ischaemic attack

Transient ischaemic attack (TIA) is defined here as focal neurological symptoms due to focal ischaemia that have fully resolved. TIA is a medical emergency. The highest risk of stroke occurring following TIA is within the first 2 days. TIA requires rapid assessment and management to prevent stroke. If symptoms persist or are fluctuating at the time of assessment the patient should be managed as a stroke, including immediate assessment for reperfusion therapy and hospital admission.

Diagnostic work-up and implementation of optimal therapy for patients with suspected TIA should be completed within 24 hours. This requires diagnostic confirmation by a stroke specialist, ECG +/- prolonged monitoring and brain imaging (CT or MRI). According to current definitions, the finding of an ischaemic lesion on brain imaging is classified as a stroke even if symptoms have fully resolved. Patients with ischaemic lesions on diffusion MRI are at substantially higher risk of recurrent ischaemic events. If anterior circulation symptoms are present, carotid imaging (ultrasound, CTA, or MRA) is also indicated. Optimal timing for carotid endarterectomy (if required) is within 2 weeks of symptom onset.

Where specialist assessment and/or diagnostic work-up for all suspected TIA patients is not feasible within the above recommended time frames, alternative providers, ideally with support from stroke specialists and/or risk stratification to focus treatment on those at highest risk, may be required. It is highly recommended that all services develop a local TIA pathway involving primary care, emergency department, and stroke specialist teams to ensure patients are managed as rapidly and comprehensively as possible matching locally available resources. Several highly effective TIA service models have been described to suit a variety of settings (Ranta and Barber 2016 *[28]*). Ongoing education around TIA for all involved providers is important. Smaller centres are encouraged to partner with larger services to assist with the establishment of such pathways.

Where GPs are confident about identifying all potential TIA's and have access to specialist assessment within 24 hours for all referred patients, it is unclear whether the use of a risk score adds clinical value and it is reasonable to rely on clinical assessment alone. In settings where GPs would benefit from diagnostic aid and/or where specialist review may be delayed by >1 day, the use of the stroke/TIA electronic decision support tool should be considered. If the tool is unavailable, but immediate access to a specialist cannot be guaranteed, the GP can use any one of the following criteria to identify patients who require immediate hospital referral: ongoing focal neurological symptoms, >1 TIA over past 7 days, presence of atrial fibrillation, patient treated with anticoagulants or $ABCD^2$ score >3. For any patients likely to access specialist assessment with >1 day delay the GP should initiate best medical therapy immediately (antiplatelet, antihypertensive, statin – anticoagulants require brain imaging before initiation) and counsel on smoking cessation and driving implications.

In the most recent clinical audit of stroke services in Australia, 81 out of 108 hospitals reported having defined and documented processes, policies or clinical pathways for assessing TIA patients (Stroke Foundation 2015 *[7]*). 26% of hospitals admitted all patients suspected of having TIA directly to hospitals, while 73% admitted only selected patients to hospitals (Stroke Foundation 2015 *[7]*). 25 hospitals had rapid assessment TIA clinics. Although the aim of the clinics is to assess and manage patients within 48 hours, the average waiting time for an appointment to a clinic was 4 days (Stroke Foundation 2015 *[7]*).

Strong Recommendation

- All patients with suspected transient ischaemic attack (TIA), i.e. focal neurological symptoms due to focal ischaemia that have fully resolved, should have urgent clinical assessment. (Lavallee et al. 2007 *[25]*; Rothwell et al. 2007 *[26]*) *(Refer to the 'Practical Information' section for further useful information)*
- Patients with symptoms that are present or fluctuating at time of initial assessment should be treated as having a stroke and be immediately referred for emergency department and stroke specialist assessment, investigation and reperfusion therapy where appropriate. (Lavallee et al 2007 *[25]*; Rothwell et al. 2007 *[26]*)
- In pre-hospital settings, high risk indicators (e.g. crescendo TIA, current or suspected AF, current use of anticoagulants, carotid stenosis or high $ABCD^2$ score) can be used to identify patients for urgent specialist assessment. (Lavallee et al. 2007 *[25]*; Rothwell et al. 2007 *[26]*)

Practical Info

Distinguishing transient ischemic attack (TIA) from other presentations:

The most useful approach to appropriate resource allocation in the investigation of patients with suspected TIA is an accurate clinical diagnosis. Confident diagnosis of alternative causes for transient neurological symptoms will avoid unnecessary investigations and allow institution of appropriate management. If the most likely diagnosis is truly TIA then urgent investigation is required (even if a risk stratification score such as $ABCD^2$ suggests “low risk”). Careful clinical assessment will also allow more targeted investigations (e.g. suspicion of posterior circulation TIA should lead to CT angiography as carotid Doppler will not

adequately assess the posterior circulation).

TIA involves the sudden onset of a focal neurological deficit: weakness, numbness (not paraesthesia in isolation), visual loss, speech disturbance, etc. The average duration is approximately 10 minutes but all symptoms must be fully resolved within 24 hours. Carefully distinguishing dysphasia (language disturbance – incorrect word use or loss of comprehension) from dysarthria (poor articulation) is useful as dysphasia is specific and localising whereas dysarthria can be non-specific.

Common TIA mimics:
Migraine aura – can cause migratory neurological phenomena that move from one part of the body to an adjacent region over several minutes and these are often recurrent. "Positive" neurological symptoms are a key feature of migraine i.e. paraesthesia, visual flashes/blur, etc. Headache may be mild or absent but, if present, significantly reduces the probability of symptoms being due to TIA. While migraine aura may manifest as limb weakness or dysphasia, a first occurrence of these symptoms should prompt further investigation as for TIA.

Benign paroxysmal positional vertigo (BPPV) – isolated vertigo is very rarely ischaemic in origin (i.e. vertigo without associated ataxia, diplopia, dysarthria, numbness or weakness). "Dizzy" patients require careful questioning to distinguish the sense of motion that defines vertigo from non-specific light-headedness (which is not a feature of TIA). Brief, positionally provoked vertigo is usually due to BPPV and can be diagnosed and then treated with a Hallpike and Epley manoeuvre. Non-vertiginous dizziness often relates to blood pressure changes and is not an indication for carotid vascular imaging.

Transient global amnesia (TGA) – isolated anterograde amnesia with repetitive questioning, without loss of personal identity (which would indicate psychogenic fugue) and with otherwise normal neurological function generally indicates TGA rather than TIA. This is not associated with an increased risk of stroke.

Syncope – loss of consciousness and pre-syncopal sensations in the absence of focal neurology should not be considered TIA. Although very rarely a basilar artery territory TIA could lead to loss of consciousness, there should be evidence of focal posterior circulation symptoms before or after the loss of consciousness e.g. diplopia, vertigo, weakness, or numbness. Patients with prior cerebrovascular disease who experience syncope can develop focal neurology after the event related to hypoperfusion. However, a focal presentation would generally require investigation as a TIA.

Hypoglycaemia – very low blood glucose levels occasionally lead to focal neurology in addition to more typical hypoglycaemic symptoms of diaphoresis and confusion and this should be considered in the differential diagnosis of TIA in diabetic patients taking medications that predispose them to hypoglycaemia.

Delirium – most episodes of delirium last too long to be a TIA. Delirium is characterised by altered attention/conscious state without focal neurology (apart from perhaps dysarthria) which is inconsistent with TIA. However, in patients with prior stroke, focal deficits may re-emerge and complicate assessment. Careful questioning is required to distinguish non-focal "confusion" (disorientation to time/place/person) from focal dysphasia or inattention that may be indicative of true TIA.

Amyloid "spells" – these events may perfectly mimic TIA but are often recurrent and stereotyped and may exhibit migrainous-like spread from one body region to another. They are due to cerebral amyloid angiopathy which can cause focal "convexal" subarachnoid haemorrhage. This is not associated with headache but can generate cortical spreading depression and migratory phenomena similar to migraine aura. CT brain (and preferably susceptibility-weighted MRI) is therefore essential to avoid harmful use of antithrombotics.

Focal seizure activity – seizures are usually distinguishable from TIA. "Positive" symptoms – clonic or myoclonic jerks, colourful/and or pulsating visual phenomena and migration of symptoms over seconds to 1–2 minutes are clinical clues. An unwitnessed seizure can be followed by Todd's paresis (weakness, dysphasia, etc.) which may resolve over a time period similar to a TIA but is generally accompanied by a postictal drowsy and confused state with amnesia. Very occasionally, a TIA can present with limb shaking as a hypoperfusion phenomenon (e.g. critical carotid stenosis). These events usually have identifiable provoking factors that lead to drops in BP (changes in posture, blood pressure lowering medication, heavy meal, etc.) and do not involve the face.

Functional disorders – these can be challenging but more often present with ongoing symptoms and therefore enter the differential diagnosis of stroke more than TIA. "Collapsing" weakness and positive Hoover's sign are useful if examined during the event. Symptoms of dissociation ("out of body" or "loss of contact") and bilateral extremity paraesthesia (hyperventilation) may be useful.

Key Info

Benefits and harms

Substantial net benefits of the recommended alternative

The risk of stroke is greatest in the first few hours and days after a TIA. Two studies in UK and France using historical controls reported an 80% risk reduction in recurrent stroke at 90 days when rapid access clinics to assess, investigate and initiate intensive secondary prevention medications were established (Lavallee et al. 2007 *[25]*; Rothwell et al. 2007 *[26]*). There were no harms identified.

Certainty of the Evidence Moderate

The evidence is largely based on non-randomised studies comparing stroke incidence following TIA before and after implementing rapid access TIA management or comparing outcomes to historical controls (Lavallee et al. 2007 *[25]*; Rothwell et al. 2007 *[26]*). This introduces a potential risk of bias that could result in overestimation of the treatment effect without accounting for other factors that may have reduced post-TIA stroke risk over recent years (e.g. more widespread use of cardiovascular risk management at baseline), and the comparators may not represent the true baseline rate of recurrent stroke. However, the large size of effect makes us moderately confident that it was effective in reducing recurrent stroke.

Preference and values Substantial variability is expected or uncertain

Some patients may prefer to be managed by their general practitioner closer to home or may experience barriers to rapidly accessing specialists. This needs to be considered when designing local patient focussed services, keeping in mind that the best evidence available does indicate that outcomes are optimised if early specialist or specialist assisted assessment is achieved.

Resources and other considerations No important issues with the recommended alternative

Resources considerations

There is evidence from a single centre study conducted in Australia that non-admission based care with follow-up in an outpatient clinic was more effective in terms of strokes prevented and cost-saving compared to admission-based care for patients presenting to the emergency department with suspected TIA (Sanders et al. 2015 *[29]*).

Implementation consideration

There are organisational indicators collected in the National Stroke Audit on whether hospitals have defined and documented processes, policies or clinical pathways for assessing suspected TIA patients. Organisational indicators are also collected on whether all, or only selected, TIA patients are admitted to hospital.

Rationale

Transient ischaemic attacks (TIA) are predictors for subsequent stroke. The risk of stroke is greatest in the first few hours and days after a TIA. The high risk of disabling and fatal stroke within a few days of a TIA is the basis for recommending urgent intervention. This means that patients with potential TIA should be medically assessed as soon as they present and those with symptoms consistent with TIA investigated promptly. If not immediately available, investigations should be completed within 2 days. Two non-randomised studies showed rapid assessment and management of TIA patients could potentially reduce recurrent stroke (Lavallee et al. 2007 *[25]*; Rothwell et al. 2007 *[26]*).

Clinical Question/ PICO

Population: All adults with suspected TIA
Intervention: Rapid assessment and treatment
Comparator: Control

Summary

One UK study (EXPRESS) measured the rate of recurrent stroke before and after the set-up of a TIA clinic, in which patients with suspected TIA were immediately assessed and treated (Rothwell et al. 2007 *[26]*). The 90-day risk of recurrent stroke in the patients referred to the study clinic was 10.3% (32/310 patients) before the clinic and 2.1% (6/281 patients) after (adjusted hazard ratio 0.20, 95% CI 0.08-0.49; p=0.0001). The reduction in risk was independent of age and sex, and early treatment did not increase the risk of intracerebral haemorrhage or other bleeding. A French study (SOS-TIA) set up a 24/7 rapid TIA clinic attached to a large urban stroke unit hospital (Lavallee et al. 2007 *[25]*). They also found an 80% reduction in 90-day recurrent stroke rate compared to that predicted by the $ABCD^2$ tool (1.24% actual vs 5.96% expected risk).

Both studies have high methodological quality but it is questionable if the comparators represent the true rate of recurrent stroke in the population. On the other hand, the large scale of risk reduction still shows that rapid assessment and treatment is likely to be beneficial for patients with suspected TIA.

Outcome Timeframe	Study results and measurements	Absolute effect estimates Control	 Rapid assessment and treatment	Certainty of the Evidence (Quality of evidence)	Plain text summary
Recurrent stroke 90 days 8 Critical	Based on data from 2,357 patients in 2 studies.	Two non-randomised studies evaluated rapid assessment and treatment of TIA and both found significant reduction of recurrent stroke of around 80%.		Moderate Potential risk of bias, and upgraded due to Very large magnitude of effect [1]	Rapid assessment and management of suspected TIA patients probably reduces recurrent stroke

1. **Risk of bias: Serious .** For observational studies, these two have high methodological quality; the comparator was recurrent stroke rate before the intervention, and recurrent stroke predicted by ABCD2 which may introduce confounding ; **Inconsistency: No serious . Indirectness: No serious . Imprecision: No serious . Publication bias: No serious . Upgrade: Very large magnitude of effect .**

References

[25] Lavallée PC, Meseguer E, Abboud H, Cabrejo L, Olivot J-M, Simon O, Mazighi M, Nifle C, Niclot P, Lapergue B, Klein IF, Brochet E, Steg PG, Lesèche G, Labreuche J, Touboul P-J, Amarenco P : A transient ischaemic attack clinic with round-the-clock access (SOS-TIA): feasibility and effects.. The Lancet. Neurology 2007;6(11):953-60 Pubmed

[26] Rothwell PM, Giles MF, Chandratheva A, Marquardt L, Geraghty O, Redgrave JNE, Lovelock CE, Binney LE, Bull LM, Cuthbertson FC, Welch SJV, Bosch S, Alexander FC, Carasco-Alexander F, Silver LE, Gutnikov SA, Mehta Z : Effect of urgent treatment of transient ischaemic attack and minor stroke on early recurrent stroke (EXPRESS study): a prospective population-based sequential comparison.. Lancet (London, England) 2007;370(9596):1432-42 Pubmed

Strong Recommendation

When TIA patients present to primary care, the use of TIA electronic decision support, when available, is recommended to improve diagnostic and triage decisions. (Ranta et al. 2015 *[15]*)

Practical Info

Stroke/TIA decision support tool

The evidence-based Stroke/TIA decision support tool referred to in the new Stroke Guidelines is provided by BPAC Clinical Solutions. BPAC Clinical Solutions has been developing health informatics software for primary care, designed specifically to support health practitioners in the management of patients. BPAC Clinical Solutions' clinically led team has pioneered a range of proven solutions, including screening, risk assessment and management, referrals, and analytics, and these are fully integrated into the existing workflow and clinical software, ensuring a seamless user experience.

The Stroke/TIA integrated decision support tool has been available to GP practices around New Zealand since its national launch in July 2015. Approximately 1000 practices now have access to the module and it has been used to assist clinician decision-making for over 1800 patients to date.

The tool consists of a data entry form and an expert-generated guideline-based computer algorithm. The tool provides diagnostic help, triage advice, and prompts immediate prescription of best medical therapy.

A three-minute instructional video demonstrating the functionality available in the New Zealand tool can be watched at www.bestpractice.net.nz/stroke-tia

How to access to access the TIA/Stroke module:

Australia

BPAC Clinical Solutions is looking to release the Stroke/TIA integrated clinical decision support tool in Australia in 2018.

BPAC Clinical Solutions already delivers electronic referrals in Australia via its SeNT (Secure Electronic Network Transfer) project in Queensland, New South Wales and Victoria. BPAC Clinical Solutions has been integrated with a number of GP software systems in Australia as well as HHS software providers, and is linked with Health Pathways. Depending on the GP practice software, the module will be launched in the context of the selected patient in the practice software and pre-populate with relevant information from the patient's medical record.
Until the release of the practice management integrated version the tool will be available as a stand-alone web application demonstration via the following link: https://www.bestpractice.org.nz/nl_login.asp?guideline=card_stroke_tia
For any queries about the BPAC Clinical Solutions Stroke/TIA tool or other Australian products, please contact the team on Freephone 1800 852 481 or email info@bpacsolutions.com

Key Info

Benefits and harms — Substantial net benefits of the recommended alternative

TIA electronic decision support is intended to assist primary care providers in optimising early assessment and management of patients with TIA and stroke. Use of the tool improves guideline adherence and reduces secondary stroke (30 per 1000) without increasing adverse events (Ranta et al. 2015 *[15]*).

Certainty of the Evidence — Moderate

This evidence is based on a cluster randomised controlled trial; the only randomised controlled trial in the TIA literature around optimising patient management in primary care (Ranta et al. 2015 *[15]*). There are some methodological limitations related to the cluster design and moderate sample size.

Preference and values — Substantial variability is expected or uncertain

It is very likely that patients prefer being managed in accordance with guidelines and having the reassurance that a TIA diagnosis is not overlooked by their GP. In addition, some patients may prefer comprehensive management in primary care avoiding hospital referral if a TIA diagnosis is unlikely or even if a diagnosis is confirmed in a setting where specialist access is challenging and the general practitioner can access all of the required interventions. Other patients may prefer having the reassurance of being assessed by a specialist for potential TIA regardless of the likelihood of this concern being justified.

Resources and other considerations — No important issues with the recommended alternative

Resources considerations
There is evidence that TIA electronic decision support in primary care is cost-saving, with average costs per patient being NZ$1,470 lower in supported clinics than in clinics not provided with this support (cost reference year 2012) (Ranta et al. 2014 *[15]*).

Rationale

Only one cluster randomised controlled trial investigated decision support tools in primary care to improve patient outcomes, and it was shown to significantly reduce stroke occurrence with no increase in adverse events (Ranta et al. 2015 *[15]*). Moreover, most of the patients would prefer to have their potential TIA managed in accordance with best-practice guidelines.

Clinical Question/ PICO

Population: All adults with suspected TIA in primary care setting
Intervention: Decision support tool
Comparator: Confirmed diagnosis of recurrent stroke

Summary

The study on an electronic decision support tool from Ranta et al. (2015) *[15]* is the only randomised controlled trial on this topic. It provides moderate evidence on a safe and potentially effective tool in reducing stroke occurrence when used in the primary care setting.

Our literature search identified a number of studies on diagnostic performance of TIA recognition tools but none of them showed superior performance. The Dawson score (Lassersen et al. 2015 *[16]*) achieved high sensitivity of 92.3% but low specificity of 18.1% in 513 suspected TIA referrals from primary care. However, it was retrospectively assessed by a research team based on primary care referral notes which may not reflect the accuracy when used prospectively by primary care clinicians. The assessors were not blinded either, which raises concerns for detection bias. Sung et al (2011) *[18]* assessed six symptom-related questions on The Questionnaire for Verifying Stroke-Free Status (QVSS) in 155 patients referred from secondary services. The sensitivity of answering 'yes' to at least one of any of the six symptom questions was 0.82, and the specificity was 0.62. However, it has similar issues of detection bias and directness of evidence. Clarey et al. (2014) *[17]* calculated the absolute cardiovascular risk (ACVR) score for 179 participants presenting as possible TIA and minor stroke in Australian general practices. They did not find improved diagnostic accuracy of ACVR beyond that of age and sex.

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Confirmed diagnosis of recurrent stroke	Decision support tool	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
Occurrence of stroke 90 days 8 Critical	Odds Ratio 0.27 (CI 95% 0.05 - 1.41) Based on data from 291 patients in 1 studies. [1] (Randomized controlled) Follow up 90 days	42 per 1000	12 per 1000 Difference: **30 fewer** per 1000 (CI 95% 40 fewer - 16 more)	**Moderate** Some imprecision and possible risk of bias [2]	TIA decision support tool probably decreases occurrence of stroke
Adverse events [3] 7 Critical	Odds Ratio 1.25 (CI 95% 0.48 - 3.24) Based on data from 291 patients in 1 studies. (Randomized controlled)	42 per 1000	52 per 1000 Difference: **10 more** per 1000 (CI 95% 21 fewer - 82 more)	**Moderate** Due to serious risk of bias [4]	TIA recognition tool in primary care probably has little or no difference on adverse events

1. Primary study [15]. **Baseline/comparator::** Control arm of reference used for intervention .
2. **Risk of bias: No serious .** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias ; **Inconsistency: No serious . Indirectness: No serious . Imprecision: Serious .** Only data from one study, Wide confidence intervals ; **Publication bias: No serious .**
3. Any event in which the tool's diagnosis or triage recommendations may have adversely affected patients.
4. **Risk of bias: Serious .** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias ; **Inconsistency: No serious . Indirectness: No serious . Imprecision: No serious .** Wide confidence intervals and only one study, but the this outcome is less critical: all adverse events were from medication side effects and reversible ; **Publication bias: No serious .**

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Weak Recommendation Against

In TIA patients, use of the ABCD^2 risk score in isolation to determine the urgency of investigation may delay recognition of atrial fibrillation and symptomatic carotid stenosis in some patients and should be avoided. (Wardlaw et al. 2015 *[8]*)

Key Info

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

Several risk scores have been proposed to stratify the risk of recurrent ischaemic events and have sometimes been used as a means of prioritising the urgency of investigation for TIA. However, studies have indicated that the most commonly used risk score (ABCD^2) and its more recent adaptations (e.g. ABCD^3) classify an important proportion of TIA patients with atrial fibrillation and symptomatic carotid stenosis in the "low risk" category, potentially exposing them to detrimental treatment delays and risk of recurrent ischaemic events (Wardlaw et al. 2015 *[8]*; Sanders et al. 2012 *[9]*; Galvin et al. 2011 *[10]*; Merwick et al. 2010 *[24]*).

Certainty of the Evidence — Moderate

Moderate quality of evidence from multiple systematic reviews of observational studies with large sample size reporting similar results (downgraded for statistical heterogeneity).

Preference and values — No substantial variability expected

Areas of major debate
Some clinicians argue that risk stratification tools have such low utility they should not be used when appropriate referrals and subsequent specialist assessments can be made. However, others believe they have value in supporting primary care physicians' decision-making when considered along with other high risk indicators.

Resources and other considerations — No important issues with the recommended alternative

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

Implementation considerations
There is an organisational indicator collected in the National Stroke Audit on whether patient selection for admission incorporates one of the published TIA risk stratification scores.

Rationale

Risk stratification in TIA patients has been used in the past in an attempt to prioritise rapid investigation of high-risk patients in settings with limited resources. However, approximately 25% of patients classified as "low risk" for recurrent ischaemic events by ABCD^2 have atrial fibrillation or symptomatic carotid stenosis which requires an important change in management (Wardlaw et al. 2015 *[8]*; Sanders et al. 2012 *[9]*; Galvin et al. 2011 *[10]*). These factors can only be identified through investigations, which challenges the validity of resource prioritisation for TIA patients.

The major challenge in TIA is diagnostic specificity, i.e. ensuring that resources are appropriately focused on patients likely to have true ischaemic aetiology rather than non-specific symptoms. There may be some role for clinical scores to improve diagnostic accuracy in settings that lack rapid access to specialist assessment.

In the environment of immediate assessment in an emergency department or dedicated TIA clinic, investigation of patients with true TIA should occur immediately and prioritisation is not relevant.

Clinical Question/ PICO

Population: All adults with suspected TIA
Intervention: Risk prediction scores
Comparator: Confirmed diagnosis of recurrent stroke

Summary

ABCD² is by far the most extensively studied risk prediction score for recurrent stroke in adults with suspected TIA. A meta-analysis of 13,766 TIA patients from 29 studies showed that the ABCD² score probably did not reliably discriminate those at low and high risk of recurrent stroke, and did not identify patients with carotid stenosis or AF needing urgent intervention (Wardlaw et al. 2015 *[8]*). Other systematic reviews came to similar conclusion. Sanders et al. (2012) *[9]* found a high sensitivity of 0.89 (0.87–0.91) and low specificity of 0.34 (0.33–0.35) for the cutoff value of 4. At 5% baseline stroke risk, ABCD² > 3 indicated an absolute increase in 7-day stroke risk of only 2.0% while a score ?equal or less than 3 indicated a 2.9% decrease in risk. Galvin et al. (2011) *[10]* also indicated over-prediction of recurrent stroke in all risk categories at 90 days.

There are a number of risk prediction tools in the literature. Perry et al. (2014) *[13]* prospectively enrolled and analysed 3906 patients, and derived a Canadian TIA score that consists of 13 variables. They reported a c-statistic of 0.77 (95% confidence interval, 0.73–0.82) for prediction of subsequent stroke within 7 days (c-statistics indicate discrimination better than chance at >0·5). Arsava et al. (2011) *[14]* calculated used a Web-based stroke recurrence estimator (http://www.nmr.mgh.harvard.edu/RRE/) in a retrospective series of 257 patients and found the sensitivity and specificity of a score of >=2 for predicting 7-day stroke risk were 87% and 73%, respectively. Merwick et al. (2010) *[24]* proposed an ABCD³ score based on preclinical information and ABCD ^{3}-I based on imaging and other secondary care assessments. N = 2654 patients were included in the derivation sample and 1232 in the validation sample. ABCD³ score (range 0-9 points) was derived by assigning 2 points for dual transient ischaemic attack (an earlier transient ischaemic attack within 7 days of the index event). C statistics for the ABCD³ score were 0·78 at 2 days, 0·80 at 7 days, 0·79 at 28 days, and 0·77 at 90 days, compared with C statistics for the ABCD² score of 0·71 at 2 days (p=0·083), 0·71 at 7 days (p=0·012), 0·71 at 28 days (p=0·021), and 0·69 at 90 days (p=0·018). Stenosis of at least 50% on carotid imaging (2 points) and abnormal DWI (2 points) were added to the ABCD³-imaging (ABCD³-I) score (0-13 points). Note that with the change in definition of TIA these DWI positive patients would now be diagnosed as having a minor stroke. C statistics for the ABCD³-I score were 0·90 at 2 days (compared with ABCD² score p=0·035), 0·92 at 7 days (p=0·001), 0·85 at 28 days (p=0·028), and 0·79 at 90 days (p=0·073). The 90-day net reclassification improvement compared with ABCD² was 29·1% for ABCD³ (p=0·0003) and 39·4% for ABCD³-I (p=0·034). Dai et al. (2015) *[12]* suggested replacing the use of clinical history of more than one TIA with more than one DWI lesion on separate occasions or in different locations would increase predictive accuracy and net reclassification value for 90-day stroke risk. However, none of these tools has shown satisfactory performance that can be replicated across different settings and populations.

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Confirmed diagnosis of recurrent stroke Risk prediction scores	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
Prediction of stroke 7 days, 90 days or greater 7 Critical	Based on data from 13,766 patients in 29 studies.	The sensitivity of the ABCD2 score equal or greater than 4 to predict stroke was 86.7 (95% CI 81.4–90.7) at 7 days and 85.4 (95% CI 81.1–88.9) at 90 days; specificity was 35.4 (95% CI 33.3–38.3) at 7 days and 36.2 (95% CI 34.0–37.6) at 90 days. Additionally, 20% of patients with ABCD2 <4 had >50% carotid stenosis or atrial fibrillation (AF).	**Moderate** Due to serious inconsistency [1]	The ABCD2 score probably does not reliably discriminate those at low and high risk of recurrent stroke, or identify patients with carotid stenosis or AF needing urgent

		intervention

1. **Risk of bias: No serious .** Methodological quality of included studies varies but mostly high quality diagnostic studies. ; **Inconsistency: Serious .** The magnitude of statistical heterogeneity was high, with I^2 > 90 %. ; **Indirectness: No serious . Imprecision: No serious . Publication bias: No serious .**

References

[8] Wardlaw JM, Brazzelli M, Chappell FM, Miranda H, Shuler K, Sandercock PAG, Dennis MS : ABCD2 score and secondary stroke prevention. Neurology 2015;85(4):373-380 Journal Website

Strong Recommendation

All TIA patients with anterior circulation symptoms should undergo early carotid imaging with CT angiography (aortic arch to cerebral vertex), carotid Doppler ultrasound or MR angiography. Carotid imaging should preferably be done during the initial assessment but should not be delayed more than 2 days (see Imaging).

Rationale

In TIA patients, early cerebrovascular imaging (CTA or MRA from aortic arch to cerebral vertex) is indicated. The presence of vascular stenosis or occlusion helps distinguish true ischaemic events from mimics and places these patients in the highest risk category for recurrent events and symptom progression (Coutts et al. 2012 *[21]*). It may also guide intensive secondary prevention (e.g. dual antiplatelets for those with significant intracranial stenoses) (Kamal et al. 2015 *[27]*).

As a minimum requirement, carotid imaging for patients with carotid territory TIA (e.g. Doppler ultrasound) is essential to identify symptomatic carotid lesions, as patients with TIA and carotid stenosis of at least 50% ipsilateral to the involved brain tissue should be considered for carotid endarterectomy.

Timely assessment is important as the risk of recurrent stroke or stroke progression is highest in the first few hours to days after TIA or minor stroke. Carotid endarterectomy is most effective when performed early (see Carotid surgery in the Secondary Prevention chapter). Urgent investigation may be facilitated by management in an emergency department or dedicated TIA clinic. When patients have presented in a delayed manner, investigation within 2 days may be acceptable.

Weak Recommendation

Patients with TIA should routinely undergo brain imaging to exclude stroke mimics and intracranial haemorrhage. MRI, when available, is recommended to improve diagnostic accuracy (see Imaging).

Rationale

The importance of brain imaging in TIA has been controversial as it affects management only in a minority of patients. However, improved diagnostic and prognostic accuracy, reassurance of absence of a cerebral haemorrhage (including focal subarachnoid bleeding related to amyloid angiopathy as a cause of transient symptoms) and exclusion of mimics are important in any setting, and therefore brain imaging is recommended. Where anticoagulation is being considered, brain imaging is especially important given the greater risk of intracerebral haemorrhage. When available, MRI has greater sensitivity and specificity in this patient population.

Strong Recommendation

Patients with suspected TIA should commence secondary prevention therapy urgently (see Secondary Prevention).

Rationale

Any delay in the initiation in secondary prevention has been associated with worse patient outcomes in the form of a higher rate of early stroke recurrence and thus it is recommended that all relevant secondary preventive medications are started as soon as possible, even though the diagnosis may still carry some degree of uncertainty. The only exception is anticoagulant therapy, which requires a head CT scan before such therapy is instituted to exclude an intracerebral haemorrhage (Rothwell et al. 2007 *[26]*).

Strong Recommendation

- All patients with TIA should be investigated for atrial fibrillation with ECG during initial assessment and referred for possible prolonged cardiac monitoring as required (see Cardiac Investigations).
- TIA patients with atrial fibrillation should commence anticoagulation therapy early after brain imaging has excluded haemorrhage, unless contraindicated (see Anticoagulant therapy in Secondary Prevention).

Rationale

The detection of atrial fibrillation in TIA patients is important to maximise secondary stroke prevention. Where atrial fibrillation is identified, prescription of anticoagulation has been associated with significant reduction in subsequent stroke.

Practice Statement

Consensus-based recommendations

- All patients and their family/carers should receive information about TIA, screening for diabetes, tailored advice on lifestyle modification strategies (smoking cessation, exercise, diabetes optimisation if relevant – see Secondary prevention), return to driving (see Driving in Community participation and long-term care) and the recognition of signs of stroke and when to seek emergency care.
- All health services should develop and use a local TIA pathway covering primary care, emergency and stroke specialist teams to ensure patients with suspected TIA are managed as rapidly and comprehensively as possible within locally available resources.

Rationale

Behavioural counselling on diabetic control and diet, exercise and smoking cessation are important components of secondary stroke prevention following TIA and should be incorporated in all management plans. Written information can help provide the patient more detailed information and can also reiterate the importance of seeking care urgently should symptoms recur. Driving restrictions apply following a TIA and need to be clearly communicated to patients to minimise risks of injury to self and others.

TIA management can be complex and routinely involves many providers across several sectors. The better coordinated these services are across this continuum, the faster and more effectively patients can access best medical care minimising the risk of secondary stroke. In addition, different environments face different geographic, logistic, and resource challenges. All of these factors should be considered when implementing a comprehensive, cohesive, well-coordinated, and locally tailored TIA service to best meet the area's population needs and achieve the best patient outcomes.

Rapid assessment in the emergency department

Initial clinical assessment remains the cornerstone in the diagnosis of stroke and TIA. Further investigations and brain imaging are undertaken to confirm the diagnosis and are essential for a decision on intervention, but the initial assessment at a minimum determines whether the patient has acute, focal or neurological deficits.

There are a number of clinical assessment tools available for emergency department staff, such as ROSIER, FAST and NIHSS. The reliability of assessment tools improves with experience and confidence, suggesting the need for a close working relationship between emergency department staff and stroke specialists, and the development of rapid referral processes.

The use of blood biomarkers for diagnostic purposes has been studied, however the evidence is inadequate to support their use in place of imaging to confirm the diagnosis of stroke and differentiate ischaemic stroke from intracerebral haemorrhage (An et al. 2013 *[35]*; Whiteley et al. 2011 *[36]*; Vanni et al. 2011 *[37]*). With the advent of effective endovascular therapy for patients with large artery occlusion, there has also been growing interest in clinical scales to identify patients likely to have large vessel occlusion. However, no clinical scale has adequate diagnostic performance for this purpose (Turc et al. 2016 *[30]*; Perez 2014 *[32]*)

According to the most recent clinical audit of stroke patients, 96 out of 108 hospitals reported having emergency department protocols for rapid triage for patients presenting with acute stroke, and 38% of patients were assessed in the emergency department (Stroke Foundation 2015 *[7]*).

Strong Recommendation

All suspected stroke patients who have been pre-notified to the stroke or ED team, and who may be candidates for reperfusion therapy, should be met at arrival and assessed by the stroke team or other experienced personnel. (Meretoja et al. 2012 *[40]*; Meretoja et al. 2013 *[39]*)

Key Info

Benefits and harms — Substantial net benefits of the recommended alternative

A rapid assessment protocol in a Helsinki hospital reduced median door-to-needle time from 105 minutes to 20 minutes, and achieved a thrombolysis rate of 31% (Meretoja et al. 2012 *[40]*). It was applied to an Australian hospital and reduced door-to-needle time from 61 minutes to 46 minutes despite only being implemented during business hours (Meretoja et al. 2013 *[39]*). Considering the current thrombolysis rate of 8% and door-to-needle time of 78 minutes in Australia (Stroke Foundation 2015 *[7]*), the intervention is likely to substantially improve the current practice.

Certainty of the Evidence — Moderate

The evidence is based on two well-designed non-randomised studies (Meretoja et al. 2012 *[40]*; Meretoja et al. 2013 *[39]*). Although a randomised controlled trial is ideal, the certainty in effect estimate is considered to be moderate due to the large improvement and sample size.

Preference and values — No substantial variability expected

Patients are likely to want to receive rapid assessments since it has potential benefits and no harms.

Resources and other considerations — No important issues with the recommended alternative

Resources considerations

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

Implementation consideration

There is a clinical indicator collected on whether patients were screened in the emergency department using a validated tool. This clinical indicator is included in the Acute Stroke Clinical Care Standard, specifically excluding patients who were in-hospital strokes, inter-hospital transfers or unconscious. Additionally, an organisational indicator is collected on whether hospitals have emergency department protocols in place for rapid triage of patients presenting with acute stroke.

Rationale

Early reperfusion therapies have been proven to improve patients' outcomes (see section Thrombolysis in chapter Acute Medical and Surgical Management). A protocol of rapid assessment after pre-notification to the emergency department in a Helsinki hospital (Meretoja et al. 2012 *[40]*) reduced door-to-needle time and reached a thrombolysis rate of 31% (compared to 8% in the most recent clinical audit data in Australia (Stroke Foundation 2015 *[7]*)). This protocol was then successfully applied to an Australian hospital (Meretoja et al. 2013 *[39]*).

Clinical Question/ PICO

Population: Adults with suspected stroke
Intervention: Rapid management
Comparator: Usual care

Summary

Meretoja et al. (2012) *[40]* reported the results of interventions to reduce treatment delays for stroke patients treated with intravenous alteplase. From 1998 to 2011, ischaemic stroke patients treated with alteplase at a Helsinki hospital were prospectively registered and followed up at 3 months. During this period, 12 measures for reducing treatment delays were gradually introduced, including high priority dispatch, pre-notification, relocation of CT to the emergency room, and delivery of alteplase treatment on the CT table. CT scans were interpreted by stroke physicians without waiting for radiology reports, with advanced imaging only conducted when uncertainty was present. Door-to-needle times (for non-basilar artery occlusion patients) were reduced throughout the study period, from an initial median of 105 minutes to 20 minutes in 2011. 31% of ischaemic stroke patients were treated with alteplase in 2011. However, patients not eligible for alteplase treatment were admitted to other hospitals in the province, meaning the overall alteplase treatment rate for the province was 16%.

Based on these results, Meretoja et al. (2013) *[39]* attempted to apply the same protocol at the Royal Melbourne Hospital. Stroke and stroke mimic patients were prospectively registered in the Royal Melbourne Hospital Stroke Registry between 2003 and 2012. Applicable elements of the Helsinki model were introduced during office hours (8 am to 5 pm Monday to Friday) beginning in May 2012, with out-of-hours care remaining the same. Elements of the Helsinki model introduced included pre-notification of the stroke team, patients going directly to CT on ambulance stretchers after a brief assessment of cardiorespiratory stability, and initiating alteplase treatment on the CT table. Other elements were modified due to differences between the original Helsinki hospital and the Royal Melbourne setting, such as registering patient details and calling the GP before arrival due to the lack of electronic patient records. Door-to-needle times significantly decreased from 2011 (median 61 minutes) to 2012 (median 46 minutes), driven by the in-hours door-to-needle time, which decreased significantly from 43 to 25 minutes. The study authors concluded that reductions in door-to-needle time should be possible in a variety of settings by attempting to do as much preparation as possible before patient arrival.

References

[39] Meretoja A, Weir L, Ugalde M, Yassi N, Yan B, Hand P, Truesdale M, Davis SM, Campbell BCV : Helsinki model cut stroke thrombolysis delays to 25 minutes in Melbourne in only 4 months.. Neurology 2013;81(12):1071-6 Pubmed Journal

[40] Meretoja A, Strbian D, Mustanoja S, Tatlisumak T, Lindsberg PJ, Kaste M : Reducing in-hospital delay to 20 minutes in stroke thrombolysis.. Neurology 2012;79(4):306-13 Pubmed Journal

Weak Recommendation

The use of clinical screening tools to identify stroke by ED staff is recommended where an expert stroke team is unable to immediately assess a patient. (Jiang et al. 2014 *[33]*; Whiteley et al. 2011 *[34]*)

Key Info

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

Stroke screening tools may be useful in the initial, rapid identification of acute stroke patients. The ROSIER and FAST scale have a sensitivity of 81-87% for identifying acute stroke and TIA patients but their specificity is low (39% to 44%) (Jiang et al. 2014 *[33]*; Whiteley et al. 2011 *[34]*).

Certainty of the Evidence — Moderate

The overall quality of evidence based on two diagnostic studies is moderate (Jiang et al. 2014 *[33]*; Whiteley et al. 2011 *[34]*).

Preference and values — No substantial variability expected

Despite a moderate diagnostic performance, clinical screening tools are likely to be preferred by suspected stroke patients to assist rapid identification when an expert stroke team is not immediately available.

Resources and other considerations — Important issues, or potential issues not investigated

Resources considerations

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

Rationale

Stroke screening tools can assist in the identification of stroke in the initial ED assessment. FAST and ROSIER have been validated and have a strong correlation for large vessel occlusion (Jiang et al. 2014 *[33]*; Whiteley et al. 2011 *[34]*).

Clinical Question/ PICO

Population: Adults with suspected stroke
Intervention: Stroke screening tool
Comparator: Confirmed diagnosis

Summary

The ROSIER and FAST scale have a sensitivity of 81–87% for identifying acute stroke and TIA patients but their specificity is low (39% to 44%) (Jiang et al. 2011 *[33]*; Whiteley et al. 2014 *[34]*).

Outcome Timeframe	Study results and measurements	Absolute effect estimates Confirmed diagnosis Stroke screening tool	Certainty of the Evidence (Quality of evidence)	Plain text summary
Identification of stroke or TIA 7 Critical	Based on data from 1,071 patients in 2 studies.	Two diagnostic studies, one prospective (N = 715) and one cross-sectional (N = 356), assessed the sensitivity and specificity of the ROSIER or FAST scales for predicting stroke or TIA among patients with suspected stroke. They were found to have a sensitivity for 81-87% and specificity of 39% to 44%.	Moderate Due to serious risk of bias [1]	The ROSIER and FAST scale have a sensitivity for 81-87% of identifying acute stroke and TIA patients but their specificity is low.

1. **Risk of bias: Serious .** Incomplete data and/or large loss to follow up ; **Inconsistency: No serious . Indirectness: No serious . Imprecision: No serious . Publication bias: No serious .**

References

[33] Jiang H-L, Chan CP-Y, Leung Y-K, Li Y-M, Graham CA, Rainer TH : Evaluation of the Recognition of Stroke in the Emergency Room (ROSIER) scale in Chinese patients in Hong Kong.. PloS one 2014;9(10):e109762 Pubmed Journal

[34] Whiteley WN, Wardlaw JM, Dennis MS, Sandercock PAG : Clinical scores for the identification of stroke and transient ischaemic attack in the emergency department: a cross-sectional study.. Journal of neurology, neurosurgery, and psychiatry 2011;82(9):1006-10 Pubmed Journal

Recommendation Strength Not Set

Practice points

- Initial diagnosis should be reviewed by a clinician experienced in the evaluation of stroke.
- Stroke severity should be assessed and recorded on admission by a trained clinician using a validated tool (e.g. NIHSS).
- A blood glucose reading should be taken to improve specificity (hypoglycaemia can present as a ‘stroke mimic’).

Rationale

Early assessment by a ‘stroke’ clinician will provide continuity of care and the identification of patients suitable for stroke intervention. There is a potential risk that concentration of skill with the stroke team may lead to slower treatment if that team is not present (e.g. after hours), due to reduced familiarity of the emergency department staff with stroke assessment protocols.

Clinicians should use a validated tool to enable an appropriate response and timely treatment.

Early identification of a low blood sugar level can lead to blood glucose correction and detection of hypoglycaemia mimicking stroke.

Investigations

Once a clinical diagnosis of stroke has been made, additional investigations are used to confirm the diagnosis and to determine the cause of the event, specifically if it is cardiac or carotid in origin. Routine investigations should include full blood count, electrolytes, erythrocyte sedimentation rate, C-reactive protein, renal function, cholesterol and glucose levels, although direct evidence is lacking for each of these investigations. An ECG should also be conducted routinely to detect AF. If clinical history, imaging and routine investigations do not adequately identify the underlying cause then further investigations may be warranted.

Imaging

While stroke and TIA are clinical diagnoses, brain imaging is needed to confirm cerebral ischaemia or intracerebral haemorrhage (ICH) and exclude stroke mimics. To confirm the diagnosis and differentiate ICH from ischaemic stroke, MRI is widely considered the imaging modality of choice. However, the longer imaging time compared to CT and the limited availability of MRI scanners in many centres limit the routine application of MRI, and it is likely that CT will remain the most frequently used imaging modality for the foreseeable future. Advanced MRI and CT imaging techniques may be used to identify ischaemic and potentially viable brain tissue and thus guide intervention decisions in the hyperacute phase.

According to the most recent clinical audit of stroke services in Australia, 99% of stroke patients underwent brain scanning, among whom 79% had a CT scan, 3% had MRI, and 16% had both (Stroke Foundation 2015 *[7]*). The median time from arrival in ED to brain scan was 1:32 hours, and 32% of patients had the brain scan within an hour of arrival (Stroke Foundation 2015 *[7]*). In terms of vascular imaging, the scan of carotid arteries was performed in 61% of patients (Stroke Foundation 2015 *[7]*).

Brain imaging

Strong Recommendation

All patients with suspected stroke who are candidates for reperfusion therapies should undergo brain imaging immediately. All other suspected stroke patients should have an urgent brain CT or MRI ('urgent' being immediately where facilities are available and preferably within 60 minutes). (Brazzelli et al. 2009 *[41]*)

Practical Info

In the current Australian context CT is much more easily accessible than MRI and therefore facilitates faster initiation of reperfusion therapies.

Brain imaging is the "rate limiting step" in therapy decisions and should therefore be prioritised in the system of care. Ambulance pre-notification of suspected stroke patients and direct transport to the CT scanner on the ambulance stretcher is strongly encouraged.

Key Info

Benefits and harms — Substantial net benefits of the recommended alternative

Ischaemic stroke and intracerebral haemorrhage cannot be reliably differentiated on clinical grounds. Brain imaging with CT or MRI is therefore essential for accurate diagnosis and determination of management. Treatment is time-critical with benefit declining rapidly with passing minutes. Brain imaging should therefore occur immediately for patients who are potential candidates for reperfusion treatments. Rapid confirmation of the diagnosis of stroke facilitates direct access to stroke units, which improves outcomes for all stroke patients and the distinction between intracerebral haemorrhage and ischaemic stroke changes management (e.g. blood pressure and thromboprophylaxis), hence the recommendation that all stroke patients should have brain imaging within 60 minutes of arrival in hospital (see Stroke unit care and Acute blood pressure lowering therapy in Acute medical and surgical management chapter and Deep venous thrombosis in Managing complications chapter).

Although MRI is more sensitive than non-contrast CT for diagnosis of ischaemic stroke, it may not be immediately accessible, leading to treatment delays (Brazzelli et al. 2009 *[41]*). There are also some patients who cannot have MRI due to metallic implants and the cost is greater than CT.

Certainty of the Evidence — High

The evidence is based on observational studies but this is standard for studies of diagnostic accuracy.

Preference and values

No substantial variability expected

In general CT brain imaging is preferred in the Australian setting due to accessibility.

Resources and other considerations

Important issues, or potential issues not investigated

Resources considerations

Earnshaw et al. (2012) *[53]* found MRI to be more effective and cost-saving than unenhanced CT selection of patients for thrombolysis, but MRI was less effective and more costly than CT perfusion imaging.

Implementation considerations

There is a clinical indicator collected in the National Stroke Audit on whether patients underwent brain imaging and, if so, what type. There are additional clinical indicators collected on the median time from arrival in the emergency department to the time of brain imaging and whether the patient was assessed for the administering of tPA. There are organisational indicators collected in the National Stroke Audit on whether hospitals have access to CT scanning within 1 hour of presentation to hospital for patients potentially eligible for thrombolysis and whether this access is available 24/7.

Rationale

Ischaemic stroke and intracerebral haemorrhage cannot be reliably differentiated on clinical grounds. Brain imaging with CT or MRI is therefore essential to accurate diagnosis and determination of management. Treatment is time-critical with benefit declining rapidly with passing minutes. Brain imaging should therefore occur immediately for patients who are potential candidates for reperfusion treatments. Rapid confirmation of the diagnosis of stroke facilitates direct access to stroke units which improves outcomes for all stroke patients and the distinction between intracerebral haemorrhage and ischaemic stroke changes management (e.g. blood pressure and thromboprophylaxis), hence the recommendation that all stroke patients should have brain imaging within 60 minutes of arrival in hospital (see Stroke unit care and Acute blood pressure lowering therapy in Acute medical and surgical management chapter and Deep venous thrombosis in Managing complications chapter).

Although MRI is more sensitive than non-contrast CT for diagnosis of ischaemic stroke (Brazzelli et al. 2009 *[41]*), it may not be immediately accessible leading to treatment delays. There are also some patients who cannot have MRI due to metallic implants and the cost is greater than CT.

Clinical Question/ PICO

Population: Adults with suspected stroke
Intervention: CT
Comparator: Confirmed diagnosis of stroke

Outcome Timeframe	Study results and measurements	Absolute effect estimates Confirmed diagnosis of stroke CT	Certainty of the Evidence (Quality of evidence)	Plain text summary
Diagnosis of ischaemic stroke 7 Critical	Based on data from 226 patients in 7 studies. [1]	In Cochrane review, CT within 12 hours of stroke onset had median sensitivity 45% and median specificity 100%	High Although patient test population was largely lacking stroke mimics, Upgraded due to Large magnitude of effect [2]	Non-contrast CT within 12 hours of stroke onset has moderate sensitivity and high specificity

1. Systematic review [41].
2. **Inconsistency: No serious . Indirectness: No serious . Imprecision: No serious . Publication bias: No serious . Upgrade: Large magnitude of effect .**

References

[41] Brazzelli M, Sandercock PA, Chappell FM, Celani MG, Righetti E, Arestis N, Wardlaw JM, Deeks JJ : Magnetic resonance imaging versus computed tomography for detection of acute vascular lesions in patients presenting with stroke symptoms.. The Cochrane database of systematic reviews 2009;(4):CD007424 Pubmed Journal

Clinical Question/ PICO

Population: Adults with suspected stroke
Intervention: MRI
Comparator: Confirmed diagnosis of stroke

Outcome Timeframe	Study results and measurements	Absolute effect estimates Confirmed diagnosis of stroke MRI	Certainty of the Evidence (Quality of evidence)	Plain text summary
Diagnosis of ischaemic stroke 7 Critical	Based on data from 226 patients in 7 studies. [1]	In Cochrane review, MRI for diagnosis of ischaemic stroke had a pooled estimate of Sensitivity = 100% (median) and Specificity = 100% (median) in comparison to non-contrast CT which had a median sensitivity of 45% and median specificity of 100%.	High Although patient test population was largely lacking stroke mimics, Upgraded due to Very large magnitude of effect [2]	Diffusion MRI increases accuracy of diagnosis of ischaemic stroke compared with non-contrast CT

1. Systematic review [41].
2. **Inconsistency: No serious . Indirectness: No serious . Imprecision: No serious . Publication bias: No serious . Upgrade: Very large magnitude of effect .**

References

[41] Brazzelli M, Sandercock PA, Chappell FM, Celani MG, Righetti E, Arestis N, Wardlaw JM, Deeks JJ : Magnetic resonance imaging versus computed tomography for detection of acute vascular lesions in patients presenting with stroke symptoms.. The Cochrane database of systematic reviews 2009;(4):CD007424 Pubmed Journal

Weak Recommendation

In patients with suspected stroke and TIA, MRI is more sensitive and specific than non-contrast CT and is the preferred modality when diagnostic confirmation is required. (Brazzelli et al. 2009 *[41]*)

Practical Info

Where MRI access is limited a "diffusion-only" protocol may allow the diagnostic benefit of MRI with a very rapid scan time.

The pattern of diffusion lesion may also provide clues to stroke aetiology, e.g. multiple vascular territory involvement may indicate a cardioembolic source. Some patients with resolved symptoms will have their diagnosis altered from TIA to stroke by the finding of a lesion on diffusion MRI, which places them in a higher risk category for stroke recurrence.

Key Info

Benefits and harms — Substantial net benefits of the recommended alternative

MRI is markedly more sensitive than non-contrast CT for diagnosis of ischaemic stroke (Brazzelli et al. 2009 *[41]*). Specificity and differentiation of stroke mimics are also better using MRI. This is particularly applicable to minor stroke patients, in whom non-contrast CT is often normal, and some patients with resolved symptoms will have their diagnosis altered from TIA to stroke by the finding of a lesion on diffusion MRI. Patients with diffusion lesions are at higher risk of stroke recurrence. A finding of multi-territory diffusion lesions can indicate pathogenesis (i.e. central embolic source). There are, however, some patients who cannot have MRI due to metallic implants and the cost is greater than CT.

Certainty of the Evidence — High

The evidence is based on observational studies but this is standard for studies of diagnostic accuracy.

Preference and values — Substantial variability is expected or uncertain

If the patient is able to have MRI and resources are available then MRI would be preferred. However, MRI may not be available in all institutions, which may delay treatment with stroke reperfusion treatment.

Resources and other considerations — Important issues, or potential issues not investigated

Resources considerations

Economic evaluations comparing MRI and CT have been conducted for a European setting. Economic evaluations comparing MRI and CT have been conducted for a European setting. Earnshaw et al. 2012 *[53]* found MRI to be more effective and cost-saving than unenhanced CT selection of patients for thrombolysis, but MRI was dominated by CT perfusion imaging. Wardlaw et al. 2014 *[19]* found that MRI was not cost-effective (given a willingness to pay of £30,000 per QALY gained) compared to CT imaging for the routine diagnosis and management of TIA and minor stroke in a variety of scenarios tested. In a single centre study in Europe, it was found that MRI was cost-effective at an additional €11,869 per QALY gained compared to CT-based methods (cost reference year 2004) *[62]*.

Rationale

MRI is substantially more sensitive for diagnosis of ischaemic stroke and may provide clues to stroke aetiology if multi-territory infarction is detected (Brazzelli et al. 2009 *[41]*). This is particularly applicable to minor stroke patients who may have a normal CT brain and patients with resolved symptoms who may have their diagnosis converted from TIA to stroke with an attendant increase in their estimated risk of stroke recurrence. However, MRI is not universally available and the frequency with which it changes management is uncertain.

Clinical Question/ PICO

Population: Adults with suspected stroke
Intervention: MRI
Comparator: Confirmed diagnosis of stroke

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Confirmed diagnosis of stroke MRI	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
Diagnosis of ischaemic stroke 7 Critical	Based on data from 226 patients in 7 studies. [1]	In Cochrane review, MRI for diagnosis of ischaemic stroke had a pooled estimate of Sensitivity = 100% (median) and Specificity = 100% (median) in comparison to non-contrast CT which had a median sensitivity of 45% and median specificity of 100%.	**High** Although patient test population was largely lacking stroke mimics, Upgraded due to Very large magnitude of effect [2]	Diffusion MRI increases accuracy of diagnosis of ischaemic stroke compared with non-contrast CT

1. Systematic review [41].
2. **Inconsistency: No serious . Indirectness: No serious . Imprecision: No serious . Publication bias: No serious . Upgrade: Very large magnitude of effect .**

References

[41] Brazzelli M, Sandercock PA, Chappell FM, Celani MG, Righetti E, Arestis N, Wardlaw JM, Deeks JJ : Magnetic resonance imaging versus computed tomography for detection of acute vascular lesions in patients presenting with stroke symptoms.. The Cochrane database of systematic reviews 2009;(4):CD007424 Pubmed Journal

Practice Statement

Consensus-based recommendation

Either CT or MRI are acceptable acute imaging options but these need to be immediately accessible to avoid delaying reperfusion therapies.

Rationale

MRI has advantages over CT in terms of diagnostic precision but safety checks for metallic implants, scanner access and patient contraindications and claustrophobia are currently practical limitations on the use of MRI in acute stroke. The randomised trials of reperfusion therapies predominantly used CT-based imaging. The fastest imaging approach that can deliver the necessary

information should be used.

Strong Recommendation

If using CT to identify hyperdense thrombus, thin slice (< 2 mm) non-contrast CT should be used rather than the standard 5 mm slices to improve diagnostic sensitivity for vessel occlusion. (Mair et al. 2015 *[46]*)

Practical Info

CT scanners can reconstruct the single CT brain acquisition with varying slice thickness and in varying planes (i.e. without any added radiation or acquisition time). Thin slices (< 2 mm thickness) reduce partial voluming effects and make hyperdense thrombus within a vessel more conspicuous, achieving ~90% sensitivity for large vessel occlusion. These thin slices should not be used to assess grey-white differentiation (early ischaemic change) as they have increased image noise.

Key Info

Benefits and harms — Substantial net benefits of the recommended alternative

Thin slice non-contrast CT is a re-format of the standard acquisition and therefore does not require any extra radiation or acquisition time. The benefit in sensitivity to vessel occlusion is marked (Mair et al. 2015 *[46]*).

Certainty of the Evidence — High

The evidence is based on observational studies but this is standard for studies of diagnostic accuracy.

Preference and values — No substantial variability expected

No substantial variability is expected as thin slice non-contrast CT improves diagnostic accuracy with no extra cost.

Resources and other considerations — Factor not considered

Rationale

Thin slice reconstructions of the non-contrast CT substantially improve diagnostic sensitivity for large vessel occlusion and do not come at any cost in terms of radiation or time.

Clinical Question/ PICO

Population: Adults with suspected stroke
Intervention: Thin slice non-contrast CT
Comparator: Confirmed diagnosis of vessel occlusion

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Confirmed diagnosis of vessel occlusion — Thin slice CT	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
Diagnosis of vessel occlusion	Based on data from 1,175 patients in 16	In systematic review (Mair 2015), hyperdense artery sign had 52% sensitivity	**High**	Thin slice (<2mm) non-contrast CT increases diagnostic sensitivity for

7 Critical	studies. [1]	and 95% specificity. There was a significant association between CT slice-thickness and sensitivity of HAS (r = −0.72; P = 0.002), but no significant relationship for specificity. The one paper that used 1mm thin slices had 100% sensitivity with similar specificity. Another paper not included in the systematic review (Riedel 2012) had 94% sensitivity.	vessel occlusion compared with 5mm slices.

1. Systematic review [46]. **Supporting references:** [56],

References

[46] Mair G, Boyd EV, Chappell FM, von Kummer R, Lindley RI, Sandercock P, Wardlaw JM : Sensitivity and specificity of the hyperdense artery sign for arterial obstruction in acute ischemic stroke.. Stroke; a journal of cerebral circulation 2015;46(1):102-7 Pubmed Journal

[56] Riedel CH, Zoubie J, Ulmer S, Gierthmuehlen J, Jansen O : Thin-slice reconstructions of nonenhanced CT images allow for detection of thrombus in acute stroke.. Stroke; a journal of cerebral circulation 2012;43(9):2319-23 Pubmed Journal

Weak Recommendation

CT perfusion imaging may be used in addition to routine imaging to improve diagnostic and prognostic accuracy. (Biesbroek et al. 2012 *[49]*)

Practical Info

CT perfusion imaging involves repeated imaging of the brain during the passage of an intravenous contrast bolus. Delayed blood flow arrival can indicate the presence of ischaemic stroke. Regions of severely reduced blood flow are likely to be irreversibly injured and large regions are associated with a worse prognosis. Despite the diagnostic and prognostic benefits of CT perfusion, studies to date have not shown modification of reperfusion treatment effect, i.e. patients still appear to benefit to some degree from reperfusion therapies delivered within standard time windows, despite quite large areas of irreversible injury. Whether patient selection based on CT perfusion may allow extension of the therapeutic time window for intervention is the subject of ongoing randomised trials.

Key Info

Benefits and harms

Substantial net benefits of the recommended alternative

CT perfusion is markedly more sensitive than non-contrast CT for diagnosis of ischaemic stroke, especially when using scanners capable of whole brain coverage (Biesbroek et al. 2012 *[49]*). CT perfusion is also more sensitive than CT angiography in patients with small distal vessel occlusions (Biesbroek et al. 2012 *[49]*). There are, however, some patients with lacunar stroke or reperfused ischaemic stroke who are not detected using CT perfusion, for whom diffusion MRI can detect the lesion.

Certainty of the Evidence

High

The evidence is based on observational studies but this is standard for studies of diagnostic accuracy.

Preference and values

Substantial variability is expected or uncertain

There is some extra contrast, radiation dose and time required to perform CT perfusion.

Resources and other considerations

No important issues with the recommended alternative

Resources considerations

CT perfusion imaging was more effective and cost-saving than usual CT-based methods for the selection of patients for thrombolysis (Jackson et al. 2010 *[54]*), and multimodal CT was also found to be more effective and cost saving over non-contrast CT (Young et al. 2010 *[55]*). Earnshaw et al. (2012) *[53]* found MRI to be dominant over unenhanced CT selection of patients for thrombolysis, but MRI was less effective and more costly than CT perfusion imaging.

Rationale

CT perfusion undoubtedly improves diagnostic and prognostic accuracy (Biesbroek et al. 2012 *[49]*). However, the extra time, contrast and radiation involved need to be balanced against the lack of definitive evidence that use of CT perfusion improves patient outcomes and hence the weaker recommendation.

Clinical Question/ PICO

Population: Adults with suspected stroke
Intervention: CT perfusion imaging
Comparator: Confirmed diagnosis of stroke

Outcome Timeframe	Study results and measurements	Absolute effect estimates Confirmed diagnosis of stroke CT Perfusion	Certainty of the Evidence (Quality of evidence)	Plain text summary
Diagnosis of ischaemic stroke	Based on data from 1,107 patients in 15 studies. [1]	Systematic review and meta-analysis of 15 observational studies - CT perfusion sensitivity approximately 80% (95% CI: 72-86%), higher with whole brain coverage.	High	CT perfusion has greater sensitivity than non-contrast CT and CT angiography with high specificity

1. Systematic review [49].

References

[49] Biesbroek JM, Niesten JM, Dankbaar JW, Biessels GJ, Velthuis BK, Reitsma JB, van der Schaaf IC : Diagnostic accuracy of CT perfusion imaging for detecting acute ischemic stroke: a systematic review and meta-analysis.. Cerebrovascular diseases (Basel, Switzerland) 2013;35(6):493-501 Pubmed Journal

Recommendation Strength Not Set

Practice points

- If a patient with stroke develops neurological deterioration, immediate clinical assessment and further brain imaging (CT or MRI) should be considered.
- Routine brain imaging approximately 24 hours after reperfusion therapies have been administered is recommended to identify haemorrhagic transformation and delineate the extent of infarction, both of which are important when making decisions about antithrombotic therapy and DVT prophylaxis.

Rationale

Changes in patient clinical status may reflect treatable or reversible pathology and should be rapidly investigated with brain imaging.

Repeating imaging routinely around 24 hours after reperfusion treatment is regarded as good practice to exclude significant haemorrhagic transformation that would alter subsequent antithrombotic management, as well as confirming the size of infarct which reflects the effectiveness of treatment and prognosis, and has implications for timing of anticoagulation in eligible patients.

Vascular imaging

Strong Recommendation

- All patients who would potentially be candidates for endovascular thrombectomy should have vascular imaging from aortic arch to cerebral vertex (CTA or MRA) to establish the presence of vascular occlusion as a target for thrombectomy and to assess proximal vascular access. (Goyal et al. 2016 *[52]*; Broderick et al. 2013 *[58]*)
- All other patients with carotid territory symptoms who would potentially be candidates for carotid re-vascularisation should have early vascular imaging to identify stenosis in the ipsilateral carotid artery. CT angiography (if not already performed as part of assessment for reperfusion therapies), Doppler ultrasound or contrast-enhanced MR angiography are all reasonable options depending on local experience and availability. (Netuka et al. 2016 *[42]*; Chappell et al. 2009 *[43]*; Nonent et al. 2011 *[44]*; Anzidei et al. 2012 *[69]*)

Practical Info

Full cerebrovascular imaging of the aortic arch to cerebral vertex is strongly encouraged in all ischaemic stroke and TIA patients to facilitate accurate diagnosis of stroke aetiology and prognosis. Carotid imaging to determine eligibility for endarterectomy is a minimum requirement and should be performed as soon as possible using whichever modality is available locally. Aortic arch to vertex vascular imaging is essential for patients who are potential candidates for endovascular clot retrieval to confirm a target for intervention and assess proximal vascular access. It is important to note that mild clinical severity does not exclude the presence of intra-cranial vessel occlusion. Approximately 10% of patients with minor stroke or even resolved symptoms have a major vessel occlusion and so mild clinical severity should not be used as an exclusion from vascular imaging with CTA or MRA. The presence or absence of vessel occlusion is a key determinant of risk of recurrent ischaemia or stroke progression. Patients with vessel occlusion are at substantial risk of subsequent clinical deterioration, whereas those without have a very low risk of stroke progression. Basilar artery occlusion is not always easy to differentiate from anterior circulation stroke on clinical grounds and hemiparesis is more common than tetraparesis. As the time window for intervention in basilar artery occlusion may be up to 24 hours at some centres, routine CT angiography would reduce the risk of missing the opportunity to treat this otherwise devastating condition.

Key Info

Benefits and harms

Substantial net benefits of the recommended alternative

Carotid imaging is critically important for people with carotid stenosis to identify candidates for endarterectomy which substantially reduces the risk of recurrent stroke in appropriate patients.

CT angiography (CTA) is highly accurate and shows the entire vascular tree, which has major advantages in accurately

diagnosing stroke aetiology. CTA does involve ionising radiation and iodinated contrast, which may be associated with a low risk of contrast nephropathy in patients with severe pre-existing kidney disease. CTA is a routine part of initial brain imaging at many centres and is essential for patients who may be considered for endovascular thrombectomy. All randomised trials that demonstrated the benefits of endovascular thrombectomy used non-invasive vessel imaging (predominantly CTA) to assess eligibility (Goyal et al. 2016 *[52]*). The IMS-3 trial did not use CTA and was neutral overall but did demonstrate benefit in the subgroup of patients with demonstrated vessel occlusion (Broderick et al 2013 *[58]*).

If carotid imaging using CTA has not already been performed, Doppler ultrasound is widely available and requires no contrast or ionising radiation, but is operator dependent and visualises a relatively small region of the carotid circulation. Contrast-enhanced MR angiography is accurate but less widely available, and gadolinium contrast is contraindicated in kidney disease.

Certainty of the Evidence Low

The evidence is based on observational data (standard for diagnostic accuracy studies).

Preference and values No substantial variability expected

No issues were identified.

Resources and other considerations No important issues with the recommended alternative

<u>Resources considerations</u>
In economic evaluations duplex ultrasonography (US), computed tomographic (CT) angiography, contrast material-enhanced magnetic resonance (MR) angiography and a combination of these modalities have been compared for patients with TIA or minor ischaemic stroke suspected of having carotid artery stenosis.

There is evidence from two economic evaluations that ultrasound to identify patients requiring surgery for carotid stenosis was cost-effective per QALY gained (Buskens et al. 2004 *[59]*) and cost-effective per stroke prevented (Wardlaw et al. 2006 *[60]*) when compared to angiography. Adding MR angiography to ultrasound was not found to be cost-effective at an additional €1,500,000 per QALY gained compared to ultrasound alone (Buskens et al. 2004 *[59]*). In a cost-utility analysis, CT angiography with ultrasound was found to be cost-saving and more effective than intra-arterial angiography and ultrasound (Brown et al. 2008 *[61]*).

In another economic evaluation, it was found that US and CT angiography for people with 70–99% stenosis was a more effective and cost-saving strategy compared to other imaging modalities except when compared to the use of CT angiography for men with 70–99% stenosis, costing an additional €71,419 per QALY gained (reference year 2007) (Tholen et al. 2010 *[76]*).

<u>Implementation considerations</u>
There is a clinical indicator collected in the National Stroke Audit on whether patients underwent carotid imaging. There are also organisational indicators collected on whether hospitals have access to carotid imaging within 24 hours of admission and whether hospitals have access to, and use, non-invasive angiography.

Rationale

People with carotid artery stenosis (CAS) may require carotid endarterectomy and therefore the accuracy of measuring the stenosis is important for indication of the CEA procedure. In the comparison between CT angiography, digital subtraction angiography, Doppler ultrasonography and MR angiography, the strongest correlation coefficient and the best allocation of stenosis into clinical significant groups (<50%, 50–69%, >=70%) was observed for CTA. Netuka concluded that CTA yielded the best accuracy in detection of carotid stenosis provided all axial slices of the stenosis are checked and carefully analysed (Netuka et al. 2016 *[42]*). In an individual patient data meta-analysis (Chappell et al. 2009 *[43]*) where ultrasonography, CTA, MR angiography and contrast material-enhanced MT angiography were compared to diagnose both severe and moderate symptomatic CAS, contrast-enhanced MR angiography was the most accurate for cases where stenosis was 70–99%. Benefits outweigh harms for both interventions and no issues were identified regarding values and preferences.

Clinical Question/ PICO

Population: Patients with carotid artery stenosis

Intervention: Imaging
Comparator: Surgical specimen

Summary

Netuka et al. (2016) *[42]* found that CTA underestimated histological measurement by 2.4% (based on European Carotid Surgery Trial [ECST] methodology) and 11.9% (based on North American Symptomatic Carotid Endarterectomy Trial [NASCET] methodology). Digital subtraction angiography (DSA) underestimated the histological measurement by 7% (ECST) and 12.2% (NASCET). MRA overestimated the histological measurement by 2.6% (ECST) and underestimated by 0.6% (NASCET). Doppler ultrasonography (DUS) overestimated the stenosis by 1.8%.

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Surgical specimen	Imaging	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
Accuracy of characterization of carotid stenosis	Based on data from 152 patients in 1 studies. [1]	Correlation coefficient with histological findings was highest for CTA (r = 0.7), followed by DSA (r = 0.6), and relatively weak for MRA and DUS (r = 0.4).		**Low** Due to serious imprecision and serious risk of bias [2]	CTA may have the best accuracy in detecting carotid stenosis, followed by DSA and MRA.

1. Primary study **Supporting references:** [42],
2. **Risk of bias: Serious .** high risk of bias according to QUADAS-2: potential issues in selecting patients and blinding of assessors ; **Inconsistency: No serious . Indirectness: No serious . Imprecision: Serious .** Only data from one study, Low number of patients ; **Publication bias: No serious .**

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Clinical Question/ PICO

Population: Patients suspected of having carotid artery stenosis
Intervention: Ultrasound, CT and MR angiography
Comparator: Digital subtraction angiography

Summary

Since the meta-analysis by Chappell et al. (2009) *[43]*, there were a few small diagnostic studies with similar results.

Anzidei et al. (2012) *[69]* studied a total of 170 patients with previous cerebrovascular events and suspected carotid artery stenoses. They underwent colour Doppler ultrasound (CDUS), first-pass (FP) and steady-state (SS) contrast-enhanced

magnetic resonance angiography (MRA) and computed tomography angiography (CTA) of the carotid arteries using digital subtraction angiography (DSA) as the reference standard. The area under the curve (AUC) for degree of stenosis was: CDUS 0.85±0.02, FP MRA 0.982±0.005, SS MRA 0.994±0.002 and CTA 0.997±0.001.

Nonent et al. (2011) *[44]* compared contrast-enhanced magnetic resonance angiography (CE-MRA), Doppler ultrasound (DUS) with DSA in 56 patients. They found CE-MRA had a sensitivity and specificity of 96–98% and 66–83% respectively for carotid stenoses ≥50% and a sensitivity and specificity of 94% and 76–84% respectively for carotid stenoses ≥70%. Combined concordant CE-MRA and DUS had a sensitivity and specificity of 100% and 85–90% respectively for carotid stenoses ≥50% and a sensitivity and specificity of 96–100% and 80–87% respectively for carotid stenoses ≥70%.

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Digital subtraction angiography	Ultrasound, CT and MR angiography	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
Accuracy of characterization of carotid stenosis	Based on data from 1,074 patients in 9 studies.	Individual patient data meta-analysis found contrast-enhanced MR angiography was the most accurate (sensitivity, 0.85 [30 of 35]; 95% confidence interval [CI]: 0.69, 0.93; and specificity, 0.85 [67 of 78]; 95% CI: 0.76, 0.92) for 70%–99% symptomatic stenosis. Sensitivity for a 50%–69% stenosis was poor, although data were limited.		Moderate Due to serious risk of bias [1]	CE-MR probably has the best diagnostic accuracy for 70%-99% symptomatic stenosis

1. **Risk of bias: Serious .** Inadequate reporting for selection of patients and blinding of assessors according to QUADAS-2 ; **Inconsistency: No serious . Indirectness: No serious . Imprecision: No serious . Publication bias: No serious .**

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Recommendation Strength Not Set

Practice points

- In ischaemic stroke and TIA patients, routinely imaging the entire vasculature from aortic arch to cerebral vertex with CTA or MRA is encouraged to improve diagnosis, recognition of stroke aetiology and assessment of prognosis.
- The administration of intravenous iodinated contrast for CT angiography/perfusion, when clinically indicated, should not be delayed by concerns regarding renal function. Post-hydration with intravenous 0.9% saline is advisable. (RANZCR guidelines 2016 *[64]*; Ang et al. 2015 *[63]*).

Rationale

Vascular imaging in ischaemic stroke and TIA patients can guide management beyond simply identifying carotid stenosis requiring endarterectomy. Other vessel pathologies (e.g. dissection) and pathology at sites other than the carotid bifurcation (e.g. aortic arch atheroma, vertebrobasilar disease, intracranial stenosis) can be identified if the complete vascular network is imaged. Patients with high grade stenosis or occlusion are at substantially higher risk of recurrent ischaemia.

Recommendation Strength Not Set

Practice point

Vascular imaging should not be performed for syncope or other non-focal neurological presentations.

Cardiac investigations

Echocardiography is an important tool in the detection of cardiac source of embolism. In patients where the stroke mechanism is uncertain after relevant intracranial or extra-cranial imaging, transthoracic echocardiography (TTE) should be considered. The timing and urgency of the test depends on the level of suspicion of cardioembolic source. Both TTE and trans-oesophageal echocardiography (TOE) have advantages and disadvantages and the use of TOE after a normal TTE should be individualised.

Atrial fibrillation (AF) is detected with electrocardiography (ECG). The optimal duration and device for ECG monitoring remain to be determined. ECG monitoring is also used in the early phase of stroke to identify cardiac complications including arrhythmia.

Weak Recommendation

Initial ECG monitoring should be undertaken for all patients with stroke. The duration and mode of monitoring should be guided by individual patient factors but would generally be recommended for at least the first 24 hours. (Kurka et al. 2015 *[66]*)

Key Info

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

The early phase after stroke can be associated with cardiac complications including arrhythmia, and cardiac monitoring is advised in the initial period. This may also diagnose unrecognised paroxysmal atrial fibrillation relevant to stroke aetiology.

Certainty of the Evidence — Moderate

This recommendation is based on observational data but that is acceptable for diagnostic studies.

Preference and values Substantial variability is expected or uncertain

ECG monitoring is non-invasive and well tolerated, although not universally available in stroke units.

Resources and other considerations Important issues, or potential issues not investigated

Resources considerations

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

Rationale

Only one study examined the utility of telemetric monitoring in acute stroke patients prospectively. In this study, the automated detection missed no events (including atrial fibrillation) but the overall rate of false alarm was 27.4%. If one considers Holter monitoring as "continuous monitoring" then more studies are available. There is evidence to suggest that Holter monitoring, telemetric monitoring and standard ECGs are complementary methods in detecting atrial fibrillation in the acute stroke setting and no particular method is superior (Kurka et al 2015 *[66]*; Lazzaro et al. 2012 *[72]*; Douen et al. 2008 *[73]*; Gunalp et al. 2006 *[74]*).

Clinical Question/ PICO

Population: Adults with acute stroke
Intervention: Continuous ECG monitoring
Comparator: Standard ECG

Summary

There is very limited literature comparing ECG vs continuous monitoring in detection of atrial fibrillation (AF) in acute stroke patients if one considers continuous monitoring as telemetric monitoring only (excluding Holter monitoring). In the single study available (Kurka et al. 2015 *[66]*), 151 patients were included, 73.5% had ischaemic stroke, 18.5% had TIA and 8% had cerebral haemorrhage. A total of 4809.5 monitoring hours were elevated. 35 patients had known AF prior to admission, 6 had AF detected on admission ECG and 10 had AF detected during continuous monitoring.

When Holter monitoring is considered as well there is more literature available, but the evidence for the superiority of any particular monitoring method is limited. An observational study by Lazzaro et al. (2012) *[72]* assessed outcomes for 133 stroke and TIA patients registered prospectively in a stroke registry who received both Holter and continuous cardiac telemetry monitoring. Holter monitoring detected significantly more atrial fibrillation (6% vs 0%). However, the small size was small, with a small number of atrial fibrillation cases. In contrast, Douen et al. (2008) *[73]* studied 144 patients with ischaemic stroke. Atrial fibrillation was detected in 15 patients by serial ECG, but out of the 12 AF cases who also had Holter monitoring, Holter monitoring only identified 6 (50%), suggesting Holter may underestimate atrial fibrillation. Gunalp et al. (2006) *[74]* had previously found Holter monitoring to be superior to serial ECG for detection of arrhythmias in an observational study of 26 patients with thromboembolic stroke and sinus rhythm. On the basis of these mixed results, there is no clear evidence for the superiority of any particular monitoring method.

Outcome Timeframe	Study results and measurements	Absolute effect estimates Standard ECG	Continuous ECG monitoring	Certainty of the Evidence (Quality of evidence)	Plain text summary
Detection of atrial fibrillation 7 Critical	Based on data from 151 patients in 1 studies. [1]	Only one study specifically reported the rate of AF detection on admission ECG vs telemetric monitoring		**Moderate** Due to serious imprecision [2]	Continuous ECG monitoring using automated arrhythmia detection is highly sensitive in acute stroke but has a high rate of false alarm

1. Primary study **Supporting references:** [66],
2. **Inconsistency: No serious . Indirectness: No serious . Imprecision: Serious .** Only data from one study ; **Publication bias: No serious .**

References

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Strong Recommendation

For patients with embolic stroke of uncertain source, longer term ECG monitoring (external or implantable) should be used. (Afzal et al. 2015 *[67]*)

Practical Info

Embolic stroke of uncertain source (ESUS) is a relatively recently defined subgroup of what has previously been called "cryptogenic stroke". It aims to define a group at higher risk of occult paroxysmal atrial fibrillation and comprises a non-lacunar infarct in the absence of significant proximal vessel disease, a normal echocardiogram and at least 24 hours of unremarkable ECG monitoring.

Investigation for occult atrial fibrillation has traditionally involved one or more periods of Holter monitoring, although the evidence clearly shows this is insensitive. External loop recorders can be worn for up to 30 days subject to patient tolerance of the device. Implantable loop recorders can provide up to 3 years of continuous monitoring and simulations indicate that 30-day monitoring or repeated Holter monitoring would detect AF in only a minority of patients otherwise detected using implantable recorders. However, the cost is substantial and may not be reimbursed. Whilst there is some question about the relevance of AF detected many months after the stroke to its aetiology, late-detected AF remains a significant risk factor for subsequent stroke and, in the trials of extended duration monitoring, led to the commencement of anticoagulation in the majority of patients in whom AF was

detected.

Key Info

Benefits and harms — Substantial net benefits of the recommended alternative

The detection of unrecognised paroxysmal atrial fibrillation is critically important to reduce the risk of recurrent stroke as antiplatelet agents are not effective and anticoagulation is required (see section Antiplatelet in chapter Secondary Prevention). Longer durations of monitoring are associated with increased AF detection. Twenty-four-hour Holter monitoring has been commonly used, but randomised controlled trials have demonstrated a substantial proportion of patients with paroxysmal AF were not detected using this approach (Afzal et al. 2015 *[67]*; Kamel et al. 2013 *[71]*). External loop recorder devices can be worn up to 30 days, but simulations based on implantable loop recorders indicate that a substantial proportion of AF was detected beyond the first 30 days. Device availability and reimbursement may be limiting factors. Safety of implantable loop recorders is acceptable, with very few adverse events reported.

Certainty of the Evidence — Moderate

Multiple randomised controlled trials reporting consistent results, with some potential risk of bias.

Preference and values — Substantial variability is expected or uncertain

The availability and reimbursement for extended cardiac monitoring are variable and may limit implementation. A minor procedure (skin incision) is required for loop recorder implantation. Wearable devices are associated with a degree of discomfort and patient adherence may be an issue.

Resources and other considerations — No important issues with the recommended alternative

Resources considerations

There is evidence from an economic evaluation by Mayer et al. (2013) *[75]* that 7-day Holter monitoring is highly cost effective for detecting paroxysmal atrial fibrillation in patients with ischaemic stroke in comparison to 24-hour Holter monitoring [71] In the least effective scenario tested in sensitivity analysis, 7-day Holter monitoring cost an additional €8,354 per QALY gained compared to 24-hour Holter monitoring when looking at benefits over a lifetime (cost reference year 2011).

Rationale

There is clear evidence that a longer duration of monitoring is associated with higher frequency of atrial fibrillation (AF) detection in patients with embolic stroke of uncertain source (Afzal et al. 2015 *[67]*; Kamel et al. 2013 *[71]*). When AF is detected and anticoagulation is commenced, the benefits for stroke prevention are well-established (see section Anticoagulant therapy in the Secondary Prevention chapter). Whether external or implantable monitors are used will depend on local availability and resources. Simulations based on implantable loop recorder data indicate that the majority of detected atrial fibrillation occurs beyond the first 30 days (the current maximum duration of external loop recording).

Clinical Question/ PICO

Population: Adults with stroke
Intervention: Long term ECG monitoring
Comparator: Short term ECG monitoring

Summary

To date, there are three high-quality randomised controlled trials investigating the detection of atrial fibrillation with long term ECG monitoring. A meta-analysis by Afzal et al. pooled data and reported OR of 4.54 (95%CI 2.92–7.06) of detecting atrial fibrillation with long-term monitoring compared to routine outpatient follow-up (Afzal et al. 2015 *[67]*). The three randomised controlled trials reported in the systematic review used different technologies with varying duration of monitoring (7–180 days) and definition of atrial fibrillation (20 seconds to greater than 30 seconds) when compared to "routine practice" which is mostly 24-hr Holter monitoring (Afzal et al. 2015 *[67]*) . A small pilot trial did not find any atrial

fibrillation in 21 days of telemetry monitoring or outpatient follow-up and the authors believed it was due to low compliance – patients wore monitors for only 64% of assigned days (Kamel et al. 2013 *[71]*). Afzal et al. (2015) also pooled data from 13 observational studies and found that implantable loop recorders (ILR) detected more atrial fibrillation than wearable devices (23.3% compared to 13.6%) *[67]*.

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Short term ECG monitoring	Long term ECG monitoring	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
Detection of atrial fibrillation 7 Critical	Odds Ratio 4.54 (CI 95% 2.92 - 7.06) Based on data from 1,098 patients in 3 studies. (Randomized controlled) Follow up Varied from 7 to 180 days	24 per 1000	100 per 1000 Difference: 76 more per 1000 (CI 95% 124 more - 43 more)	**Moderate** Due to serious risk of bias [1]	Long term ECG monitoring probably improves detection of atrial fibrillation

1. **Risk of bias: Serious .** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias ; **Inconsistency: No serious . Indirectness: No serious . Imprecision: No serious . Publication bias: No serious .**

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Weak Recommendation

Further cardiac investigations should be performed where clarification of stroke aetiology is required after initial investigations. In patients with ischaemic stroke, echocardiography should be considered based on individual patient factors. Transoesophageal echocardiography is more sensitive for suspected valvular, left atrial and aortic arch pathology. (Holmes et al. 2014 *[68]*)

Key Info

Benefits and harms Substantial net benefits of the recommended alternative

Echocardiography identifies more potential cardiac risk factors for strokes. Findings range from major risk factors such as severe valvular disease to minor risk factors such as patent foramen ovale (Holmes et al. 2014 *[68]*).

Certainty of the Evidence Low

Diagnostic studies with some potential risk of bias and a wide range of performances in detecting different conditions.

Preference and values No substantial variability expected

None expected.

Resources and other considerations Important issues, or potential issues not investigated

Resources considerations

Routine cardiac imaging using echocardiography was not cost-effective (given a willingness to pay of US$50,000 per QALY gained) for identifying and treating intracardiac thrombus in patients with stroke or TIA (Meenan et al. 2007 *[77]*). Economic evaluations of cardiac investigations used to identify other stroke mechanisms are required.

Rationale

Echocardiography identifies more potential cardiac risk factors for strokes. Holmes et al. (2014) performed a systematic review comparing diagnostic performance of transthoracic echocardiography (TTE) and transoesophageal echocardiography (TOE) in the identification of cardiac source of stroke and TIA (excluding AF). Patent foramen ovale (PFO), atrial septal aneurysm and mitral valve prolapse were the most commonly detected cardiac risk factors. In most cases, TTE and TOE have similar specificity and TTE had lower sensitivity. The reported sensitivity ranges widely and therefore one cannot be certain how many patients may be missed due to a low sensitivity (Holmes et al. 2014 *[68]*).

Clinical Question/ PICO

Population: Adults with cardiac conditions as potential sources of stroke or TIA
Intervention: Echocardiography
Comparator: Reference standard

Summary

Holmes et al. (2014) *[68]* performed a systematic review comparing diagnostic performance of transthoracic echocardiography (TTE) and transoesophageal echocardiography (TOE) in the identification of the cardiac source of stroke and TIA (excluding atrial fibrillation). Patent foramen ovale (PFO), atrial septal aneurysm and mitral valve prolapse were the most commonly detected cardiac risk factors. In most cases, TTE and TOE have similar specificity and TTE had lower sensitivity. The reported sensitivity varies widely and therefore one cannot be certain how many patients may be missed due to a low sensitivity. Detection of PFO with TTE, for example, has a sensitivity ranging from 0 to 94% when compared with TOE, with a pooled point estimate of 34%.

Tanaka et al. (2014) *[70]* evaluated the association between the volume of the left atrial appendage measured by real-time three-dimensional TOE and presence of paroxysmal atrial fibrillation. The optimal cut-off for left atrial appendage peak flow velocity was 39·0 cm/s (sensitivity, 54·6%; specificity, 89·7%). This may be a promising method for detecting atrial fibrillation, but more studies will be needed to validate its diagnostic performance.

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Reference standard Echocardiography	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
Detection of cardiac source of stroke		Based on a meta-analysis of diagnostic studies comparing TTE and TOE, TTE has high specificity of mostly 100% across various cardiac conditions but sensitivity	**Low** Due to serious risk of bias, Due to serious	TOE and TTE have comparable performance in specificity, but TTE may

7 Critical	ranging from 0 to 100%.	inconsistency [1]	have a much lower sensitivity in detecting cardiac source of stroke.

1. **Risk of bias: Serious .** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias ; **Inconsistency: Serious .** Sensitivity for different conditions ranges from 0 to 0.99 ;

References

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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: 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

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

EMG	Electromyographic feedback
EMS	Emergency medical services
ESD	Early supported discharge
ESS	European Stroke Scale
FAST	Face, Arm, Speech, Time
FEES	Fibre-optic endoscopic examination of swallowing
FeSS	Fever, Sugar, Swallowing
FFP	Fresh frozen plasma
FIM	Functional independence measure
GP	General practitioner
HR	Hazard ratio
HRQOL	Health related quality of life
HRT	Hormone replacement therapy
IA	Intra-arterial
ICH	Intracerebral haemorrhage
ICU	Intensive care unit
INR	International normalised ratio
IPC	Intermittent pneumatic compression
IV	Intravenous
LMWH	Low molecular weight heparin
LOS	Length of stay
MCA	Middle cerebral artery
MD	Mean difference
MI	Myocardial infarction
MNA	Mini Nutritional Assessment
MR	Magnetic resonance

MRA	Magnetic resonance angiography
MRI	Magnetic resonance imaging
mRS	Modified rankin scale
MST	Malnutrition screening tool
MUST	Malnutrition universal screening tool
N	Number of participants in a trial
NASCET	North American Symptomatic Carotid Endarterectomy Trial
NG	Nasogastric
NHMRC	National Health and Medical Research Council
NIHSS	National Institutes of Health Stroke Scale
NMES	Neuromuscular electrical stimulation
NNH	Numbers needed to harm
NNT	Numbers needed to treat
OR	Odds ratio
OT	Occupational therapist
PBS	Pharmaceutical Benefits Scheme
PE	Pulmonary embolism
PEG	Percutaneous endoscopic gastrostomy
PFO	Patent foramen ovale
PPV	Positive predictive value
QALYs	Quality-adjusted life years
QOL	Quality of life
RCT	Randomised controlled trial
rFVIIa	recombinant activated factor VII
RHS	Right hemisphere syndrome
ROC	Receiver operator curve

ROM	Range of motion
ROSIER	Recognition of stroke in the emergency room
RR	Relative risk
RRR	Relative risk reduction
rTMS	repetitive transcranial magnetic stimulation
rt-PA	Recombinant tissue plasminogen activator
SBP	Systolic blood pressure
SC	Subcutaneous
SD	Standard deviation
SE	Standard error
SES	Standardised effect size
SGA	Subjective global assessment
sICH	symptomatic intracerebral haemorrhage
SMD	Standardised mean difference
SSS	Scandinavian stroke scale
TEE	Transoesophageal echocardiography
TIA	Transient ischaemic attack
TOE	Transoesophageal echocardiography
TOR-BSST	Toronto Bedside Swallowing Screening test
tPA	Tissue plasmogen activator
TTE	Transthoracic echocardiography
UFH	Unfractionated heparin
UK	United Kingdom
UL	Upper limb
VF or VFS	Videofluoroscopy
VR	Virtual reality

VTE	Venous thromboembolism
WMD	Weighted mean difference

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