National Institute for Health and Care Excellence

FINAL

Stroke and transient ischaemic attack in over 16s: diagnosis and initial management

[C] Evidence review for TIA imaging

NICE Guideline NG128

Intervention evidence review

May 2019

FINAL

This evidence review was developed by the National Guideline Centre

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1 Brain imaging after transient ischaemic attack (TIA)

1.1 Review question: After TIA, what is the optimal brain imaging strategy?

1.2 Introduction

The diagnosis of TIA is difficult, especially for non-specialist clinicians because the symptoms have, by definition, resolved, and there is no perfect diagnostic test. Making a diagnosis of a TIA is important because a) people with suspected TIA can have a range of other conditions (e.g. tumours or intracerebral haemorrhage, so called 'mimics') and b) people with confirmed TIA are at high risk of future ischemic stroke. The goal of assessment of suspected TIA is to establish the diagnosis and reduce the potential for future strokes by starting preventive treatments. Brain imaging might be helpful in excluding alternative diagnoses, improving risk prediction, or guiding treatment, but its role remains controversial. Previous NICE guidance and an HTA[12] advise that specialist assessment is necessary before making decisions regarding imaging in suspected TIA, and suggest that the role of MRI remains unproven. Variation across organisations suggests that previous recommendations have not been implemented appropriately and CT imaging is still being performed routinely (including prior to specialist assessment). Inappropriate radiation exposure from CT causes risk to the patient while the routine use of CT or MRI might be an inappropriate use of resources which offer no clinical benefit.

Computed tomography (CT) is insensitive to the small areas of acute ischaemia likely to underlie most TIA syndromes, while magnetic resonance imaging is very sensitive in detecting both acute ischaemia (in about 50% of patients) and haemorrhage of any age. Clinicians remain uncertain about the value of either CT or MRI in assessing suspected TIA. Since 2008 further evidence has emerged regarding the value of MRI in predicting the risk of future ischaemic events, including ischaemic strokes.[6] The pattern of diffusion weighted imaging (DWI) lesions can also help in determining the likely mechanism of ischemic stroke or TIA. In light of these advances in knowledge about imaging technologies in TIA, an evidence review was required to investigate the best imaging strategy in patients presenting with suspected TIA.

1.3 PICO table

For full details see the review protocol in appendix A.

Table 1: PICO characteristics of review question

Population	People aged over 16 with suspected or confirmed TIA
Interventions	Magnetic resonance diffusion weighted imaging (MR DWI) MR DWI and computed tomography (CT) CT
Comparisons	Any combination of the above
Outcomes	Critical Stroke Mortality Important Modified Rankin scale (mRS)

	Quality of life Change in diagnosis or clinical management
Study design	Randomised controlled trials (diagnostic test and treat studies) Systematic reviews and meta-analyses of the above Prospective observational studies with a test and treat design if no RCTs are identified

1.4 Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual.[10] Methods specific to this review question are described in the review protocol in appendix A.

Declarations of interest were recorded according to NICE's 2014 conflicts of interest policy upto March 2018, and NICE's 2018 conflicts of interest policy from April 2018.

1.5 Clinical evidence

1.5.1 Included studies

No relevant clinical studies comparing MR DWI and CT or any combination in a randomised or observational test and treat study design were identified.

See also the study selection flow chart in appendix C.

1.5.2 Excluded studies

See the excluded studies list in appendix E.

An HTA[12] was identified that looked at whether MR with DWI is cost-effective in stroke prevention compared with CT brain scanning in all patients with TIA or minor stroke. The relevant chapter for this evidence review was planned to be a systematic review and meta-analysis of sensitivity/specificity of imaging strategies. However, no studies reporting sensitivity/specificity were identified and so the report assessed the frequency of DWI visible lesions in people with TIA or minor stroke. This HTA was highlighted in the NICE surveillance report and also as a key paper when discussing the protocol with the committee, however it did not meet the protocol criteria for this question. The committee were particularly interested in diagnostic test and treat outcomes. That is what happens downstream after imaging in terms of observed stroke, mortality, functional outcome and changes decision making and clinical management, to allow comparison of imaging strategies.

1.6 Economic evidence

1.6.1 Included studies

No relevant health economic studies were included.

1.6.2 Excluded studies

One economic study relating to this review question was excluded.[12]

This was an HTA published in 2014 that aimed to assess the cost effectiveness of routine MRI, including DWI, compared to routine CT in patients with TIA and minor stroke using economic modelling. It used a UK NHS perspective and QALYs as the health outcome measure. The population analysed was broader than the guideline review question as it included minor stroke as well as TIA (clinically TIA by definition has symptom resolution [within 24hrs and typically around 10 minutes] and in minor stroke symptoms persist after 24hrs; radiologically minor stroke will be DWI positive but TIA may not be; management and outcomes may also vary; some data in the model varied between people with TIA and minor stroke such as proportion of people with haemorrhage). The interventions compared were relevant for the review although did not cover all the options considered relevant by the committee – for example selective use of CT scanning in those with a 'red flag' for an alternative diagnosis that CT could detect. The model was comprehensive and model inputs were informed by systematic reviews. However, it was excluded becausethe clinical evidence the model was based on did not meet the inclusion criteria for the clinical review for the guideline. Specifically, as discussed above, the committee agreed that for the guideline evidence review diagnostic test and treat studies which compare clinical outcomes between groups where different diagnostic strategies have been used in people with TIA were the most useful evidence to inform decision making but no such studies were identified.

This is listed in appendix E, with reasons for exclusion given. See also study selection flowchart in appendix D.

1.6.3 Unit costs

Table 2: UK costs of outpatient imaging

Currency Description	Unit Cost
Magnetic Resonance Imaging of Head	
Magnetic Resonance Imaging Scan, One Area, without Contrast, 19 years and over	£139
Computed Tomography of Head	
Computerised Tomography Scan of One Area, without Contrast, 19 years and over	£86

Source: NHS Reference Costs, 2016-2017

1.7 Resource costs

The recommendation made by the committee based on this review (see section **Error! R eference source not found.**) that CT imaging is not offered unless there is diagnostic doubt may have a substantial impact on resources to the NHS in England. The committee agreed this recommendation will reduce costs through greatly reducing the population requiring CT imaging in emergency departments. Additional savings are likely to be made by improving the flow of people with TIA to the TIA clinic and in the timeliness of delivering secondary

prevention, which reduces the risk of stroke. Further work is being carried out to quantify the potential resource impact in this area.

The committee has also made a recommendation based on this review (see section **Error! R eference source not found.**) that urgent MRI (including diffusion-weighted and blood sensitive sequences) to detect ischaemia, haemorrhage or alternative pathologies should be 'considered' following expert assessment in the TIA clinic. Unlike for stronger recommendations stating that interventions should be adopted, it is not possible to make a judgement about the potential resource impact to the NHS of recommendations regarding interventions that could be used, as uptake is too difficult to predict. The committee was not confident of the effect of this recommendation on MRI requests. They acknowledged that this recommendation may increase the number of MRI requests compared to current practice. However, they also noted that it was not necessarily the case as the decision to do an MRI will not generally be affected by the results of a previous CT scan.Tthe committee was confident that CT imaging will decrease and so expect that this may offset the potential increase in MRI requests. The committee was uncertain whether overall these recommendations will be cost saving.

1.8 Evidence statements

1.8.1 Clinical evidence statements

- No relevant published evidence was identified.

1.8.2 Health economic evidence statements

- No relevant economic evaluations were identified.

1.9 The committee's discussion of the evidence

1.9.1 Interpreting the evidence

1.9.1.1 The outcomes that matter most

This review focused on the 'optimal' brain imaging strategy in terms of improvement in patient outcomes. Critical outcomes for this review were stroke and mortality. Important outcomes were identified as functional outcome (mRS), quality of life and change in diagnosis or clinical management.

This review examined diagnostic test and treat outcomes, as the committee were particularly interested in the downstream outcomes after imaging. This included stroke, mortality, functional outcome and changes in decision making and clinical management. The committee agreed that diagnostic accuracy outcomes were not the most important factor in deciding on a strategy and therefore these would not provide as useful an insight for making a practice recommendation.

No evidence was identified for this question.

1.9.1.2 The quality of the evidence

No relevant clinical studies comparing MR, DWI and CT alone or any combination in a test and treat study design were identified. Therefore, there was no evidence to directly answer the question of whether brain imaging (unenhanced CT or MRI) after suspected TIA affects either subsequent treatment or early risk of stroke, or whether brain imaging of all suspected TIA cases is appropriate or cost effective.

An HTA[12] was identified that aimed to perform a systematic review and meta-analysis on the diagnostic accuracy of MR with DWI compared with CT brain scanning in all patients with TIA or minor stroke. However, this was excluded because it did not meet the protocol for this question. This was because no test-and-treat trials or studies that directly compared MR DWI with CT scanning were included.

1.9.1.3 Benefits and harms

In the absence of any evidence, the committee based discussions on clinical experience and knowledge. The committee agreed that CT is most useful when there is a clinical suspicion of finding an alternative diagnosis that CT could detect, and should not be applied routinely to all suspected TIA cases. If exclusion of intracerebral bleeding is a clinical priority, for example, for those on anticoagulants or with a known bleeding disorder, or other reasons to suspect intracerebral bleeding (subdural haematoma, convexity subarachnoid haemorrhage, or intracerebral haemorrhage), then an unenhanced CT head scan should be performed. CT scans are indicated in the presence of 'red flag' clinical (for example headache, anticoagulation, head injury, repetitive stereotyped events) which suggest that the cause may not be a TIA. The committee anticipates that in these cases, those presenting to the ED would have the CT scan performed in ED, but those who present to primary care should be urgently referred to secondary care where the scan would be done if appropriate.

The committee discussed that routine CT imaging is common in current practice and could waste resources, extend the length of stay in ED, and expose people to unnecessary radiation. Therefore, they made a strong recommendation that CT brain scanning should not be offered to people with a suspected TIA unless there is clinical suspicion of an alternative diagnosis that CT could detect.

The committee discussed the possible risks of not offering CT brain imaging to all people with a suspected TIA. They agreed that, in the absence of specific 'red flag' clinical indicators

(for example, headache, anticoagulation) it is rare for a CT scan to reveal an alternative diagnosis requiring a different referral pathway, and therefore the numbers of referrals to TIA clinics should not increase greatly. The risk of missing a TIA diagnosis by not performing a CT scan is also low because the committee agreed that the best diagnosis of TIA is by clinical assessment.

Additionally, based on the opinion and experience of the committee, urgent MRI, within 24 hours, should be considered after expert assessment in the TIA clinic to detect the presence and distribution of cerebral ischaemia, or alternative pathologies (TIA mimics, such as tumours, demyelinating disorders or convexity subarachnoid haemorrhage). MRI may also be needed to confirm the vascular territory of ischaemia before a decision is made to refer for a carotid endarterectomy, and may suggest alternative stroke mechanisms, such as cardiac embolism, large artery thrombo-embolism, haemodynamic compromise, or small vessel occlusion. MRI can also improve the assessment of future risk of stroke. However, the committee believed it was important to leave flexibility for clinicians in the TIA clinic to decide on the need for brain imaging based on the clinical scenario and agreed that MRI will not be required for all patients in a TIA clinic; therefore, the recommendation was to 'consider' MRI to allow for clinical discretion on an individual case basis. The potential harms for MRI are less than CT as there is no ionising radiation.

There was remaining uncertainty about whether urgent, routine MRI scanning versus standard care improves the outcomes of suspected TIA patients and so a priority research recommendation was framed in this area. The committee noted that this should be a cluster randomised test-and-treat trial comparing urgent routine MRI to usual care for all cases of suspected TIA within a TIA clinic.

1.9.2 Cost effectiveness and resource use

No cost effectiveness evidence was included for the optimal brain imaging strategy after TIA review.

In the absence of economic evidence, the committee considered the unit costs of MR and CT imaging. In the outpatient setting, non-contrast CT and MRI scans of one area currently cost £86 and £139, respectively. The committee noted that the unit costs of the imaging strategies are high and the population of those with suspected TIA is large. In addition, there is wide variation in current practice and issues surrounding access to imaging, particularly MRI.

In current practice, CT imaging is widely used in the ED in patients with suspected TIA to rule out other diagnoses, for example, intracerebral haemorrhage or a mass lesion. There is usually limited access to MRI in the ED. As CT imaging only identifies persistent deficits, people with TIA often have normal CT scans and are then sent to the TIA clinic where they may receive further imaging, usually MRI. Currently people with suspected TIA can experience delays in their transit through the ED, while awaiting CT imaging. The committee agreed that when a diagnosis of TIA is confidently suspected, CT imaging should not be routinely offered. The committee noted that CT imaging is only useful in specific cases when there is a clinical suspicion of alternative diagnoses which may be detected by CT, for example mass lesions or intracerebral haemorrhage.

The committee was confident this recommendation will reduce costs through greatly reducing the population requiring CT imaging in emergency departments, without negatively affecting patient outcomes. Furthermore, the committee expects that, by not routinely CT scanning patients with suspected TIA, there will be improvements in the flow of people with suspected TIA to the TIA clinic and in the timeliness of delivering secondary prevention, which is likely to improve patient outcomes and reduce downstream costs.

The committee agreed that the 'gold standard' diagnostic strategy for TIA is expert clinical assessment. The committee agreed that MRI is much more sensitive to acute cerebral ischaemia than CT imaging, with a sensitivity that decreases over time. MRI enables the

detection and localisation of ischaemia, which allows clarification of the stroke mechanism and improved assessment of future risk. The committee agreed that the stroke physician/neurologist in the TIA clinic should dictate the need for imaging, noting that MRI will not be informative for all people with suspected TIA, such as those presenting late. The committee was not confident of the effect of this recommendation on MRI requests. They acknowledged that this recommendation may increase the number of MRI requests. However, they also noted that it was not necessarily the case as the decision to do an MRI will not generally be affected by the results of a previous CT scan. The committee was confident that CT imaging will decrease and so expect that this will offset any potential increase in MRI requests. The committee was uncertain whether overall these recommendations will be cost saving. They highlighted that they were not recommending routine early MRI for all instead of a CT as there was not evidence to support this and made a research recommendation in this area.

The committee noted that access to high quality MRI scanners is limited in some trusts and in particular in smaller hospitals. This could impact the implementation of the recommendation if more MRI scanning is required. The committee further discussed that undertaking an MRI scan takes more time than a CT of the head without contrast, although newer MRI scanners are faster. The number of MRI slots per day is currently limited, so there may be a need for dedicated MRI slots for people with suspected TIA.

In conclusion, no cost effectiveness evidence was identified for the optimal brain imaging strategy after TIA. The committee chose to recommend that CT scans are not offered to those with suspected TIA, unless there is clinical suspicion of a CT detectable alternative diagnosis. People with suspected TIA should undergo expert assessment, during which an MRI scan may be considered. The committee thought that recommending against the use of CT scans may offset any potential increase in costs due to the possible increase in use of MRI scans. The committee chose to recommend that further research be done which considers whether routine MRI screening for all those arriving in TIA clinics improves outcomes.

1.9.3 Other factors the committee took into account

The committee noted that imaging is performed routinely in some services, and sometimes involves both CT and MRI. This suggests that current NICE recommendations in CG68 are not being implemented appropriately.

The committee agreed that uncertainty about the need for brain scanning in this group remains, with variations between clinics in protocols for scanning people with suspected TIA. Often CT is used because of lack of access to MRI.

Regarding MRI, the committee acknowledged that timely access to MRI is not currently standard in TIA clinics. Delayed access reduces the utility of MR-DWI for detecting transient ischemic events as sensitivity reduces over time and, therefore, further reinforces the need for early expert assessment and timely access to MRI.

The committee noted that brain imaging is often performed simultaneously with vascular imaging of the intracerebral and extracranial arteries but did not assess this strategy as the question addressed was about brain imaging only.

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Appendices

Appendix A: Review protocols

Table 3: Review protocol: TIA Imaging

Field	Content
Review question	After TIA, what is the optimal brain imaging strategy?
Type of review question	Diagnostic (diagnostic test and treat studies only) A review of health economic evidence related to the same review question was conducted in parallel with this review. For details see the health economic review protocol for this NICE guideline.
Objective of the review	To determine whether MR DWI is effective in diagnosing TIA, compared with CT brain scanning, to guide secondary stroke prevention.
Eligibility criteria – population / disease / condition / issue / domain	People aged over 16 with suspected or confirmed TIA
Eligibility criteria – intervention(s) / exposure(s) / prognostic factor(s)	Diagnsotic tests: • MR diffusion weighted imaging (MR DWI) • MR DWI and CT • CT Subsequent treatments for secondary stroke prevention if TIA is diagnosed include: • antiplatelet agents, • blood pressure management, • anticoagulation in selected patients e.g. people with AF, • exclusion of diabetes, • management of dyslipidaemia including statins, • diet and lifestyle advice, particularly smoking cessation.
Eligibility criteria – comparator(s) / control or reference (gold) standard	Diagnsotic tests: • MR diffusion weighted imaging (MR DWI) • MR DWI and CT • CT Subsequent treatments for secondary stroke prevention if TIA is diagnosed: • antiplatelet agents, • blood pressure management, • anticoagulation in selected patients e.g. people with AF, • exclusion of diabetes, • management of dyslipidaemia including statins, • diet and lifestyle advice, particularly smoking cessation.
Outcomes and prioritisation	Critical Stroke at 7 days, 90 days and 1 year Mortality at 7 days, 90 days and 1 year Important Modified Rankin Scale at 90 days and 1 year Quality of life at 90 days and 1 year

Field	Content
	Change in diagnosis or clinical management
Eligibility criteria – study design	Randomised controlled trials (diagnostic test and treat studies) Systematic reviews and meta-analyses of the above Prospective observational studies if no RCTs are identified
Other inclusion exclusion criteria	Inclusion Include studies on 'minor stroke' and downgrade for indirectness Language: Restrict to English only Settings: Hospital, Emergency department, Specialist stroke unit, Mobile units Exclusion Haemorrhagic stroke
Proposed sensitivity / subgroup analysis, or meta-regression	Subgroups to investigate if heterogeneity is present Time from symptom onset to imaging (<24hr/>24hr, <1 week/> 1 week) ABCD2 score
Selection process – duplicate screening / selection / analysis	Studies are sifted by title and abstract. Potentially significant publications obtained in full text are then assessed against the inclusion criteria specified in this protocol.
Data management (software)	• EndNote will be used for reference management, sifting, citations and bibliographies. • EviBASE will be used for data extraction and quality assessment for clinical studies. • MS Excel will be used for data extraction and critical appraisal for health economic studies. • Pairwise meta-analyses will be performed using Cochrane Review Manager (RevMan5). • GRADEpro will be used to assess the quality of evidence for each outcome.
Information sources – databases and dates	Databases: Medline, Embase, Cochrane Library, CINAHL, Social Care Online, PsycINFO Language: Restrict to English only Date restriction: none Key papers: 1. Boulanger JM, Coutts SB, Eliasziw M et al. Diffusion-weighted imaging-negative patients with transient ischemic attack are at risk of recurrent transient events. Stroke 2007;38(8):2367–2369. 2. Prabhakaran S, Chong JY, Sacco RL. Impact of abnormal diffusion-weighted imaging results on short term outcome following transient ischemic attack. Archives of Neurology 2007;64(8):1105–1109. 3. Calvet D. Management and outcome of patients with transient ischemic attack admitted to a stroke unit. Cerebrovascular Diseases 2007;24(1):80–85. 4. Coutts SB, Simon JE, Eliasziw M et al. Triaging transient ischemic attack and minor stroke patients using acute magnetic resonance imaging. Annals of Neurology 2005;57(6):848–854. 5. Purroy F, Montaner J, Rovira A et al. Higher risk of further vascular events among transient ischemic attack patients with diffusion-weighted imaging acute ischemic lesions. Stroke 2004;35(10):2313–2319.

Field	Content
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Identify if an update	No (recommendation made in CG68, but no specific review). 5 studies were included in the original guideline in explanatory text, but not reviewed. Recommendations from CG68 1.2.1.2 People who have had a suspected TIA who are at high risk of stroke (for example, an ABCD2 score of 4 or above, or with crescendo TIA) in whom the vascular territory or pathology is uncertain should undergo urgent brain imaging (preferably diffusion-weighted MRI [magnetic resonance imaging]). 1.2.1.3 People who have had a suspected TIA who are at lower risk of stroke (for example, an ABCD2 score of less than 4) in whom the vascular territory or pathology is uncertain should undergo brain imaging (preferably diffusion-weighted MRI). 1.2.2.1 People who have had a suspected TIA who need brain imaging (that is, those in whom vascular territory or pathology is uncertain) should undergo diffusion-weighted MRI except where contraindicated, in which case CT (computed tomography) scanning should be used.
Author contacts	https://www.nice.org.uk/guidance/indevelopment/gid-ng10071
Highlight if amendment to previous protocol	For details please see section 4.5 of Developing NICE guidelines: the manual.
Search strategy – for one database	For details please see appendix B
Data collection process – forms / duplicate	A standardised evidence table format will be used, and published as appendix D of the evidence report.
Data items – define all variables to be collected	For details please see evidence tables in Appendix D (clinical evidence tables) or H (health economic evidence tables).
Methods for assessing bias at outcome / study level	Standard study checklists were used to critically appraise individual studies. For details please see section 6.2 of Developing NICE guidelines: the manual The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/
Criteria for quantitative synthesis	For details please see section 6.4 of Developing NICE guidelines: the manual.
Methods for quantitative analysis – combining studies and exploring (in)consistency	For details please see the separate Methods report for this guideline.
Meta-bias assessment –	For details please see section 6.2 of Developing NICE guidelines: the

Field	Content
publication bias, selective reporting bias	manual.
Confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual.
Rationale / context – what is known	For details please see the introduction to the evidence review.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the evidence review. The committee was convened by the National Guideline Centre (NGC) and chaired by Jason Kendall in line with section 3 of Developing NICE guidelines: the manual. Staff from NGC undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the evidence review in collaboration with the committee. For details please see Developing NICE guidelines: the manual.
Sources of funding / support	NGC is funded by NICE and hosted by the Royal College of Physicians.
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Roles of sponsor	NICE funds NGC to develop guidelines for those working in the NHS, public health and social care in England.
PROSPERO registration number	Not registered

Table 4: Health economic review protocol

Review question	All questions – health economic evidence
Objectives	To identify health economic studies relevant to any of the review questions.
Search criteria	• Populations, interventions and comparators must be as specified in the clinical review protocol above. • Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Search strategy	A health economic study search will be undertaken using population-specific terms and a health economic study filter – see appendix B2 of reviews. For questions being updated, the search will be run from 2007, which was the cut-off date for the searches conducted for NICE guideline CG68. For the new review question on endovascular therapy, the search will be run from 2007 as studies published before 2007 are not likely to be relevant.
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2002, abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Studies published after 2002 that were included in the previous guideline will be reassessed for inclusion and may be included or selectively excluded based on their

relevance to the questions covered in this update and whether more applicable evidence is also identified.

Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual (2014).[10]

Inclusion and exclusion criteria

- If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile.
- If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile.
- If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included.

Where there is discretion

The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation as excluded health economic studies in appendix H.

The health economist will be guided by the following hierarchies.

Setting:

- UK NHS (most applicable).
- OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden).
- OECD countries with predominantly private health insurance systems (for example, Switzerland).
- Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations.

Health economic study type:

- Cost–utility analysis (most applicable).
- Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis).
- Comparative cost analysis.
- Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations.

Year of analysis:

- The more recent the study, the more applicable it will be.
- Studies published in 2002 or later (including any such studies included in the previous guideline) but that depend on unit costs and resource data entirely or predominantly from before 2002 will be rated as 'Not applicable'.
- Studies published before 2002 (including any such studies included in the previous guideline) will be excluded before being assessed for applicability and methodological limitations.

	Quality and relevance of effectiveness data used in the health economic analysis: • The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

Appendix B: Literature search strategies

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual 2014, updated 2017 https://www.nice.org.uk/guidance/pmg20/resources/developing-nice-guidelines-the-manual-pdf-72286708700869

For more detailed information, please see the Methodology Review.

B.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well described in title, abstract or indexes and therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 5: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 19 February 2018	Exclusions Randomised controlled trials Systematic review studies Diagnostic tests studies
Embase (OVID)	1974 – 19 February 2018	Exclusions Randomised controlled trials Systematic review studies Diagnostic tests studies
The Cochrane Library (Wiley)	Cochrane Reviews to 2018 Issue 2 of 12 CENTRAL to 2018 Issue 1 of 12 DARE, and NHSEED to 2015 Issue 2 of 4 HTA to 2016 Issue 2 of 4	None

Medline (Ovid) search terms

1.	((mini or minor or mild or acute) adj2 (stroke or strokes)).ti,ab.
2.	exp Brain Ischemia/
3.	((brain or brainstem or cerebr* or cerebell* or vertebrobasil* or verte brobasil* or hemisphere* or intracran* or intracerebral or infratentorial or supratentorial or mca*1 or anterior circulation or carotid or crescendo or transient or lacunar) adj3 isch?emi*).ti,ab.
4.	Ischemic Attack, Transient/
5.	(isch?emi* adj2 attack*).ti,ab.
6.	TIA*.ti,ab.
7.	or/1-6
8.	letter/
9.	editorial/

10.	news/
11.	exp historical article/
12.	Anecdotes as Topic/
13.	comment/
14.	case report/
15.	(letter or comment*).ti.
16.	or/8-15
17.	randomized controlled trial/ or random*.ti,ab.
18.	16 not 17
19.	animals/ not humans/
20.	exp Animals, Laboratory/
21.	exp Animal Experimentation/
22.	exp Models, Animal/
23.	exp Rodentia/
24.	(rat or rats or mouse or mice).ti.
25.	or/18-24
26.	7 not 25
27.	limit 26 to English language
28.	(exp child/ or exp pediatrics/ or exp infant/) not (exp adolescent/ or exp adult/ or exp middle age/ or exp aged/)
29.	27 not 28
30.	exp tomography/
31.	tomograph*.ti,ab.
32.	(NCCT or CT or UHCT).ti,ab.
33.	((CAT or body) adj2 scan*).ti,ab.
34.	or/30-33
35.	Magnetic Resonance Imaging/
36.	((magnetic or nuclear) adj2 resonance adj3 imag*).ti,ab.
37.	(MRI or NMR or NMRI or fMRI or MR or DWI).ti,ab.
38.	Diffusion Magnetic Resonance Imaging/
39.	((diffusion-weighted or T2-weighted) adj2 imag*).ti,ab.
40.	or/35-39
41.	29 and 34 and 40
42.	Meta-Analysis/
43.	Meta-Analysis as Topic/
44.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
45.	((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
46.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
47.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
48.	(search* adj4 literature).ab.
49.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
50.	cochrane.jw.
51.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.

52.	or/42-51
53.	randomized controlled trial.pt.
54.	controlled clinical trial.pt.
55.	randomi#ed.ab.
56.	placebo.ab.
57.	randomly.ab.
58.	clinical trials as topic.sh.
59.	trial.ti.
60.	or/53-59
61.	exp "sensitivity and specificity"/
62.	(sensitivity or specificity).ti,ab.
63.	((pre test or pretest or post test) adj probability).ti,ab.
64.	(predictive value* or PPV or NPV).ti,ab.
65.	likelihood ratio*.ti,ab.
66.	likelihood function/
67.	((area under adj4 curve) or AUC).ti,ab.
68.	(receive* operat* characteristic* or receive* operat* curve* or ROC curve*).ti,ab.
69.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness)).ti,ab.
70.	gold standard.ab.
71.	or/61-70
72.	41 and (52 or 60 or 71)
73.	93 or 72

Embase (Ovid) search terms

1.	((mini or minor or mild or acute) adj2 (stroke or strokes)).ti,ab.
2.	*brain ischemia/ or *hypoxic ischemic encephalopathy/
3.	((brain or brainstem or cerebr* or cerebell* or vertebrobasil* or verte brobasil* or hemisphere* or intracran* or intracerebral or infratentorial or supratentorial or mca*1 or anterior circulation or carotid or crescendo or transient or lacunar) adj3 isch?emi*).ti,ab.
4.	*Transient ischemic attack/
5.	(isch?emi* adj2 attack*).ti,ab.
6.	TIA*.ti,ab.
7.	or/1-6
8.	letter.pt. or letter/
9.	note.pt.
10.	editorial.pt.
11.	case report/ or case study/
12.	(letter or comment*).ti.
13.	or/8-12
14.	randomized controlled trial/ or random*.ti,ab.
15.	13 not 14
16.	animal/ not human/
17.	nonhuman/
18.	exp Animal Experiment/
19.	exp Experimental Animal/

20.	animal model/
21.	exp Rodent/
22.	(rat or rats or mouse or mice).ti.
23.	or/15-22
24.	7 not 23
25.	limit 24 to English language
26.	(exp child/ or exp pediatrics/) not (exp adult/ or exp adolescent/)
27.	25 not 26
28.	exp x-ray computed tomography/
29.	tomograph*.ti,ab.
30.	(NCCT or CT or UHCT).ti,ab.
31.	((CAT or body) adj2 scan*).ti,ab.
32.	or/28-31
33.	nuclear magnetic resonance imaging/
34.	((magnetic or nuclear) adj2 resonance adj3 imag*).ti,ab.
35.	(MRI or NMR or NMRI or fMRI or MR or DWI).ti,ab.
36.	diffusion weighted imaging/
37.	((diffusion-weighted or T2-weighted) adj2 imag*).ti,ab.
38.	or/33-37
39.	27 and 32 and 38
40.	systematic review/
41.	Meta-Analysis/
42.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
43.	((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
44.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
45.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
46.	(search* adj4 literature).ab.
47.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
48.	cochrane.jw.
49.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
50.	or/40-49
51.	random*.ti,ab.
52.	factorial*.ti,ab.
53.	(crossover* or cross over*).ti,ab.
54.	((doubl* or singl*) adj blind*).ti,ab.
55.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
56.	crossover procedure/
57.	single blind procedure/
58.	randomized controlled trial/
59.	double blind procedure/
60.	or/51-59
61.	exp "sensitivity and specificity"/
62.	(sensitivity or specificity).ti,ab.

63.	((pre test or pretest or post test) adj probability).ti,ab.
64.	(predictive value* or PPV or NPV).ti,ab.
65.	likelihood ratio*.ti,ab.
66.	((area under adj4 curve) or AUC).ti,ab.
67.	(receive* operat* characteristic* or receive* operat* curve* or ROC curve*).ti,ab.
68.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness)).ti,ab.
69.	diagnostic accuracy/
70.	diagnostic test accuracy study/
71.	gold standard.ab.
72.	or/61-71
73.	39 and (50 or 60 or 72)

Cochrane Library (Wiley) search terms

#1.	(mini or minor or mild or acute) near/2 (stroke or strokes):ti,ab
#2.	MeSH descriptor: [Brain Ischemia] explode all trees
#3.	((brain or brainstem or cerebr* or cerebell* or vertebrobasil* or verte brobasil* or hemisphere* or intracran* or intracerebral or infratentorial or supratentorial or mca*1 or anterior circulation or carotid or crescendo or transient or lacunar) near/3 isch?emi*):ti,ab
#4.	MeSH descriptor: [Ischemic Attack, Transient] explode all trees
#5.	(isch?emi* near/2 attack*):ti,ab
#6.	TIA*:ti,ab
#7.	(or #1-#6)
#8.	MeSH descriptor: [Tomography, X-Ray Computed] explode all trees
#9.	tomograph*:ti,ab
#10.	(NCCT or CT or UHCT):ti,ab
#11.	((CAT or body) near/2 scan*):ti,ab
#12.	(or #8-#11)
#13.	MeSH descriptor: [Magnetic Resonance Imaging] this term only
#14.	((magnetic or nuclear) near/2 resonance near/3 imag*):ti,ab
#15.	(MRI or NMR or NMRI or fMRI or MR or DWI):ti,ab
#16.	MeSH descriptor: [Diffusion Magnetic Resonance Imaging] this term only
#17.	((diffusion-weighted or T2-weighted) near/2 imag*):ti,ab
#18.	(or #13-#17)
#19.	#7 and #12 and #18

B.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to the stroke population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics studies.

Table 6: Database parameters and filters used

Database	Dates searched	Search filter used
Medline	01 January 2007 – 06 August 2018	Exclusions Health economics studies
Embase	01 January 2007 – 06 August 2018	Exclusions Health economics studies
Centre for Research and Dissemination (CRD)	HTA - 01 January 2007 – 10 November 2017 NHSEED - 01 January 2007 – March 2015	None

Medline (Ovid) search terms

1.	exp Stroke/
2.	(stroke or strokes).ti,ab.
3.	((cerebro* or cerebral*) adj2 (accident* or apoplexy)).ti,ab.
4.	(CVA or poststroke or poststrokes).ti,ab.
5.	exp Intracranial Hemorrhages/
6.	(brain adj2 (attack*1 or hemorrhag* or haemorrhag* or bleed* or infarct*)).ti,ab.
7.	((intracerebral or intracranial or cerebral* or cerebro* or cerebrum or cerebellum or subarachnoid* or choroidal or basal ganglia or subdural) adj3 (hemorrhag* or haemorrhag* or bleed*)).ti,ab.
8.	exp Brain infarction/
9.	exp Carotid Artery Thrombosis/
10.	((brain or brainstem or cerebr* or cerebell* or vertebrobasil* or verte brobasil* or hemisphere* or intracran* or intracerebral or infratentorial or supratentorial or mca*1 or anterior circulation or carotid or transient or lacunar) adj3 (infarct* or thrombo* or emboli* or occlus* or hypoxi*)).ti,ab.
11.	exp Brain Ischemia/
12.	((brain or brainstem or cerebr* or cerebell* or vertebrobasil* or verte brobasil* or hemisphere* or intracran* or intracerebral or infratentorial or supratentorial or mca*1 or anterior circulation or carotid or crescendo or transient or lacunar) adj3 isch?emi*).ti,ab.
13.	Ischemic Attack, Transient/
14.	(isch?emi* adj2 attack*).ti,ab.
15.	TIA.ti,ab.
16.	or/1-15
17.	letter/
18.	editorial/
19.	news/
20.	exp historical article/
21.	Anecdotes as Topic/
22.	comment/
23.	case report/
24.	(letter or comment*).ti.
25.	or/17-24
26.	randomized controlled trial/ or random*.ti,ab.

27.	25 not 26
28.	animals/ not humans/
29.	exp Animals, Laboratory/
30.	exp Animal Experimentation/
31.	exp Models, Animal/
32.	exp Rodentia/
33.	(rat or rats or mouse or mice).ti.
34.	or/27-33
35.	16 not 34
36.	limit 35 to English language
37.	(exp child/ or exp pediatrics/ or exp infant/) not (exp adolescent/ or exp adult/ or exp middle age/ or exp aged/)
38.	36 not 37
39.	economics/
40.	value of life/
41.	exp "costs and cost analysis"/
42.	exp Economics, Hospital/
43.	exp Economics, medical/
44.	Economics, nursing/
45.	economics, pharmaceutical/
46.	exp "Fees and Charges"/
47.	exp budgets/
48.	budget*.ti,ab.
49.	cost*.ti.
50.	(economic* or pharmaco?economic*).ti.
51.	(price* or pricing*).ti,ab.
52.	(cost* adj2 (effectiv* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
53.	(financ* or fee or fees).ti,ab.
54.	(value adj2 (money or monetary)).ti,ab.
55.	or/39-54
56.	38 and 55

Embase (Ovid) search terms

1.	*cerebrovascular accident/ or cardioembolic stroke/ or exp experimental stroke/ or lacunar stroke/
2.	(stroke or strokes).ti,ab.
3.	((cerebro* or cerebral*) adj2 (accident* or apoplexy)).ti,ab.
4.	(CVA or poststroke or poststrokes).ti,ab.
5.	*brain hemorrhage/ or *brain ventricle hemorrhage/ or *cerebellum hemorrhage/ or *subarachnoid hemorrhage/
6.	(brain adj2 (attack*1 or hemorrhag* or haemorrhag* or bleed* or infarct*)).ti,ab.
7.	((intracerebral or intracranial or cerebral* or cerebro* or cerebrum or cerebellum or subarachnoid* or choroidal or basal ganglia or subdural) adj3 (hemorrhag* or haemorrhag* or bleed*)).ti,ab.
8.	*brain infarction/ or *brain infarction size/ or *brain stem infarction/ or *cerebellum infarction/
9.	*Carotid Artery Thrombosis/

10.	((brain or brainstem or cerebr* or cerebell* or vertebrobasil* or verte brobasil* or hemisphere* or intracran* or intracerebral or infratentorial or supratentorial or mca*1 or anterior circulation or carotid or transient or lacunar) adj3 (infarct* or thrombo* or emboli* or occlus* or hypoxi*)).ti,ab.
11.	*brain ischemia/ or *hypoxic ischemic encephalopathy/
12.	((brain or brainstem or cerebr* or cerebell* or vertebrobasil* or verte brobasil* or hemisphere* or intracran* or intracerebral or infratentorial or supratentorial or mca*1 or anterior circulation or carotid or crescendo or transient or lacunar) adj3 isch?emi*).ti,ab.
13.	*Transient ischemic attack/
14.	(isch?emi* adj2 attack*).ti,ab.
15.	TIA.ti,ab.
16.	or/1-15
17.	letter.pt. or letter/
18.	note.pt.
19.	editorial.pt.
20.	case report/ or case study/
21.	(letter or comment*).ti.
22.	or/17-21
23.	randomized controlled trial/ or random*.ti,ab.
24.	22 not 23
25.	animal/ not human/
26.	nonhuman/
27.	exp Animal Experiment/
28.	exp Experimental Animal/
29.	animal model/
30.	exp Rodent/
31.	(rat or rats or mouse or mice).ti.
32.	or/24-31
33.	16 not 32
34.	(exp child/ or exp pediatrics/) not (exp adult/ or exp adolescent/)
35.	33 not 34
36.	health economics/
37.	exp economic evaluation/
38.	exp health care cost/
39.	exp fee/
40.	budget/
41.	funding/
42.	budget*.ti,ab.
43.	cost*.ti.
44.	(economic* or pharmaco?economic*).ti.
45.	(price* or pricing*).ti,ab.
46.	(cost* adj2 (effectiv* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.

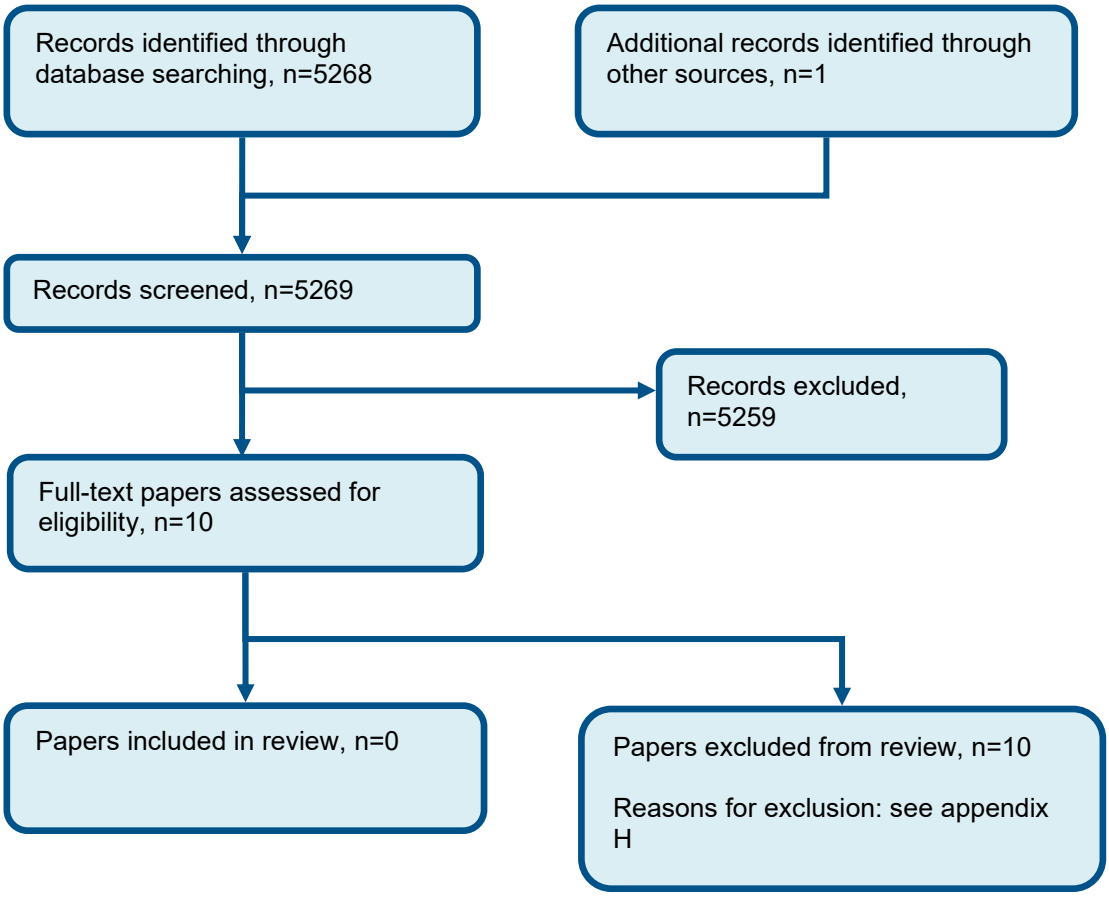
47.	(finance* or fee or fees).ti,ab.
48.	(value adj2 (money or monetary)).ti,ab.
49.	or/36-48
50.	35 and 49

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Stroke EXPLODE 1 2
#2.	((stroke or strokes))
#3.	(((cerebro* or cerebral*) adj2 (accident* or apoplexy)))
#4.	((CVA or poststroke or poststrokes))
#5.	MeSH DESCRIPTOR Intracranial Hemorrhages EXPLODE ALL TREES
#6.	((brain adj2 (attack*1 or hemorrhag* or haemorrhag* or bleed* or infarct*)))
#7.	(((intracerebral or intracranial or cerebral* or cerebro* or cerebrum or cerebellum or subarachnoid* or choroidal or basal ganglia or subdural) adj3 (hemorrhag* or haemorrhag* or bleed*)))
#8.	MeSH DESCRIPTOR Brain Infarction EXPLODE ALL TREES
#9.	MeSH DESCRIPTOR Carotid Artery Thrombosis EXPLODE ALL TREES
#10.	(((brain or brainstem or cerebr* or cerebell* or vertebrobasil* or verte brobasil* or hemisphere* or intracran* or intracerebral or infratentorial or supratentorial or mca*1 or anterior circulation or carotid or transient or lacunar) adj3 (infarct* or thrombo* or emboli* or occlus* or hypoxi*)))
#11.	MeSH DESCRIPTOR Brain Ischemia EXPLODE ALL TREES
#12.	(((brain or brainstem or cerebr* or cerebell* or vertebrobasil* or verte brobasil* or hemisphere* or intracran* or intracerebral or infratentorial or supratentorial or mca*1 or anterior circulation or carotid or crescendo or transient or lacunar) adj3 isch?emi*))
#13.	MeSH DESCRIPTOR Ischemic Attack, Transient EXPLODE ALL TREES
#14.	((isch?emi* adj2 attack*))
#15.	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14

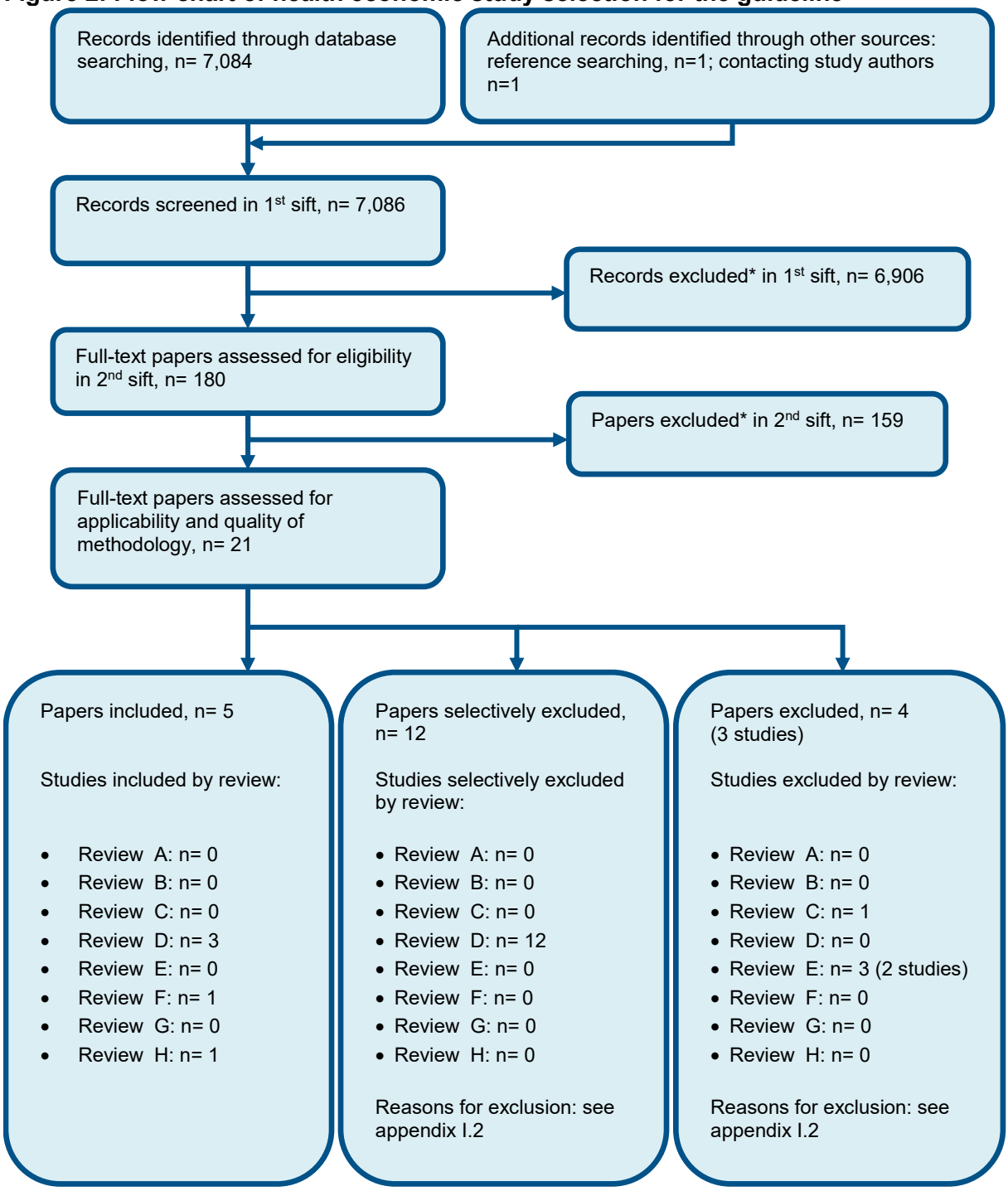
Appendix C: Clinical evidence selection

Figure 1: Flow chart of clinical study selection for the review of brain imaging in TIA



Appendix D: Health economic evidence selection

Figure 2: Flow chart of health economic study selection for the guideline



* Non-relevant population, intervention, comparison, design or setting; non-English language

Appendix E: Excluded studies

E.1 Excluded clinical studies

Table 7: Studies excluded from the clinical review

Coutts, 2012 [1]	Incorrect study type; no direct comparison
Coutts, 2012 [2]	Incorrect study type
Coutts, 2009 [3]	Incorrect study type; no direct comparison
Coutts, 2005 [4]	Incorrect study type; no direct comparison
Hefzy, 2013 [5]	Incorrect population
Kleinman, 2015 [7]	Incorrect intervention
Moreau, 2013 [8]	Incorrect study type
Moreau, 2013 [9]	Incorrect intervention
Souillard-Scemama, 2015 [11]	Incorrect study type; non systematic review
Wardlaw 2014 [12]	Incorrect study type

E.2 Excluded health economic studies

Table 8: Studies excluded from the health economic review

Reference	Reason for exclusion
Wardlaw 2014[12]	This analysis was an HTA published in 2014 that aimed to assess the cost effectiveness of routine MRI, including DWI, compared to routine CT in patients with TIA and minor stroke using economic modelling. It used a UK NHS perspective and QALYs as the health outcome measure. The population analysed was broader than the guideline review question as it included minor stroke as well as TIA (clinically TIA by definition has symptom resolution [within 24hrs and typically around 10 minutes] and in minor stroke symptoms persist after 24hrs; radiologically minor stroke will be DWI positive but TIA may not be; management and outcomes may also vary; some data in the model varied between people with TIA and minor stroke such as proportion of people with haemorrhage). The interventions compared were relevant for the review although did not cover all the options considered relevant by the committee – for example selective use of CT scanning in those with a 'red flag' for an alternative diagnosis that CT could detect. The model was comprehensive and model inputs were informed by systematic reviews. However, it was excluded because the clinical evidence the model was based on did not meet the inclusion criteria for the clinical review for the guideline. Specifically, the committee agreed that for the guideline evidence review diagnostic test and treat studies which compare clinical outcomes between groups where different diagnostic strategies have been used in people with TIA were the most useful evidence to inform decision making but no such studies were identified.

Appendix F: Research recommendation

F.1 Does early MRI brain scanning improve outcomes after suspected transient ischemic attack (TIA)?

Why this is important:

Stroke is the single largest cause of adult disability and the third most common cause of death in the UK. People with TIA are at higher risk for a subsequent stroke. The diagnosis of TIA is made by specialist assessment and remains a clinical diagnosis based primarily on the clinical history of the TIA event. Secondary prevention strategies are based on this assessment and are vital to reduce the risk of future stroke. It is not known whether information provided by an early MRI brain scan – within 24-48 hours of the TIA event – improves on the clinical assessment, secondary prevention strategies or overall outcomes after TIA.

Criteria for selecting high-priority research recommendations:

PICO question	Population: People aged over 16 years of age with suspected transient ischemic attack (TIA) Intervention(s): Routine MRI for all patients within 24-48 hours of TIA event. Comparison: Standard care based on clinical judgement and local protocols (i.e. no brain imaging, MRI at various time points or CT brain imaging if there is diagnostic doubt). Outcome(s): Stroke following TIA, mortality, recurrent vascular events, certainty of diagnosis, change in clinical management as a result of the MRI, improved elucidation of TIA mechanism, brain complications (bleeds), radiation exposure (from reduction in use of CT scans), quality of life
Importance to patients or the population	People who have a TIA are a high risk group for future disabling stroke. If doing an MRI in all those with a suspected TIA had a favourable impact on the risk of stroke then there would be a positive impact with fewer people left disabled, and with impaired quality of life. If doing an MRI improved the understanding of the underlying cause of a TIA (for example by paroxysmal atrial fibrillation [PAF], cerebral amyloid angiopathy [CAA]) this would improve secondary prevention strategies and lead to fewer incident strokes. There may also be reduced radiation exposure as a consequence of fewer CT head scans required.
Relevance to NICE guidance	Currently there is a lack of evidence of the benefits of brain imaging with MRI following TIA. An answer to this question would mean access to a more robust evidence base and would enable an analysis of cost effectiveness. A future NICE committee could then answer the question – should everyone with a suspected TIA have an MRI brain scan within 24 hours of the event?
Relevance to the NHS	The type and extent of brain imaging for people with suspected TIA is highly variable within the NHS. Some suspected TIA patients have no brain imaging, some have CT brain scans and others MRI at variable time points following the TIA. New NICE guidance on this issue would really help stroke services and imaging departments plan for future brain imaging requirements for people with suspected TIA. If there was good evidence for MRI brain imaging after TIA then this would have an impact on service delivery within radiology departments. It may lead to far fewer CT head scans being performed in this cohort. If routine MRI for all patients reduces the number of recurrent vascular events, then the upfront costs of imaging may be recuperated through a reduction in downstream costs such as rehabilitiation and long term care. This could result in cost savings for the NHS.

National priorities	There will be a new 'stroke strategic plan' launched in 2018/19 by The Stroke Association and NHS England. TIA and stroke will be covered in this document and responsive services for people with suspected TIA will be a priority area.
Current evidence base	The evidence review in the clinical guideline found no test-and-treat trials directly comparing CT brain imaging with MR imaging after TIA and there was a lack of a good comprehensive evidence base for MR imaging after TIA. There was also a lack of studies on cost effectiveness of brain imaging after suspected TIA.
Equality	Not relevant to this question. All groups would be considered in the research.
Study design	The most appropriate design would be a cluster (wedge) randomised test-and-treat trial design where people with suspected TIA are randomised in specific clusters to MRI at different early time points following the initial event or to standard care. Cluster randomisation is the most appropriate and practical design because it will allow each TIA service to operate under a single protocol at a given time. It would not be feasible for clinicians to randomise each case to MRI or control within one TIA service. Within a proposed intervention group (i.e. those having MRI) there would be a treatment algorithm for participating clinicians depending on the MRI findings. Treatment decisions and outcomes could then be analysed in the MRI and standard care (no MRI) clusters.
Feasibility	Most stroke services have daily TIA clinics seeing 900 or more suspected TIAs per year. The cost of an additional MRI scan is about £250. Service support costs should be low as there are daily clinics in most services from which the study could be run. Access of additional cases to MRI scanners will be the main issue for participating centres. As the stroke clinical research network is already established it is likely many centres would want to participate in such a study and utilise their research nurses to help recruitment.
Other comments	
Importance	• High: the research is essential to inform future updates of key recommendations in the guideline.