Software with artificial intelligence-derived algorithms for analysing CT brain scans in people with a suspected acute stroke: a systematic review and cost-effectiveness analysis

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Marie Westwood, Nigel Armstrong, and Charlotte Ahmadu planned and performed the systematic review and interpretation of evidence. Bram Ramaekers, Sabine Grimm, and Ben Wijnen planned and performed the cost effectiveness analyses and interpreted the results. Nigel Armstrong and Charlotte Ahmadu contributed to the planning and interpretation of the cost effectiveness analyses, acquisition of input data and conducted the model peer review. Shelley de Kock and Caro Noake

devised and performed the literature searches and provided information support to the project. Marie Westwood and Manuela Joore provided senior advice and support to the systematic review and cost effectiveness analyses, respectively. All parties were involved in drafting and/or commenting on the report.

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ABSTRACT

Background

Stroke is a serious life-threatening medical condition, the timely and effective management of which substantially impacts patients' outcomes. A number of artificial intelligence (AI)-derived software technologies have been developed, intended to facilitate the review of computed tomography (CT) images of the brain in patients with suspected stroke. These products are not intended to provide a diagnosis, but to support review and reporting by healthcare professionals.

Objectives

To evaluate the clinical and cost effectiveness of using AI-derived software to support the review of CT brain scans in acute stroke, in the National Health Service (NHS) setting.

Methods

Twenty-five databases were searched to July 2021. Review methods followed published guidelines. Study quality was assessed using appropriate risk of bias tools. Results were primarily summarised using a narrative synthesis, structured by a research question, AI-derived software technology and study type.

The health economic analysis focussed on the addition of AI-derived software assisted review of CT angiography (CTA) brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke. The de novo model (developed in R Shiny) consisted of a decision tree (short-term) and a state transition model (long-term) to calculate the mean expected costs and quality adjusted life years (QALYs) for people with ischaemic stroke and suspected large vessel occlusion (LVO) comparing AI-derived software assisted review to usual care.

Results

Twenty-two studies (30 publications) were included in the review. The majority (18/22 studies) concerned AI-derived software for the interpretation of (CTA) to detect LVO. No study evaluated an AI-derived software technology used as specified in the inclusion criteria for this assessment. For AI-derived software technology alone, the sensitivity and specificity estimates for proximal anterior circulation LVO were 95.4% (95% confidence interval (CI): 92.7% to 97.1%) and 79.4% (95% CI: 75.8% to 82.6%) for Rapid CTA, 91.2% (95% CI: 77.0% to 97.0%) and 85.0 (95% CI: 64.0% to 94.8%) for Viz LVO, 83.8% (95% CI: 77.3% to 88.7%) and 95.7% (95% CI: 91.0% to 98.0%) for Brainomix e-CTA, and 98.1% (95% CI: 94.5% to 99.3%) and 98.2% (95% CI: 95.5% to 99.3%) for Avicenna CINA LVO, based on one study each.

These studies were not considered appropriate to inform cost effectiveness modelling but formed the basis by which the accuracy of AI plus human reader could be elicited by expert opinion. Probabilistic analyses based on the expert elicitation to inform the sensitivity of the diagnostic pathway indicated that the addition of AI to detect LVO is potentially more effective (QALY gain of 0.003), more costly (increased costs of £8.61) and cost effective for willingness to pay thresholds of £3,380 per QALY and higher.

Conclusions

The available evidence is not suitable to determine the clinical effectiveness of using AI-derived software to support the review of CT brain scans in acute stroke.

The economic analyses did not provide evidence to prefer the AI-derived software strategy over current clinical practice. However, results indicated that if the addition of AI-derived software assisted review for guiding mechanical thrombectomy treatment decisions increased the sensitivity of the diagnostic pathway (i.e., reduced the proportion of undetected LVO's), this may be considered cost-effective.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

Technical terms and abbreviations are used throughout this report. The meaning is usually clear from the context, but a glossary is provided for the non-specialist reader.

AF	atrial fibrillation
AI	artificial intelligence
AiC	academic in confidence
AIS	acute ischaemic stroke
ASPECTS	Alberta Stroke Program Early CT Score
CADTH	Canadian Agency for Drugs and Technologies in Health
CBCT	cone beam computed tomography
CBF	cerebral blood flow
CBV	cerebral blood volume
CCT	controlled clinical trial
CDSR	Cochrane Database of Systematic Reviews
CEAC	cost-effectiveness acceptability curve
CEAF	cost-effectiveness acceptability frontier
CENTRAL	Cochrane Central Register of Controlled Trials
CI	confidence interval
CRD	Centre for Reviews and Dissemination
CSC	comprehensive stroke centre
CT	computed tomography
CTA	computed tomography angiography
CTP	computed tomography perfusion
CV	coefficient of variation
DAR	Diagnostic Assessment Report
DARE	Database of Abstracts of Reviews of Effects
DICOM	Digital Imaging Communications in Medicine
DM	diabetes mellitus
DTA	diagnostic test accuracy
ED	emergency department
EED	Economic Evaluations Database
ELC	expected loss curve
FAST	face arm speech test
FN	false negative
FP	false positive
GDPR	General Data Protection Regulation
HES	Hospital Episode Statistics
HIPAA	Health Insurance Portability and Accountability Act
HR	hazard ratio
HRQoL	health-related quality of life
HSROC	hierarchical summary receiver operating characteristic
HTA	Health technology Assessment
ICA	internal carotid artery
ICER	incremental cost effectiveness ratio

ICH	intracranial haemorrhage
INAHTA	International Network of Agencies for Health Technology Assessment
IQR	interquartile range
LILACS	Latin American and Caribbean Health Sciences Literature
LVO	large vessel occlusion
LY	life year
MCA	middle cerebral artery
MD	mean difference
MRI	magnetic resonance imaging
mRS	Modified Rankin Score
MTT	mean transit time
NA	not applicable
NCCT	non-contrast computed tomography
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NIH	National Institute of Health
NIHSS	National Institute of Health Stroke Scale
NIHR	National Institute for Health Research
NPV	negative predictive value
NR	not reported
ONS	Office for National Statistics
OR	odds ratio
PACS	picture archiving and communications systems
PPV	positive predictive value
PSA	probabilistic sensitivity analysis
PSC	primary stroke centre
PSSRU	Personal Social Services Research Unit
QALY	quality-adjusted life year
RCT	randomised controlled trial
RIS	radiology information systems
ROC	receiver operating characteristic
ROSIER	Recognition of Stroke In Emergency Rooms
SCI	Science Citation Index
SD	standard deviation
sICH	symptomatic intracranial haemorrhage
SIGN	Scottish Intercollegiate Guidelines Network
SROC	summary receiver operating characteristic
SSNAP	Sentinel Stroke National Audit Programme
TIA	transient ischaemic attack
Tmax	time to maximum
TN	true negative
TP	true positive

GLOSSARY

Cost effectiveness analysis	An economic analysis that converts effects into health terms and describes the costs for additional health gain.
Decision modelling	A mathematical construct that allows the comparison of the relationship between costs and outcomes of alternative healthcare interventions.
False negative	Incorrect negative test result – number of diseased persons with a negative test result.
False positive	Incorrect positive test result – number of non-diseased persons with a positive test result.
Incremental cost effectiveness ratio (ICER)	The difference in the mean costs of two interventions in the population of interest divided by the difference in the mean outcomes in the population of interest.
Index test	The test whose performance is being evaluated.
Meta-analysis	Statistical techniques used to combine the results of two or more studies and obtain a combined estimate of effect.
Meta-regression	Statistical technique used to explore the relationship between study characteristics and study results.
Opportunity costs	The cost of forgone outcomes that could have been achieved through alternative investments.
Publication bias	Bias arising from the preferential publication of studies with statistically significant results.
Quality of life	An individual's emotional, social and physical well-being and their ability to perform the ordinary tasks of living.
Quality-adjusted life year (QALY)	A measure of health gain, used in economic evaluations, in which survival duration is weighted or adjusted by the patient's quality of life during the survival period.
Receiver Operating Characteristic (ROC) curve	A graph which illustrates the trade-offs between sensitivity and specificity which result from varying the diagnostic threshold.
Reference standard	The best currently available method for diagnosing the target condition. The index test is compared against this to allow calculation of estimates of accuracy.
Sensitivity	Proportion of people with the target disorder who have a positive test result.
Specificity	Proportion of people without the target disorder who have a negative test result.
State-transition model	A model in which individuals move (**transition**) between disease **states** as their condition changes over time. Time spent in each disease **state** for a single **model** cycle (and **transitions** between **states**) is associated with a cost and a health outcome.
True negative	Correct negative test result – number of non-diseases persons with a negative test result.
True positive	Correct positive test result – number of diseased persons with a positive test result.

SCIENTIFIC SUMMARY

Background

The primary population for this assessment is people presenting or attending secondary care with a suspected acute stroke, who were last known to be well within 24 hours. Stroke is a serious life-threatening medical condition defined by the World Health Organization (WHO) as a clinical syndrome consisting of '*rapidly developing clinical signs of focal (at times global) disturbance of cerebral function, lasting more than 24 hours or leading to death with no apparent cause other than that of vascular origin.'* Timely and effective management of the patients with suspected stroke substantially impacts patients' outcomes.

A number of software products with AI-derived software technologies have been developed, which are intended to facilitate the review of computed tomography (CT) images of the brain in patients with suspected stroke. These products are not intended to provide a diagnosis, but to support review and reporting healthcare professionals.

Objectives

This assessment aimed to evaluate the clinical and cost effectiveness of using AI-derived software to support the review of CT brain scans in acute stroke, in the NHS setting. Three research questions were considered.

1. Does AI-derived software assisted review of non-enhanced CT brain scans for guiding thrombolysis treatment decisions for people with suspected acute stroke represent a clinically and cost-effective use of NHS resources?

2a. Does AI-derived software assisted review of CT angiography (CTA) brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke represent a clinically and cost-effective use of NHS resources?

2b. Does AI-derived software assisted review of CT perfusion brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke after a CTA brain scan represent a clinically and cost-effective use of NHS resources?

Methods

Assessment of clinical effectiveness

Twenty-five databases, including MEDLINE and EMBASE, research registers, conference proceedings and a pre-print resource were searched for relevant studies from inception to July 2021; up-date searches were conducted in October 2021. Search results were screened for relevance independently by two reviewers. Full text inclusion assessment, data extraction, and quality

assessment were conducted by one reviewer and checked by a second. The methodological quality of included diagnostic test accuracy (DTA) studies was assessed using QUADAS-2. The methodological quality of observational 'before and after' studies was assessed using a checklist, devised by the authors, for this review.

The hierarchical summary receiver operating characteristic (HSROC) model was used to estimate summary sensitivity and specificity with 95% confidence intervals (CIs) and prediction regions around the summary points, and to derive HSROC curves for meta-analyses of DTAs, where four or more studies evaluated the same intervention for a given research question. All other results, including those of 'before and after' studies, were summarised in a narrative synthesis, grouped by research question addressed, AI-derived software evaluated and study type.

Assessment of cost effectiveness

The health economic analysis focussed on research question 2a:

Does AI-derived software assisted review of CT angiography brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke represent a clinically and cost-effective use of NHS resources?

All diagnostic accuracy studies, identified by the systematic review conducted for this assessment, assessed the accuracy of AI-derived software technologies as stand-alone interventions. As a result, information about how AI-derived software technologies would perform when used as an adjunct/aid to human readers (i.e., as recommended by the manufacturers, as specified for this assessment and as they would be used in clinical practice) is lacking. This is because the accuracy of the device by itself tells us nothing about how, or indeed if, it might improve the accuracy of a human reader. It would not make sense to infer that any of the variation in sensitivity observed between standalone AIs can tell us something about precisely the variation in a hypothetical, small improvement in sensitivity of the human reader. In order to perform cost effectiveness analysis (CEA), we elicited expert opinion to estimate the diagnostic accuracy of AI as adjunct to human reader. Experts were provided with the evidence on AI alone and human reader alone. Because it was considered too difficult for experts to differentiate between different AI-derived software assisted review technologies, AI-derived software assisted review in general (not specified by manufacturer or specific technology) is considered.

The de novo model (developed in R Shiny) consisted of a decision tree (short-term) and a state transition model (long-term) to calculate the mean expected costs and quality adjusted life years (QALYs) for people with ischaemic stroke and suspected LVO.

The decision tree was used to estimate short term costs and consequences (first 90 days). Subsequently, patients with LVO are classified as either eligible for thrombectomy or not eligible. Those with both LVO and eligibility for thrombectomy are further classified, based on the sensitivity of the diagnostic strategy, into whether a LVO was detected (and thus thrombectomy received) or not. Based on the classification in the decision tree, patients were subdivided into health states according to the modified Rankin Scale (mRS). Notably, patients without LVO were subdivided, based on the specificity of the diagnostic strategy, into whether a LVO was incorrectly detected or not. If a LVO was incorrectly detected (i.e., false positive), this had cost consequences only (e.g., due to potential unnecessary transfer to experienced stroke centre qualified to perform thrombectomy). The long-term consequences in terms of costs and QALYs were estimated using a state transition cohort model with a lifetime time horizon (annual cycle length) and health states defined as per mRS states.

Probabilistic sensitivity analyses, deterministic sensitivity analyses and scenario analyses were performed.

Results

Assessment of clinical effectiveness

Twenty-two studies (30 publications) were included in the review. For nine of the 13 manufacturers of AI-derived software included in the scope, no studies were identified; all included studies concerned AI-derived software produced by Avicenna, Brainomix, iSchemaView or Viz. The majority (18/22 studies) reported data concerning research question 2a (i.e., evaluated AI-derived software for the interpretation of CTA). All included studies either assed the diagnostic accuracy of AI-derived software alone (i.e., **not** as it would be used in clinical practice, as recommended by the manufacturers and as specified in the inclusion criteria for this assessment) or were 'before and after' observational studies reporting information about the effects of implementing AI-derived software in treated patients.

Eleven studies provided information about the accuracy of various AI-derived software technologies for the detection of LVO on CTA scans in patients with acute ischaemic stroke. Where the target condition included occlusions of ICA, carotid terminus, or the M1- or M2-segments of the MCA, the sensitivity and specificity estimates were 95.4% (95% CI: 92.7% to 97.1%) and 79.4% (95% CI: 75.8% to 82.6%) for Rapid CTA, 91.2% (95% CI: 77.0% to 97.0%) and 85.0 (95% CI: 64.0% to 94.8%) for Viz LVO, 83.8% (95% CI: 77.3% to 88.7%) and 95.7% (95% CI: 91.0% to 98.0%) for Brainomix e-CTA, and 98.1% (95% CI: 94.5% to 99.3%) and 98.2% (95% CI: 95.5% to 99.3%) for Avicenna CINA LVO, based on one study each. There was some evidence to indicate that, where studies included more distal

(e.g., M3-segment of the MCA) elements of the anterior circulation or included posterior circulation in their definition of the target condition, sensitivity was reduced. All four studies that provided information about the effects of implementing Viz LVO and one study that provided information about the effects of implementing Rapid CTA reported that implementation was associated with reductions in time to treatment for thrombectomy patients and, where reported, with no significant change in clinical outcomes (mRS). However, it should be noted that two of the studies of Viz LVO and the study of Rapid CTA evaluated implementation in the context of providing an automated alert system (i.e., **not** as specified in the scope for this assessment); it is plausible that reductions in time to intervention, observed in these studies, may be driven by this 'early alert' step. The information provided by studies of this type is also limited in that it concerns only treated (i.e., test positive) patients; no information is provided about test negative patients, and hence there is no information about the extent to which AI-derived software, as implemented, may miss patients with LVO.

There is no evidence about the accuracy of AI-derived software when used as an aid to human interpretation; all evidence concerns only stand-alone AI. This might imply that a CEA is not feasible for any of the three research questions. However, we conducted a CEA in relation to the research question (2a) where there is most evidence about the performance of AI-derived software technologies alone and one study comparing an AI-derived software technology alone with human reader alone. These studies were not considered appropriate to inform cost effectiveness modelling but formed the basis by which the accuracy of AI plus human reader could be elicited by expert opinion.

Assessment of cost effectiveness

Base case analysis

The probabilistic results indicated that the addition of AI to detect LVO is potentially more effective (QALY gain of 0.003), more costly (increased costs of £8.61) and cost effective for willingness to pay thresholds of £3,380 per QALY and higher. The cost effectiveness plane illustrated the negative correlation between incremental costs and incremental QALYs, i.e., if a technology is more effective it also tends to be less costly. The cost effectiveness acceptability curve indicated that at willingness to pay values of £20,000 and £30,000 per QALY gained the probabilities of current practice with AI being cost effective are 54% and 56% respectively. The expected risk per patient associated with adding AI, at willingness to pay values of £20,000 and £30,000 per QALY gained, are £80 and £95 respectively (these were £122 and £163 respectively without adding AI; see expected loss curves). On a population level (assuming 87,635 annual patients in the UK) the estimated annual risks

associated with adding AI are £7,0 million and £8,4 million, at willingness to pay values of £20,000 and £30,000 per QALY gained respectively.

Secondary analysisSensitivity and scenario analyses

Sensitivity analyses indicated that the sensitivity of both technologies (i.e., with and without the addition of AI-derived software assisted review) was the most important input parameter. In addition, the proportion of patients with LVO that are eligible for mechanical thrombectomy is important to determine the most optimal strategy in terms of costs and QALYs. For the estimated costs, specificity, the additional costs of the AI technology, costs related to mRS4 and mRS5 were input parameters (in addition to those mentioned above) that can change the strategy that is most expensive. Consistently, the most influential scenario analyses were related to the sensitivity (for both strategies), the proportion of LVO patients eligible for mechanical thrombectomy with AI, removing the general population mortality cap and the additional costs of the AI technology.

Conclusions

The available evidence is not suitable to determine the clinical effectiveness of using AI-derived software to support the review of CT brain scans in acute stroke.

The economic analyses did not provide evidence to prefer the AI-derived software strategy over current clinical practice. However, results indicated that if the addition of AI-derived software assisted review for guiding mechanical thrombectomy treatment decisions increased the sensitivity of the diagnostic pathway (i.e., reduced the proportion of undetected LVOs) this may be considered cost-effective. Nevertheless, the sensitivity of AI-derived software assisted review when added to current clinical practice is largely uncertain and likely depends on the implementation of AI-derived software assisted review.

PLAIN ENGLISH SUMMARY

Stroke is a serious life-threatening medical condition caused by severely compromised blood supply to the brain. Restriction or stopping of the blood flow to the brain causes limited flow of oxygen and nutrients to the brain leading to the death of brain cells.

Timely and effective management of the patients with suspected stroke substantially impacts outcomes. Patients should preferably be cared for in designated specialised stroke units. However, some patients may initially be seen in places where some treatments (e.g., thrombectomy and neurosurgery) are not available and may need to be transferred.

Artificial intelligence (AI) derived software exists which is intended to facilitate the review of CT images of the brain in stroke. This assessment considered the effectiveness and value for money of using this software to help healthcare professionals with the review of CT brain scans.

Despite the growing number of research studies about AI-derived software for the review of CT brain scans in stroke patients, there is very little evidence to tell us how well this software works in practice. Studies have either assessed the accuracy of AI-derived software on its own (i.e., not with a healthcare professional's judgement, as it would be used in clinical practice and as recommended by the manufacturers) or assessed the effects of implementing AI-derived software in 'real world' clinical settings for treated patients only (i.e., no information is provided about the extent to which AI-derived software may miss patients). If the addition of AI-derived software assisted review to the diagnostic pathway for guiding mechanical thrombectomy treatment decisions were to reduce the proportion of undetected LVOs, it may be considered cost-effective. However, it is unclear how well AI-derived software assisted review works when added to current clinical practice. This also likely depends on how AI-derived software assisted review is implemented in current clinical practice.

1. OBJECTIVE

The overall objective of this assessment was to evaluate the clinical and cost effectiveness of using artificial intelligence (AI)-derived software to support the review of computed tomography (CT) brain scans in acute stroke, in the National Health Service (NHS) setting. The following research questions were defined to address the stated objective:

2. Does AI-derived software assisted review of non-enhanced CT brain scans for guiding thrombolysis treatment decisions for people with suspected acute stroke represent a clinically and cost-effective use of NHS resources?

2a. Does AI-derived software assisted review of CT angiography (CTA) brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke represent a clinically and cost-effective use of NHS resources?

2b. Does AI-derived software assisted review of CT perfusion brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke after a CTA brain scan represent a clinically and cost-effective use of NHS resources?

2. BACKGROUND AND DEFINITION OF THE DECISION PROBLEM(S)

2.1 Population

The primary population for this assessment is people presenting or attending secondary care with a suspected acute stroke, who were last known to be well within 24 hours. Within this population separate groups are considered for each research question (see Section 3).

Depending on the availability of evidence, the following subpopulation may be considered: People over the age of 80 years with small vessel disease and calcification of the cerebrovasculature.

The condition

Stroke is a serious life-threatening medical condition defined by the World Health Organization (WHO) as a clinical syndrome consisting of "*rapidly developing clinical signs of focal (at times global) disturbance of cerebral function, lasting more than 24 hours or leading to death with no apparent cause other than that of vascular origin"*.[1] Stroke can occur without any warning and leads to interruption or restriction of the blood flow to the brain causing reduction of the flow of oxygen and nutrients to the brain and subsequently brain cell death. The effects of a stroke depend on which area of the brain is affected, the extent of damage and the time to treatment.[2]

There are two main types of stroke:

- ischaemic stroke – the most frequently occurring type of stroke resulting from reduced blood flow due to arterial occlusion. Approximately 87.1% of patients in the United Kingdom (UK) will suffer from this type of stroke. Arterial blockage can be caused by the formation of atherosclerotic plaques (fatty deposits building up in the walls of arteries). As well as narrowing the artery, making it harder for blood to pass through it, the fatty deposits can break down or become inflamed. When this happens a blood clot forms, which can block the artery or a clot can travel from a distant location, such as from the heart or blood vessels in the neck and block the blood vessel in the brain (embolisation); the majority of the ischaemic strokes are caused by this mechanism rather than *in situ* thrombosis. Other causes of ischaemic stroke are small vessel disease leading to vessel damage, heart conditions (i.e., atrial fibrillation, patent foramen ovale, endocarditis) or arterial dissection.[2, 3]

- haemorrhagic stroke (also referred to as intracranial haemorrhage (ICH) or cerebral haemorrhage) – accounts for approximately 12.5% of all strokes in the UK and is caused by bleeding from blood vessels in or around the brain. This type of stroke can be intracerebral

(bleed within the brain) or subarachnoid (bleed on the surface of the brain in the subarachnoid space). Intracerebral haemorrhagic stroke is most associated with high blood pressure, resulting in the bursting of an artery, whereas subarachnoid haemorrhagic stroke is most frequently caused by a burst aneurysm.[2, 3]

A transient ischaemic attack (TIA), sometimes known as a mini stroke, is differentiated from ischaemic stroke in that symptoms are time limited/self-resolving. Patients who have experienced one or more TIAs are at increased risk for ischaemic stroke.[2] The diagnosis of TIA is not considered in this assessment.

In 2018-2019, there were 224,172 stroke hospital admissions (including stroke mimics) in the UK and the in-hospital crude mortality rate for 2017-2019 was reported to be 13.4%.[4] In the same year, there were over 1.2m stroke survivors in the UK with stroke prevalence (defined as patients who have had a stroke or TIA on a GP practice register) ranging from 1.77% in England to 2.28% in Scotland.[5]

2.1.1 Symptoms and risk factors

Common symptoms include drooping of one side of the face, problems with speaking and vision, loss of sensation in an arm or leg and slurred or garbled speech. Other symptoms can include nausea, vomiting, vertigo and decreased level of consciousness.[2]

The Sentinel Stroke National Audit Programme (SSNAP), the UK national healthcare quality improvement programme, collects patient data from England, Wales and Northern Ireland and provides information on patient characteristics, outcomes, and the infrastructure of stroke services. Among 89,280 stroke patients for whom data were collected between April 2019 and March 2020, the median age of patients with acute stroke in the UK was 77.[3] The risk of stroke increases with age due to continuous changes in brain arteries.[2] Females accounted for 48% of all acute stroke patients in the UK.[3]

It is estimated that approximately 90% of strokes are attributable to risk factors that can be modified during a patient's lifetime e.g., management of high blood pressure, diabetes, changes in smoking habits and addressing physical inactivity.[2] According to SSNAP, 55.1% and 22.5% of acute stroke patients in the UK suffered from hypertension and diabetes before their stroke, respectively.[3]

2.1.2 Diagnosis and treatment

Timely and effective management of the patients with suspected stroke substantially impacts patients' outcomes. As stroke mimics account for approximately 20% to 25% of all acute

presentations, the patient history is crucial to establish the potential cause of patient's symptoms and avoid misdiagnosis.[6]

Outside the hospital setting, patients with suspected stroke should be assessed using Face Arm Speech Test (FAST) and they must be transported to the hospital as quickly as possible, preferably to a stroke unit.[7] Specialised stroke units are trained in the management of stroke patients and have access to specialist medical staff, diagnostic imaging equipment, time-sensitive procedures such as thrombectomy and thrombolysis and other services. In the UK, these units are known as comprehensive stroke centres, defined as centres providing hyper-acute, acute, and inpatient rehabilitation including thrombectomy and neurosurgery services. Non-specialist units, however, may be unable to provide access to specialist medical staff or some crucial medical procedures which can affect the timely and effective selection and treatment of patients suffering from a stroke. In the UK, these units are known as acute stroke centres, defined as centres which provide hyper-acute, acute, and inpatient rehabilitation, but excluding thrombectomy and neurosurgery; all acute stroke centres are expected to have an intra hospital thrombectomy transfer pathway to transfer patients from acute stroke centres to comprehensive stroke centres.

In the emergency room, patients should be assessed with the Recognition of Stroke in the Emergency Room (ROSIER) scale.[7, 8] After admission, a CT or a magnetic resonance imaging (MRI) brain scan should be performed at the next available imaging slot and within an hour from arrival to rule out other causes of symptoms, provide information on the potential cause, show the extent of damage and decide on the best treatment option.[2] A CT scan is quick and effective method ruling out intracranial haemorrhage which is often sufficient to make thrombolysis decisions for patients with ischaemic stroke. However, the specificity of CT scan might be compromised in patients with acute ischaemia due to ongoing changes in the brain since the symptom onset.[6] Other tests may be needed, especially for patients with haemorrhagic stroke, to provide more information on the cause of stroke. In the UK, only 55.2% of acute stroke patients are scanned within 1 hour from admission, with the numbers rising to 95.5% for a scan within 12 hours from patient admission.[3] Admission directly to a stroke unit, and assessment by a stroke specialist, can lead to improved patient outcomes and reduction in complications. Patients who are seen in a specialist stroke unit are also more likely to receive more targeted secondary care.[2] Based on the SSNAP, between April 2019 and March 2020, the stroke unit was the first ward of admission for 79.9% of acute stroke patients in the UK.[3]

Some patients, however, may be initially transported to other units where direct specialist care is not available.

Patients with an ischaemic stroke can be treated with thrombolysis which uses alteplase to dissolve the clot blocking the artery in the brain.[2] The shorter the time between symptom onset and thrombolysis, the higher a patient's chance of better recovery, however, only a limited number of patients can benefit from this treatment due to the number of contraindications and potential complications that need to be considered. For stroke patients with unknown time of symptom onset, a recent systematic review showed that patients treated with alteplase thrombolysis had over three-times greater risk of symptomatic intracranial haemorrhage (sICH; a side effect of thrombolysis) when compared to patients receiving conservative medical treatment. There was no increase in the risk of death at 3 months and patients had a similar likelihood of functional independence.[9] Treatment with alteplase is also associated with an increased risk of ICH, compared to conservative treatment, in patients with a clearly defined time of stroke onset.[10]

Some ischaemic stroke patients may benefit from thrombectomy (i.e., extraction of arterial obstruction with a device). Thrombectomy is considered if the obstruction is present in a large artery[11] and has been shown to be superior to best medical therapy alone (e.g., thrombolysis alone) for patients with anterior circulation large artery occlusion.[6] [12] In patients with an ischaemic stroke, thrombolysis can be administered before mechanical thrombectomy without an increase in the incidence of sICH or mortality at 90 days when compared to thrombectomy alone. Similarly, there is no difference between treatments (thrombolysis plus thrombectomy versus thrombectomy alone) in the rates of successful recanalization or the level of patients' functional independence at 90 days.[13]

Patients with haemorrhagic stroke require intensive blood pressure-lowering medications or reversal of antithrombotic medications at the early stages of their treatment. Patients may undergo surgery to seal a burst aneurysm or relieve the pressure on the brain. Severe headaches can be addressed with pain relief medications.[2]

More information regarding the patient pathway, available treatments, and patient eligibility for treatment in the NHS setting is provided in Section 2.3.

2.2 Intervention technologies

Over recent years, a number of software products with AI-derived algorithms have been developed, which are intended to facilitate the review of CT images of the brain in conditions such as stroke. These products are not intended to provide a diagnosis, but rather to support the review of scans, reporting by a radiologist and prioritisation of critical cases.

For patients with suspected stroke, software using AI-derived algorithms may be a useful tool in the early stages of the treatment pathway, particularly where neuroradiologist assessment of the CT

images is not directly available. The use of AI-derived algorithms may potentially speed up the process of reviewing CT scans by identifying, quantifying, and notifying about clinically relevant brain structures related to acute stroke. Highlighting stroke-related changes in the patient' brain may assist in confirming a stroke, and along with other patient information, expedite the patient transfer and support assessments of the suitability of time-sensitive treatments such as thrombolysis and thrombectomy leading to improvement of patient outcomes. Other potential benefits include improved report turnaround time and enabling rapid review of scans by a multi-site clinical team.

These software products are typically designed to be incorporated into standard radiology CT workstations. This means they can work with existing forms of brain imaging (including non-contrast CT (NCCT), CTA and CT perfusion (CTP) imaging), radiology information systems (RIS) and picture archiving and communication systems (PACS). They are typically hosted on a web cloud which is separate from image exchange portals used to transfer images between care providers.

The Royal College of Radiologists published a position statement in AI in medical imaging[14] and subsequently published guidance on integrating AI with the radiology reporting workflows (RIS and PACS).[15] The guidance recommends that:

- '*AI must be integrated in reporting (radiology information system [RIS] and picture archiving and communication system [PACS]) workflows seamlessly and in a way that does not add extra burden to radiologists.*
- *The accuracy of the AI algorithms must be clearly declared for radiologists and others making decisions on patient management.*
- *AI findings must be communicated to the RIS via existing, widely used global technical standards (HL7).*
- *AI findings must be communicated to the PACS using existing, widely used global technical standards (Digital Imaging Communications in Medicine [DICOM]).*
- *The workflow must be robust enough to ensure AI analysis is complete and available on PACS before a human reporter starts image interpretation.'*[15]

In March 2020, NICE published Medtech innovation briefing 207 (MIB207; "Artificial intelligence for analysing CT brain scans")[16] describing AI-derived software for CT brain scans. Based on MIB207, "*the intended place in therapy would be to support radiologists in secondary care when they are reviewing CT brain scans of people with suspected brain abnormalities. The technology may be of most benefit when images are not first reviewed by neuroradiologists*."[16]

Several companies offer software with AI-derived algorithms for analysing CT brain scans in people with a suspected acute stroke. Some companies offer software that can be used to analyse NCCT, CTA and CTP scans (or have agreements between companies to offer their algorithms as a package), whereas others have software that can only analyse one of these types of scans. Some software packages do not have a dedicated platform through which they are delivered but may be housed on multivendor platforms for example Blackford analysis.

These technologies are classed as medical devices and require CE mark. Details of the technologies to be considered in this assessment are provided below. Where less detail is given, this is because only information available in the public domain was able to be used.

Table 1: Summary of types of CT scans analysed by AI-derived software platforms included in this assessment

Platform	Available to the NHS	Type of CT scan analysed		
		NCCT	CTA	CTP
icobrain ct**	✓			✓
Aidoc	✓	✓	✓	
Aidoc + icobrain	NYD	✓	✓	✓
RapidAI	✓	✓*	✓	✓
e-stroke	✓	✓*	✓	✓
Viz	✓	✓	✓	✓
qER**	NYD	✓		
Zebra-Med	TBC	✓		
CT Perfusion 4D	TBC			✓
Brainscan	TBC	✓		
Cercare stroke**	NYD			✓
Cina head**	✓	✓*	✓	
Accipio**	✓	✓		
Biomind	TBC	✓		

ASPECTS: Alberta Stroke Program Early CT Score; CT: computed tomography; CTA: CT angiography; CTP: CT perfusion; NCCT: non-contrast-enhanced CT; NHS: National Health Service; NYD: not yet deployed
*Gives ASPECTS score by assessing non-enhanced CT
**Provided through a multivendor platform, Blackford analysis. *Icobrain ct can also be provided stand alone*

2.2.1 icobrain ct

icobrain ct (Icometrix) is a CE marked (class 1 medical device) neuroimaging platform which uses AI-derived algorithms to detect abnormalities in brain CT scans. icobrain ct can generate two output reports related to stroke diagnosis:

- Report 1, from icobrain CTP (CT perfusion), details a quantitative assessment of perfusion in the brain based on a CT scan done with contrast. It analyses the flow of blood in areas of the brain to determine the presence of potentially salvageable tissues in ischaemic stroke. The

analysis includes a calculation of abnormality in parameters such as mean transit time (MTT), cerebral blood flow (CBF), cerebral blood volume (CBV) and time to maximum (Tmax) of residue function.

- Report 2, from icobrain tbi (traumatic brain injury), can give a quantitative assessment of intracranial haemorrhage (ICH) based on a non-enhanced CT scan. This report also has application in traumatic brain injury. Some of the non-contrast CT parameters measured include midline shift and asymmetry index between the left and right lateral ventricle.

The company notes that its AI-derived neuroimaging platform integrates with existing RIS and PACS. The software is intended for automatic labelling, visualization, and volumetric quantification of segmentable brain structures from a set of CT images. It receives digital images as input and generates an electronic report on quantitative parameters and annotated images. Results can be viewed as visual reports through digital imaging and communication in medicine (DICOM) output images, email notifications and on a web browser. The report highlights stroke-related changes that guide clinician diagnosis. Data transfer from and into the PACS is done securely over a software icobridge, installed on site. icobrain ct has had two major releases, Versions 4.0 and 5.0. The company notes that performance of icobrain in detecting ICH and for CT perfusion analysis has been tested on a series of scenarios that cover specific aspects of the software performance. icobrain ct algorithms send and receive information over a secure cloud 'Icometrix'. Icometrix is ISO13485 and ISO27001 certified and UK General Data protection Regulation (GDPR) and United States of America (USA) Health Insurance Portability and Accountability Act (HIPAA) compliant for privacy and security.

The company provides a training manual for health professionals which gives guidance on how to use the software and interpret reports. Customer support is also available from the company. Prior to deployment in clinical practice the company carries out a clinical and technical test phase. icobrain ct is currently a self-certified class 1 medical device under the Medical Device Directive, the company notes that it will be up classified to a class 2a medical device under the Medical Device Regulation, in line with the transition from the Medical Device Directive to the Medical Device Regulation.

2.2.2 Aidoc ICH, Aidoc LVO, Aidoc mobile

The Aidoc software (also called "BriefCase" [Aidoc]) is a CE marked (class 1 medical device) AI triage and notification platform. This neuroimaging platform uses AI-derived algorithms to detect abnormalities in brain CT scans. Algorithms related to stroke diagnosis include:

- Aidoc ICH for detecting suspected intracranial haemorrhage on non-contrast head CT
- Aidoc LVO for detecting suspected LVOs on CTA

The third component of the platform relevant to stroke diagnosis is Aidoc mobile, which is for communication between clinical stakeholders in the stroke pathway to facilitate peer review.

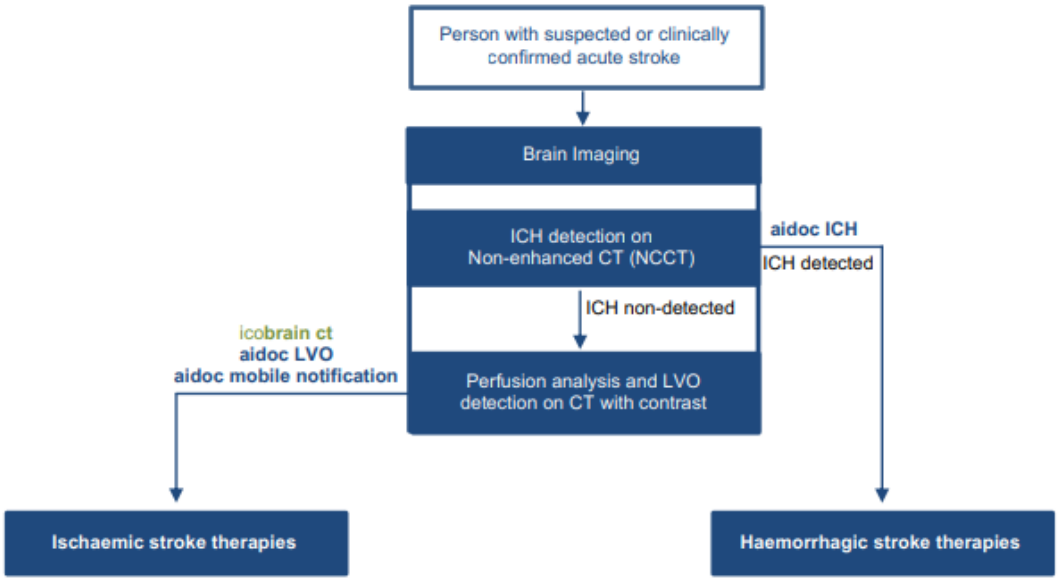
The company notes that its software can integrate with existing radiology workstation including PACS, reporting system and radiology workflow solutions. The platform can prioritise worklist, triage, and generate notification on suspected stroke cases. Analysis done by the AI-derived software is intended to supplement CT scan review by a neuroradiologist or stroke specialist.

The company provides an initial product training which lasts around 30 minutes and where necessary additional training on specific workflows can be provided. Recurring annual training is also available to review new features, enhancements, and algorithms. Prior to deployment of the software on a site, the company through its AI operations centre carries out an automated performance assessment. Aidoc is ISO13485 and ISO27001 certified. The Aidoc software is currently a self-certified class 1 medical device under the Medical Device Directive, the company notes that it will be up classified to a class 2a medical device under the Medical Device Regulation, in line with the transition from the Medical Device Directive to the Medical Device Regulation.

2.2.3 Icometrix and Aidoc 'comprehensive stroke solution'

Aidoc and Icometrix have partnered to provide a stroke solution in which the Aidoc software detects intracranial haemorrhage and large vessel occlusion and the icobrain software is used for CT perfusion analysis to detect ischaemic stroke. Figure 1 shows how the technologies are intended to be implemented in clinical practice.

Figure 1: Icometrix and Aidoc 'comprehensive stroke solution' pathway



2.2.4 Rapid ASPECTS, Rapid ICH, Rapid CTA, Rapid LVO, Rapid CTP)

RapidAI (iSchemaView) is a CE marked (class 2a medical device) neuroimaging platform which uses AI-derived software for detecting abnormalities in brain CT scans. The CT algorithms relevant to stroke diagnosis are:

- Rapid ICH is an image processing software that analyses non-enhanced CT head scans to detect, and flag suspected intracranial haemorrhage. Cases with suspected findings can be notified through email and the mobile application. The notification includes compressed images that are for informational purposes only and not intended to be diagnostic. The notified clinician is responsible for viewing non-compressed images on a diagnostic viewer and carrying out necessary patient evaluation.

- Rapid CTA is an image processing software that analyses head CT angiograms scans to provide neurologic vasculature maps with indications of hemispheric differences in the intracranial internal carotid artery (ICA)/middle cerebral artery (MCA) region which may indicate a large vessel occlusion.

- Rapid LVO is an image processing software that analyses head CT angiograms scans to highlight and notify cases with suspected large vessel occlusion

- Rapid CTP enables the assessment of salvageable brain tissue through the delivery of quantified and colour-coded CT perfusion maps that identify brain regions with reduced cerebral blood flow, volume, and transit time that exceed pre-specified thresholds. Imaging

datasets acquired from CT or Cone Beam Computed Tomography (CBCT) or MR Perfusion and Mismatch, MR Diffusion, and CT/MR Angiography are analysed to measure parameters that determine suitability for thrombectomy.

- RAPID ASPECTS is not intended for the primary interpretation of CT images. It assists the clinician in evaluating patients presenting for diagnostic imaging with known MCA or ICA occlusion, to assess the extent of disease on non-contrast CT scans. Extent of disease refers to the number of Alberta Stroke Program Early CT Score (ASPECTS) regions affected. Image data and AI analysis of morphological features is used to generate a single ASPECT score. This score is useful in characterising early signs of brain ischaemia, areas of irreversible tissue injury and to help the clinician assess patient eligibility for thrombectomy or thrombolysis.

The RapidAI platform runs on a standard computer or a virtual platform, such as VMware, and can be used to perform image viewing, processing, and analysis. The software receives DICOM compliant images as input primarily CT, CTA, CBCT and Magnetic Resonance (MR). Results from on Rapid platform can be viewed as visual reports through PACS, email notifications and the Rapid mobile app. Notifications have a sound option for positive cases and can be set to user defined thresholds to enable prioritisation. Results from multiple sites can be viewed and organised in one location. RapidAI is ISO certified and complies with GDPR and data security requirements.

The company provides training which includes online role-based product training, virtual instructor-led sessions led by clinical experts and performance support content.

2.2.5 e-ASPECTS, e-CTP, e-CTA

The e-Stroke platform (Brainomix) is a CE marked (class 2a medical device) neuroimaging platform that utilises AI-derived software for detecting anomalies in brain CT scans. The platform includes the following algorithms relevant to stroke diagnosis:

- e-ASPECTS which analyses non-contrast CT scans for clot detection, signs of hypodensity and generates a heat map of regional ischaemic change, volume of the change, and an automatic ASPECTS score.

- e-CTP which analyses CT perfusion scans to generate perfusion summary maps, report parameters such as mismatch volume and ratio, hypoperfusion intensity ratio, and assesses eligibility for mechanical thrombectomy.

- e-CTA which analyses CT angiogram scans to detect the location of LVOs and to generate a CT collateral score which is used to assesses eligibility for mechanical thrombectomy.

The software integrates with current imaging systems and results can be viewed as visual reports through DICOM output images, email notifications and a web browser.

2.2.6 Viz

The Viz platform (Viz.ai) is a CE marked (class 1 medical device) software which uses static AI-derived algorithms to detect abnormalities in brain scans in clinical practice. The algorithms relevant to stroke detection include:

- Viz LVO which analyses CTA images of the brain and sends notification to the clinician if a suspected large vessel occlusion has been detected. Notifications include compressed images that can be previewed for information purposes only. They are not intended to be diagnostic. The notified clinician is responsible for viewing non-compressed images on a diagnostic viewer and carrying out necessary patient evaluation.

- Viz ICH which analyses non-contrast CT images of the brain and sends notification to the clinician if a suspected intracranial haemorrhage has been detected.

- Viz CTP has communication and analysis capabilities for CT perfusion scans. The analysis includes the calculation of parameters related to tissue perfusion and tissue blood volume.

The company notes that the Viz platform integrates with currently available CT scanners and is designed to receive DICOM images which can be transferred securely to Viz.ai's GDPR-compliant Amazon Web Services cloud. Within the cloud, Viz.ai will analyse the imaging data for specific neurovascular disease. The platform can be used by hospital networks and trained clinicians.

The Viz platform is GDPR/HIPAA compliant and has ISO and SOC-2 certifications. Viz is currently a self-certified class 1 medical device under the Medical Device Directive, the company notes that it will be up classified to a class 2a medical device under the Medical Device Regulation, in line with the transition from the Medical Device Directive to the Medical Device Regulation.

2.2.7 qER

qER (Qure.ai) is a CE marked triage and notification tool that detects and quantifies a range of brain abnormalities intracerebral bleeds and their subtypes, infarcts, mass effect, midline shift and cranial fractures following non-contrast CT imaging. Based on information from https://grand-challenge.org/aiforradiology/, qER currently has class 2a CE mark. The software populates a

radiology reporting template with preliminary findings, patient prioritisation and alert systems including mobile notifications. It integrates with current imaging systems.

2.2.8 Zebra triage

Zebra-Med (Zebra Medical Vision) is a CE marked software that detects and annotates intracranial haemorrhage after non-contrast CT imaging and automates patient prioritisation and a real-time alert system. Based on information from https://grand-challenge.org/aiforradiology/, Zebra-Med currently has class 2a CE mark. It integrates with the current imaging worklist and viewer with an accompanying alert widget.

Zebra Medical Vision has now been acquired by Nanox (November 2021) and operates as Nanox.AI Nanox Completes Merger with Zebra Medical Vision, LTD., Re-brand as Nanox.AI, and Acquisition of MDWEB, LLC., and USARAD Holdings, Inc. | Nano-X Imaging LTD. The product is now called Neuro Solution.

2.2.9 CT Perfusion 4D Neuro

CT Perfusion 4D (GE Healthcare) is a CE marked medical device for CT perfusion image analysis of images obtained by cine imaging (in the head and body) after the intravenous injection of contrast. It produces image data and generates information regarding changes in image intensity over time and in calculation of the various perfusion-related parameters (including regional blood flow, regional blood volume, mean transit time and capillary permeability).

2.2.10 Brainscan

BrainScan CT (BrainScan) is a CE marked AI-derived platform that enables automatic detection and classification of pathological changes occurring in CT examinations of the brain. Based on information from https://grand-challenge.org/aiforradiology/, BrainScan CT currently has class 2a CE mark.

2.2.11 Cercare stroke

Cercare stroke (Cercare Medical) is a CE marked AI enabled stroke CT and MRI imaging software. The technology uses inputs from perfusion maps and additional maps of oxygen extraction and metabolism to provide an overview of brain tissues status in stroke. Based on information from https://grand-challenge.org/aiforradiology/, Ceracare stroke currently has class 2a CE mark.

2.2.12 CINA head

CINA head (Avicenna) uses CE marked (class 1 medical device) AI software for detecting abnormalities in brain CT scans. The algorithms in CINA head include:

- CINA ICH which identifies suspected intracranial haemorrhage on non-contrast CT scans and prioritises them on the radiologist's worklist.

- CINA LVO detects and prioritises the review of suspected LVOs on CTA.

- CINA ASPECTS analyses non-contrast CT and creates heat maps that indicate signs of hypodensity which help characterise early ischaemic brain tissue injury.

2.2.13 ACCIPIO

Accipio (MaxQ AI) is a CE marked AI-derived software that analyses non-contrast CT scan to identify and prioritise suspected intracranial haemorrhage. Based on information from https://grand-challenge.org/aiforradiology/, Accipio currently has class 2b CE mark.

2.2.14 Biomind

Biomind (Biomind.ai) is a CE marked (class not available publicly) AI-derived software used for detecting the location of intracerebral haemorrhage on CT scans and assessing its severity.

2.3 Comparator

The comparator for this technology appraisal is review of CT brain scans, by a neuroradiologist or other healthcare professional, unassisted by AI-derived software.

2.4 Care pathway

2.4.1 Stroke care service provision

The NHS Long Term Plan[17] identifies stroke as a clinical priority and sets out (Section 3.78) the NHS's ambition to support the national scaling of technology that will assist the expansion of life-changing treatments to more patients, which includes CT perfusion scans to assess the reversibility of brain damage, improved access to MRI scanning and the potential use of AI in the interpretation of CT and MRI scans to support clinical decisions regarding suitability for thrombolysis and thrombectomy.

The National Stroke Service Model: Integrated Stroke Delivery Networks[18] outlines best practices for stroke care, people with a suspected stroke should typically receive care within 4 hours in a hospital with a:

- Comprehensive stroke centre that provides hyper-acute, acute, and inpatient rehabilitation including thrombectomy and neurosurgery services or in an

- Acute stroke centre which provides hyper-acute, acute, and inpatient rehabilitation, but *excluding thrombectomy and neurosurgery*. All acute stroke centres are expected to have an

intra hospital thrombectomy transfer pathway to transfer patients from acute stroke centres to comprehensive stroke centres.

Hyper-acute stroke care usually covers the first 72 hours after a person is admitted. Services provided in the hyperacute phase include specialist clinical assessment, urgent imaging and skilled clinical interpretation of images, delivery of intravenous thrombolysis 24 hours a day, 7 days a week and transfer or treatment for thrombectomy. Imaging ensures that appropriate diagnosis is made, and time-dependent interventions are delivered. The guidance describes an optimal stroke imaging pathway (Figure 2).

2.4.2 Initial assessment

The diagnosis and initial management of patients with suspected stroke are discussed in National Institute for Health and Care Excellence (NICE) guideline NG128 ("Stroke and transient ischaemic attack in over 16s: diagnosis and initial management").[7] For a diagnosis of stroke or TIA, patients with sudden onset of neurological symptoms outside of hospital should be assessed using e.g., Face Arm Speech Test (FAST) tool and check for a potential episode of hypoglycaemia. For patients admitted to the emergency department, the early diagnosis should be established using e.g., a ROSIER tool.[7]

The NG128 recommends "*Admit everyone with suspected stroke directly to a specialist acute stroke unit after initial assessment, from either the community, the emergency department, or outpatient clinics. (An acute stroke unit is a discrete area in the hospital that is staffed by a specialist stroke multidisciplinary team. It has access to equipment for monitoring and rehabilitating patients. Regular multidisciplinary team meetings occur for goal setting.)"*[7] Similarly, Quality standard QS2 ("Stroke in adults") published by NICE[1] states "*Adults presenting at an accident and emergency (A&E) department with suspected stroke are admitted to a specialist acute stroke unit within 4 hours of arrival.*"

For patients with an initial diagnosis of acute stroke and an indication of prompt brain imaging, NG128[7] recommends immediate (i.e., "*ideally the next slot and definitely within 1 hour, whichever is sooner*") brain imaging with a non-enhanced CT to rule out or confirm intracranial haemorrhage, if any of the following apply:

- indications for thrombolysis or thrombectomy,
- on anticoagulant treatment,
- a known bleeding tendency,
- a depressed level of consciousness (Glasgow Coma Score below 13),

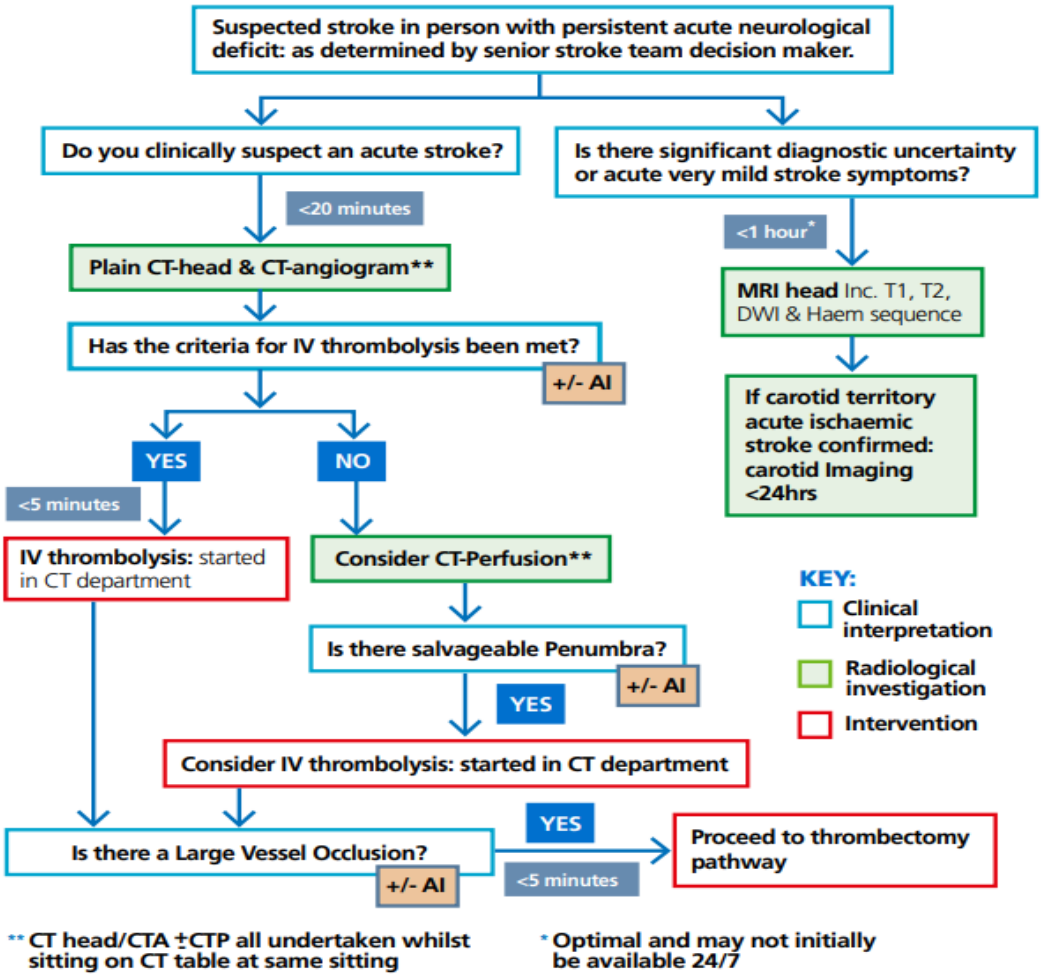
- unexplained progressive or fluctuating symptoms,
- papilloedema, neck stiffness or fever,
- severe headache at onset of stroke symptoms.

For patients with ischaemic stoke, CT with contrast angiography should be performed following an initial non-enhanced CT scan to confirm the presence of occlusion and/or clot. Addition of CT perfusion imaging, or MR equivalent, is recommended if thrombectomy is indicated beyond 6 hours of symptom onset in order to assess potential salvage of brain tissue.[7]

Patients with suspected acute stroke without indication for immediate brain imaging should be scanned as soon as possible and within 24 hours of symptom onset.[7]

The National Stroke Service Model guidance[18] describes an optimal stroke imaging pathway (see Figure 2) and recommends that stroke imaging, interpretation and transfer decisions are made within 20 minutes of patient's arrival.

Figure 2: National Stroke Service Model optimal imaging pathway



Source: The National Stroke Service Model: Integrated Stroke delivery Networks[18]

2.4.3 Treatment

Initially, patients with acute stroke must have their blood glucose concentration maintained and can be offered supplemental oxygen therapy if oxygen saturation drops below 95%.[7] The treatment options for patients with suspected or confirmed ischaemic or haemorrhagic stroke are summarised below.

Ischaemic stroke

For patients with suspected or clinically confirmed ischaemic stroke, NG128[7] and technology appraisal guidance 264 (TA264; Alteplase for treating acute ischaemic stroke)[19] recommends thrombolysis with alteplase (within its marketing authorisation) if:

- treatment is started as early as possible within 4.5 hours of onset of stroke symptoms,
- and intracranial haemorrhage has been excluded by appropriate imaging techniques.

Alteplase should be administered in a well organised stroke service with appropriately trained staff to deliver thrombolysis and monitor for any complications, nurse staff trained in acute stroke care and immediate access to brain imaging with professionals trained to interpret images. The procedure can also be carried out in the emergency department if staff are appropriately trained and supported and patients can be managed after the procedure in an acute stroke service.[7]

Thrombectomy for ischaemic stroke is recommended by NICE with more information available in interventional procedures guidance 548 (IPG548; "Mechanical clot retrieval for treating acute ischaemic stroke Interventional procedures guidance").[20]

For patients with acute ischaemic stroke and confirmed occlusion of the proximal anterior circulation demonstrated by CT or MR angiography, thrombectomy should be offered as soon as possible (if not contraindicated and within 6 hours of symptom onset), together with intravenous thrombolysis (within 4.5 hours).[7] Thrombectomy alone should be offered for the same patient population (acute ischaemic stroke and confirmed occlusion of the proximal anterior circulation demonstrated by CT or MR angiography) last known to be well between 6 hours to 24 hours (including wake-up strokes), with the potential to salvage brain tissue as shown by CT perfusion or diffusion-weighted MRI sequence.[7]

For patients last known to be well up to 24 hours (including wake-up strokes) with AIS and who have confirmed occlusion of the proximal posterior circulation demonstrated by CT or MR angiography

and the potential salvage brain tissue (as shown by CT perfusion or diffusion-weighted MRI sequence), thrombectomy is recommended together with intravenous thrombolysis.[7, 21]

Patients with ischaemic stroke are recommended to receive pharmacological treatment i.e., aspirin (or an alternative antiplatelet agent if there is intolerance to aspirin) within 24 hours. Anticoagulant therapy with heparin and then warfarin is recommended for people diagnosed with cerebral venous sinus thrombosis (including those with secondary cerebral haemorrhage).[7]

Haemorrhagic stroke

Surgical intervention following primary intracerebral haemorrhage can be considered for previously fit people. Initial medical treatment, instead of surgical intervention, should be offered for patients with:

- small deep haemorrhages,
- lobar haemorrhage without either hydrocephalus or rapid neurological deterioration,
- a large haemorrhage and significant comorbidities before the stroke,
- a score on the Glasgow Coma Scale of below 8 unless this is because of hydrocephalus,
- posterior fossa haemorrhage.[7]

The NG128 recommends a reversal of anticoagulation treatment using a combination of prothrombin complex concentrate and intravenous vitamin K, in people with a primary intracerebral haemorrhage who were receiving warfarin before their stroke.[7]

3. ASSESSMENT OF CLINICAL EFFECTIVENESS

Systematic review methods followed the principles outlined in the Centre for Reviews and Dissemination (CRD) guidance for undertaking reviews in health care[22], NICE Diagnostics Assessment Programme manual[23] and the Cochrane Handbook for Diagnostic Test Accuracy Reviews.[24]

3.1 Systematic review methods

3.1.1 Search strategy

Searches were undertaken to identify interventions using AI to diagnose acute stroke, as recommended in the CRD guidance for undertaking reviews in health care and the Cochrane Handbook for Diagnostic Test Accuracy Reviews.[22, 24]

Candidate search terms were identified from target references, browsing database thesauri (e.g., MEDLINE MeSH and Embase). Strategy development involved an iterative approach testing candidate text and indexing terms across a sample of bibliographic databases, so as to reach a satisfactory balance of sensitivity and specificity. Search strategies were developed specifically for each database and the keywords and thesaurus terms were adapted according to the configuration of each database. No restrictions on language, publication status or date were applied.

- MEDLINE (Ovid): 1946–2021/07/07
- MEDLINE In-Process Citations (Ovid): up to 2021/07/07
- MEDLINE Daily Update (Ovid): up to 2021/07/07
- MEDLINE Epub Ahead of Print (Ovid): up to 2021/07/07
- Embase (Ovid): 1974-2021/07/07
- Cochrane Database of Systematic Reviews (CDSR) (Wiley): up to 2021/07/Iss7
- Cochrane Central Register of Controlled Trials (CENTRAL) (Wiley): up to 2021/07/Iss7
- Science Citation Index (SCI) (Web of Science): 1988-2021/07/06
- Database of Abstracts of Reviews of Effects (DARE) (Internet) (https://www.crd.york.ac.uk/CRDWeb/): up to 2015/03/31
- Health Technology Assessment Database (HTA) (Internet) (https://www.crd.york.ac.uk/CRDWeb/): up to 2018/03/31
- KSR Evidence (KSR Ltd): up to 2021/07/07
- Epistemonikos (Internet) (https://www.epistemonikos.org/): up to 2021/07/07
- International Network of Agencies for Health Technology Assessment (INAHTA) Publication (Internet) http://www.inahta.org/: up to 2021/07/06
- NIHR Health Technology Assessment Programme (Internet) (https://www.nihr.ac.uk/): up to 2021/07/02
- Aggressive Research Intelligence Facility (ARIF) database (Internet) (http://www.birmingham.ac.uk/research/activity/mds/projects/HaPS/PHEB/ARIF/index.aspx): searched 2021/07/02
- PROSPERO (International Prospective Register of Systematic Reviews) (Internet) (http://www.crd.york.ac.uk/prospero/): up to 7 July 2021

- International Platform of Registered Systematic Review and Meta-analysis Protocols (Internet) (Home - INPLASY): up to 2021/07/02
- Latin American and Caribbean Health Sciences Literature (LILACS) (Internet) (http://regional.bvsalud.org/php/index.php?lang=en): up to 2021/07/02

The main Embase search strategy was independently peer reviewed by a second Information Specialist, using the PRESS-EBC checklist.[25]

Completed and ongoing trials were identified by searches of the following resources:

- NIH ClinicalTrials.gov (Internet) (http://www.clinicaltrials.gov/): up to 2021/07/02
- EU Clinical Trials Register (Internet) (https://www.clinicaltrialsregister.eu/ctr-search/search): up to 2021/07/28
- WHO International Clinical Trials Registry Platform (ICTRP) (Internet) (http://www.who.int/ictrp/en/: up to 2021/07/02
- ScanMedicine (Internet) (https://scanmedicine.com/): up to 2021/07/02

Conference Proceedings

To identify conference proceedings, searches in Embase were not restricted to exclude conference abstracts. Additional searches were also undertaken of the following specific conference proceedings resources:

- Northern Light Life Sciences Conference Abstracts (Ovid): 2010-2021/Wk25
- Conference Proceedings Citation Index (Web of Science): 1988–2021/07/06

Named technologies

An additional search was undertaken combining named AI technologies and terms for stroke in order to ensure no relevant studies were missed. These supplementary searches were restricted from 2017 to the present and were undertaken in the following resources:

- MEDLINE (Ovid): 1946-2021/09/03
- MEDLINE In-Process Citations (Ovid): up to 2021/09/03
- MEDLINE Daily Update (Ovid): up to 2021/09/03
- MEDLINE Epub Ahead of Print (Ovid): up to 2021/09/03
- Embase (Ovid): 1974-2021/09/03
- Northern Light Life Sciences Conference Abstracts (Ovid): 2010-2021/Wk34

Preprints Search

Given the fast-moving nature of this topic, the decision was made to conduct a further search of the medRxiv preprint server. All results retrieved from this resource were treated with due caution given the warning from the website's homepage that "*Preprints are preliminary reports of work that have not been certified by peer review. They should not be relied on to guide clinical practice or health-related behaviour and should not be reported in news media as established information*." [26]

- MedRxiv (Internet) (https://www.medrxiv.org): up to 2021/09/29

Guidelines

A search of the following resources from 2017 to present was conducted in order to identify the latest guidelines for stroke:

- TRIP database [Internet] (https://www.tripdatabase.com/): up to 2021/10/26
- Guidelines International Network (GIN) [Internet] (https://g-i-n.net/international-guidelines-library/): up to 2021/10/20
- Health Technology Assessment Database (HTA) (CRD): up to 2018/03
- National Institute for Health and Care Excellence (NICE)[Internet](https://www.nice.org.uk/guidance/): up to 2021/10/20
- NIHR Health Technology Assessment (HTA)[Internet](https://www.nihr.ac.uk/): up to 2021/10/20
- ECRI Guidelines Trust [Internet](https://guidelines.ecri.org/): up to 2021/10/20
- NHS Evidence (Internet) (https://www.evidence.nhs.uk/): up to 2021/10/20
- International HTA Database (INAHTA) [Internet](https://database.inahta.org/): up to 2021/10/20

Update searches

To ensure no new relevant papers had been published since the original core strategies were run in July 2021, the main Embase and MEDLINE searches were rerun in their entirety in October 2021 before submission of the draft report. Results were deduplicated against the original search results and for completeness the MedRxiv preprints search was also updated:

- MEDLINE (Ovid): 1946-21/10/15
- MEDLINE In-Process Citations (Ovid): up to 21/10/15
- MEDLINE Daily Update (Ovid): up to 21/10/15
- MEDLINE Epub Ahead of Print (Ovid): up to 21/10/15
- Embase (Ovid): 1974-2021/10/18
- MedRxiv (Internet) (https://www.medrxiv.org): up to 2021/10/20

Search strategies for all the resources listed above are presented in Appendix 1.

Hand searching

The bibliographies of included articles and relevant systematic reviews were checked for additional studies.

All identified references were downloaded in Endnote software for further assessment and handling. Results for the searches described above were imported into a single project library and deduplicated against each other. All search results (both clinical and economics) were screened for all areas of interest. Rigorous records were maintained as part of the searching process. Individual records within the Endnote reference library were tagged with search information, including the name of the searcher, date searched, database name and host, strategy name and iteration.

3.1.2 Inclusion and exclusion criteria

Separate inclusion criteria were developed for each of the three research questions, and these are summarised in Table 2.

Comparative studies, which reported secondary outcomes only (time to intervention and acceptability to clinicians), were included, in order to maximise the available information for these outcomes. However, it should be noted that these outcomes alone are not sufficient to inform meaningful estimates of the clinical and cost effectiveness of software using AI-derived algorithms for analysing CT brain scans in people with a suspected acute stroke; because it is possible, for example, for the use of such software to reduce time to intervention whilst also being associated with poorer clinical outcomes, secondary outcome data are only useful for decision making when combined with data on higher-level outcomes (clinical outcomes or measures of diagnostic performance).

Table 2: Inclusion criteria

Decision question 1	**Is the use of AI-derived software to assist review of non-enhanced CT brain scans to guide thrombolysis treatment decisions for people with suspected acute stroke a clinically effective intervention?**	
Research question	**What is the diagnostic performance of AI-derived software assisted review of plain CT brain scans to rule-out ICH and to rule-in ischaemic stroke in people with suspected acute stroke?**	**What are the clinical effects of using AI-derived software assisted review of plain CT brain scans to guide thrombolysis treatment decisions in people with suspected acute stroke?**
Participants:	Adults (≥18 years old) attending a secondary care stroke centre with suspected acute stroke and who were last known to be well within 24 hours	
Interventions (index test):	AI-derived software assisted review of plain CT brain scan by a healthcare professional other than a neuroradiologist	AI-derived software assisted plain CT brain scan review by a neuroradiologist or other healthcare professional
Comparators:	AI-derived software assisted plain CT brain scan review by a healthcare professional other than a neuroradiologist, using a different AI-derived technology, or unassisted plain CT brain scan review by a healthcare professional other than a neuroradiologist	Unassisted plain CT brain scan review by a neuroradiologist or other healthcare professional
Reference standard:	Unassisted plain CT brain scan review by a neuroradiologist, or by a consensus panel	Not applicable
Outcomes:	Test accuracy (the numbers of true positive, false negative, false positive and true negative test results), for the target conditions ICH and ischaemic stroke. *Where reported, information will also be extracted on technical failure rates, time to intervention and ease of use/acceptability to clinicians	Clinical/patient-perceived outcomes: mortality, function (e.g., mRS), health-related quality of life, adverse events (e.g., bleed subsequent to thrombolysis), length of hospital stay. *Where reported, information will be extracted on technical failure rates, time to thrombolysis/rate of thrombolysis within the clinically appropriate time window, time in emergency department prior to admission or discharge and ease of use/acceptability to clinicians
Study design:	Diagnostic accuracy studies	All comparative study designs: study designs will be included in a hierarchical manner (RCTs, CCTs, observational studies), i.e., CCTs and observational studies will only be considered for inclusion where no

		RCTs are identified, or where there are concerns about the applicability (e.g., non-UK settings) or risk of bias for identified RCTs
Decision question 2a	**Is the use of AI-derived software to assist review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?**	
Research question	**What is the diagnostic performance of AI-derived software assisted review of CTA brain scans to guide thrombolysis treatment decisions in people with confirmed ischaemic acute stroke?**	**What are the clinical effects of using AI-derived software assisted review of CTA to guide mechanical thrombectomy treatment decisions in people with confirmed ischaemic stroke?**
Participants:	Adults (≥18 years old) attending a secondary care stroke centre with AIS, who were last known to be well within 6 hours	
Interventions (index test):	AI-derived software assisted CTA brain scan review by a healthcare professional other than a neuroradiologist	AI-derived software assisted CTA brain scan review by a neuroradiologist or other healthcare professional
Comparators:	AI-derived software assisted CTA brain scan review by a healthcare professional other than a neuroradiologist, using a different AI-derived technology, or unassisted CTA brain scan review by a healthcare professional other than a neuroradiologist	Unassisted CTA brain scan review by a neuroradiologist or other healthcare professional
Reference standard:	Unassisted CTA scan review by a neuroradiologist, or by a consensus panel	Not applicable
Outcomes:	Test accuracy (the numbers of true positive, false negative, false positive and true negative test results) for the target condition (large vessel occlusion/occlusion of the proximal anterior circulation) *Where reported, information will also be extracted on technical failure rates, time to start of interventional procedure (insertion of catheter) and ease of use/acceptability to clinicians	Clinical/patient-perceived outcomes: mortality, function (e.g., mRS), health-related quality of life, procedure-related adverse events (e.g., bleed subsequent to thrombolysis), length of hospital stay. *Where reported, information will be extracted on technical failure rates, time to start of interventional procedure (insertion of catheter), reperfusion rates and ease of use/acceptability to clinicians
Study design:	Diagnostic accuracy studies	All comparative study designs: study designs will be included in a

		hierarchical manner (RCTs, CCTs, observational studies), i.e., CCTs and observational studies will only be considered for inclusion where no RCTs are identified, or where there are concerns about the applicability (e.g., non-UK settings) or risk of bias for identified RCTs
Decision question 2b	**Is the use of AI-derived software-assisted review of CT perfusion brain scans to guide mechanical thrombectomy treatment decisions for people with an ischaemic stroke, after a CTA brain scan, a clinically effective intervention?**	
Research question	**What is the diagnostic performance of AI-derived software assisted review of CTA and CT perfusion brain scans to guide thrombolysis treatment decisions in people with confirmed ischaemic acute stroke?**	**What are the clinical effects of using AI-derived software assisted review of CTA and CT perfusion brain scans to guide mechanical thrombectomy treatment decisions in people with confirmed ischaemic stroke?**
Participants:	Adults (≥18 years old) attending a secondary care stroke centre with suspected acute stroke, who were last known to be well more than 6 hours previously, but within 24 hours, and in whom ischaemic stroke has been confirmed on plain CT	
Interventions (index test):	AI-derived software assisted CTA and CT perfusion brain scan review by a healthcare professional other than a neuroradiologist	1. AI-derived software assisted CTA and AI-derived software assisted CT perfusion brain scan review by a neuroradiologist or other healthcare professional 2. Unassisted CTA and AI-derived software assisted CT perfusion brain scan review by a neuroradiologist or other healthcare professional
Comparators:	AI-derived software assisted CTA and CT perfusion brain scan review by a healthcare professional other than a neuroradiologist, using a different AI-derived technology, or unassisted CTA and CT perfusion brain scan review by a healthcare professional other than a neuroradiologist	Unassisted CTA brain scan review by a neuroradiologist or other healthcare professional and unassisted CT perfusion brain scan review by a neuroradiologist
Reference standard:	Unassisted CTA and CT perfusion scan review by a neuroradiologist, or by a consensus panel	Not applicable
Outcomes:	Test accuracy (the numbers of true positive, false negative, false positive and true negative test results) for the target	Clinical/patient-perceived outcomes: mortality, function (e.g., mRS), health-related quality of life, procedure-related adverse events (e.g.,

	conditions (large vessel occlusion/occlusion of the proximal anterior circulation for CTA and presence of salvageable tissue for CT perfusion) *Where reported, information will also be extracted on technical failure rates, time to start of interventional procedure (insertion of catheter) and ease of use/acceptability to clinicians	bleed subsequent to thrombolysis), length of hospital stay. *Where reported, information will be extracted on technical failure rates, time to start of interventional procedure (insertion of catheter), reperfusion rates and ease of use/acceptability to clinicians
Study design:	Diagnostic accuracy studies	All comparative study designs: study designs will be included in a hierarchical manner (RCTs, CCTs, observational studies), i.e., CCTs and observational studies will only be considered for inclusion where no RCTs are identified, or where there are concerns about the applicability (e.g., non-UK settings) or risk of bias for identified RCTs
*Secondary outcomes, which are not sufficient to inform decision making in the absence of higher-level outcomes data		

3.1.3 Inclusion screening and data extraction

Two reviewers independently screened the titles and abstracts of all reports identified by searches and any discrepancies were discussed and resolved by consensus. Full copies of all studies deemed potentially relevant were obtained and the same two reviewers independently assessed these for inclusion; any disagreements were resolved by consensus. Details of studies excluded at the full paper screening stage are presented in Appendix 4, along with reasons for exclusion.

Studies cited in materials provided by the manufacturers of software with AI-derived algorithms for analysing CT brain scans in people with suspected stroke were first checked against the project reference database, in Endnote X20; any studies not already identified by our searches were screened for inclusion following the process described above.

Where available, data were extracted on the following: study design/details, participant characteristics, details of the AI-derived software (e.g., manufacturer, version used, mode of implementation), details of the CT scanner and imaging protocol(s), details of comparator (i.e., who reviewed the scans), clinical outcomes (e.g., Modified Rankin Score (mRS)), 2x2 data to calculate test performance outcome measures (sensitivity, specificity positive predictive value (PPV) and negative predictive value (NPV)), technical failure rates and time to intervention (time from imaging to intravenous thrombolysis or to groin puncture for mechanical thrombectomy). Data were extracted by one reviewer using standard data extraction forms. A second reviewer checked data extraction and any disagreements were resolved by consensus or discussion with a third reviewer.

3.1.4 Quality assessment

The methodological quality of studies reporting diagnostic accuracy data was assessed using QUADAS-2.[27] The methodological quality of observational 'before and after' studies was assessed using a checklist, devised by the authors, for this review. Quality assessment was undertaken by one reviewer and checked by a second reviewer, and any disagreements were resolved by consensus or discussion with a third reviewer.

The results of the quality assessments are summarised and presented in tables (Section 3.2.2) and are provided in full, by study, in Appendix 3.

3.1.5 Methods of analysis/synthesis

Where multiple studies evaluated the accuracy of the same AI-derived software for the same target condition, the hierarchical summary receiver operating characteristic (HSROC) model was used to estimate summary sensitivity and specificity with 95% CIs and prediction regions around the

summary points, and to plot HSROC curves. Pooled results were only obtained from meta-analyses involving four or more studies.[28-30] This approach allows for between-study heterogeneity in sensitivity and specificity, and for the trade-off (negative correlation) between sensitivity and specificity commonly seen in diagnostic meta-analyses. Analyses were performed in Stata 13 (StataCorp LP, College Station, Texas, USA), mainly using the *metandi* command.

All other results, including those from 'before and after' studies of the implementation of AI-derived software technologies, were summarised in a narrative synthesis.

The results of included studies are grouped by research question addressed, AI-derived software evaluated and study type.

3.2 Results of the assessment of clinical effectiveness assessment

The literature searches of bibliographic databases conducted for this assessment identified 6145 unique references, after deduplication. Following initial screening of titles and abstracts, 193 were considered to be potentially relevant and ordered for full paper screening; of these, two publications[31, 32] could not be obtained and 27 were included in the review.[33-59] An additional two publications,[60, 61] cited in documents supplied by the technology manufacturers, met the inclusion criteria for this assessment and were included in the review; one of these[60] was an additional conference abstract, relating to a study for which our searches had already identified two publications,[37, 38] and the other[61] was published in a journal not indexed in the databases searched. One further un-published article was provided, AiC, by a specialist committee member.[62] All remaining potentially relevant studies cited in documents supplied by the technology manufacturers had already been identified by bibliographic database searches. Figure 3 shows the flow of studies through the review process, and Appendix 4 provides details, with reasons for exclusion, of all publications excluded at the full paper screening stage.

3.2.1 Overview of included studies

Based on the searches and inclusion criteria described above, a total of 30 publications[33-61] relating to 22 studies[33-36, 39-41, 43-46, 48-52, 55, 56, 59-62] were included in the review; the results section of this report cites studies using the primary publication and, where this is different, the publication in which the referenced data were reported.

The studies included in this review evaluated AI-derived software technologies produced by iSchemaView (iSchemaView, Menlo Park, CA), Viz (Viz.ai Inc., San Francisco CA), Brainomix (Brainomix, Oxford, UK) and Avicenna (Avicenna.ai, La Ciotat, France). For iSchemaView, three studies evaluated Rapid CTA, [33, 35, 36] two studies evaluated Rapid LVO,[41, 55] one study evaluated Rapid

CTP[50] and two studies assessed the effects of implementing RapidAI (comprising Rapid CTA and Rapid CTP).[34, 49] Eight studies evaluated Viz LVO[40, 43, 45, 46, 52, 59-61] and one study evaluated Viz ICH.[39] For Brainomix, one study evaluated e-CTA,[56] one study evaluated e-ASPECTS,[62] one study assessed the effects of implementing the e-ASPECTS and e-CTA components of the e-Stroke Suite[44] and one study evaluated an un-specified 'AI-based algorithm developed by Brainomix'.[48] The remaining study evaluated CINA LVO, produced by Avicenna.[51] **We did not identify any studies that evaluated the remaining AI-derived software technologies described in Section 2.2 of this report.**

We did not identify any studies, conducted in the UK which met the inclusion criteria for this assessment. [redacted].[62] Twelve of the 22 included studies were conducted in the USA,[33, 34, 39, 40, 43, 45, 46, 51, 52, 59-61] one study each was conducted in Australia,[36] Canada,[55] Germany[56] and Hungary,[44] three studies were multi-centre studies conducted in the USA, Brazil and Switzerland,[41] in the USA and the Netherlands,[50] and [redacted],[62] the remaining three studies did not report information on geographic location.[35, 48, 49]

Eight of the 22 included studies reported receiving some support from the manufacturers of AI-derived software technologies (including shareholdings, consulting fees and employment in relation to individual study authors),[35, 36, 41, 46, 51, 56, 59, 61] three studies reported receiving no funding,[33, 34, 52] two studies were publicly funded,[50, 62] and nine studies reported no information about funding.[39, 40, 43-45, 48, 49, 55, 60]

Full details of the characteristics of study participants, study inclusion and exclusion criteria, AI-derived software technologies evaluated, and reference standard (for diagnostic test accuracy studies) or comparator (for before and after studies) are reported in the data extraction tables presented in Appendix 2 (Tables 32 and 33).

Figure 3: Flow of studies through the review process

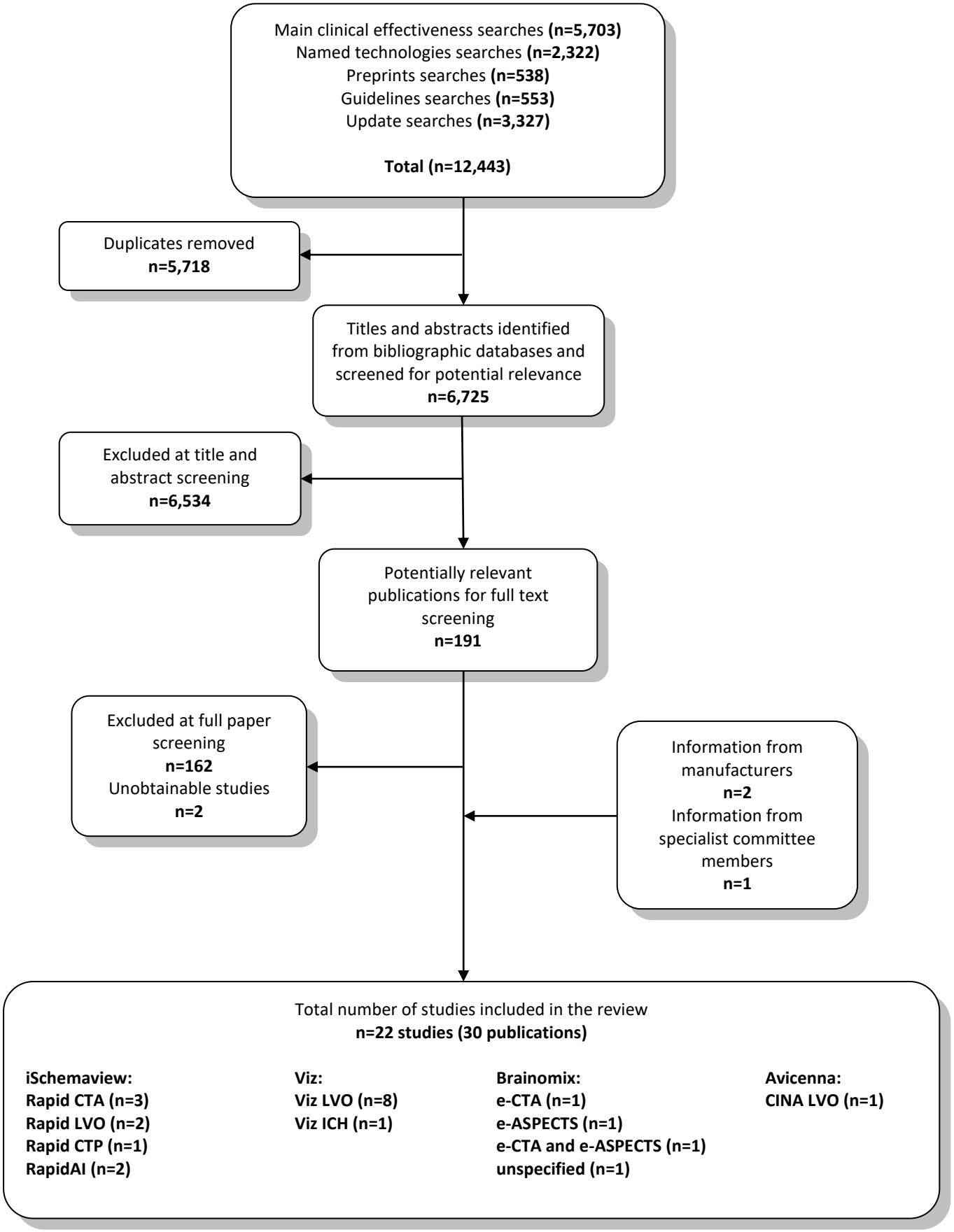


Table 3: Overview of included diagnostic test accuracy studies

Study details	Country	N	Target condition(s) reported	Subgroups reported
(Q1) Is AI-derived software assisted review of non-enhanced CT brain scans for guiding thrombolysis treatment decisions for people with suspected acute stroke a clinically effective intervention?				
Viz ICH				
Barriera 2018d[39]	USA	284	ICH	None
Brainomix (unspecified)				
Herweh 2020[48]	NR	160	ICH	None
Brainomix e-ASPECTS				
Mair 2021[62]	[redacted]	[redacted]	[redacted]	[redacted]
(Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective use intervention?				
iSchemaView Rapid CTA				
Amukotuwa 2019a[*35]	NR	926	Intracranial anterior circulation LVO (ICA, carotid terminus or M1- segment of the MCA) ICA occlusion M1-segment MCA occlusion M2-segment MCA occlusion Intracranial anterior LVO (ICA, carotid terminus or M1- segment of the MCA) or M2-segment of the MCA occlusion	None
Amukotuwa 2019b[*36]	Australia	477	Intracranial anterior circulation LVO (ICA, carotid terminus or M1- segment of the MCA) M2-segment MCA occlusion Intracranial anterior LVO (ICA, carotid	None

Study details	Country	N	Target condition(s) reported	Subgroups reported
			terminus or M1- segment of the MCA) or M2-segment of the MCA occlusion	
iSchemaView Rapid LVO				
Dehkharghani 2021[41] Dehkharghani 2021[42]	USA; Switzerland; Brazil	217	Intracranial anterior circulation LVO (ICA, carotid terminus or M1- segment of the MCA)	Age: 20-39 years; 40-59 years; ≥60 years CT scanner: GE Medical Systems; Siemens; Toshiba
Paz 2021[55]	Canada	151	LVO (ICA, carotid terminus or M1-segment of the MCA) or M2/3-segment of the MCA occlusion	None
Viz LVO				
Barreira 2018a[60] Barreira 2018b[37] Rodrigues 2019a[38]	USA	875	Intracranial anterior circulation LVO (ICA, carotid terminus or M1- segment of the MCA)	None
Chatterjee 2018[40]	USA	54	Intracranial anterior LVO (ICA, carotid terminus or M1- segment of the MCA) or M2-segment of the MCA occlusion	None
Dornbos 2020[43]	USA	680	Intracranial anterior LVO (ICA, carotid terminus or M1- segment of the MCA), distal M2-segment of the MCA or posterior circulation occlusion	None
Shalitin 2020[61]	USA	2544	LVO (not defined)	None
Yahav-Dovrat 2021[59]	USA	1167	LVO (not defined)	'Stroke protocol' patients
Brainomix e-CTA				
Seker 2020[56] Seker 2019a[57] Seker 2019b[58]	Germany	301	Proximal (ICA or proximal M1 segment of the MCA) or distal (distal M1 segment or proximal M2 segment of the MCA) LVO Proximal LVO (terminal ICA and proximal	None

Study details	Country	N	Target condition(s) reported	Subgroups reported
			M1 segment of the MCA)	
Avicenna CINA LVO				
McLouth 2021[51]	USA	378	Intracranial anterior LVO (ICA, carotid terminus or M1- segment of the MCA) or M2-segment of the MCA occlusion	Age: 18-39 years; 40-70 years; >70 years Male/Female CT scanner: GE Medical Systems; Philips; Siemens; Canon (formerly Toshiba)
(Q2b) Is AI-derived software assisted review of CT perfusion brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke after a CTA brain scan a clinically effective intervention?				
iSchemaView Rapid CTP				
Kauw 2020[50]	Netherlands; USA	176	Suitability for thrombectomy	None

*Overlapping study populations
Publications in **bold** have provided data for inclusion in this assessment
AIS: acute ischaemic stroke; CT: computed tomography; CTA: computed tomography angiography; ICA: internal carotid artery; ICH: intracranial haemorrhage; LVO: large vessel occlusion; MCA: middle cerebral artery; N: number

Table 4: Overview of included observational 'before and after' studies

Study details	Country	N	Time to intervention outcome reported	Clinical outcome(s) reported
(Q1) Is AI-derived software assisted review of non-enhanced CT brain scans for guiding thrombolysis treatment decisions for people with suspected acute stroke a clinically effective intervention? AND (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?				
Brainomix e-ASPECTS and e-CTA				
Gunda 2020[44]	Hungary	797	Time from CTA to groin puncture (thrombectomy) Time from door to needle (thrombolysis)	None
(Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?				

Study details	Country	N	Time to intervention outcome reported	Clinical outcome(s) reported
iSchemaView Rapid CTA				
Adhya 2021[33]	USA	310	Time from CTA to groin puncture (thrombectomy)	90-day mRS
Viz LVO				
Hassan 2021a[45]	USA	188	Time from door to groin puncture (thrombectomy), within CSC	mRS at discharge; in-hospital mortality; in-hospital complications; length of hospital stay
Hassan 2020[46] Hassan 2021b[47]	USA	43	Time from CTA at PSC to groin puncture at CSC in patients transferred for thrombectomy	mRS at discharge; in-hospital mortality; in-hospital complications; length of hospital stay
Morey 2020a[52] Morey 2020b[53] Morey 2021[54]	USA	55	Time from CTA to skin puncture (thrombectomy)	90-day mRS
(Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention? **AND** **(Q2b) Is AI-derived software assisted review of CT perfusion brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke after a CTA brain scan a clinically effective intervention?**				
iSchemaView RapidAI mobile application				
Al-Kawaz 2021[34]	USA	64	Time from door to groin puncture (thrombectomy)	None
iSchemaView Rapid (unspecified)				
Kamal 2017[49]	NR	168	Time from door to groin puncture (thrombectomy)	None

*Overlapping study populations
Publications in **bold** have provided data for inclusion in this assessment
CSC: comprehensive stroke centre; CTA: computed tomography angiography; mRS: modified Rankin Scale; PSC: primary stroke centre

3.2.2 Study quality

The methodological quality of the 15 studies[36, 39-41, 43, 48, 50, 51, 55, 56, 59-62] that reported diagnostic test accuracy data was assessed using QUADAS-2.[27] No study reported accuracy data for more than one AI-derived software technology. Studies were generally poorly reported and information about how the AI-derived software technology (index text) was implemented, e.g., threshold or criteria used to determine the presence or absence of the target condition, was lacking. Five studies were published as conference abstracts only,[39, 40, 43, 48, 60] and two studies were pre-publication (not yet peer reviewed) texts.[55, 62] All but one[61] of the included studies were retrospective analyses and the remaining study[61] did not report sufficient information to determine whether participants were recruited prospectively or retrospectively. The main potential sources of bias in the included diagnostic test accuracy studies relate to patient spectrum. There were also concerns regarding the applicability of the patient population and the index test to the research questions specified for this assessment (Section 1 and Section 3.1.2, Table 2). The results of QUADAS-2 assessments are summarised in Table 5; full QUADAS-2 assessments for each study are provided in Appendix 3. A summary of the risks of bias and applicability concerns within each QUADAS-2 domain is provided below.

Patient spectrum

Five studies were rated as high risk of bias for patient selection.[39, 41, 48, 51, 56] Three of these studies were diagnostic case-control studies.[39, 41, 56] Diagnostic case-control studies enrol patients known to have the target condition (cases) and controls without the target condition, i.e., they do not include a representative sample of the patients in whom the test would be used in clinical practice (e.g., all patients presenting with symptoms suggestive of AIS); because they exclude patients with unclear diagnoses or alternative explanations for the presenting symptoms (differential diagnoses), these studies may produce exaggerated estimates of test accuracy.[63, 64] One study was rated high risk of bias for patient selection because patients were excluded for reasons which were not specified in the reported methods.[48] The remaining study[51] was rated high risk of bias for patient selection because it included patients identified using a key-word search of a database; it was considered that potential inconsistencies in database indexing could result in inclusion of a different spectrum of patients than if a consecutive or random sample had been enrolled. A further eight studies were rated as unclear risk of bias because they did not provide sufficient details to make a judgement on whether appropriate steps were taken to minimise bias when enrolling patients.[35, 40, 43, 50, 55, 60-62]

Only two of the included studies were considered to have low concerns regarding the applicability of the included patients to the research questions specified for this assessment.[36, 62] The three

diagnostic case-control studies were rated as having high concerns regarding applicability because the inclusion of patients known to have the target condition and controls without the target condition was not considered to be representative of the spectrum of patients in who the AI-derived software technologies (index tests) would be used in clinical practice.[39, 41, 56] The remaining 10 studies were considered to have unclear applicability, because they did not report any information about the time from symptom onset or 'last known well' for included participants.[36, 40, 43, 48, 50, 51, 55, 59-61]

Index test

Eleven studies were rated as unclear risk of bias for the index test because no information was reported about how the AI-derived software technology (index text) was implemented, e.g., threshold or criteria used to determine the presence or absence of the target condition.[39, 40, 43, 48, 50, 51, 55, 56, 59-61] Eight of these studies also reported no information about the version of the software assessed and, hence, it was unclear whether the results of these studies would be applicable to currently available versions.[40, 43, 48, 50, 55, 56, 59, 61]

All studies were considered to have high concern regarding the applicability of the index test to the research questions specified for this assessment; this was because, in all cases, the AI-derived software technology was evaluated as a stand-alone intervention, rather than as an adjunct or aid to human interpretation (i.e., **not** as it would be used in clinical practice, as its use is recommended by the manufacturers and as specified in the inclusion criteria for this assessment).

Reference standard

One study was rated as high risk of bias and high concerns regarding applicability, with respect to the refence standard and its application.[50] In this study, images were processed by RAPID CTP then reviewed for potential causes of post-processing failure, by two clinicians in consensus, who were blinded to clinical data but had access to all imaging data available at the time of patient evaluation (i.e., not blinded to the index test results).[50] The 2x2 data needed to calculate measures of test accuracy could only be derived by using treatment received (thrombectomy or no thrombectomy) as the reference standard and hence the reference standard was not considered to be applicable to the research questions specified for this assessment, as defined by the inclusion criteria (Table 2).[50] One further study was rated as having high concerns with respect to the applicability of the reference standard.[62] [redacted]

[redacted][62] Eight further studies were rated as unclear risk of bias with respect to the reference standard and its implementation,[39, 40, 43, 48, 51, 55, 60, 61] because insufficient information was reported to determine whether the human readers providing the reference standard imaging interpretation were blinded to the output from the AI-derived software technology (index test); four of these studies were also considered to have provided insufficient information to determine whether the reference standard likely to correctly classify the target condition and were rated unclear with respect to reference standard applicability.[40, 43, 55, 61]

Patient flow

All but one[55] of the studies reporting test accuracy data were rated low risk of bias with respect to patient flow. The remaining study[55] was rated unclear risk of bias because no information was reported about the reference standard for interpretation of images, and hence it was not clear that all participants had received the same reference standard.

Table 5: Summary of QUADAS-2 results

Study details	**RISK OF BIAS**				**APPLICABILITY CONCERNS**		
	Patient selection	**Index test**	**Reference standard**	**Flow and timing**	**Patient selection**	**Index test**	**Reference standard**
Amukotuwa 2019a[35]	?	☺	☺	☺	?	☹	☺
Amukotuwa 2019b[36]	☺	☺	☺	☺	☺	☹	☺
Barreira 2018a[60]	?	?	?	☺	?	☹	☺
Barreira 2018d[39]	☹	?	?	☺	☹	☹	☺
Chatterjee 2018[40]	?	?	?	☺	?	☹	?
Dehkharghani 2021[41]	☹	☺	☺	☺	☹	☹	☺
Dornbos 2020[43]	?	?	?	☺	?	☹	?
Herweh 2020[48]	☹	?	?	☺	?	☹	☺
Kauw 2020[50]	?	?	☹	☺	?	☹	☹
Mair 2021[62]	?	☺	☺	☺	☺	☹	☹
McLouth 2021[51]	☹	?	?	☺	?	☹	☺
Paz 2021[55]	?	?	?	?	?	☹	?
Seker 2020[56]	☹	?	☺	☺	☹	☹	☺
Shalitin 2020[61]	?	?	?	☺	?	☹	?
Yahav-Dovrat 2021[59]	☺	?	☺	☺	?	☹	☺

☺Low Risk ☹High Risk ? Unclear Risk

The methodological quality of the seven[33, 34, 44-46, 49, 52] observational 'before and after' studies was assessed using a checklist, devised by the authors, for this review. The results of this assessment are summarised in Table 6 and reported, in full, for each study, in Appendix 3.

All of these studies were retrospective studies, which assessed the effects of implementing an AI-derived software technology in real world settings. In all studies, the primary outcome was a measure of time to intervention (thrombectomy and, in one study,[44] thrombectomy or thrombolysis). As noted in Section 3.1.2, time to intervention outcomes alone are not sufficient to inform meaningful estimates of the clinical and cost effectiveness of AI-derived software technologies. It is important to measure clinical outcomes alongside time to intervention outcomes because it is possible, for example, for the implementation of AI-derived software technologies to reduce time to intervention whilst also being associated with poorer clinical outcomes. Only four of the studies in this section reported a clear clinical outcome measure along with time to intervention.[33, 45, 46, 52] In addition, with respect to the applicability of these studies to the current decision problem, Four[33, 46, 49, 52] of the seven studies evaluated the implementation of an AI-derived software technology in the context of providing an automated alert system (i.e., **not** as specified in the scope for this assessment) and two further studies were reported as conference abstracts that did not provide sufficient detail to determine how the AI-derived software technology had been implemented.[44, 45]

Observational comparative studies provide a lower level of evidence with respect to the effects of an intervention than RCTs. Where observational study designs are used to provide estimates of effect, it is important to control, as far as possible, for potential confounding factors (factors other than the intervention that may affect the outcome or outcomes being assessed), for example, by matching participants in the intervention and comparator groups on key risk factors. Two of the studies in this section did not report sufficient information to assess whether participants were comparable before and after the implementation of the AI-derived software technology, with respect to baseline demographic characteristics, co-morbid conditions and risk factors.[33, 44] Two further studies reported information indicating that the before and after implementation populations differed with respect to one or more key characteristics.[45, 52] In addition, only three studies[33, 44, 46] reported that there were no changes in the care pathway, other than the implementation of then AI-derived software technology, between the two time periods assessed; the remaining studies did not report sufficient information to determine whether any other changes had occurred.

Studies in this section were generally poorly reported, with no study providing a clear description of the imaging criteria used to select patients for treatment (thrombectomy or thrombolysis), and only

two[34, 46] studies reporting information about how the AI-derived software technology was implemented (e.g., at what point in the care pathway was the AI-derived software technology and by whom were the results used/interpreted). Information about participant selection was also poorly reported; four studies[33, 34, 44, 49] did not report sufficient information to determine whether the spectrum of included participants was applicable to the research questions specified for this assessment (Q2 in Table 6), and three studies[34, 49, 52] did not report sufficient information to assess whether study inclusion criteria were similar before and after implementation of the AI-derived software technology.

No study in this section compared clinical outcomes along with time to intervention, in populations that were comparable (with respect to key baseline characteristics) before and after the implementation of the AI-derived software technology, and where the AI-derived software technology was the only change to the care pathway.

Table 6: Summary of quality assessment results for observational 'before and after' studies

Study details	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9
Adhya 2021[33]	N	U	Y	U	Y	N	N	N	Y
Al-Kawaz 2021[34]	N	U	U	Y	U	Y	N	NA	N
Gunda 2020[44]	N	U	Y	U	Y	N	N	Y	N
Hassan 2020[46]	N	Y	Y	N	Y	Y	N	Y	Y
Hassan 2021a[45]	N	Y	Y	Y	U	N	N	NA	Y
Kamal 2017[49]	N	U	U	Y	U	N	N	NA	U
Morey 2020a[52]	N	Y	U	N	U	N	N	NA	Y

Questions (Q):

1. Did the study have a prospective design?
2. Did the study population include an appropriate spectrum of patients?
   - Adults (≥18 years old) attending a secondary care stroke centre with suspected acute stroke and who were last known to be well within 24 hours
   - Adults (≥18 years old) attending a secondary care stroke centre with acute ischaemic stroke, who were last known to be well within 6 hours
   - Adults (≥18 years old) attending a secondary care stroke centre with suspected acute stroke, who were last known to be well more than 6 hours previously, but within 24 hours, and in whom ischaemic stroke has been confirmed on plain CT
3. Were the criteria used to select patients for CT imaging similar, before and after the introduction of the AI intervention?
4. Were the study populations, before and after the introduction of the AI intervention, similar with respect to baseline demographic characteristics (e.g., age, male/female), co-morbid conditions (e.g., hypertension, diabetes, atrial fibrillation) and risk factors (e.g., smoking status, previous history)?
5. Other than the availability of AI software, was the care pathway similar before and after the introduction of the AI intervention?
6. Was the implementation of the AI intervention clearly described? (e.g., how and when it was used to assist human readers and what was the level of training and experience of the human readers)
7. Were the CT imaging criteria used to select patients for treatment (e.g., thrombectomy) clearly reported for both the periods before and after the introduction of the AI intervention?
8. In addition to time to intervention outcomes, did the study report the proportion of patients who received treatment (e.g., thrombectomy) before and after the introduction of the AI intervention?
9. In addition to time to intervention outcomes, did the study report clinical outcomes (e.g., 90-day mRS) before and after the introduction of the AI intervention?

Y: yes, N:no, NA: not applicable; U: unclear

3.2.3 Research question 1

Is the use of AI-derived software to assist review of non-enhanced CT brain scans to guide thrombolysis treatment decisions for people with suspected acute stroke a clinically effective intervention?

Four studies[39, 44, 48, 62] reported some limited information relevant to research question one and three of these four studies were reported as conference abstracts only.[39, 44, 48] The results of these studies are summarised below and detailed study characteristics are provided in Appendix 2. Three studies provided data on the diagnostic performance of AI-derived software technologies for the detection of ICH in patients with suspected AIS (Table 7); one study evaluated Viz ICH in a random sample taken from a cohort of stroke patients with and without ICH,[39] the second study evaluated an un-specified Brainomix AI-derived software technology in patients with suspected AIS[48] and the final study evaluated Brainomix e-ASPECTS in a clinically representative of patients admitted to hospital with stroke.[62] The sensitivity and specificity estimates were 90.2% (95% CI: 83.9% to 94.2%) and 100% (95% CI: 97.5% to 100%) for Viz ICH,[39] 91.1% (95% CI: 82.8% to 95.6%) and 88.9 (95% CI: 80.2% to 94.0%) for the un-specified Brainomix AI-derived software technology,[48] [redacted][62] [redacted][62] It should be noted that all of these studies were retrospective analyses, of previously acquired images, which assessed the performance of the AI-derived software technology alone; no study provided information about the performance of an AI-derived software technology as an adjunct or aid to human interpretation (as it would be used in clinical practice, as its use is recommended by the manufacturer and as specified in the inclusion criteria for this assessment).

The remaining publication[44] reported an observational 'before and after' study, evaluating the effects on time to treatment of implementing the e-ASPECTS and e-CTA modules of Brainomix e-Stroke in a centre which did not offer thrombectomy (patients requiring thrombectomy were transferred to another unit); the results of this study are summarised in Table 8. The publication stated that *'delivery of stroke care was otherwise unchanged.'* e-ASPECTS analyses non-contrast CT scans for clot detection, signs of hypodensity and generates a heat map of regional ischaemic change, volume of the change and an automatic ASPECTS score, and e-CTA analyses CT perfusion scans to generate perfusion summary maps, report parameters such as mismatch volume and ratio, hypoperfusion intensity ratio, and assesses eligibility for mechanical thrombectomy, hence, only the implementation of e-ASPECTS is relevant to research question 1. However, the effects of

implementation were not reported separately for e-ASPECTS and e-CTA.[44] The proportion of patients receiving thrombolysis was 11.5% before implementation and 18.1% after implementation (absolute numbers not reported), and the proportion of patients transferred for thrombectomy was 2.8% before implementation and 4.8% after implementation (absolute numbers not reported).[44] For patients receiving thrombolysis, the mean time from door to treatment was 44 minutes before implementation and 41 minutes after implementation (no estimates of variance reported).[44] For patients transferred for thrombectomy, the mean time from first CT to groin puncture was 174 minutes before implementation and 145 minutes after implementation (no estimates of variance reported).[44] It should also be noted that this study did not report any information comparing clinical outcomes before and after implementation, such as would be needed to inform decision making.

We did not identify any studies, conducted in patients with suspected AIS, that evaluated Aidoc ICH, Rapid ICH, Rapid ASPECTS, qER, Zebra-Med, Brainscan, Avicenna CINA ICH, Avicenna CINA ASPECTS, MaxQ AI Accipio, or Biomind, the remaining AI-derived software technologies used in the analysis of NCCT images, as indicated in Table 1 and described in Section 2.2 of this report.

Table 7: Accuracy of AI-derived software technologies for the detection of ICH in stroke patients

Study details	AI-derived software technology	Target condition	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Barreira 2018d[39]	Viz ICH	ICH	119	0	13	152	90.2 (83.9, 94.2)	100 (97.5, 100)	100 (96.9, 100)	92.1 (87.0, 95.3)
Herweh 2020[48]	(un-specified) Brainomix		72	9	7	72	91.1 (82.8, 95.6)	88.9 (80.2, 94.0)	88.9 (80.2, 94.0)	91.1 (82.8, 95.6)
Mair 2021 [62]	Brainomix e-ASPECTS		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
		AIS								

AIS: acute ischaemic stroke; CI: confidence interval; FN: false negative; FP: false positive; ICH: intracranial haemorrhage; NPV: negative predictive value; PPV: positive predictive value; TN: true negative; TP: true positive

Table 8: Effects of implementing AI-derived software technologies for the analysis of NCCT and CTA in stroke patients

Study details	AI-derived software technology	Time to treatment outcome	Pre-implementation	Post-implementation	Clinical outcome	Pre-implementation	Post-implementation
Gunda 2020[44]	Brainomix e-ASPECTS and e-CTA	Mean (sd) minutes from door to needle, (iv thrombolysis)	44 (NR), (n=46)	41 (NR), (n=72)	None reported	NA	NA
		Mean (sd) minutes from door to groin puncture (thrombectomy)	174 (NR), (n=11)	145 (NR), (n=19)	None reported	NA	NA

ASPECTS: Alberta stroke programme early CT score; CI: confidence interval; CTA: computed tomography angiography; iv: intravenous; NA: not applicable; NR: not reported; sd: standard deviation

3.2.4 Research question 2a

Is the use of AI-derived software to assist review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?

Eighteen studies reported information relevant to research question 2a.[33-36, 40, 41, 43-46, 49, 51, 52, 55, 56, 59-61] Eleven studies reported sufficient information to allow calculation of measures of the diagnostic performance of AI-derived software technologies for the detection of LVO;[35, 36, 40, 41, 43, 51, 55, 56, 59-61] two studies evaluated Rapid CTA[35, 36] and two studies evaluated Rapid LVO,[41, 55] five studies evaluated Viz LVO,[40, 43, 59-61] one study evaluated Brainomix e-CTA,[56] and one study evaluated Avicenna CINA LVO.[51] The remaining seven studies in this section were observational 'before and after' studies, which evaluated the effects of implementing AI-derived software technologies in clinical practice. [33, 34, 44-46, 49, 52] Four studies reported, specifically, on the implementation of AI-derived software technologies for the analysis of CTA images, one on the implementation of Rapid CTA[33] and three on the implementation of Viz LVO.[45, 46, 52] The remaining three studies assessed the effects of implementation of AI-derived software technologies which were unclearly reported or included multiple components;[34, 44, 49] one study[44] reported on the implementation of e-ASPECTS and e-CTA and is described in Section 3.2.3 and Table 8, and two studies[34, 49] reported on the implementation of Rapid technologies and are described in Section 3.2.5 and Table 17. One study, which provided diagnostic performance data for Viz LVO, also reported the effect of implementing Viz LVO on time from door to groin puncture, in patients who were transferred for thrombectomy.[43]

The results of studies in this Section are grouped by AI-derived software technology. Detailed study characteristics are provided in Appendix 2.

We did not identify any studies, conducted in patients with AIS, that evaluated Aidoc LVO, the remaining AI-derived software technology used in the analysis of CTA images, as indicated in Table 1 and described in Section 2.2 of this report.

Rapid CTA and Rapid LVO

Two studies reported sufficient data to calculate the sensitivity and specificty of Rapid CTA for the detection of intracranial anterior circulation LVO, at the relative vessel density <75% to 60% (green)*

* The RAPID CTA algorithm perfoms the following operations: (1) imports the CTA raw data in DICOM format; (2) motion and tilt corrects the images; (3) trims the CTA data to restrict coverage from the C1 vertebra to the vertex; (4) elastically aligns a human head

threshold.[35, 36] Data from these studies were not pooled, as the study populations overlapped (see Table 9). The sensitivity and specificity estimates from the larger study study[35] were 96.9% (95% CI: 94.3% to 98.3%) and 74.3% (95% CI: 70.6% to 77.7%), respectively. Further analysis from this study indicated that sensitivity and specificity estimates did not change substantially when M2-segment occlusions were included in the target condition; the estimated sensitivity was 95.4% (95% CI: 92.7% to 97.1%) and the estimated specificity was 79.4% (95% CI: 75.8% to 82.6%).[35] This study also provided separate sensitivity and specificity estimates for Rapid CTA for detection of occlusions of the ICA, and M1- and M2-segments of the MCA, using varying optimised thresholds (see Table 9).[35]

Two studies reported sufficient data to allow calculation of sensitivity and specifity estimates for Rapid LVO.[41, 55] One study provided data to calculate the sensitivity and specificty of Rapid LVO for the detection of intracranial anterior circulation LVO, at the relative vessel density <60% (green)* threshold; the sensitivity and specificity estimates were 96.3% (95% CI: 90.9% to 98.6%) and 98.1% (95% CI: 93.5% to 99.5%), respectively.[41] The results of sub-group analyses from this study[41] indicated that the sensitivity and specificty of Rapid LVO for the detection of intracranial anterior circulation LVO did not vary substantially with patient age or between the different CT scanners used to acquire images (see Table 9). The sensitivity and specificity estimates for Rapid LVO, calculated from the second study, were substantially lower; the sensitivity estimate was 63.6% (95% CI: 51.6% to 74.2%) and the specificity estimate was 85.9% (95% CI: 76.9% to 91.7).[55] However, this study included a wider range of anatomical locations in its definition of LVO (see Table 9).[55]

It should be noted that all of the studies that provided data on the diagnostic performance of Rapid CTA or Rapid LVO were retrospective analyses, of previously acquired images, which assessed the performance of the AI-derived software technology alone; no study provided information about the performance of an AI-derived software technology as an adjunct or aid to human interpretation (as it would be used in clinical practice, as its use is recommended by the manufacturer and as specified in the inclusion criteria for this assessment).

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template with the CTA data; (5) warps template of anatomic structures (e.g. bones and blood vessels) on to the CTA to create masks; (6) removes the skull base and calvarium using the bone mask; (7) identifies and dichotomises (into small and large diameter) intracranial vessels; (8) determines vessel density by assessing the length of large calibre vessels in the suprasellar cistern (supraclinoid IVA) and proximal Sylvian cistern (M1-MCA) as well as the sum of density values (Hounsfield units) of the voxels constituting these vessels; (9) determines vessel density for small calibre vessels (distal M1, M2, and M3 segments) further distally in and adjacent to the Sylvian cistern; (10) performs left-right comparison to determine the relative vessel density ratio, within the suprasellar and proximal Sylvian cistern and progressing distally; (11) creates axial, coronal and sagittal MIP of the intracranial vasculature from the bone-masked CTA; **(12) highlights the areas of reduced relative interhemispheric vessel density on these MIPs using colour thresholds 75% to 80% (blue), 60% to 74% (green), 45% to 59% (yellow and <45% (red)**; (13) sends these MIPs as de-identified outputs to the PACS.

Full diagnostic performance data for Rapid CTA and Rapid LVO are provided in Table 9.

The remaining study of Rapid CTA was an observational 'before and after' study, which reported some limited information about the effects of implementing Rapid CTA in a 'real world' clincal setting (see Table 10).[33] The article reporting this study stated that: *'All interventional equipment, endovascular therapists, neuroradiology staff, and hospitals serviced were identical during the study period, and the only significant change was the installation of Rapid CTA.'* Data from this study appear to indicate that the implentation of Rapid CTA was associated with a reduction in the mean time from CTA to groin puncture, for patients undergoing thrombectomy, from 92 minutes before implemention to 68 minutes after implementation, however, no estimates of variance were reported.[33] There was no significant difference in the proportion of patients who were functionally independent (mRS ≤2) following implementation of Rapid CTA, odds ratio (OR) 1.75 (95% CI: 0.84 to 3.67). It should also be noted that this study evaluated the implementation of an Rapid CTA in the context of providing an automated alert system (i.e., not as specified in the scope for this assessment).[33] Two further studies reported information about the effects on time to treatment of implementing an un-specified Rapid product[49] and the RapidAI Mobile Application.[34] Neither study provided separate results for the effects of the CTA and CTP analysis algorithms in Rapid; the results of these studies are described in Section 3.2.5 and Table 17.

It should be noted that, although studies of this type provide some information about the effects of implementing Rapid AI-derived software technologies in 'real world' clinical settings, the information provided is limited to those patients who underwent thrombectomy, i.e., there is no information about the effects of implementation of these technologies, with respect to identification of patients who are candidates for thrombectomy.

Table 9: Accuracy of Rapid AI-derived software technologies for the identification of LVO

Study details	Population	Target condition	Threshold	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Rapid CTA											
Amukotuwa 2019a[35]	All	Intracranial anterior circulation LVO (ICA, carotid terminus or M1-segment of the MCA)	<75% to 60% relative vessel density (green)	310	151	10	437	96.9 (94.3, 98.3)	74.3 (70.6, 77.7)	67.2 (62.8, 71.4)	97.8 (95.9, 98.8)
Amukotuwa 2019b[*36]			<75% relative vessel density[**]	73	93	5	303	93.6 (85.9, 97.2)	76.5 (72.1, 80.4)	44.0 (36.6, 51.6)	98.4 (96.3, 99.3)
Amukotuwa 2019a[35]		Intracranial anterior LVO (ICA, carotid terminus or M1-segment of the MCA) or M2-segment of the MCA occlusion	<75% to 60% relative vessel density (green)	351	112	17	431	95.4 (92.7, 97.1)	79.4 (75.8, 82.6)	75.8 (71.7, 79.5)	96.2 (94.0, 97.6)
Amukotuwa 2019b[*36]			<75% relative vessel density[**]	97	70	9	301	91.5 (84.6, 95.5)	81.1 (76.8, 84.8)	58.1 (50.5, 65.3)	97.1 (94.6, 98.5)
Amukotuwa 2019a[35]		ICA occlusion	<60% to 45% relative vessel density (yellow)	129	7	4	459	97.0 (92.5, 98.8)	86.4 (83.3, 89.1)	64.2 (57.3, 70.5)	99.1 (97.8, 99.7)
Amukotuwa 2019a[35]		M1-segment MCA occlusion	<75% to 60% relative vessel density (green)	281	108	9	423	96.9 (94.2, 98.4)	79.7 (76.0, 82.9)	72.2 (67.6, 76.5)	97.9 (96.1, 98.9)
Amukotuwa 2019a[35]		M2-segment MCA occlusion	<80% to 75% relative vessel density (blue)	54	133	6	398	90.0 (79.9, 95.3)	75.0 (71.1, 78.5)	28.9 (22.9, 35.7)	98.5 (96.8, 99.3)
Amukotuwa 2019b[*36]			<75% relative vessel density[**]	24	144	4	305	85.7 (68.5, 94.3)	67.9 (63.5, 72.1)	14.3 (9.8, 20.4)	98.7 (96.7, 99.5)
Rapid LVO											
Dehkharghani 2021[41]	All	Intracranial anterior circulation LVO (ICA, carotid terminus or M1-segment of the MCA)	<60% relative vessel density	105	2	4	106	96.3 (90.9, 98.6)	98.1 (93.5, 99.5)	98.1 (93.4, 99.5)	96.4 (91.0, 98.6)

Paz 2021[55]		LVO (ICA, carotid terminus or M1-segment of the MCA) or M2/3-segment of the MCA occlusion	NR	42	12	24	73	63.6 (51.6, 74.2)	85.9 (76.9, 91.7)	77.8 (65.1, 86.8)	75.3 (65.8, 82.8)
Dehkharghani 2021[41]	Subgroup, age 20-39 years	Intracranial anterior circulation LVO (ICA, carotid terminus or M1-segment of the MCA)	<60% relative vessel density	7	0	0	10	100 (64.6, 100)	100 (72.2, 100)	100 (64.6, 100)	100 (72.2, 100)
	Subgroup, age 20-39 years			29	1	0	38	100 (88.3, 100)	97.4 (86.8, 99.5)	96.7 (83.3, 99.4)	100 (90.8, 100)
	Subgroup, age ≥60 years			69	1	4	57	94.5 (86.7, 97.8)	98.3 (90.9, 99.7)	98.6 (92.3, 99.7)	93.4 (84.3, 97.4)
	Subgroup, GE Medical Systems scanner			62	1	2	32	96.9 (89.3, 99.1)	97.0 (84.7, 99.5)	98.4 (91.5, 99.7)	94.1 (80.9, 98.4)
	Subgroup, Siemens scanner			14	1	0	45	100 (78.5, 100)	97.8 (88.7, 99.6)	93.3 (70.2, 98.8)	100 (92.1, 100)
	Subgroup, Toshiba scanner			26	0	2	28	92.9 (77.4, 98.0)	100 (87.9, 100)	100 (87.1, 100)	93.3 (78.7, 98.2)

[*] sub-set of Amukotuwa 2019a,[35]

[**] inclusive of 60% to 75% green, 45% to 59% yellow and <45% red

CI: confidence interval; FN: false negative; FP: false positive; ICA: internal carotid artery; LVO: larger vessel occlusion; MCA: middle cerebral artery; NPV: negative predictive value; PPV: positive predictive value; TN: true negative; TP: true positive

Table 10: Effects of implementing Rapid CTA for the analysis of CTA in patients with AIS, who are potential candidates for thrombectomy

Study details	Time to treatment outcome	Pre-implementation	Post-implementation	Clinical outcome	Pre-implementation	Post-implementation
Adhya 2021[33]	Mean (sd) minutes from CTA to groin puncture (thrombectomy), setting unclear	92 (NR), (n=74)	68 (NR), (n=72)	Mean (sd) 90-day mRS	4.47 (NR), (n=74)	3.9 (NR), (n=67)
				Proportion with 90-day mRS ≤2	17/74 (23%)	23/67 (34%)

CTA: computed tomography angiography; mRS: modified Rankin Score; NR: not reported; sd: standard deviation

Viz LVO

Five studies reported sufficient information to calculate measures of the diagnostic performance of Viz LVO.[40, 43, 59-61] The target condition varied across studies, with respect to the anatomical location of occlusions,[40, 43, 60] and two studies did not provide any definition of LVO.[59, 61] The summary estimates of sensitivity and specificity, derived from all five studies, were 88.0% (95% CI: 76.9% to 94.2%) and 89.9% (95% CI: 85.5% to 93.0%), respectively (Figure 4). A sensitivity analysis, excluding one study where the reported target condition included posterior circulation occlusions,[43] resulted in a higher summary estimate of sensitivity (91.3% (95% CI: 84.9% to 95.1%)) and a similar summary estimate of specificity (89.3 (95% CI: 83.5% to 93.2%)), (Figure 5). One study also reported that, for those patients who were transferred between centres for thrombectomy (number not reported), the median time from door to groin puncture was significantly shorter after implementation of Viz LVO, 141 (95% CI: 128.5 to 168) minutes, compared to before implementation, 185 (95% CI: 151 to 241) minutes, p=0.027.[43] This study did not report any comparison of clinical outcomes for the periods before and after implementation of Viz LVO.[43]

It should be noted that all five studies that provided data on the diagnostic performance of Viz LVO were retrospective analyses, of previously acquired images, which assessed the performance of the AI-derived software technology alone; no study provided information about the performance Viz LVO as an adjunct or aid to human interpretation (as it would be used in clinical practice, as its use is recommended by the manufacturer and as specified in the inclusion criteria for this assessment).

Full diagnostic performance data for Viz LVO are provided in Table 12.

Three further observational 'before and after' studies, reported information about the effects of implementing Viz LVO in clincal settings (see Table 13).[45, 46, 52] One study reported that, for patients transferred between centres for thrombectomy, the median time from CTA to groin puncture was significantly shorter after implementation of Viz LVO, 127 (range: 39 to 622) minutes, compared to before implementation, 216 (range: 109 to 608) minutes, p=0.026.[46] This study also reported a small reduction in the length of hospital stay after implementation of Viz LVO, mean difference (MD) -2.5 (95% CI: -4.7 to -0.3) days, and no significant change in the proportion of patients who were functionally independent at 90 days post-procedure (mRS ≤2), OR 1.67 (95% CI: 0.45 to 6.23), or rates of in-hospital complications, OR 0.60 (95% CI: 0.06 to 6.28), or in-hospital mortality, OR 1.33 (95% CI: 0.31 to 5.73).[46] A second study, from the same research group, reported that the mean time from door to groin puncture was also reduced, following implementation of Viz LVO, for patients who were treated with thrombectomy within centre, MD -86.7 (95% CI: -125.9 to -47.5) minutes.[45] Again, this study found no significant change in the proportion of patients who were functionally

independent at 90 days post-procedure (mRS ≤2), OR 0.88 (95% CI: 0.46 to 1.69), or rates of in-hospital complications, OR 0.87 (95% CI: 0.46 to 1.62), or in-hospital mortality, OR 1.10 (95% CI: 0.55 to 2.21) and, additionally, reported no significant change (p=0.103) in the median length of hospital stay.[45] The final study reported a significant reduction in the meantime from CTA to groin puncture, MD -44.6 (95% CI: -68.6 to -20.6) minutes, after implementation of Viz LVO, for patients transferred between centres for thrombectomy.[52] This study also reported no significant change in the mean 90 day mRS after implementation of Viz LVO, MD -1.0 (95% CI: -2.1 to 0.1).[52]

All four studies[43, 45, 46, 52] that provided information about the effects of implementing Viz LVO in clincal settings reported that implementation was associated with reductions in time to treatment for thrombectomy patients and, where reported, with no significant change in clinical outcomes.[45, 46, 52] However, it should be noted that two of these studies[46, 52] evaluated the implementation of Viz LVO in the context of providing an automated alert system (i.e., **not** as specified in the scope for this assessment) and the remaining two studies[43, 45] were reported as conference abstracts that did not provide sufficient information to determine how Viz LVO had been implemented. It should also be noted that, although these studies provide some information about the effects of implementing Viz LVO in a 'real world' clinical settings, the information provided is limited to those patients who underwent thrombectomy, i.e., there is no information about the performance of Viz LVO, on the identification of patients who are candidates for thrombectomy.

Figure 4: HSROC – All studies Viz LVO

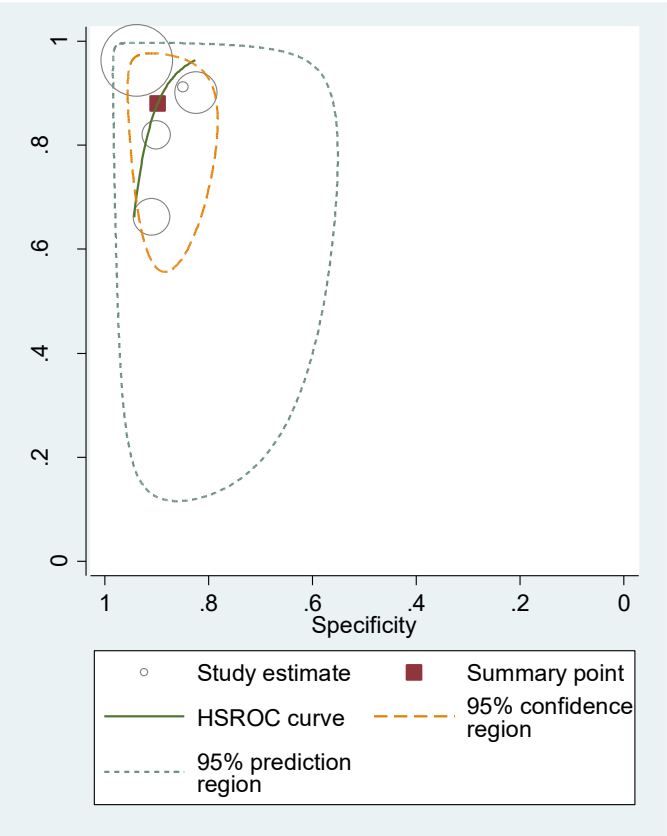


Figure 5: HSROC – Sensitivity analysis Viz LVO

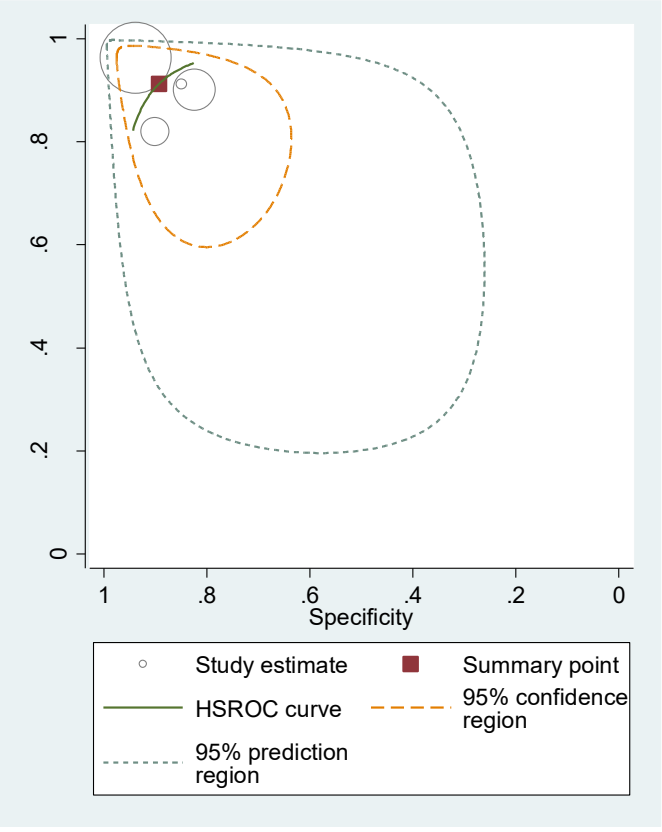


Table 11: Accuracy of Viz LVO for the identification of LVO

Study details	Population	Target condition	Threshold	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Barreira 2018a[60]	All	Intracranial anterior circulation LVO (ICA, carotid terminus or M1-segment of the MCA)	NR	362	83	40	390	90.0 (86.7, 92.6)	82.5 (78.8, 85.6)	81.3 (77.5, 84.7)	90.7 (87.6, 93.1)
Chatterjee 2018[40]		Intracranial anterior LVO (ICA, carotid terminus or M1-segment of the MCA) or M2-segment of the MCA occlusion		31	3	3	17	91.2 (77.0, 97.0)	85.0 (64.0, 94.8)	91.2 (77.0, 97.0)	85.0 (64.0, 94.8)
Dornbos 2020[43]		Intracranial anterior LVO (ICA, carotid terminus or M1-segment of the MCA), distal M2-segment of the MCA or posterior circulation occlusion		45	55	23	557	66.2 (54.3, 76.3)	91.0 (88.5, 93.0)	45.0 (35.6, 54.8)	96.0 (94.1, 97.3)
Shalitin 2020[61]		LVO (not defined)		157	147	6	2234	96.3 (92.2, 98.3)	93.8 (92.8, 94.7)	51.6 (46.0, 57.2)	99.7 (99.4, 99.9)
Yahav-Dovrat 2021[59]	All 'stroke protocol'	LVO (not defined)		59	33	13	299	81.9 (71.5, 89.1)	90.1(86.4, 92.8)	64.1 (53.9, 73.2)	95.8 (93.0, 97.5)
Summary estimate (5 studies)[40, 43, 59-61]								**88.0 (76.9, 94.2)**	**89.9 (85.5, 93.0)**		
Sensitivity analysis, excluding Dornbos 2020[43]								**91.3 (84.9, 95.1)**	**89.3 (83.5, 93.2)**		

CI: confidence interval; FN: false negative; FP: false positive; ICA: internal carotid artery; LVO: larger vessel occlusion; MCA: middle cerebral artery; NPV: negative predictive value; PPV: positive predictive value; TN: true negative; TP: true positive

Table 12: Effects of implementing Viz LVO for the analysis of CTA in patients with AIS, who are potential candidates for thrombectomy

Study details	Time to treatment outcome	Pre-implementation	Post-implementation	Mean difference (95% CI)	Clinical outcome	Pre-implementation	Post-implementation	Mean difference (95% CI) or OR (95% CI)
Dornbos 2020[43]	Median (IQR) minutes from door to groin puncture, for transferred patients	185 (151, 241), (n=NR)	141 (128.5, 168), (n=NR)	NC	None reported	NA	NA	NA
Hassan 2020[46]	Median (min, max) minutes from CTA to groin puncture, for transferred patients	216 (109, 608), (n=28)	127 (39, 622), (n=11)	NC	90-day mRS ≤2	8/28	6/15	1.67 (0.45, 6.23)*
					In-hospital complications	3/28	1/15	0.60 (0.06, 6.28)*
					In-hospital mortality	6/28	4/15	1.33 (0.31, 5.73)*
					Mean (sd) Hospital stay (days)	9.7 (4.9), (n=28)	7.2 (2.5), (n=15)	-2.5 (-4.7, -0.3)*
Hassan 2021a[45]	Mean (sd) minutes from door to groin puncture, within centre	206.6 (169.1), (n=86)	119.9 (83.0), (n=102)	-86.7 (-125.9, -47.5)*	90-day mRS ≤2	24/86	26/102	0.88 (0.46, 1.69)*
					In-hospital complications	27/86	29/102	0.87 (0.46, 1.62)*
					In-hospital mortality	18/86	23/102	1.10 (0.55, 2.21)*
					Median (IQR) Hospital stay (days)	7.0 (4.0, 11.0)	7.5 (4.0, 12.0)	NC
Morey 2020a[52]	Mean (sd) minutes from CTA to groin puncture, for transferred patients	161.3 (51.1), (n=29)	146.7 (39.4), (n=26)	-44.6 (-68.6, -20.6)*	Mean (sd) 90-day mRS	4.3 (2.1), (n=29)	3.3 (1.9), (n=26)	-1.0 (-2.1, 0.1)*

* Calculated value

CI: confidence interval; CTA: computed tomography angiography; IQR: inter-quartile range; mRS: modified Rankin Score; NA: not applicable: NC: not calculable; NR: not reported; OR: odds ratio; sd: standard deviation

Brainomix e-CTA

One study reported sufficient information to calculate the sensitivity and specificity of Brainomix e-CTA for the detection of proximal (ICA or proximal M1-segment of the MCA) or distal (distal M1-segmant or proximal M2-segment of the MCA) LVO (Table 13).[56] The sensitivity and specificity estimates were 83.8% (95% CI: 77.3% to 88.7%) and 95.7% (95% CI: 91.0% to 98.0%). When patients with distal LVOs were excluded for the analysis the estimated sensitivity and specificity values, for the detection of proximal LVOs were 91.6% (95% CI: 84.3% to 95.7%) and 97.9% (95% CI: 93.9% to 99.3%). The reference standard for this study was provided by a board-certified Neuroradiologist with more than 10 years of experience and unrestricted access to all clinical and imaging data, including data on interventional therapy and follow-up.[56] Using a sub-set of 144 patients, this study also provided comparative accuracy data for e-CTA versus human readers (a board-certified Neuroradiologist, a Radiology resident and two Neurology residents), for the detection of proximal (ICA or proximal M1-segment of the MCA) or distal (distal M1-segmant or proximal M2-segment of the MCA) LVO; these data are summarised in Table 14.[56] It should be noted that, whilst this study provides a comparison of the diagnostic performance of e-CTA alone versus human readers with varying levels of expertise, it does not provide any information about the performance of e-CTA when implemented as an adjunct to a human reader (i.e., as it would be implemented in clinical practice as its use is recommended by the manufacturer and as specified in the inclusion criteria for this assessment).

One additional study[44] reported information about the effects of implementing the e-ASPECTS and e-CTA modules of Brainomix e-Stroke in a centre which did not offer thrombectomy (patients requiring thrombectomy were transferred to another unit).[44] The results of this study, summarised in Section 3.2.3 and Table 8, appeared to indicate that implementation was associated with a reduction in mean time from first CT to groin puncture for patients treated with thrombectomy. It should also be noted that this study did not report any information comparing clinical outcomes before and after implementation, such as would be needed to inform decision making.

Table 13: Accuracy of Brainomix e-CTA for the identification of LVO

Study details	Population	Target condition	Threshold	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Seker 2020[56]	All	Proximal (ICA or proximal M1 segment of the MCA) or distal (distal M1 segment or proximal M2 segment of the MCA) LVO	NR	134	6	26	135	83.8 (77.3, 88.7)	95.7 (91.0, 98.0)	95.7 (91.0, 98.0)	83.9 (77.4, 88.7)
	Subgroup, excluding distal LVO	Proximal LVO		87	3	8	138	91.6 (84.3, 95.7)	97.9 (93.9, 99.3)	96.7 (90.7, 98.9)	94.5 (89.6, 97.2)

CI: confidence interval; FN: false negative; FP: false positive; ICA: internal carotid artery; LVO: larger vessel occlusion; MCA: middle cerebral artery; NPV: negative predictive value; PPV: positive predictive value; TN: true negative; TP: true positive

Table 14: Comparative aaccuracy of Brainomix e-CTA versus human readers for the identification of LVO

Study details	Population	Reader	Threshold	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Seker 2020[56]	All	e-CTA	NR	59	3	11	71	84.3 (74.0, 91.0)	95.9 (88.7, 98.6)	95.2 (86.7, 98.3)	86.6 (77.6, 92.3)
		Neuroradiologist		68	1	2	73	97.1 (90.2, 99.2)	98.6 (92.7, 99.8)	98.6 (92.2, 99.7)	97.3 (90.8, 99.3)
		Radiology resident		67	6	3	68	95.7 (88.1, 98.5)	91.9 (83.4, 96.2)	91.8 (83.2, 96.2)	95.8 (88.3, 98.6)
		Neurology resident 1		60	7	10	67	85.7 (75.7, 92.1)	90.5 (81.7, 95.3)	89.6 (80.0, 94.8)	87.0 (77.7, 92.8)
		Neurology resident 2		64	0	6	74	91.4 (82.5, 96.0)	100 (95.1, 100)	100 (94.3, 100)	92.5 (84.6, 96.5)

CI: confidence interval; CTA: computed tomography angiography; FN: false negative; FP: false positive; NPV: negative predictive value; PPV: positive predictive value; TN: true negative; TP: true positive

Avicenna CINA LVO

One study reported sufficient data to calculate the sensitivity and specificity of CINA LVO for the detection intracranial anterior LVO or M2-segment occlusion of the MCA (Table 15).[51] The sensitivity and specificity estimates were 98.1% (95% CI: 94.5% to 99.3%) and 98.2% (95% CI: 95.5% to 99.3%), respectively.[51] The results of sub-group analyses indicated that the sensitivity and specificty of CINA LVO for the detection of intracranial anterior LVO or M2-segment occlusion of the MCA did not vary substantially with patient age or between the different CT scanners used to acquire images (see Table 15). It should be noted this study was a retrospective analysis of previously acquired images, which assessed the performance of the CINA LVO technology alone; it does not provide information about the performance of the AI-derived software technology as an adjunct or aid to human interpretation (i.e., as it would be used in clinical practice, as its use is recommended by the manufacturer and as specified in the inclusion criteria for this assessment).

No studies were identified which evaluated the effects of implementing CINA LVO in clinical practice.

Table 15: Accuracy of Avicenna CINA LVO for the identification of LVO

Study details	Population	Target condition	Threshold	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
McLouth 2021[51]	All	Intracranial anterior LVO (ICA, carotid terminus or M1-segment of the MCA) or M2-segment of the MCA occlusion	NR	153	4	3	218	98.1 (94.5, 99.3)	98.2 (95.5, 99.3)	97.5 (93.6, 99.0)	98.6 (96.1, 99.5)
	Subgroup, age 18-39 years			4	0	1	21	80.0 (37.6, 96.4)	100 (84.5, 100)	100 (51.0, 100)	95.5 (78.2, 99.2)
	Subgroup, age 40-70 years			65	3	0	108	100 (94.4, 100)	97.3 (92.4, 99.1)	95.6 (87.8, 98.5)	100 (96.6, 100)
	Subgroup, age >70 years			83	1	2	90	97.6 (91.8, 99.4)	98.9 (94.0, 99.8)	98.8 (93.6, 99.8)	97.8 (92.4, 99.4)
	Subgroup, male			73	2	1	109	98.6 (92.7, 99.8)	98.2 (93.7, 99.5)	97.3 (90.8, 99.3)	99.1 (95.0, 99.8)
	Subgroup, female			78	2	2	104	97.5 (91.3, 99.3)	98.1 (93.4, 99.5)	97.5 (91.3, 99.3)	98.1 (93.4, 99.5)
	Subgroup, GE Medical Systems scanner			46	4	4	75	92.0 (81.2, 96.8)	94.9 (87.7, 98.0)	92.0 (81.2, 96.8)	94.9 (87.7, 98.0)
	Subgroup, Philips scanner			52	2	10	73	83.9 (72.8, 91.0)	97.3 (90.8, 99.3)	96.3 (87.5, 99.0)	88.0 (79.2, 93.3)
	Subgroup, Siemens scanner			29	4	1	39	96.7 (83.3, 99.4)	90.7 (78.4, 96.3)	87.9 (72.7, 95.2)	97.5 (87.1, 99.6)
	Subgroup, Canon (formerly Toshiba) scanner			13	0	1	23	92.9 (68.5, 98.7)	100 (85.7, 100)	100 (77.2, 100)	95.8 (79.8, 99.3)

CI: confidence interval; FN: false negative; FP: false positive; ICA: internal carotid artery; LVO: larger vessel occlusion; MCA: middle cerebral artery; NPV: negative predictive value; PPV: positive predictive value; TN: true negative; TP: true positive

3.2.5 Research question 2b

Is the use of AI-derived software assisted review of CT perfusion brain scans to guide mechanical thrombectomy treatment decisions for people with an ischaemic stroke, after a CTA brain scan, a clinically effective intervention?

Three studies, two reported as journal articles[34, 50] and one as a conference abstract,[49] provided some limited information relevant to research question 2b. All three studies evaluated iSchemaView Rapid products. The results of these studies are summarised below, and detailed study characteristics are provided in Appendix 2.

One article reported sufficient information to allow the calculation of measures of the diagnostic performance of Rapid CTP for identifying patients who are suitable candidates for thrombectomy (Table 16).[50] The objectives of the study concerned the quantification and characterisation of failures occurring during the automated post-processing of imaging data with Rapid CTP. The study was a retrospective analysis of AIS patients, from a database, who had undergone CTP for thrombectomy; potential causes of Rapid CTP post-processing failures were evaluated by two clinicians (experience not specified) in consensus, who had access to all imaging data available at the time of patient evaluation and failures were re-processed manually using IntelliSpace software (Philips, Best, The Netherlands). A total of 176 AIS patients were included in the analysis and Rapid CTP post-processing failures accrued in 20 (11%) patients. Causes for failures were severe motion (n=14, 70%), streak artifact (n=3, 15%), and poor arrival of contrast (n=3, 15%). Of the 176 patients, 126 (72%) received thrombectomy, based on clinical information and interpretation of CTP imaging which included correction for failures. Based on information about the results of Rapid CTP image analysis provided in the paper and using treatment received as the reference standard, it was possible to calculate measures of the diagnostic performance of Rapid CTP alone (without correction) in identifying patients who are suitable candidates for thrombectomy; the estimated sensitivity was 95.2% (95% CI: 90.0% to 97.8%) and the estimated specificity was 80.0% (95% CI: 67.0% to 88.8%), and the estimates of PPV and NPV were 92.3% (95% CI: 86.4% to 95.8%) and 87.0% (95% CI: 74.3% to 93.9%), respectively.

The remaining two publications reported the results of observational 'before and after' studies, evaluating the effects on time to treatment and clinical outcome of implementing Rapid (details not specified) in the context of providing an automated e-mail alert system[49] (i.e., not as specified in the scope for this assessment) and the RapidAI Mobile Application.[34] Neither study provided separate results for the effects of the CTA and CTP analysis algorithms in Rapid. The results of these studies

are summarised in Table 17. One study reported no significant change in the mean time from door to groin puncture, in thrombectomy patients, following the implementation of RapidAI, MD 2.0 (95% CI: -12.9 to 16.9) minutes.[49] Clinical outcome, as indicated by the proportion of patients (for whom data were available) with a mRS ≤3 (time point not specified), was also similar before, 58/119 (48.7%), and after, 23/41 (56.1%), implementation (calculated OR 1.34 (95% CI: 0.66 to 2.74)).[49] By contrast, the study that assessed the effects of implementing the RapidAI Mobile Application reported a reduction in the mean time from door to groin puncture after implementation, MD -33.2 (95% CI: -60.2 to -6.2) minutes; this study also reported that implementation of the RapidAI Mobile Application had no effect on mean 90 day mRS, 2.9 (no estimate of variance reported) both before (n=29) and after (n=26) implementation.[34]

We did not identify any studies conducted in patients with LVO, that evaluated icobrain ct, Brainomix e-CTP, Viz CTP, CT Perfusion 4D, or Ceracare Stroke, the remaining AI-derived software technologies used in the analysis of CTP images, as indicated in Table 1 and described in Section 2.2 of this report.

Table 16: Accuracy of AI-derived software technologies for the identification of candidates for thrombectomy in patients with LVO

Study details	AI-derived software technology	Target condition	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Kauw 2020[50]	Rapid CTP	Candidate for thrombectomy	120	10	6	40	95.2 (90.0, 97.8)	80.0 (67.0, 88.8)	92.3 (86.4, 95.8)	87.0 (74.3, 93.9)

CI: confidence interval; CTP: computed tomography perfusion imaging; FN: false negative; FP: false positive; NPV: negative predictive value; PPV: positive predictive value; TN: true negative; TP: true positive

Table 17: Effects of implementing AI-derived software technologies for the analysis of CTA and CTP in stroke patients with LVO, who are potential candidates for thrombectomy

Study details	AI-derived software technology	Time to treatment outcome	Pre-implementation	Post-implementation	Mean difference (95% CI)	Clinical outcome	Pre-implementation	Post-implementation
Al-Kawaz 2021[34]	RapidAI Mobile Application	Mean (sd) minutes from door to groin puncture, (thrombectomy, within centre	104.3 (57.9), (n=31)	71.1 (51.7), (n=33)	-33.2 (-60.2, -6.2)*	Mean (sd) 90-day mRS	2.9 (NR), (n=29)	2.9 (NR), (n=26)
Kamal 2017[49]	Rapid (un-specified)	Mean (sd) minutes from door to groin puncture, (thrombectomy, setting unclear	116 (61), (n=136)	118 (39), (n=50)	2 (-12.9, 16.9)*	mRS ≤3 (time point NR)	58/119	23/41

* Calculated value
CI: confidence interval; mRS: modified Rankin Score; NR: not reported; sd: standard deviation

3.2.6 Selection of diagnostic accuracy estimates for inclusion in cost effectiveness modelling

There is no evidence, in any population, about the accuracy of AI-derived software technologies in combination with clinicians. The available diagnostic accuracy studies were retrospective analyses, of previously acquired images, which assessed the performance of the AI-derived software technology alone; no study provided information about the performance of an AI-derived software technology as an adjunct or aid to clinician interpretation (as it would be used in clinical practice and as specified in the decision problem for this assessment). This might imply that a CEA is not feasible for any of the three research questions (1, 2a or 2b). However, we have chosen to conduct a CEA in relation to the research question (2a) where there is most evidence about the performance of AI-derived software technologies alone and one study comparing an AI-derived software technology alone with clinicians alone.[56] These studies were not considered appropriate to inform cost effectiveness modelling, but formed the basis by which the accuracy of AI plus human reader could be elicited by expert opinion. The expert elicitation process, undertaken to inform cost effectiveness modelling, is described in detail in Section 4.2.3.

Diagnostic accuracy datasets were selected for use in the background information provided with the expert elicitation tool, based on comparability of the target condition across the different AI-derived software technologies assessed by included studies, comparability with the target condition in the study used to inform estimates of the effectiveness of thrombectomy in cost effectiveness modelling,[65] availability of comparator data[56] and match to the target condition specified during the scoping phase of this assessment (Table 2). The common target condition was intracranial anterior circulation LVO (ICA, carotid terminus or M1- segment of the MCA) or M2-segment of the MCA occlusion and the corresponding diagnostic performance estimates, for AI-derived software technologies and the comparator (human readers alone), provided with the expert elicitation tool are given in Table 18. These estimates were presented to the clinical experts for elicitation of sensitivity and specificity of the intervention (clinician plus AI) and the comparator (clinician only). It should be noted that the estimates for clinician alone could have been used directly in the model to inform the effectiveness of the comparator. However, given that so few data were available i.e., from only one study,[56] it was considered more appropriated to use these estimates to inform expert elicitation.

The decision to undertake an expert elicitation process was made, given the complete absence of applicable evidence in the literature, with a view to providing the diagnostic appraisal committee with a framework to consider the potential cost effectiveness of AI as it would be used in practice and in order to facilitate the development of research recommendations. Nevertheless, no

comparison of different AI-derived software technologies was feasible, and the results of this CEA (reported in Section 4) need to be regarded with caution.

Table 18: Accuracy estimates used in expert elicitation for cost effectiveness modelling

Study details	Intervention/Comparator	Target condition	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Amukotuwa 2019a[35]	Rapid CTA	Intracranial anterior LVO (ICA, carotid terminus or M1- segment of the MCA) or M2-segment of the MCA occlusion	351	112	17	431	95.4 (92.7, 97.1)	79.4 (75.8, 82.6)	75.8 (71.7, 79.5)	96.2 (94.0, 97.6)
Chatterjee 2018[40]	Viz LVO	Intracranial anterior LVO (ICA, carotid terminus or M1- segment of the MCA) or M2-segment of the MCA occlusion	31	3	3	17	91.2 (77.0, 97.0)	85.0 (64.0, 94.8)	91.2 (77.0, 97.0)	85.0 (64.0, 94.8)
Seker 2020[56]	Brainomix e-CTA	Proximal (ICA or proximal M1 segment of the MCA) or distal (distal M1 segment or proximal M2 segment of the MCA) LVO	134	6	26	135	83.8 (77.3, 88.7)	95.7 (91.0, 98.0)	95.7 (91.0, 98.0)	83.9 (77.4, 88.7)
McLouth 2021[51]	Avicenna CINA LVO	Intracranial anterior LVO (ICA, carotid terminus or M1- segment of the MCA) or M2-segment of the MCA occlusion	153	4	3	218	98.1 (94.5, 99.3)	98.2 (95.5, 99.3)	97.5 (93.6, 99.0)	98.6 (96.1, 99.5)
Seker 2020[56]	Neuroradiologist	Proximal (ICA or proximal M1 segment of the MCA) or distal (distal M1 segment or proximal M2 segment of the MCA) LVO	68	1	2	73	97.1 (90.2, 99.2)	98.6 (92.7, 99.8)	98.6 (92.2, 99.7)	97.3 (90.8, 99.3)
	Radiology resident		67	6	3	68	95.7 (88.1, 98.5)	91.9 (83.4, 96.2)	91.8 (83.2, 96.2)	95.8 (88.3, 98.6)
	Neurology resident 1		60	7	10	67	85.7 (75.7, 92.1)	90.5 (81.7, 95.3)	89.6 (80.0, 94.8)	87.0 (77.7, 92.8)
	Neurology resident 2		64	0	6	74	91.4 (82.5, 96.0)	100 (95.1, 100)	100 (94.3, 100)	92.5 (84.6, 96.5)

4. ASSESSMENT OF COST EFFECTIVENESS

4.1 Review of economic analyses of software with artificial intelligence-derived algorithms for analysing CT brain scans in people with a suspected acute stroke

4.1.1 Search strategy

A series of literature searches were performed to identify published economic evaluations and cost effectiveness data and utility studies for diagnostic techniques and procedures used in the investigation of patients with stroke that were not included within the scope of the clinical effectiveness searches. The searches aimed to identify studies that could be used to support the development of a health economic model, to estimate the model input parameters and to answer the research questions of the assessment, but not to perform a systematic review. Searches were therefore pragmatic in design, and date limits applied where appropriate.

Methodological study design filters were included in the search strategies where relevant. No restrictions on language or publication status were applied. Limits were applied to remove animal studies. The main Embase strategy for each search was independently peer reviewed by a second Information Specialist, using the CADTH Peer Review checklist[25] Identified references were downloaded in Endnote software for further assessment and handling. References in retrieved articles were checked for additional studies. In addition, the Endnote library created for the clinical effectiveness section (Section 3.1.1) was also screened to identify potentially relevant economic studies.

The following databases were searched for relevant studies with from 2005-Sept 2021:

- NHS Economic Evaluation Database (NHS EED) (Internet) (https://www.crd.york.ac.uk/CRDWeb/): up to 2015/03
- MEDLINE (Ovid): 1946-2021/09/15
- MEDLINE In-Process Citations (Ovid): up to 2021/09/15
- MEDLINE Daily Update (Ovid): up to 2021/09/15
- MEDLINE Epub Ahead of Print (Ovid): up to 2021/09/15
- Embase (Ovid): 1974-2021/09/15
- EconLit (EBSCO): up to 2021/09/21
- Science Citation Index (Web of Science): 1988-2021/09/21
- Research Papers in Economics (RePEc) (http://repec.org/): up to 2021/09/21

Supplementary searches

As described by the NICE Methods Guide, the information process that supports the development of a model is “a process of assembling evidence and this reflects an iterative, emergent process of

information gathering".[66] The following additional searches were requested by the health economists as part of this process:

HRQoL and Utilities

Searches for utility weights and HRQoL papers for stroke were conducted on the following resources:

- Embase (Ovid): 1974-2021/11/01
- CEA Registry (http://www.cearegistry.org): up to 2021/07/14

Review of Reviews

In order to locate papers evaluating the effectiveness of diagnostic imaging techniques without the use of AI an additional focused search aimed at identifying existing SRs was run without date limits on the following resources:

- Cochrane Database of Systematic Reviews (CDSR) (Wiley): up to 2021/10/Iss10
- KSR Evidence (KSR Ltd) (https://ksrevidence.com/): up to 2021/10/14

Accuracy of human readers

Estimates of the performance of human readers alone (without AI) in interpreting diagnostic images in stroke were required to provide comparator data for cost effectiveness modelling. Previous searches had found insufficient data supporting this topic; therefore a single targeted search was undertaken on MEDLINE:

- MEDLINE (Ovid): 2017-2021/10/15
- MEDLINE In-Process Citations (Ovid): up to 2021/10
- MEDLINE Daily Update (Ovid): up to 2021/10
- MEDLINE Epub Ahead of Print (Ovid): up to 2021/10

Review of Reviews: Alteplase

In order to locate papers evaluating the effectiveness of intravenous thrombolysis (alteplase) in AIS, an additional focused search aimed at identifying existing systematic reviews was run without date limits on the following resources:

- Cochrane Database of Systematic Reviews (CDSR) (Wiley): up to 2021/11/Iss11
- KSR Evidence (KSR Ltd) (https://ksrevidence.com/): up to 2021/11/11

Full search strategies for all of the above are reported in Appendix 1.

4.1.2 Inclusion criteria

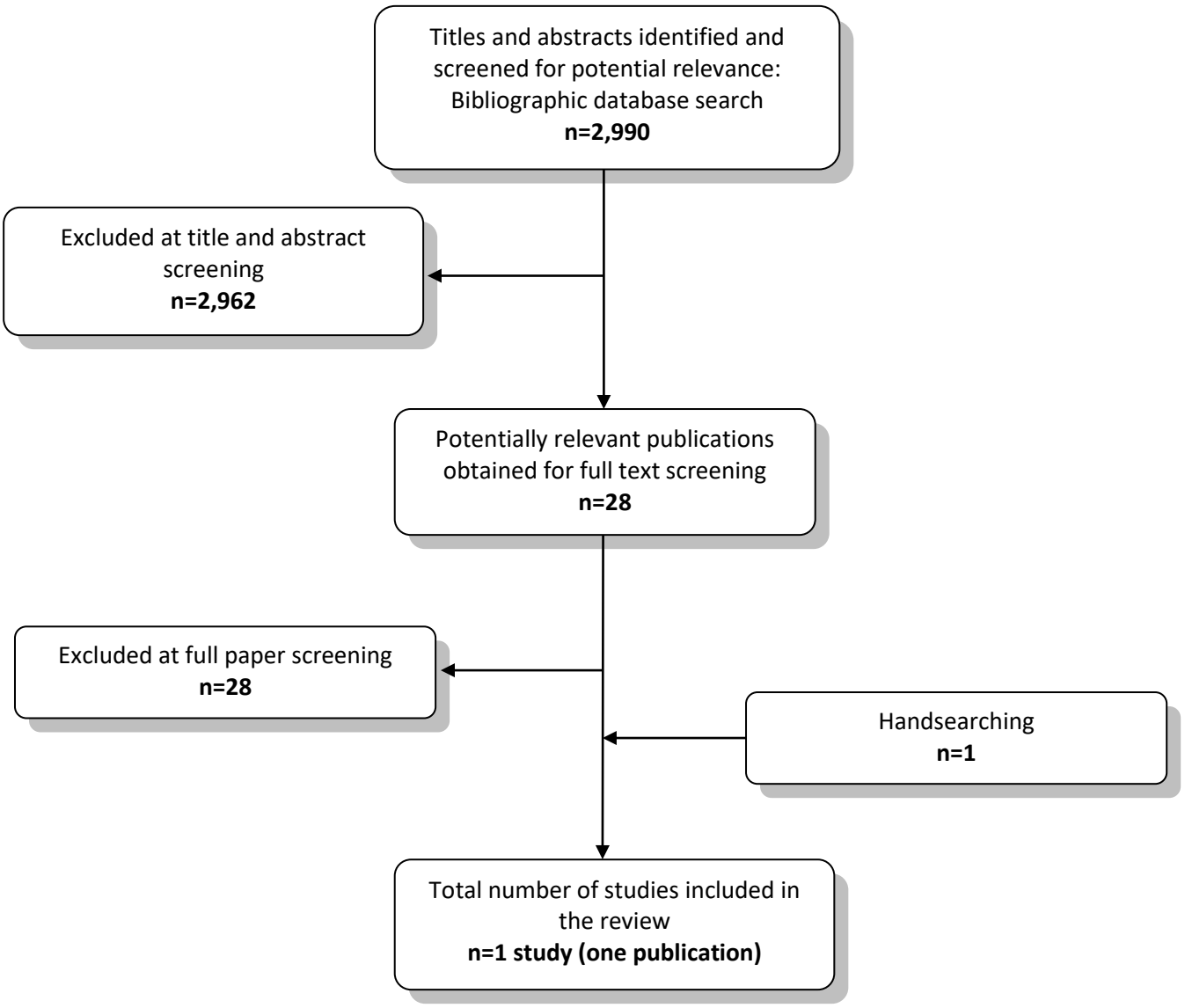
Studies reporting outcomes of a full CEA, examining (quality-adjusted) life-years, with (at least) one AI-derived software assisted review strategy, were eligible for inclusion.

4.1.3 Results

The literature search identified 2,990 records from bibliographic database searches and supplementary searching (e.g., reference/citation checking, additional database searches including the database search for the assessment of clinical effectiveness). After title and abstract screening, 28 records are considered to be potentially relevant; after full text screening one cost effectiveness study (identified by handsearching as it was published after conducting the literature search), was considered eligible for inclusion. This study is described in more detail below. Figure 6 shows the flow of studies through the review process.

An additional economic model was submitted by Bainomix to NICE. This submission was not considered in this review as it was not specifically focussed on one of the research questions nor does it adopt an approach (e.g., decision tree combined with a state transition model) typically adopted for diagnostic assessments.

Figure 6: Flowchart (review of economic analyses)



Van Leeuwen 2021

Van Leeuwen and colleagues[67] used a decision tree for the acute phase (90 days) combined with a state transition model (health states defined based on the mRS) with a life-time time horizon (the economic model is available online https://www.AIforRadiology.com). The analyses were performed from a societal UK perspective (discount rates of 1.5% and 4.0% for effects and costs respectively), while reporting the costs in 2018, US dollars for ease of interpretation (£1 = $1.283). The authors estimated the potential cost effectiveness of using AI software in ischemic stroke to aid intracranial LVO detection on CTA (with or without CTP) compared with standard care without the AI software. The population focussed on vessel occlusions in the proximal anterior circulation (ICA, A1, M1, M2) as these were considered appropriate for the selection of patients to receive mechanical thrombectomy.

For the analysis it was assumed that AI software is capable of increasing the diagnostic sensitivity, especially for the detection of M2 occlusions, without a decrease in specificity. False positives generated by the AI software were assumed to be neutralised by the judgement of the reader, preventing overtreatment. It was noted that, besides providing a more accurate diagnosis, the use of AI may lead to shorter time to treatment, especially if it reduced the need for specialist review. However, as most currently available commercial products focus on triage and interactive decision support, the analyses only considered the claim that the use of AI could provide a more accurate diagnosis, i.e., reduce the number of missed LVOs.

The early HTA assessment considered the potential value of AI software in general without focus on a specific manufacturer. The main assumption (varied in uncertainty analyses) was that in standard care (without AI software) 6% of LVOs are missed and that with the addition of AI software this can be reduced by 50% (i.e., only 3% of LVOs are missed). It was acknowledged that although published accuracy data are available for AI software in isolation, there is no evidence of the performance of AI software combined with standard practice, i.e., it is unclear to what degree AI software can reduce the LVOs missed in standard practice. The price per patient for using the AI software was assumed to be $40. Additionally included costs were treatment related costs, acute stroke costs (90 days, depending on mRS) and long-term stroke costs (annual, depending on mRS). Scenario and deterministic multi-way sensitivity analyses were performed (no probabilistic analysis).

The base-case analysis indicated that if the addition of AI software detected additional LVOs, this could potentially result in cost savings (of $156) whilst yielding additional QALYs (0.0095 QALY gained) compared with standard care without AI software. Sensitivity analyses seem to indicate that these results are sensitive to the percentage of LVOs missed by usual care, the percentage of missed

LVOs detected by the AI software and the AI software costs per patient. Additional false-positive cases due to the addition of AI software only had very minor cost consequences ($0.07 per percentage point of false positives).

The authors noted that evidence is lacking regarding the percentage of missed LVOs (with standard care) that can be detected by AI software. Notably, this percentage cannot directly be derived from the sensitivity of an AI-algorithm applied stand-alone as it is likely that the cases that were missed by a physician are also more likely to be missed by an algorithm (e.g., M2 occlusions). The authors specifically advised against using these sensitivity measures directly as model inputs.

Quality assessment (Drummond checklist[68]) of the study by van Leeuwen and colleagues[67] only indicated suboptimal score for reporting to (disaggregated/absolute) results as well as related to the uncertainty analyses (lack of CIs for stochastic data and justification for ranges over which the variables are varied).

4.2 Model structure and methodology

4.2.1 Intervention an comparators

The health economic analysis focussed on research question 2a:

> *Does AI-derived software assisted review of CT angiography brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke represent a clinically and cost-effective use of NHS resources?*

All diagnostic accuracy studies, identified by the systematic review conducted for this assessment (Section 3) assessed the accuracy of AI-derived software technologies as stand-alone interventions. As a result, information about how AI-derived software technologies would perform when used as an adjunct/aid to human readers (i.e., as recommended by the manufacturers, as specified for this assessment and as they would be used in clinical practice) is lacking. This is because the accuracy of the device by itself tells us nothing about how, or indeed if, it might improve the accuracy of a human reader. It would not make sense to infer that any of the variation in sensitivity observed between standalone AIs can tell us something about precisely the variation in a hypothetical, small improvement in sensitivity of the human reader. To still be able to perform CEA, we elicited expert opinion to estimate the diagnostic accuracy of AI as adjunct to human reader. Experts were provided with the evidence on AI alone and human reader alone. Because it was considered too difficult for experts to differentiate between different AI-derived software assisted review technologies, AI-derived software assisted review in general (not specified by manufacturer or specific technology) is considered.

4.2.2 Model structure

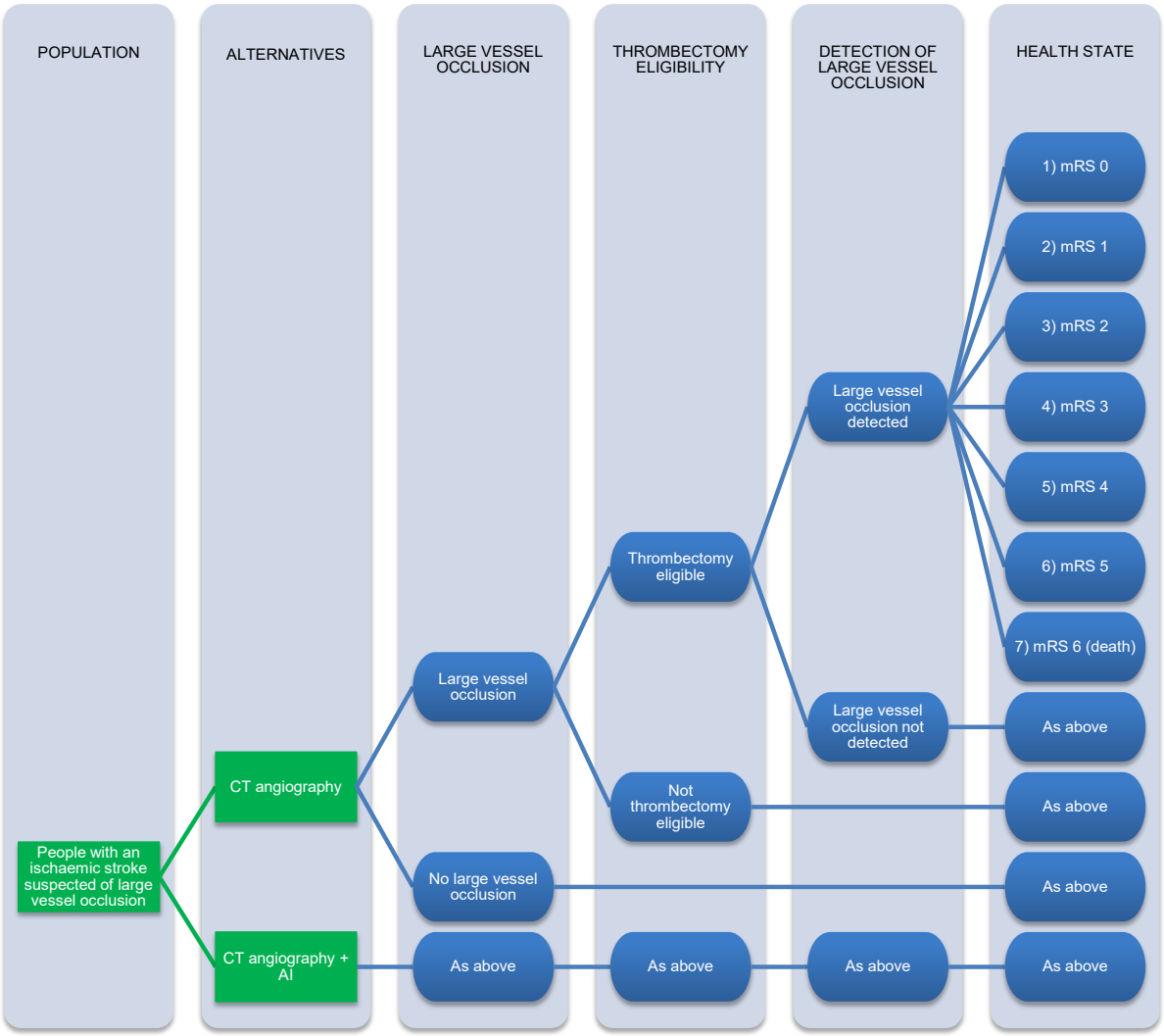
This assessment uses the CEA by van Leeuwen et al[67] (identified in the literature review as the only assessment focussing on a similar decision problem) as a starting point. In addition, recent cost effectiveness assessments (mainly on the cost effectiveness of thrombectomy) that have been identified informally (through the cost effectiveness review, checking references) have also been used to support the development of the model. Consistent with the focus of AI-derived software assisted review on triage and supporting the thrombectomy decision, the current assessment primarily considers the question of whether AI-derived software assisted review could provide a more accurate diagnosis of LVO than usual care.

The *de novo* developed model consisted of a decision tree (short-term) and a state transition model (long-term) to calculate the mean expected costs and QALYs for people with ischaemic stroke and suspected LVO.

The decision tree was used to estimate short term costs and consequences (first 90 days). For this purpose, a distinction is made between patients who have a LVO and those who do not. The definition of LVO was LVOs in the proximal anterior circulation (ICA, A1, M1, M2). This definition was chosen for two main reasons: consistency with the recommendations of NICE guidelines and with the meta-analysis by Román et al, the source of the effectiveness of thrombectomy used in the model (Section 4.2.3).[65] Subsequently, patients with LVO are classified as either eligible for thrombectomy or not eligible. Eligibility for thrombectomy is determined by a number of factors beyond the location of the occlusion, including timing and salvageability of brain tissue as determined by CT perfusion scanning (Section 2.4.2). Those with both LVO and eligibility for thrombectomy are further classified, based on the sensitivity of the diagnostic strategy, into whether a LVO was detected (and thus thrombectomy received) or not. Based on the classification in the decision tree, patients were subdivided into the health states according to the mRS. mRS is a commonly used scale for measuring the degree of disability or dependence in daily activities of people who have suffered a stroke and was the predominant outcome to define health states in published cost effectiveness models in this disease area. Notably, patients without LVO were subdivided, based on the specificity of the diagnostic strategy, into whether a LVO was incorrectly detected or not. If a LVO was incorrectly detected (i.e., false positive), this had cost consequences only (e.g., due to potential unnecessary transfer to experienced stroke centre qualified to perform thrombectomy) as, based on clinical opinion and consistent with the assessment by van Leeuwen et al,[67] it was assumed that the LVO would be classified as a false positive (i.e., in fact no LVO) before proceeding to thrombectomy. The rationale for this was that specialists (e.g., neuroradiologists or

neurointerventionalists) would review the imaging before agreeing to take patients for thrombectomy and then detect the false positive. The decision tree is shown in Figure 7.

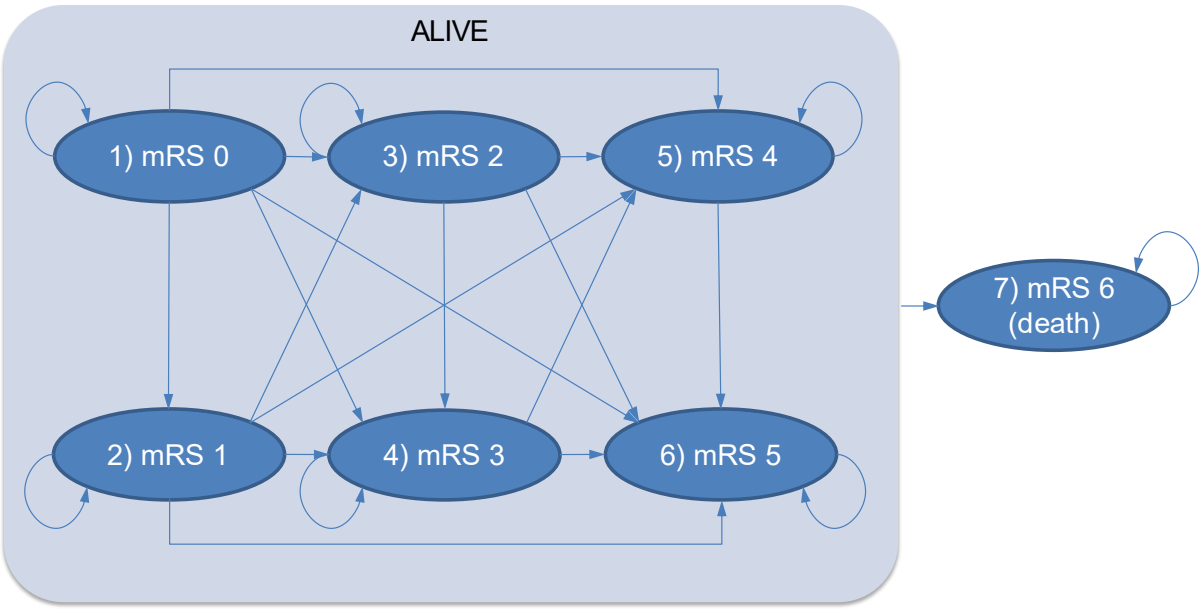
Figure 7: Decision tree structure (90 days period)



The long-term consequences in terms of costs and QALYs were estimated using a state transition cohort model (Figure 8) with a lifetime time horizon. The cycle time was 1 year. The following health states were included:

- 1) mRS 0
- 2) mRS 1
- 3) mRS 2
- 4) mRS 3
- 5) mRS 4
- 6) mRS 5
- 7) mRS 6 (death)

Figure 8: State transition model structure



The *de novo* model was developed in R Shiny[69] to leverage the benefits of using modern programming languages such as R[70] while providing an accessible interface through the Shiny package. To improve model transparency as well as model credibility and for consistency with suggested good practices and conventions, the technical implementation of the computational model was inspired by recent work of the DARTH group[71, 72] and others.[73]

4.2.3 Model parameters

Decision tree probabilities

Proportion of ischaemic strokes that are LVOs

The proportion of ischaemic strokes correctly suspected to be caused by LVOs was estimated by pooling the prevalence of LVOs in the diagnostic accuracy studies[35, 40, 51] (random effects model using logit transformation), resulting in an estimated prevalence of 46.1% (95% CI: 43.0% to 49.1%).

Eligibility for medical thrombectomy

Not all patients with LVO are eligible for thrombectomy. Based on the UK study by McMeekin et al 2017,[74] including early presenters (within 4 hours of onset) as well as late presenters and those for which the timing was unknown, the proportion of patients with LVO eligible for thrombectomy was 41.2% (95% CI: 40.6% to 41.8%).

Accuracy of clinician and AI-derived software assisted review of CT angiography (CTA) brain scans

Expert elicitation methods

As was outlined in Section 3.2.6, the available accuracy estimates were not appropriate for the decision problem. We therefore performed elicitation of expert opinion to inform sensitivity and specificity of clinician review of CTA brain scans and of AI-assisted review of CTA brain scans. In addition, we also elicited the throughput of patients with ischaemic stroke and suspected LVO per an average centre (this was not used in the end). This translated into five elicitation questions. The sensitivity question was phrased in terms of *proportion of LVOs missed* (= 1 – sensitivity). The specificity question was phrased in terms of *proportion of non-LVOs falsely classed as LVOs* (= 1 – specificity) (questions and screenshots of the EXPLICIT tool are presented in Appendix 7).

We used the EXPLICIT tool developed by Grigore et al[75] to facilitate remote expert elicitation. This tool has been validated, follows established methodological guidance for expert elicitation,[76-78] and has the advantage that it is relatively easy to use. The tool includes an informed consent form, training exercises, and explanations of some important heuristics. We also included background information on the evidence on accuracy of AI standalone and human reader alone, identified in Section 3.2.6. Experts were asked for the mode and the upper and lower bounds to each estimate. A beta-PERT distribution was then fitted. Mathematical aggregation of elicited expert estimates was performed using linear pooling, i.e., by taking the arithmetic average over all experts for each elicited quantity.

Expert elicitation results

Five UK clinical experts sent complete responses (a consultant in Emergency Medicine, a Clinical Associate Professor and Honorary Consultant Stoke Physician, a Senior Lecturer and Honorary Consultant Neurosurgeon, a Senior Clinical Lecturer and Honorary Consultant Neuroradiologist and an Honorary Consultant Neuroradiologist). The elicited mean sensitivity and specificity, as well as parameters for the beta-PERT distribution are presented in Table 19. Probability distributions are shown for the pooled experts' estimates of sensitivity (Figure 9) and specificity (Figure 10) as well as for individual experts (Figure 11).

Table 19: Results of expert elicitation

	Mean	Lower bound	Mode	Upper bound
Clinician* only sensitivity	**93.00**	83.60	94.20	97.60
Clinician* only specificity	**94.09**	88.00	94.58	98.20
AI + clinician* sensitivity	**94.13**	87.80	94.80	97.80
AI + clinician* specificity	**93.77**	84.80	94.80	98.60
*Assuming current care mix of expertise and circumstance				

Figure 9: Elicited sensitivity estimates (pooled)

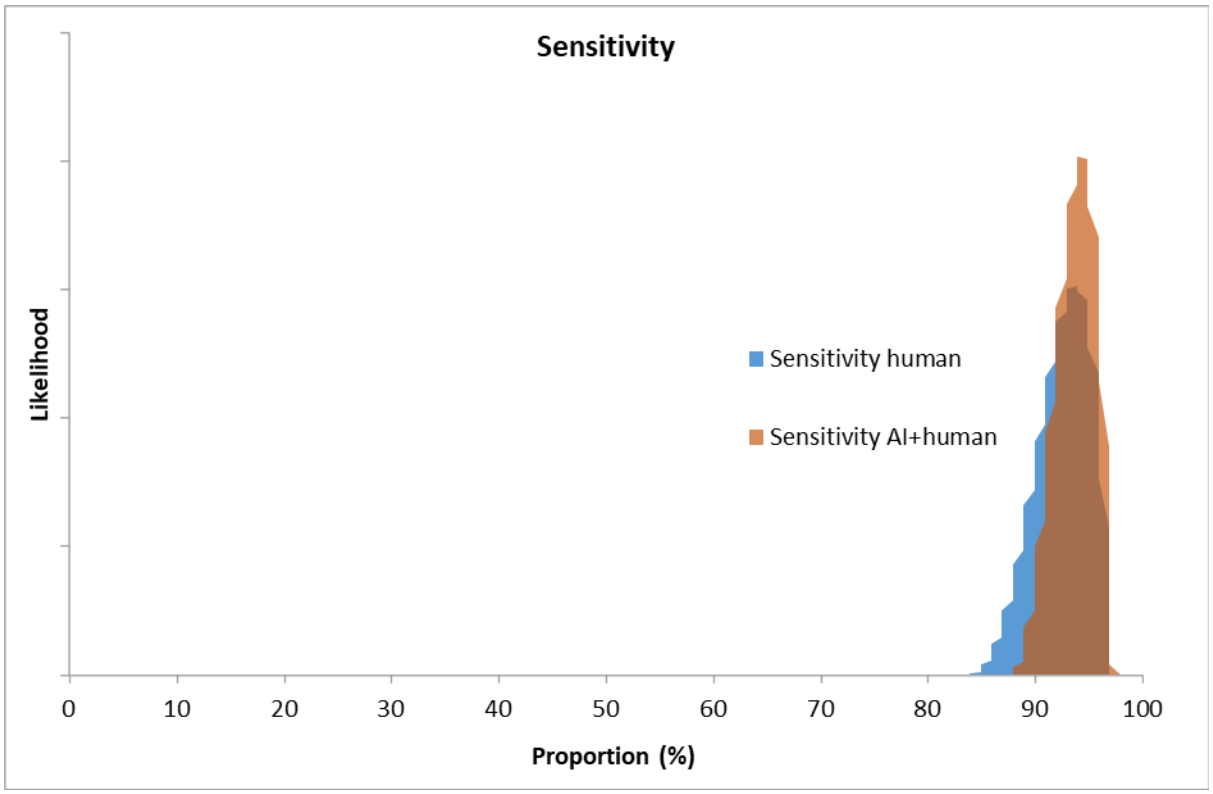


Figure 10: Elicited specificity estimates (pooled)

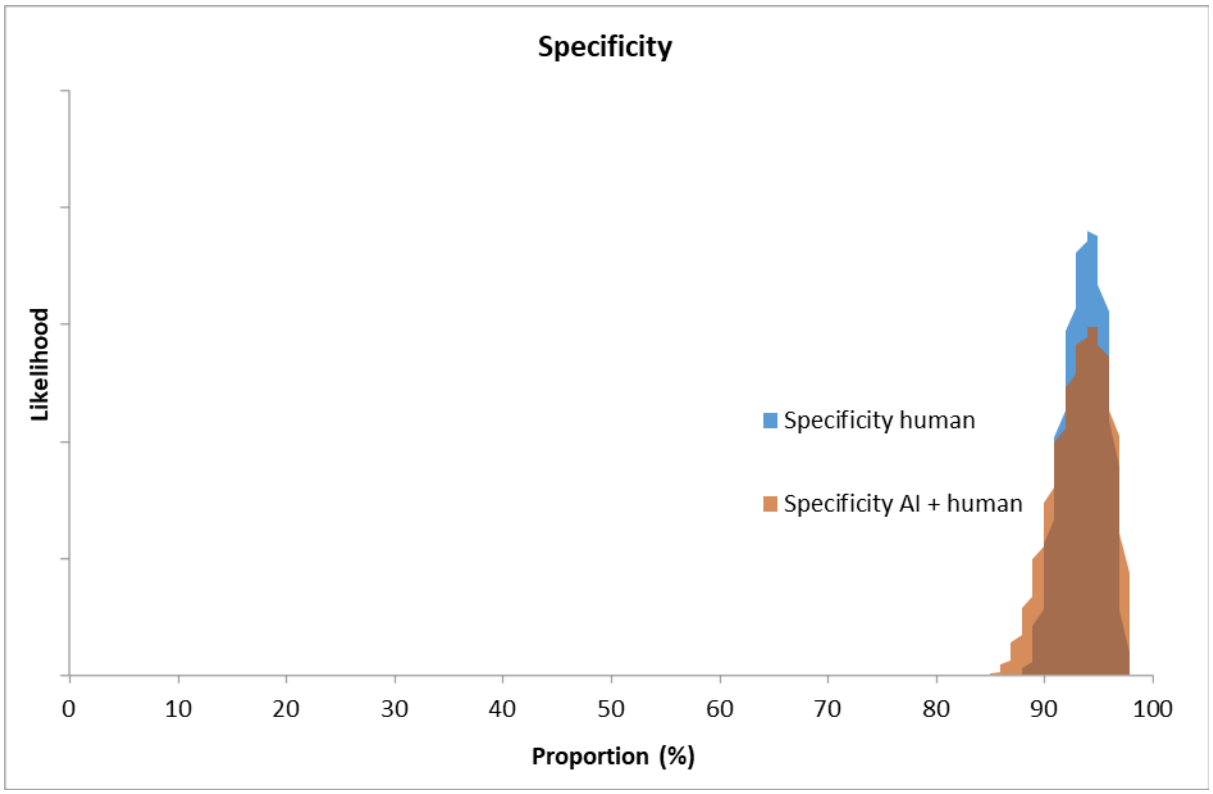
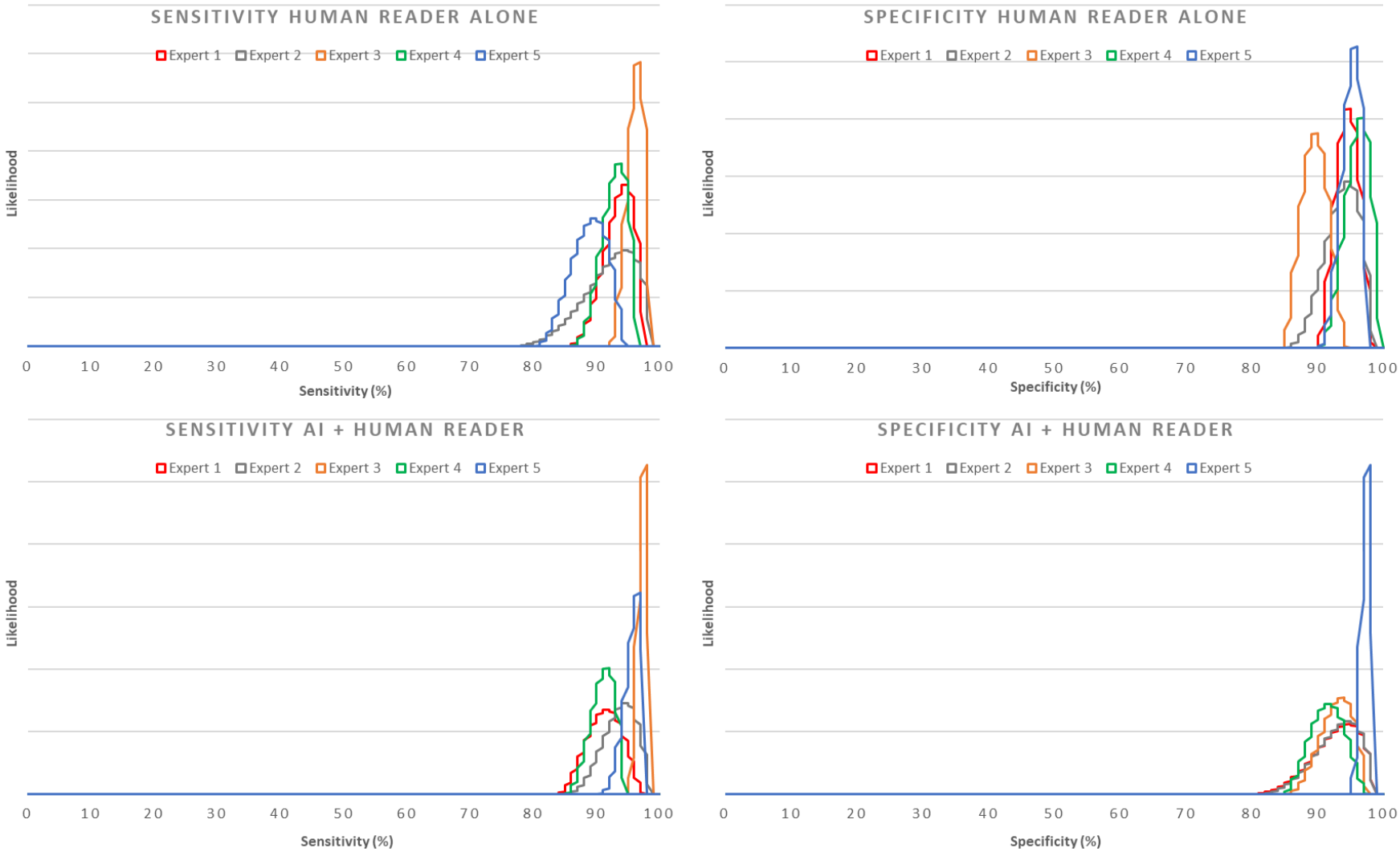


Figure 11: Probability distributions of individual experts



Initial distribution over mRS states for patients with LVO

We performed a pragmatic review to inform the distribution over the disability post stroke health states at 90 days after thrombectomy or standard medical therapy (i.e., for those ineligible for thrombectomy) at the end of the decision tree. A study by Román et al of the effectiveness of thrombectomy was identified in which mRS outcomes at 90 days were estimated based on an individual patient-level data meta-analysis,[65] combining from seven randomised trials: MR CLEAN,[79] ESCAPE,[80] EXTEND-IA,[81] SWIFT PRIME,[82] REVASCAT,[83] THRACE,[84] and PISTE.[85] This study was deemed to be the most recent meta-analysis on this topic and included all relevant, high quality, randomised trials. Eligibility for thrombectomy in those trials was also consistent with the vessel occlusions in the proximal anterior circulation [ICA, A1, M1, M2].[65] Given that Román et al[65] presented only stratified estimates of the distribution of mRS outcomes (i.e., stratified for Alberta Stroke Program Early CT Score (ASPECTS) categories), results were pooled to obtain an estimate for the full population (Table 20).

Table 20: Pooled estimates of mRS state distribution at day 90

Treatment	mRS0	mRS1	mRS2	mRS3	mRS4	mRS5	mRS6
mRS after LVO treated with IAT (n=856)	96 (11.1%)	154 (18.1%)	159 (18.6%)	137 (16.1%)	136 (15.9%)	47 (5.5%)	125 (14.7%)
mRS after LVO treated without IAT (n=862)	54 (6.3%)	84 (9.8%)	122 (14.2%)	139 (16.2%)	216 (25.1%)	94 (10.9%)	150 (17.5%)

IAT: intra-arterial thrombectomy; LVO: large vessel occlusion; mRS: modified Rankin Scale
Pooled estimates based on Román et al.[65]

It is unclear to what extent these distributions are generalisable to the current UK NHS setting, given that there is no information on the proportion of early versus late presenters, or proportion of patients receiving alteplase. The impact of potential problems with generalisability here is considered to be small as all patients will receive standard medical therapy, regardless of their true negative or false positive status. Likewise, the proportion of patients who are early presenters is the same irrespective of test outcome, which would mean that the distribution over mRS states would also be the same irrespective of test outcome.

Initial distribution over mRS states for patients without LVO

To inform the distribution of patients with small vessel occlusion (i.e., the true negatives and false positives) over mRS states, we performed a pragmatic review of five systematic reviews and meta-analyses[86-90] of studies assessing the effectiveness of thrombolysis. None of these reported the

distribution over mRS states, but individual studies included did – hence, we reviewed all studies informing these meta-analyses and ruled out those that did not report the distribution over mRS states at least 3 months after stroke, that did not focus on small vessel occlusion, that were based on small sample sizes in the thrombolysis group (n<150). Only two studies were included: Choi et al[91] and Paek et al.[92] Both were based on South Korean registries and had similar sample sizes: Choi et al[91] used a retrospective analysis of the Clinical Research Center for Stroke - 5th division registry database with n=194 in the unmatched sample; and Paek et al[92] used a prospective registry of 15 South Korean stroke centres with n=193 in the thrombolysis group (Table 21). Due to limitations to data availability with Choi et al (see NA in the Table below),[91] we used the distribution reported by Paek et al[92] in the ERG base-case. Whilst it is unclear whether this is representative of UK patients, the proportion of small vessel occlusion and the accompanying mRS distribution is the same regardless of test outcome and will therefore not be influential in terms of incremental results.

Table 21: mRS state distribution for small vessel occlusion at 90 days based on two studies (implemented in the model using a Dirichlet distribution)

Study	mRS0	mRS1	mRS2	mRS3	mRS4	mRS5	mRS6
Choi et al 2015[91] (n=194)	NA (39.2%)	NA (31.4%)	NA (11.3%)	NA (10.3%)	NA (NA%)	NA (NA%)	NA (NA%)
Paek et al 2019[92] (n=192)	42 (21.8%)	68 (35.2%)	46 (23.8%)	24 (12.4%)	9 (4.7%)	4 (2.1%)	0 (0.0%)
mRS: modified Rankin Scale; NA = not available							

Transition probabilities for the state transition model

We performed a pragmatic review to inform the transition probabilities for the state transition model using the identified CEA for thrombectomy studies as a starting point. Consistent with most CEA studies we assumed that no transitions were possible between mRS states unless a recurrent stroke occurred (only in Lobotesis et al 2016[93] patients could improve or deteriorate by one mRS state at the end of year 1). Other relevant transition probabilities included: the probability of having a recurrent stroke, and the mRS distribution after a recurrent stroke. After a recurrent stroke, we assumed that patients could either stay in their mRS state or move to a more severe mRS state. The distribution over the mRS states, after recurrent stroke, was based on that for patient's ineligible for mechanical thrombectomy (Table 20) to reflect a worse outlook after recurrent stroke compared with first stroke.

Recurrent stroke with transitions to the same or worse mRS states

In the CEA model by van Leeuwen et al,[67] the annual rate for recurrent stroke was 2.8%, based on a study by Pennlert et al.[94] In this study sex- and age- adjusted annual risk of stroke recurrence was estimated for patients at 28 days after an ischaemic stroke in the Swedish population-based Monitoring Trends and Determinants of Cardiovascular Disease (MONICA) stroke incidence registry (n=5,885 with ischaemic stroke, mean age = 64.2 (24 to 74) and proportion male = 60.6%). The index stroke occurred between 1995 to 1998. The average rate for recurrent stroke over the use calculated based on data provided in Online Supplement Table 1 of Pennlert et al[94] was 2.8%. Pennlert et al also observed that there was a decline in recurrent stroke rates over time,[94] however, we did not include this in the model.

An alternative source is the study by Mohan et al,[95] who performed a systematic review and meta-analysis of 13 included studies reporting cumulative risk of recurrence after first-ever stroke (both ischemic and haemorrhagic stroke). Three of the 13 studies were from the UK. Some of these studies dated back a long time, e.g., the oldest started data collection in 1961, whereas the newest started in 2003. The pooled cumulative risk of stroke recurrence was: 3.1% (95% CI, 1.7 to 4.4) at 30 days; 11.1% (95% CI, 9.0 to 13.3) at 1 year; 26.4% (95% CI, 20.1 to 32.8) at 5 years; and 39.2% (95% CI, 27.2 to 51.2) at 10 years after initial stroke.[95] A Weibull model was fitted but model parameters were not provided. Lobotesis et al[93] used the cumulative risk at 5 years reported by Mohan et al[95] and estimated the annual risk of recurrence for the rest of patients' lives at 2.0%.

We considered that Pennlert et al[94] provided estimates specifically for ischaemic stroke whilst these were not available from Mohan et al.[95] We therefore used estimates by Pennlert et al[94] in the base-case and explored the use of Mohan et al[95] in a scenario.

In the model, risk of recurrent stroke was the same across all mRS health states (consistent with assumptions in other CEA studies).[67, 93]

Death conditional on functional status after stroke

The study by Slot et al[96] estimated the risk of stroke-related mortality conditional on functional dependency using two cohorts: the Oxfordshire Community Stroke Project (n=320), the Lothian Stroke Register (n=448) and the First International Stroke Trial (n=1,563), all UK studies. The authors found a significant impact of functional status on the cause of death. In particular, functionally dependent patients (i.e., those with mRS scores of 3-5) were more likely to die of recurrent stroke (RR 1.68 (95% CI 1.49 to 1.91)) than functionally independent patients. Stroke-related causes of death were present in 794 (49%) of the functionally dependent patients versus 207 (29%) of the

independent patients in all three cohorts combined and included ICD codes for cerebrovascular diseases (ICD-9 430-438; ICD-10 I60-I69), either mentioned in the death certificate as a primary cause of death or a contributing factor (i.e., secondary, tertiary, or quaternary cause of death). The risk of stroke-related cause of death increased by mRS score.

We estimated (recurrent stroke-related) mortality by: 1) multiplying recurrent stroke probability with the mRS 6 probability (Table 20) and 2) applying the relative risk of dying per mRS state reported by Slot et al (Table 22) to the general population mortality.[97] The maximum probability of these two approaches was used in the economic model. This prevented underestimating mortality in the more severe mRS health states; ensured that mortality was consistent with the age-adjusted general population mortality whilst including mRS health state dependent mortality; and prevented double-counting.

Table 22: Risk of stroke-related death, by mRS, at 6 months post-stroke

mRS	RR (95% CI)
0-1	1.00 (baseline)
2	1.12 (0.82, 1.56)
3	1.66 (1.24, 2.23)
4	1.92 (1.41, 2.61)
5	2.57 (1.92, 3.43)
CI: confidence interval; mRS: modified Rankin scale; RR: relative risk OCSP and LSR cohorts combined Source: Slot et al 2009,[96] Table 4	

Health-related quality of life

To identify studies reporting utility values associated with the model health states (i.e., the mRS states), we performed a pragmatic search and review (see Section 4.1.1). In addition, we also reviewed the identified CEA studies and searched their references. If necessary, references of articles identified in that way were also searched. This pragmatic review resulted in seven studies reporting utility values for the mRS states.[98-105] The studies reporting EQ-5D time-trade-off values using the UK value set were: Ali et al,[102] Rivero-Arias et al,[99] Rebchuk et al[104] and Wang et al.[105] Ali et al[102] was a multi-country study and the sample size of UK patients and utilities valued with the UK value set was small (n=70). Rebchuk et al[104] presented utility values averaged over nine studies that collected EQ-5D data, but most of these studies did not use the UK value set. Similarly, Wang et al[105] presented utility values averaged over six studies, but not all of them using the UK value set. Therefore, we used total utility values from the study by Rivero-Arias et al[99] in the base-case (sample size of at least n=365 at 1 month and more in subsequent months). Utilities by Rebchuk et al[104] and Wang et al[105] were applied in scenarios.

Rivero-Arias et al[99] derived mRS and EQ-5D-3L information from stroke or TIA patients identified as part of the Oxford Vascular (OXVASC) study. Ordinary least squares (OLS) regression was used to predict UK EQ-5D-3L tariffs from mRS scores. Data were available at months 1, 6, 12, and 24 with sample sizes for the EQ-5D-3L varying by measurement point (n=365, n=478, n=346, and n=539 respectively).

Table 23: Utility values for mRS states

mRS	Rivero-Arias et al[99] utility values (sd)	Rebchuk et al[104] utility values (CI) [n]	Wang et al[105] utility values (sd) [n]
0	0.936 (0.127)	0.93 (0.96,0.9) [3,624]	0.97 (0.1) [3,148]
1	0.817 (0.183)	0.86 (0.89, 0.83) [2,376]	0.88 (0.16) [4,968]
2	0.681 (0.211)	0.68 (0.72, 0.64) [1,149]	0.72 (0.21) [1,950]
3	0.558 (0.284)	0.57 (0.61, 0.53) [957]	0.54 (0.25) [2,327]
4	0.265 (0.294)	0.31 (0.35, 0.26) [1,101]	0.23 (0.33) [1,618]
5	–0.054 (0.264)	0.06 (0.12, 0.00) [400]	-0.17 (0.21) [858]
CI: confidence interval; mRS: modified Rankin Scale; n; number; sd: standard deviation			

Utility values used in the model were age-adjusted using the UK population norms for the EQ-5D-3L reported by Janssen et al.[106]

Resource use and costs

Costs of AI-derived software technologies

Based on information provided by each company, mean costs per patient were calculated for using AI-derived software technologies. In the base-case analysis, a mean estimate was used based on all four technologies.

In order to calculate an overall mean price of the AI-derived software technologies, annual license fees for each device were applied to the UK situation in terms of number of comprehensive stroke centres (CSCs), primary stroke centres (PSCs), and total number of stroke patients in the UK based on the Sentinel Stroke National Audit Programme.[107] The mean cost price of AI-derived software technologies in the base-case analysis was assumed to be £49.24 (£12.31).

Table 24 presents all relevant inputs as well as intervention-specific cost estimates.

Table 24: Costs of AI-derived software technologies

Fixed estimates for each AI-technology			***Source***
Number of Comprehensive Stroke Centres (CSCs):	25		Sentinel Stroke National Audit Programme
Number of Primary Stroke Centres (PSCs):	177		Sentinel Stroke National Audit Programme
Number of stroke patients in	87,635		Sentinel Stroke National Audit

UK:			Programme
Intervention-specific inputs	**Lowest price**	**Highest price**	**Source**
Rapid CTA			
AI license Annual fee for CSC:	£20,000	N/A	Provided by company
AI license Annual fee for PSC:	£20,000	N/A	Provided by company
Training costs:	£5,000	N/A	Assumption
Total costs:	£5,050,000	N/A	
Cost per patient (Se*)	£57.63 (£14.41)		
Viz.ai			
AI license Annual fee for CSC:	£40,000	£55,000	Provided by company
AI license Annual fee for PSC:	£20,000	£30,000	Provided by company
Training costs:	£7,241	£7,241	Provided by company
Total costs:	£6,002,682	£8,147,682	
Cost per patient	£68.50	£92.97	
Mean cost per patient (Se*)	£80.73 (£20.18)		
Avicenna			
AI license Annual fee for CSC:	N/A	N/A	Avicenna only works with price per patient
AI license Annual fee for PSC:	N/A	N/A	Avicenna only works with price per patient
Training costs:	N/A	N/A	The company stated that no training was required to work with the software
Mean cost per patient (Se*)	£7.08 (£1.77)		Avicenna only works with price per patient (this price is for centres up to 5000 scans per year)
Brainomix			
AI license Annual fee for CSC:	£30,000	£30,000	Provided by company
AI license Annual fee for PSC:	£15,000	£15,000	Provided by company
Training costs:	£3,000	£8,000	Provided by company
Total costs:	£4,011,000	£5,021,000	Provided by company
Cost per patient	£45.77	£57.29	
Mean cost per patient (Se*)	£51.53 (£12.88)		
Mean cost price of AI-derived software technologies in base-case analysis			
Mean cost per patient (Se*)	£49.24 (£12.31)		

* Se was assumed to be 25% of the mean
Se: standard error

We performed a pragmatic review to inform resource use and costs parameters in the model. A study of Lobotesis et al.[93] was identified which served as the main source of input parameters related to resource use and costs. In that study, a UK healthcare provider perspective was assumed, and all (treatment) cost estimates were broken down into units and unit prices enabling us to calculate treatment costs using a bottom-up approach. In line with that study, short term costs (<90 days) consisted of costs for treatment, hospitalisation, and management of adverse events. In

Lobotesis et al (2016), to estimate treatment costs, unit costs for each cost item were presented in combination with the corresponding number of units that each cost item was used in which unit costs were sourced from Personal Social Services Research Unit (PSSRU17), Unit Costs of Health & Social Care, and treatment and device costs for the stent retriever were provided by Medtronic. Costs and resource use associated with intravenous tissue plasminogen activator were derived from the Single Technology Appraisal for alteplase (TA122).[19]

Using these number, treatment costs were calculated using a bottom-up approach (Table 25).

Table 25: Short term costs (< 90 days): costs for treatment, hospitalisation, and management of adverse events

Cost items	Unit price	Source	Units	Total price (indexed to 2020)
Mechanical thrombectomy				
Stent retriever	£3,190	Covidien internal pricing	1,2	£4,161
Catheter/support kit	£920	Covidien internal pricing	1	£1.000
Procedure Pack	£35	Covidien internal pricing	1	£38
Drapes/Gowns/Gloves	£80	Covidien internal pricing	1	£87
Sheath	£15	Expert clinical opinion	1	£16
Interventional Suite	£150	Expert clinical opinion	3	£489
Anesthetist	£157	Expert clinical opinion (cost not available in PSSRU)	4	£683
Anesthetist assistant	£58	PSSRU17 (Nurse team manager)	4	£252
Radiographer	£58	PSSRU17 (Nurse team manager)	3	£189
Consultant Interventional Neuroradiologist	£140	PSSRU17 (Medical consultant)	3	£457
Registrar	£60	PSSRU17 (Registrar)	3	£196
Nurse (band 7)	£58	PSSRU17 (Nurse team manager)	3	£189
Scrub nurse (band 5)	£49	PSSRU17 (Nurse team leader)	3	£160
Subtotal				£7,916
Intravenous thrombolysis				
Nurse activates stroke team	£49	PSSRU17 (Nurse team leader)	0,08	£4
Stroke team assessment (Registrar grade)	£60	PSSRU17 (Registrar)	0,5	£33
Blood test	£5	ISD Scotland24	1	£6

Cost items	Unit price	Source	Units	Total price (indexed to 2020)
Registrar accompanies patient to CT scan	£60	PSSRU17 (Registrar)	1	£65
Consultant reviews CT results and discusses with relatives	£140	PSSRU17 (Medical consultant)	0,5	£76
Nurse assessment	£58	PSSRU17 (Nurse team manager)	0,08	£5
IV t-PA infusion (Registrar time)	£60	PSSRU17 (Registrar)	1,25	£82
Additional 12 routine observations	£49	PSSRU17 (Nurse team leader)	1	£53
1:1 care for 5 h with senior nurse	£58	PSSRU17 (Nurse team manager)	5	£315
Junior staff review	£60	PSSRU17 (Registrar)	0,42	£27
Overnight junior staff review	£60	PSSRU17 (Registrar)	0,17	£11
Consultant review after infusion	£140	PSSRU17 (Medical consultant)	0,33	£50
Alteplase drug costs	£576	British National Formulary25	1	£626
Subtotal				£1,354
Non-thrombolytic treatment				
ER Doctor Assessment	£140	PSSRU17 (Medical consultant)	0,25	£38
Blood test	£5	ISD Scotland24	1	£6
CT scan (brain imaging)	£91	NHS Reference Costs26	1	£98
Nurse to accompany to CT scan	£49	PSSRU17 (Nurse team leader)	1	£53
Nurse assessment	£49	PSSRU17 (Nurse team leader)	0,08	£4
Routine nurse observation (4 in 24 h)	£49	PSSRU17 (Nurse team leader)	0,33	£18
Junior staff review	£60	PSSRU17 (Registrar)	0,21	£14
Consultant review at 24 h	£140	PSSRU17 (Medical consultant)	0,25	£38
Subtotal				£269

Sourced from Lobotesis et al.[93]
CT: computed tomography; ER: emergency room; PSSRU: Personal Social Services Research Unit.

In line with Van Leeuwen et al.,[67] for patients with LVO receiving mechanical thrombectomy, it was assumed that 85% would receive both mechanical thrombectomy and intravenous thrombolysis, 10% to receive intravenous thrombolysis only, and 5% to receive intravenous thrombolysis and going for mechanical thrombectomy but who appeared revascularised during angiography. Moreover, for

patients with LVO not receiving mechanical thrombectomy, it was assumed that 40% would receive intravenous thrombolysis and 60% would receive non-thrombolytic treatment.[67] Treatment costs for non-LVO patients were assumed to be equal to the costs of 1 day in the acute stroke unit based on Patel et al.[108] Lastly, the additional costs of non-LVO patients incorrectly classified as LVOs were assumed to be equal to the costs of an ambulance ride and a stroke unit day using cost estimates from Patel et al.[108] An overview of the resulting short term costs (<90 days) for each branch of the decision tree is presented in Table 26.

Table 26: Short term costs (<90 days) for each branch of the decision tree (2020 prices)

Branch in decision tree	Costs (Se)*	Source
Patients with LVO receiving mechanical thrombectomy	8,794 (2,198)	Lobotesis et al. (2016)/Van Leeuwen et al. (2020)
Patients with LVO not receiving mechanical thrombectomy	702 (176)	Lobotesis et al. (2016)/Van Leeuwen et al. (2020)
Non-LVO patients	745 (186)	Patel et al. (2020)
Non-LVO patients incorrectly classified as LVO**s**	559 (140)	Patel et al. (2020)
* Se was assumed to be equal to 25% of the mean estimates. Se: standard error		

Acute stroke costs (< 90 days) and long-term costs (annually) were attributed to the different mRS states and included costs of personal social services, such as nursing and residential care costs (i.e., for long term costs). To this extent, Lobotesis et al.[93] used data from the OXVASC study.[109] As data were only available for three levels of post-stroke disability (i.e., mRS 0–2, mRS 3–4, and mRS 5), the authors employed a consensus-based approach by using three clinical experts from whom weights were elicited. By applying a weighting on the three levels of post-stroke disability, individual costs by mRS were calculated for mRS levels/states.

Acute and long-term costs of acute ischemic stroke by mRS are presented in Table 27.

Table 27: Acute and long-term costs of acute ischemic stroke by mRS

mRS state	Mean acute costs (SD)	Mean annual long-term costs (SD)
mRS0	£3,145 (£8,333)	£2,846 (£3,998)
mRS1	£3,700 (£8,333)	£3,348 (£3,998)
mRS2	£4,255 (£8,333)	£3,850 (£3,998)
mRS3	£16,409 (£20,657)	£13,697 (£8,343)
mRS4	£22,200 (£20,657)	£18,532 (£8,343)
mRS5	£26,367 (£17,704)	£30,093 (£16,209)
mRS6 (cost of death)	£3,328 (£3,055)	-
Sourced from Lobotesis et al. 2016[93] mRS: modified Rankin Scale (assessment of global disability range from 0 (no symptoms) to 6 (death)); SD: standard deviation.		

4.2.4 Overview of main model assumptions and input parameters

The main assumptions in the health economic analyses were:

1. Consistent with the focus of the AI-derived software assisted review on triage and supporting the thrombectomy decision, the current assessment primarily considers the claim that AI-derived software assisted review could provide a more accurate diagnosis of LVO.
2. Thrombectomy eligibility is independent of the diagnostic strategy.
3. For recurrent strokes, the mRS distribution of patients without thrombectomy is used.
4. Consistent with most cost effectiveness studies in this disease area, it was assumed that transitions between health states mRS 0-5 were only possible in case a (recurrent) stroke occurred. After a recurrent stroke, patients could either stay in their mRS health state or move to a more severe mRS health state.
5. The risk of recurrent stroke was assumed the same across all mRS health states.
6. False positives have cost consequences only.

A summary of model input parameters is provided in Table 28.

Table 28: Model input parameters (generated with the f_gen_psa)(function)

Parameter	Description	Deterministic value	Probabilistic mean (95% CI)	Distribution
d_c	discount rate for costs	0.035	-	Fixed
d_e	discount rate for effects	0.035	-	Fixed
cycles	number of model cycles	40	-	Fixed
age_init	starting age	66	-	Fixed
p_male	proportion of patients that are male	0.584	-	Fixed
p_prev	prevalence of LVO	0.461	0.461 (0.430-0.491)	Logit normal
p_mt_eligible_t1	proportion of patients eligible for thrombectomy for t1	0.412	0.412 (0.406-0.418)	Beta
p_mt_eligible_t2	proportion of patients eligible for thrombectomy for t2	0.412	0.412 (0.406-0.418)	Beta
p_se_t1	sensitivity for t1 (clinician only)	0.930	0.930 (0.876-0.969)	PERT
p_sp_t1	specificity for t1 (clinician only)	0.941	0.941 (0.902-0.973)	PERT
p_se_t2	sensitivity for t2 (AI + clinician)	0.941	0.941 (0.904-0.971)	PERT
p_sp_t2	specificity for t2 (AI + clinician)	0.938	0.937 (0.885-0.978)	PERT
p_mRS0_lvo_mt	proportion of patients with mRS0 after thrombectomy	0.111	0.111 (0.091-0.133)	Dirichlet
p_mRS1_lvo_mt	proportion of patients with mRS1 after thrombectomy	0.181	0.181 (0.156-0.208)	Dirichlet
p_mRS2_lvo_mt	proportion of patients with mRS2 after thrombectomy	0.186	0.186 (0.161-0.212)	Dirichlet
p_mRS3_lvo_mt	proportion of patients with mRS3 after thrombectomy	0.161	0.161 (0.137-0.186)	Dirichlet
p_mRS4_lvo_mt	proportion of patients with mRS4 after thrombectomy	0.159	0.159 (0.135-0.185)	Dirichlet
p_mRS5_lvo_mt	proportion of patients with mRS5 after thrombectomy	0.055	0.055 (0.041-0.072)	Dirichlet
p_mRS6_lvo_mt	proportion of patients with mRS6 after thrombectomy	0.147	0.147 (0.124-0.172)	Dirichlet
p_mRS0_lvo_no_mt	proportion of patients with mRS0 with LVO but without thrombectomy	0.063	0.063 (0.048-0.080)	Dirichlet
p_mRS1_lvo_no_mt	proportion of patients with mRS1 with LVO but without thrombectomy	0.098	0.098 (0.079-0.119)	Dirichlet
p_mRS2_lvo_no_mt	proportion of patients with mRS2 with LVO but without thrombectomy	0.142	0.142 (0.119-0.167)	Dirichlet
p_mRS3_lvo_no_mt	proportion of patients with mRS3 with LVO but without thrombectomy	0.162	0.162 (0.138-0.188)	Dirichlet
p_mRS4_lvo_no_mt	proportion of patients with mRS4 with LVO but without thrombectomy	0.251	0.251 (0.222-0.280)	Dirichlet
p_mRS5_lvo_no_mt	proportion of patients with mRS5 with LVO but without thrombectomy	0.109	0.109 (0.089-0.130)	Dirichlet
p_mRS6_lvo_no_mt	proportion of patients with mRS6 with LVO but without thrombectomy	0.175	0.175 (0.150-0.200)	Dirichlet
p_mRS0_no_lvo	proportion of non-LVO patients with mRS0	0.218	0.217 (0.161-0.278)	Dirichlet
p_mRS1_no_lvo	proportion of non-LVO patients with mRS1	0.352	0.352 (0.287-0.421)	Dirichlet

Parameter	Description	Deterministic value	Probabilistic mean (95% CI)	Distribution
p_mRS2_no_lvo	proportion of non-LVO patients with mRS2	0.238	0.239 (0.181-0.301)	Dirichlet
p_mRS3_no_lvo	proportion of non-LVO patients with mRS3	0.124	0.124 (0.082-0.174)	Dirichlet
p_mRS4_no_lvo	proportion of non-LVO patients with mRS4	0.047	0.047 (0.022-0.080)	Dirichlet
p_mRS5_no_lvo	proportion of non-LVO patients with mRS5	0.021	0.021 (0.006-0.044)	Dirichlet
p_mRS6_no_lvo	proportion of non-LVO patients with mRS6	0.000	-	Fixed
p_mRS0_rec	proportion of patients with mRS0 after recurrent stroke	0.063	0.063 (0.048-0.08)	Dirichlet
p_mRS1_rec	proportion of patients with mRS1 after recurrent stroke	0.098	0.098 (0.079-0.119)	Dirichlet
p_mRS2_rec	proportion of patients with mRS2 after recurrent stroke	0.142	0.142 (0.119-0.167)	Dirichlet
p_mRS3_rec	proportion of patients with mRS3 after recurrent stroke	0.162	0.162 (0.138-0.188)	Dirichlet
p_mRS4_rec	proportion of patients with mRS4 after recurrent stroke	0.251	0.251 (0.222-0.28)	Dirichlet
p_mRS5_rec	proportion of patients with mRS5 after recurrent stroke	0.109	0.109 (0.089-0.13)	Dirichlet
p_mRS6_rec	proportion of patients with mRS6 after recurrent stroke	0.175	0.175 (0.15-0.2)	Dirichlet
p_rec_stroke	probability of recurrent stroke	0.030	0.028 (0.016-0.043)	Beta
rr_mRS0	relative risk for mortality for patients with mRS0	1.000	-	Fixed
rr_mRS1	relative risk for mortality for patients with mRS1	1.000	-	Fixed
rr_mRS2	relative risk for mortality for patients with mRS2	1.120	1.137 (0.815-1.543)	Log-normal
rr_mRS3	relative risk for mortality for patients with mRS3	1.660	1.68 (1.237-2.227)	Log-normal
rr_mRS4	relative risk for mortality for patients with mRS4	1.920	1.948 (1.417-2.628)	Log-normal
rr_mRS5	relative risk for mortality for patients with mRS5	2.570	2.596 (1.926-3.439)	Log-normal
u_mRS0	utility for patients with mRS0	0.936	0.817 (0.507-0.993)	Truncated normal
u_mRS1	utility for patients with mRS1	0.817	0.752 (0.41-0.985)	Truncated normal
u_mRS2	utility for patients with mRS2	0.681	0.656 (0.28-0.964)	Truncated normal
u_mRS3	utility for patients with mRS3	0.558	0.552 (0.165-0.909)	Truncated normal
u_mRS4	utility for patients with mRS4	0.265	0.262 (-0.132-0.658)	Truncated normal
u_mRS5	utility for patients with mRS5	-0.054	-0.054 (-0.094--0.015)	Truncated

Parameter	Description	Deterministic value	Probabilistic mean (95% CI)	Distribution
				normal
u_mRS6	utility for patients with mRS6	0.000	-	Fixed
c_mRS0_dt	decision tree costs for patients with mRS0	£3,419	£3,405 (£0-£29,384)	Gamma
c_mRS1_dt	decision tree costs for patients with mRS1	£4,022	£4,061 (£0-£31,253)	Gamma
c_mRS2_dt	decision tree costs for patients with mRS2	£4,625	£4,558 (£0-£30,417)	Gamma
c_mRS3_dt	decision tree costs for patients with mRS3	£17,837	£18,190 (£67-£81,983)	Gamma
c_mRS4_dt	decision tree costs for patients with mRS4	£24,131	£23,895 (£877-£81,859)	Gamma
c_mRS5_dt	decision tree costs for patients with mRS5	£28,661	£28,483 (£4,045-£77,477)	Gamma
c_mRS6_dt	decision tree costs for patients with mRS6	£3,618	£3,565 (£133-£12,152)	Gamma
c_mRS0	annual costs for patients with mRS0	£3,094	£3,118 (£4-£16,017)	Gamma
c_mRS1	annual costs for patients with mRS1	£3,639	£3,612 (£24-£15,874)	Gamma
c_mRS2	annual costs for patients with mRS2	£4,185	£4,176 (£82-£15,882)	Gamma
c_mRS3	annual costs for patients with mRS3	£14,889	£14,913 (£2,694-£36,909)	Gamma
c_mRS4	annual costs for patients with mRS4	£20,144	£20,112 (£6,488-£42,020)	Gamma
c_mRS5	annual costs for patients with mRS5	£32,711	£32,727 (£7,722-£74,336)	Gamma
c_mRS6	annual costs for patients with mRS6	£0	-	Fixed
c_t1	technology costs for t1	£0	-	Fixed
c_t2	technology costs for t2	£49	£49 (£28-£77)	Gamma
c_treat_mt	initial treatment costs for patients with thrombectomy	£8,794	£8,788 (£5,386-£13,130)	Beta and Gamma
c_treat_no_mt	initial treatment costs for LVO patients without thrombectomy	£702	£705 (£411-£1,131)	Beta and Gamma
c_treat_non_LVO	initial treatment costs for non-LVO patients	£745	£746 (£385-£1,220)	Beta and Gamma
c_FP	initial additional costs for non-LVO patients incorrectly classified as LVO	£559	£558 (£322-£864)	Gamma

4.3 Model analyses

Discount rates of 3.5% and a half-cycle correction were applied for both costs and effects. Expected costs, life years (LYs) and QALYs were estimated from the perspective of the NHS. The incremental cost effectiveness ratio (ICER) was calculated by dividing the incremental costs by the incremental QALYs. Probabilistic sensitivity analyses (10,000 simulations) were performed, and cost effectiveness acceptability curves (CEACs) and expected loss curves (ELC) were constructed.

4.3.1 Sensitivity analysis

Deterministic one-way sensitivity analyses were performed, using all stochastic input parameters, to assess the impact of input parameters on the estimated outcomes. The results of these analyses are presented using optimal strategy plots and plotting the input parameters versus outcomes. Info-rank plots, based on the probabilistic sensitivity analyses (PSA), are presented to explore the relative 'importance' of each parameter in terms of the expected value of information. Finally, two-way sensitivity analyses were performed, including the most influential AI-specific parameters.

4.3.2 Scenario analyses

Various deterministic scenario analyses were performed to assess the impact of assumptions on the estimated outcomes:

1. Assuming the AI technology costs are increased to £100 per patient
2. Assuming the proportion of LVO patients eligible for mechanical thrombectomy with AI is increased to 50%
3. Assuming the AI technology + clinician sensitivity is increased to 96%
4. Assuming the AI technology + clinician sensitivity is decreased to 90%
5. Assuming the LVO prevalence is increased to 50%
6. Assuming the LVO prevalence is decreased to 40%
7. Assuming recurrent strokes are LVOs eligible for thrombectomy with appropriate mRS distribution
8. Assuming recurrent strokes are non-LVOs
9. Assuming additional FP costs are increased to £2,000
10. Assuming the annual recurrent stroke probability is decreased to 2%
11. Assuming the annual recurrent stroke probability is increased to 4%
12. Assuming the proportion of patients eligible for thrombectomy is increased to 50% (both strategies)
13. Assuming the proportion of patients eligible for thrombectomy is decreased to 35%% (both strategies)

14. Utility values based on Rebchuk et al (0.93, 0.86, 0.68, 0.57, 0.31 and 0.06 for mRS 0-5)
15. Utility values based on Wang et al (0.97, 0.88, 0.72, 0.54, 0.23 and -0.17 for mRS 0-5)
16. Assuming no mortality cap (allowing mortality to be potentially lower than general population mortality)
17. Assuming no utility cap (allowing utility values to be potentially higher than general population utility values)
18. Assuming both no mortality cap and no utility cap
19. Assuming accuracy for current practice without AI is based on Seker 2020 (neuroradiologist grader)
20. Assuming accuracy for current practice without AI is based on Seker 2020 (resident graders)

4.4 Results of cost effectiveness analyses

The probabilistic base-case analyses were performed using 10,000 simulations. Although less simulations were deemed sufficient based on the convergence plots of the incremental results (see Figure 12), the number of simulations was increased to increase the stability of the estimated results (given the small incremental differences) when rerunning the PSA with a different random seed.

4.4.1 Base-case analysis

The probabilistic results indicated that the addition of AI to detect LVO is potentially more effective, (QALY gain of 0.003), more costly (increased costs of £8.61) and cost effective for willingness to pay thresholds of £3,380 per QALY and higher (Table 29). The cost effectiveness plane (Figure 12) illustrates the negative correlation between incremental costs and incremental QALYs, i.e., if a technology is more effective it also tends to be less costly. The CEAC (Figure 13) indicates that at willingness to pay thresholds of £20,000 and £30,000 per QALY gained the probabilities of current practice with AI being cost effective are 53.6% and 56.2% respectively. The expected risks per patient associated with adding AI, at willingness to pay thresholds of £20,000 and £30,000 per QALY gained, were £80 and £95 respectively (these were £122 and £163 respectively without adding AI; see expected loss curves). On a population level (assuming 87,635 patients per annum, in the UK) the estimated annual risks associated with adding AI were £7.0 million and £8.4 million, at willingness to pay thresholds of £20,000 and £30,000 per QALY gained, respectively. The deterministic results (Table 30) were similar to the probabilistic results.

Table 29: Probabilistic base-case results

Technology	Costs (£)	QALYs	Δ Costs (£)	Δ QALYs	Δ Costs (£) / Δ QALYs
Current practice without AI	116,273	5.9000	NA	NA	NA
Current practice with AI	116,281	5.9026	9	0.0025	3,380

Table 30: Deterministic results (using base-case settings)

Technology	Costs (£)	QALYs	Δ Costs (£)	Δ QALYs	Δ Costs (£) / Δ QALYs
Current practice without AI	117,267	6.2778	NA	NA	NA
Current practice with AI	117,276	6.2806	10	0.0027	3,490

Intermediate results (probabilistic base-case)

The diagnostic pathway (after the 90 day decision tree) results were similar for both strategies (Figure 14). The proportion of detected LVOs (and thus patients receiving thrombectomy) was increased from 17.6% to 17.9% when AI is added to current practice. As a result, the mRS 0-3 proportions were slightly higher while mRS 4-6 proportions were slightly lower when AI is added (differences <0.1%). Moreover, the average traces (across all PSA simulations) were very similar for both technologies (Figure 15). Similarly, to the 90 day decision tree results, the average trace differences per cycle were <0.1% with the addition of AI resulting in slightly higher proportions in the lower mRS health states. When considering the cumulative costs and QALYs over time (Figure 16), the cost difference is largest in cycle 1 (the addition of AI resulting in a cost increase of £58) decreasing over time to £9 at the end of the time horizon. In contrast, the QALY difference (Figure 17) is smallest in cycle 1 (the addition of AI resulting in a QALY increase of 0.0002) increasing over time to 0.0025 QALY (at the end of the time horizon).

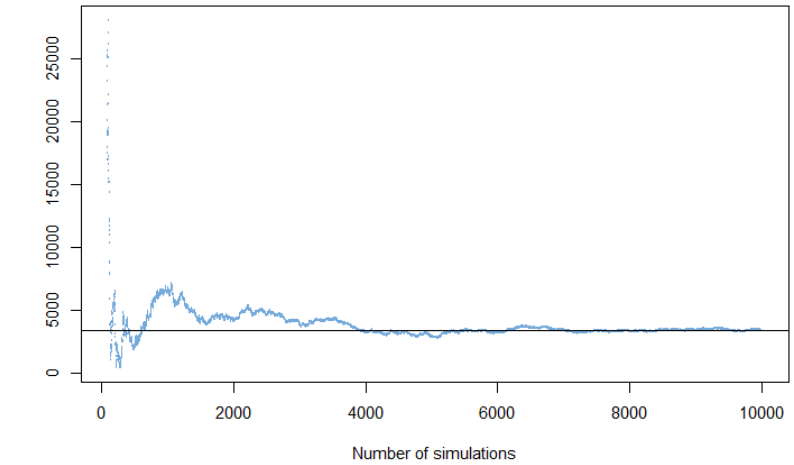
Considering the disaggregated costs, the cost increase for AI was mainly driven by the short-term costs (including the AI technology costs); while overall costs related to the mRS4 and mRS5 health states are lower (due to lower occupancy for these health states) when AI is added. Although incremental QALYs are very low and similar across health states, the increased QALYs for AI are driven by QALY differences in the mRS0 and mRS1 health states (due to higher occupancy for these health states). Finally, the estimated life years were very similar for both strategies (10.847 versus 10.848).

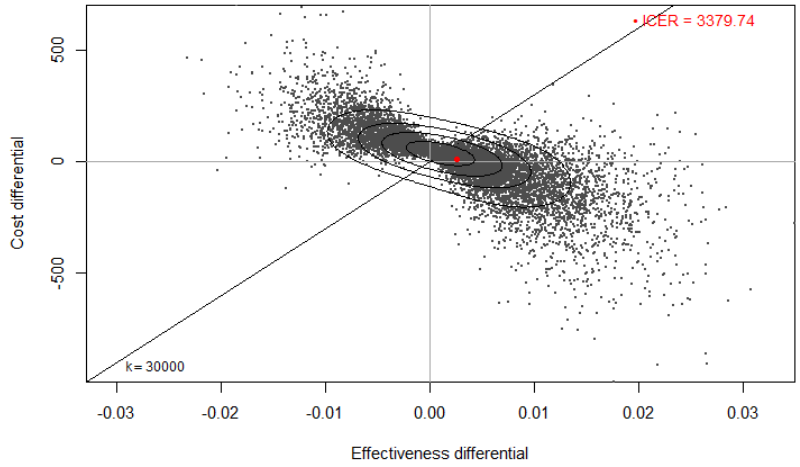
4.4.2 Sensitivity analyses

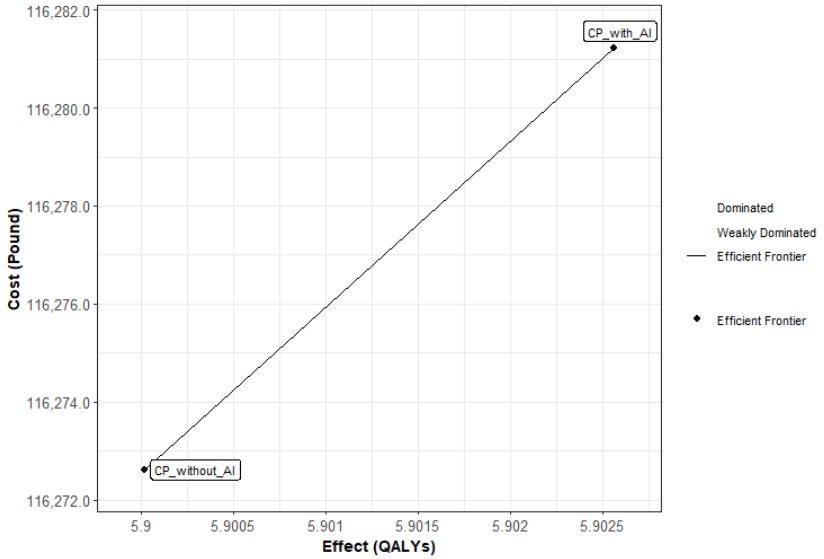
The info-rank plot indicated that the sensitivity of both technologies was the most important input parameter (Figure 18). In addition, the optimal strategy plots (Figure 19) indicated that the proportion of patients with LVO who are eligible for mechanical thrombectomy is important to determine the most optimal strategy in terms of costs and QALYs. For the estimated costs, specificity, the additional costs of the AI technology, costs related to mRS4 and mRS5 were input parameters (in addition to those mentioned above) that can change the strategy that is most optimal. Deterministic one-way sensitivity analyses for all stochastic parameters are presented in Figures 20 (costs) and Figure 21 (QALYs).

Two-way sensitivity analyses were performed (Figure 22) between: 1) AI technology sensitivity; 2) AI technology costs; and 3) the proportion of LVO patients eligible for mechanical thrombectomy with AI. These analyses indicated that (given the 95 CI of these inputs), although the AI technology sensitivity is a main driver of the results, the AI technology costs and the proportion of LVO patients eligible for mechanical thrombectomy with AI can have an impact on the minimal AI technology sensitivity required for the AI technology to be cost effective.

Figure 12: Convergence plot (iCER), cost effectiveness plane and expected incremental benefit







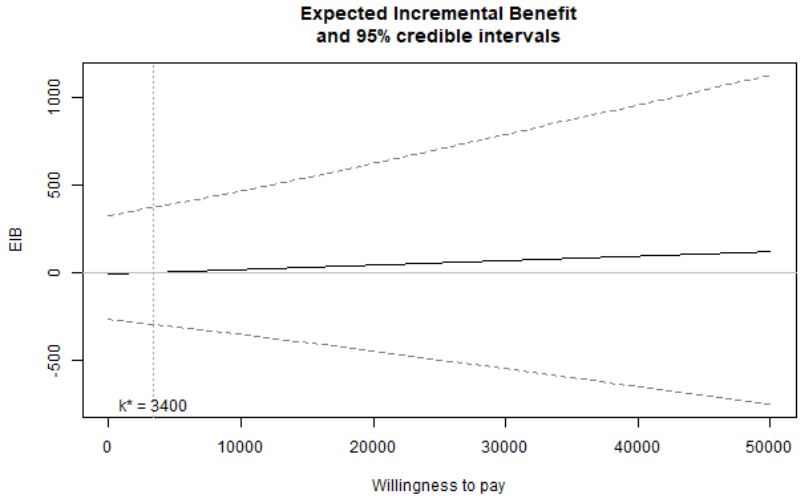


Figure 13: Cost effectiveness acceptability and expected loss curves

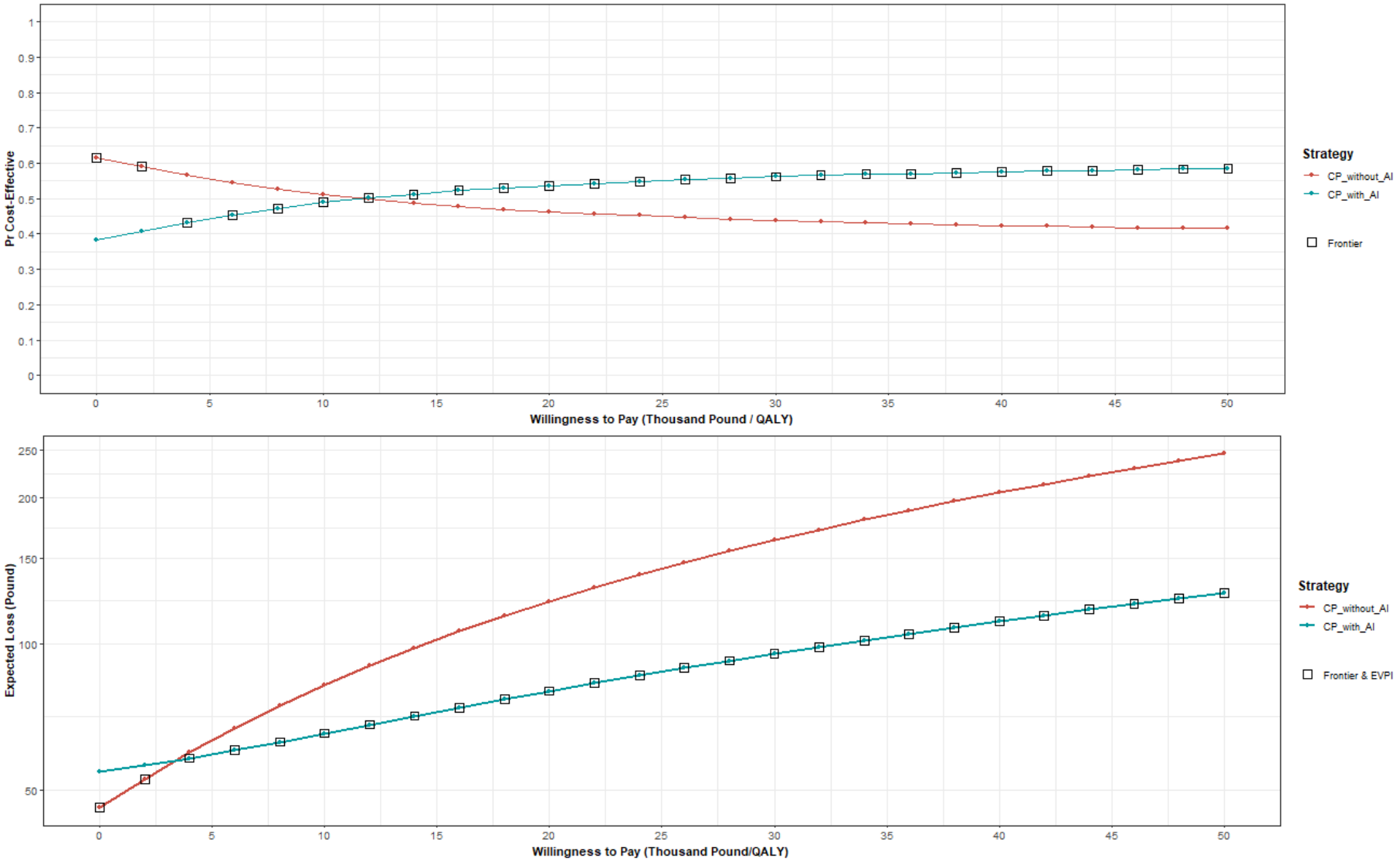


Figure 14: Diagnostic pathway results for current practice with AI (t2) and without AI (t1)

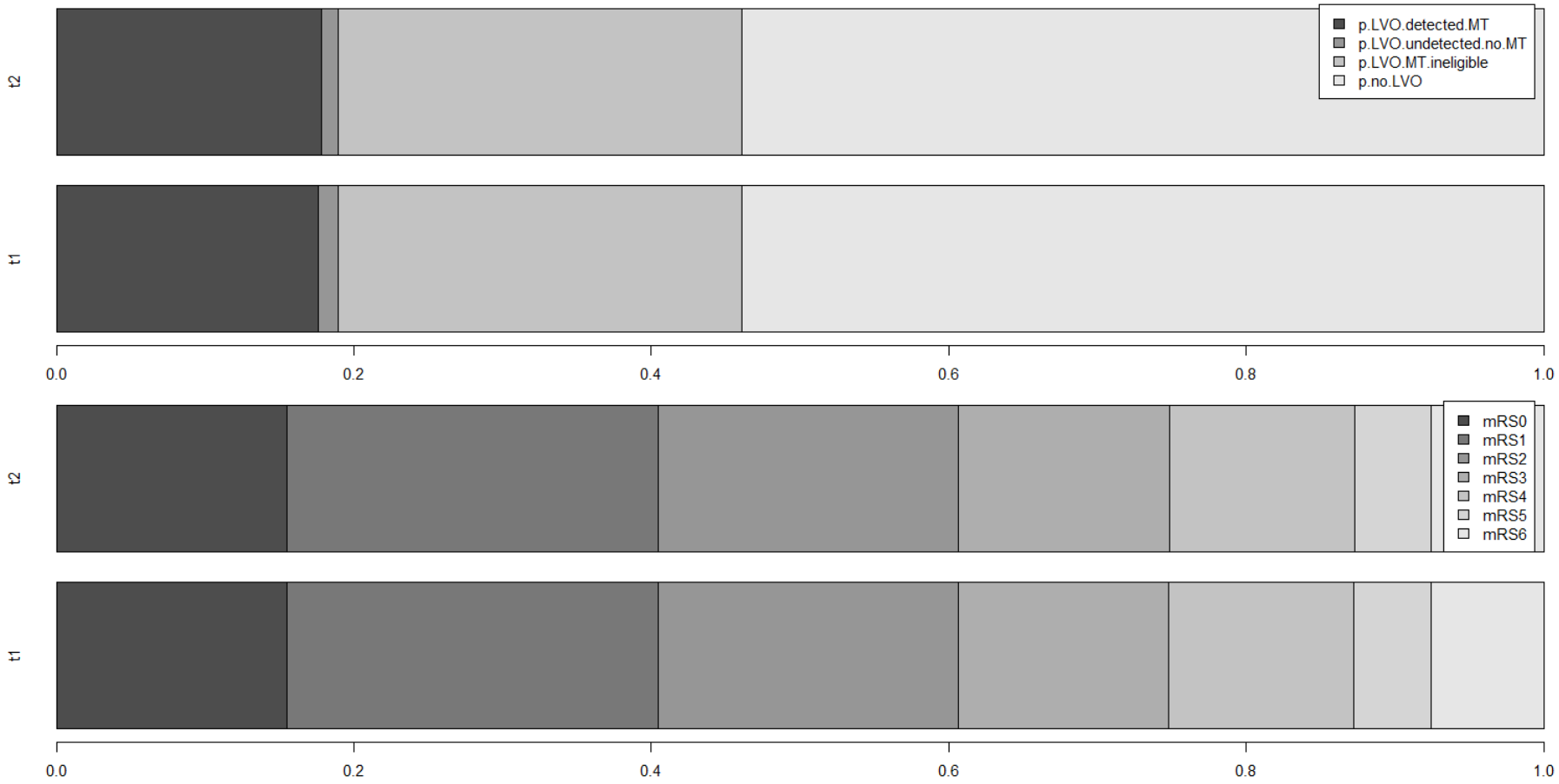


Figure 15: Average state transition trace for current practice with AI and without AI

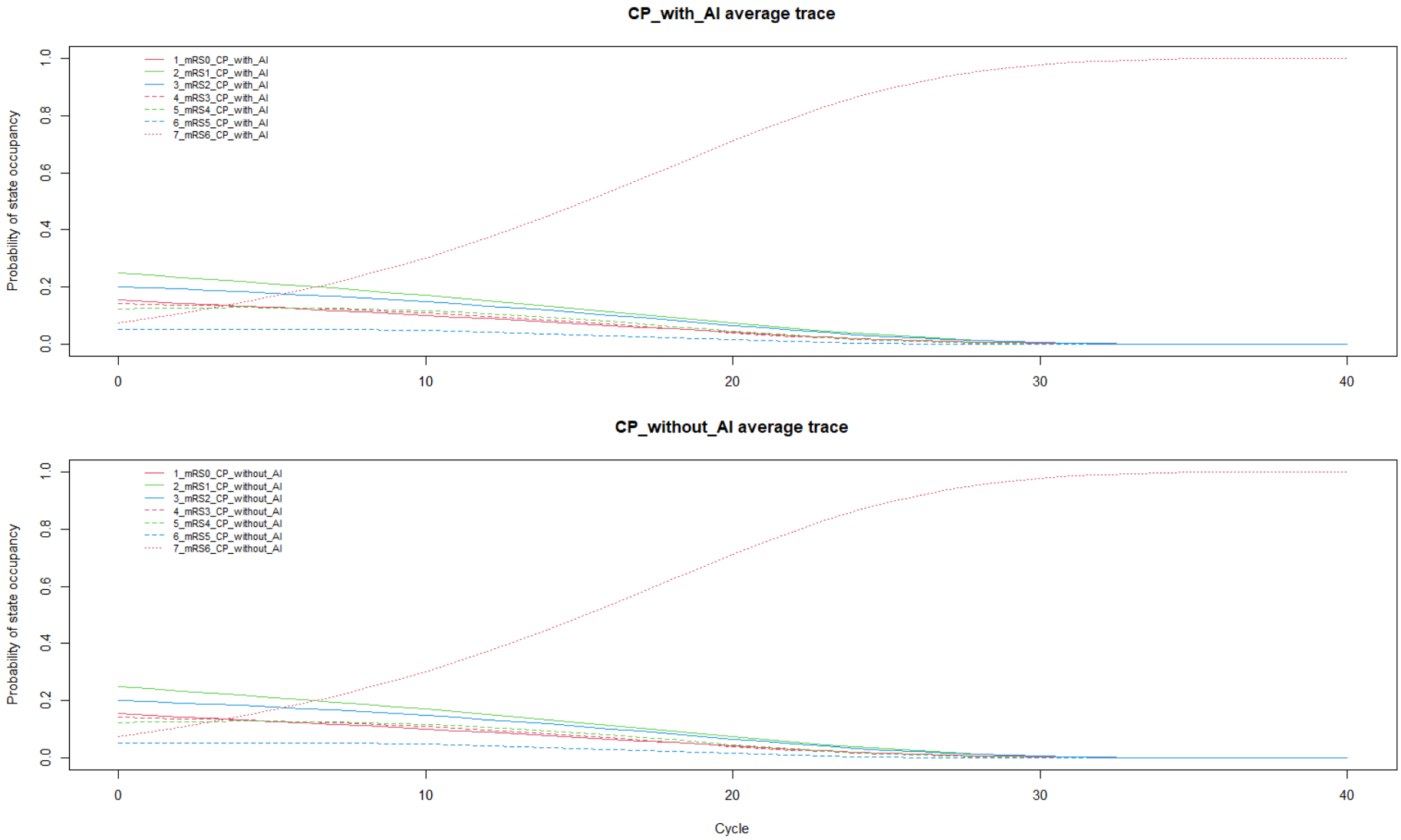


Figure 16: Cumulative costs for current practice with AI and without AI

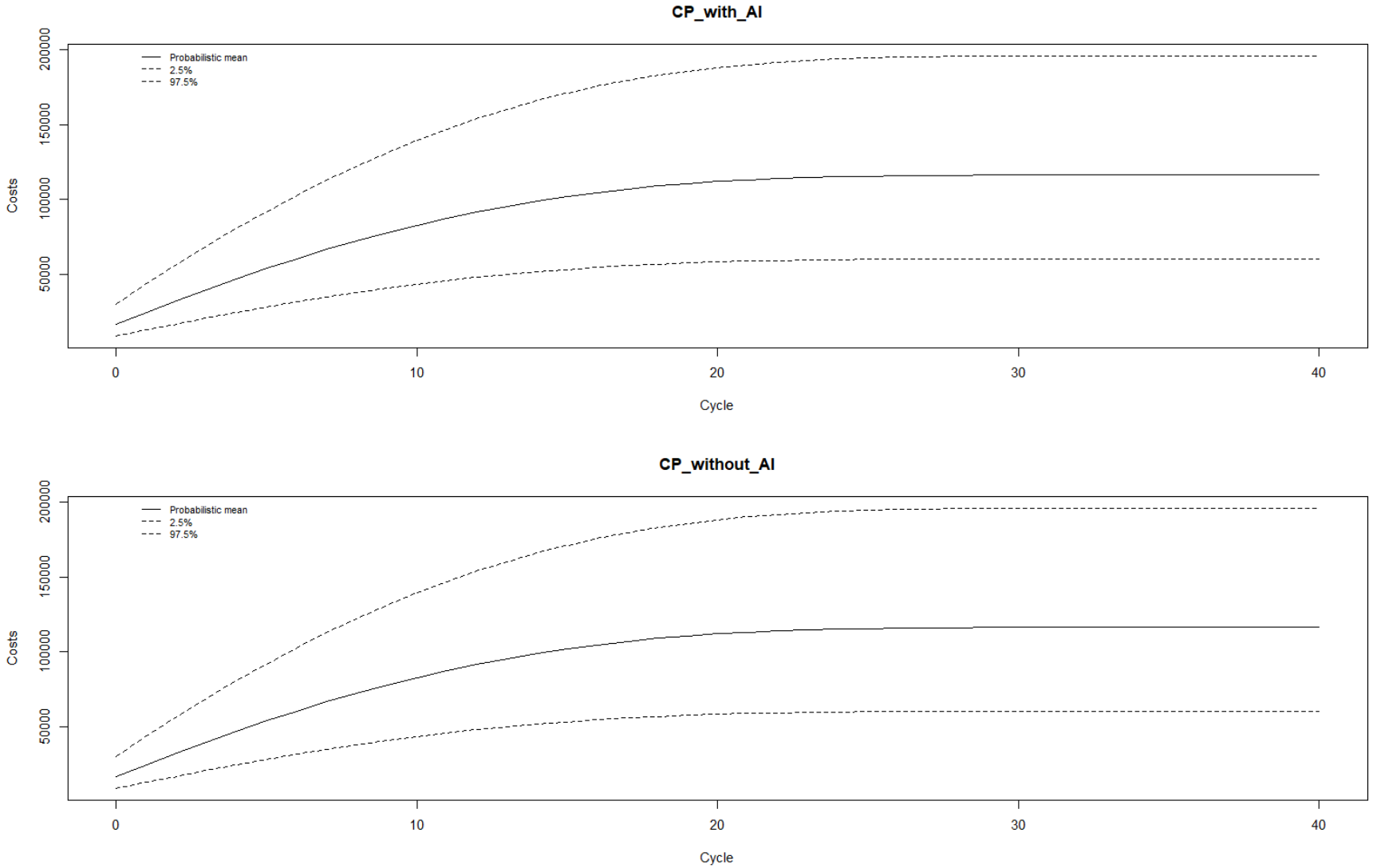


Figure 17: Cumulative QALYs for current practice with AI and without AI

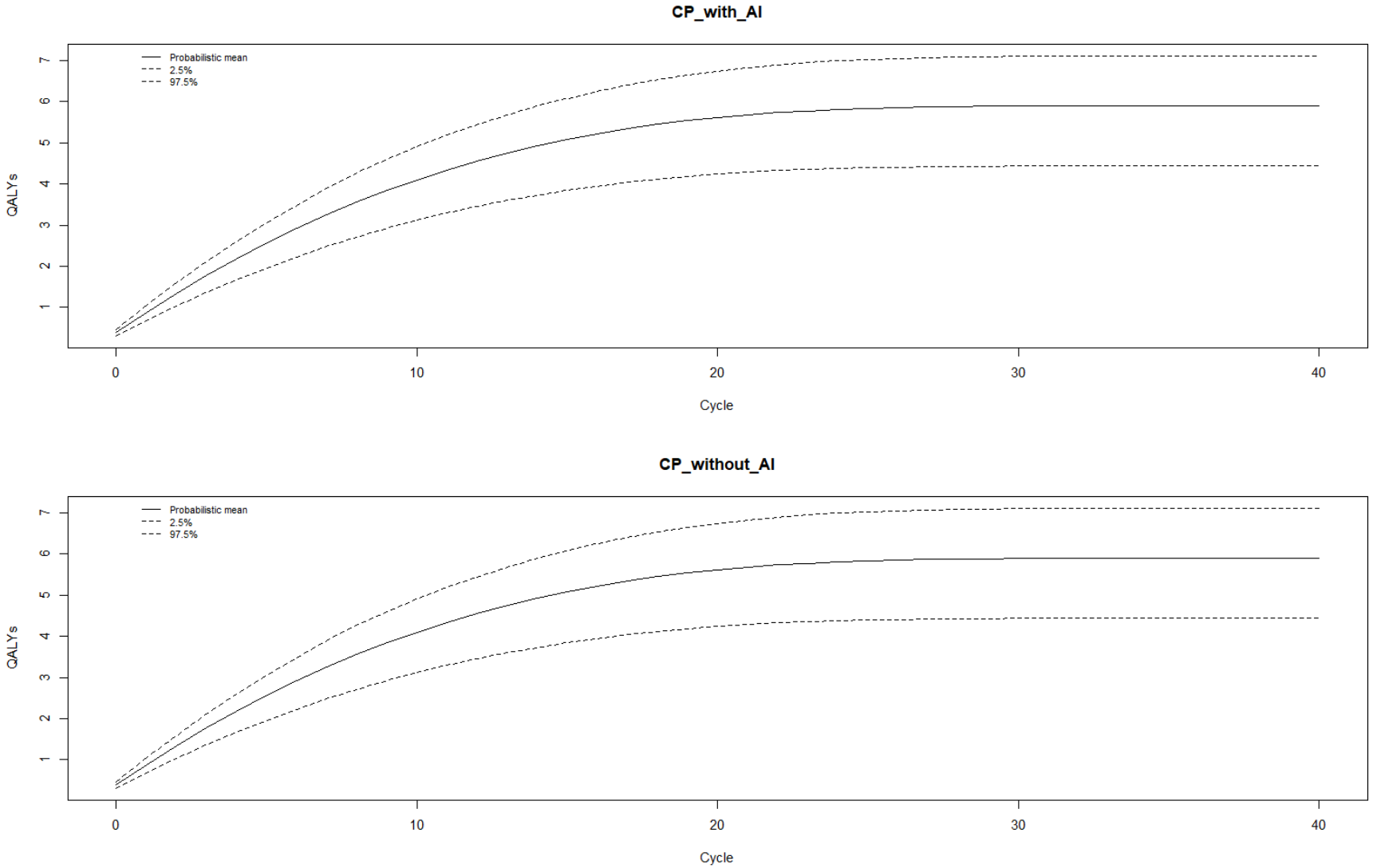
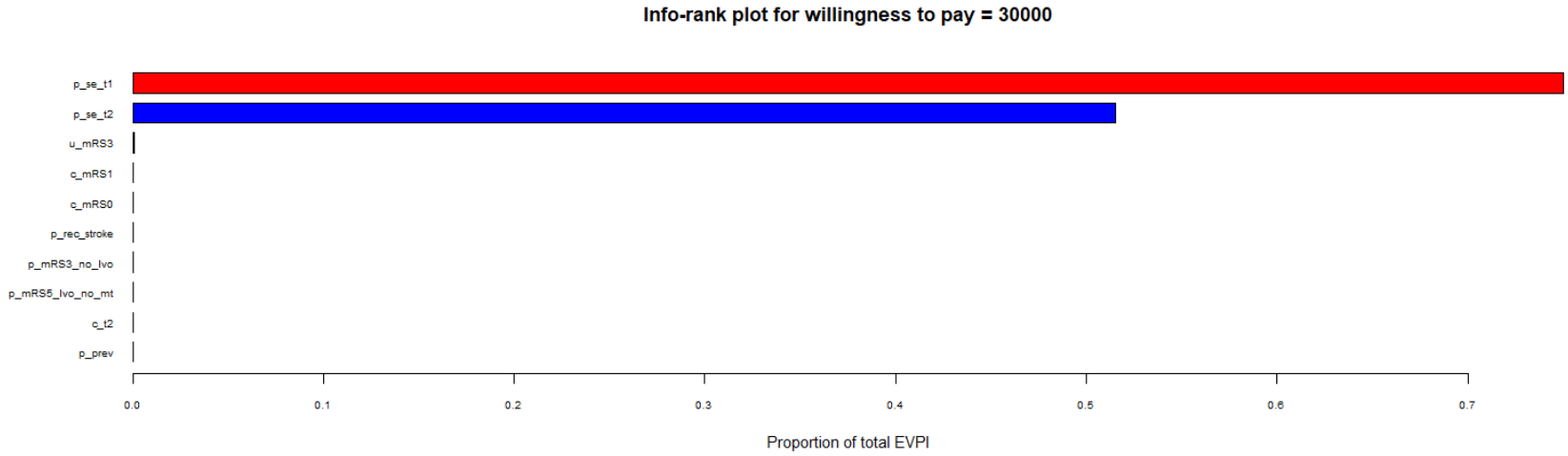


Figure 18: Info-rank plots



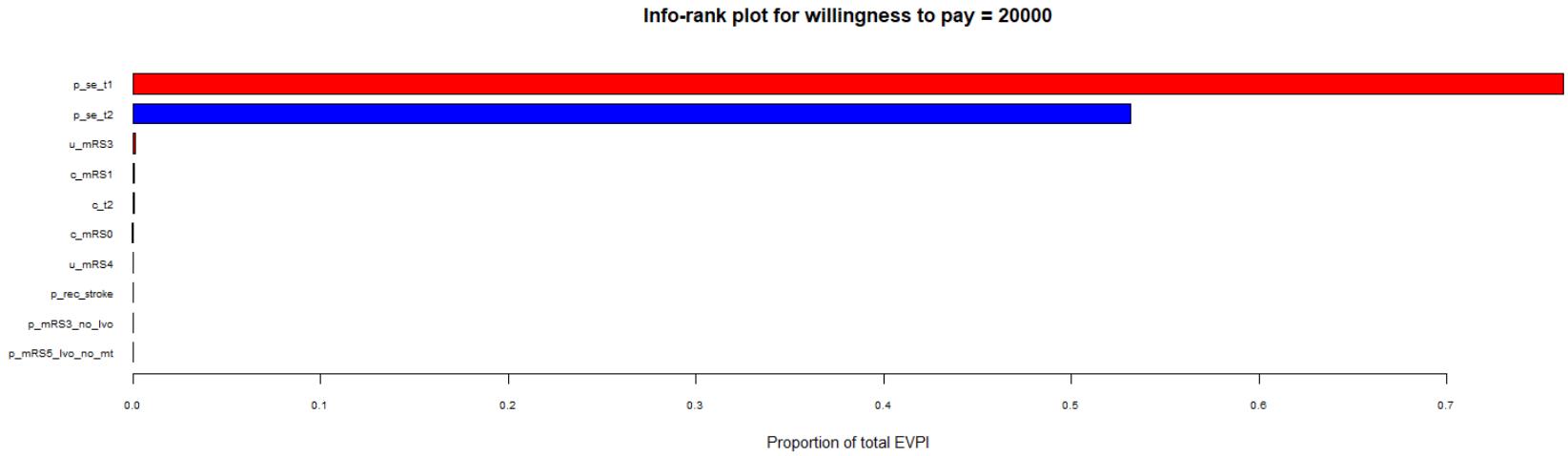
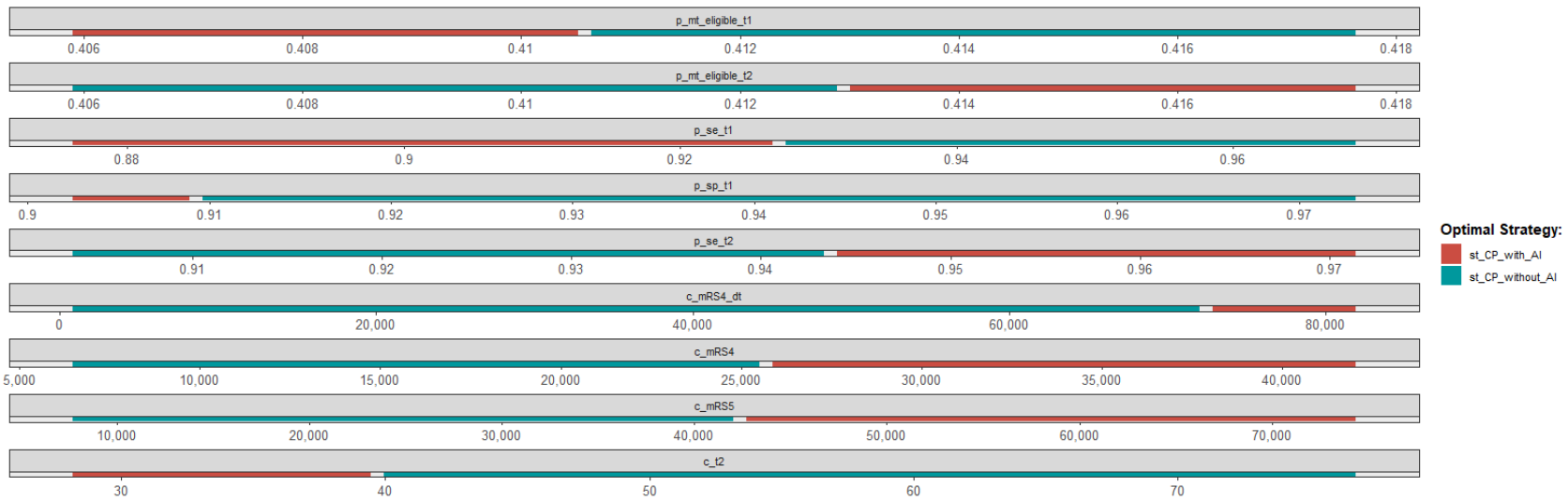


Figure 19: Optimal strategy plots

Costs



QALYs

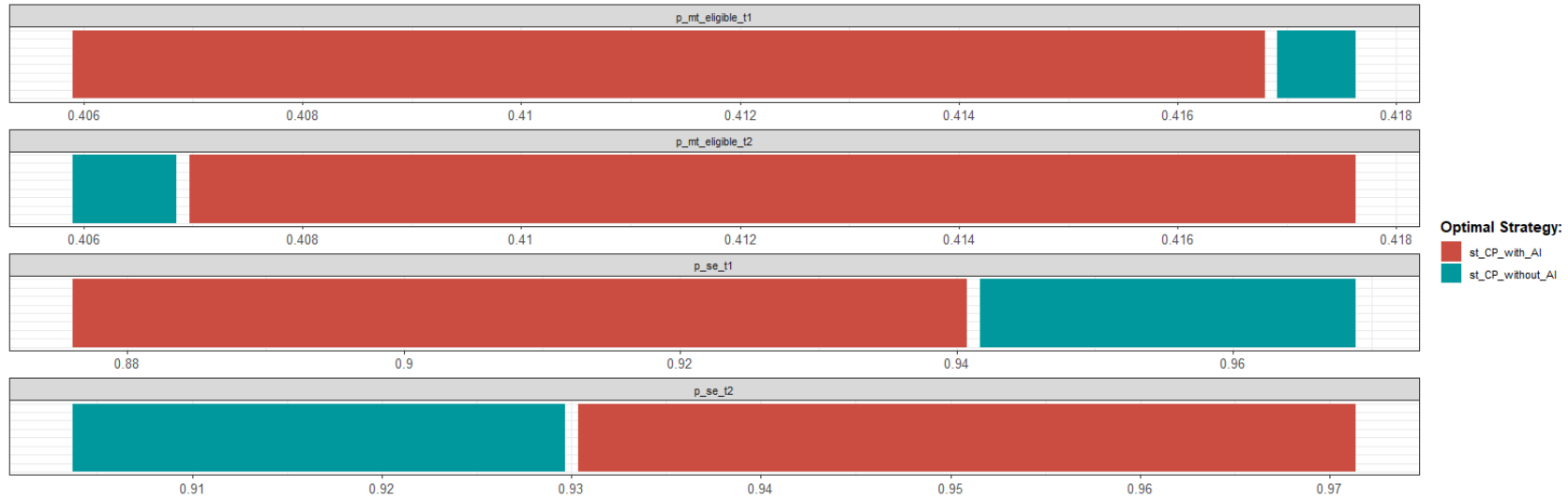


Figure 20: One-way sensitivity analyses (costs)

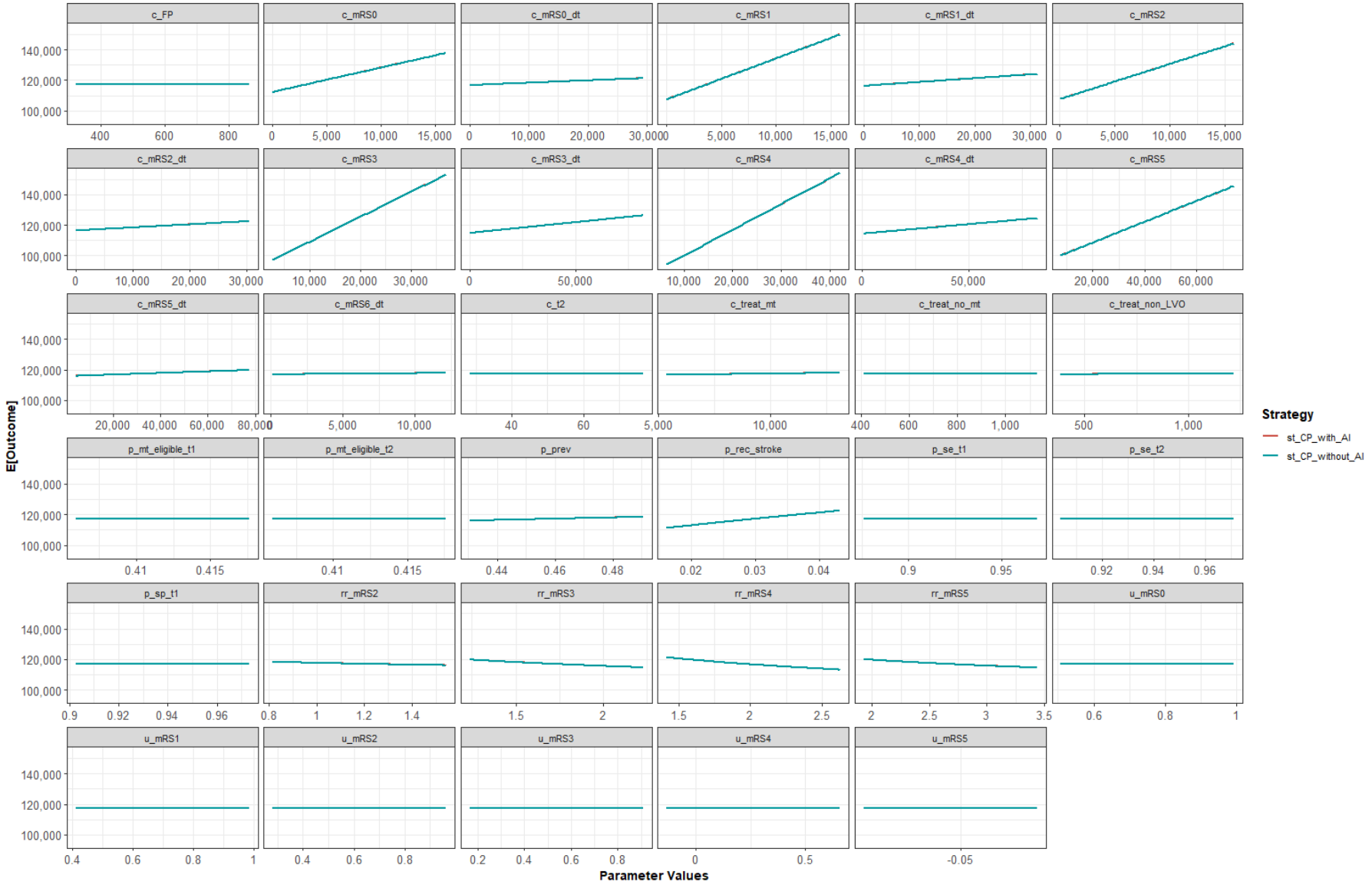


Figure 21: One-way sensitivity analyses (QALYs)

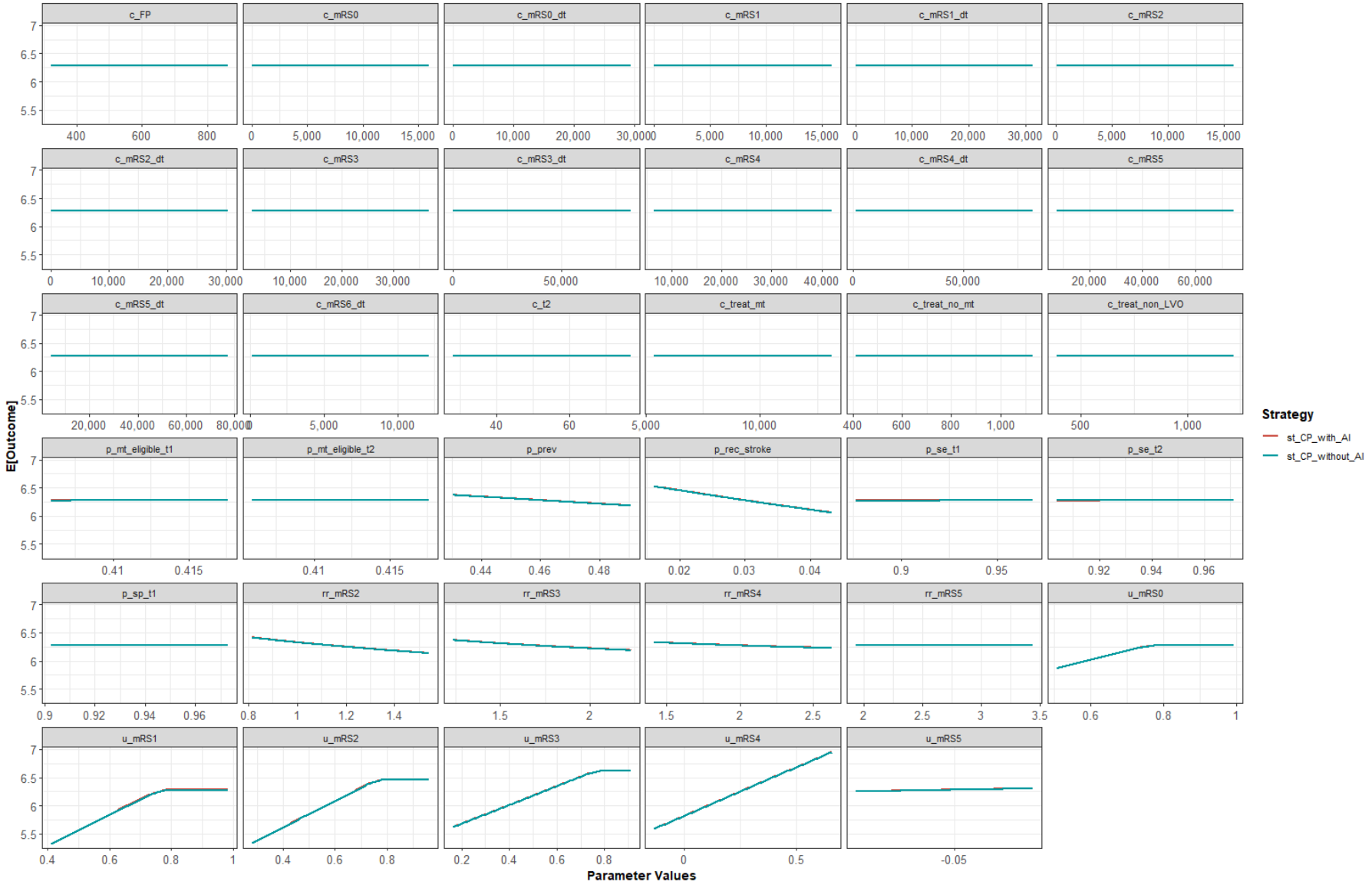
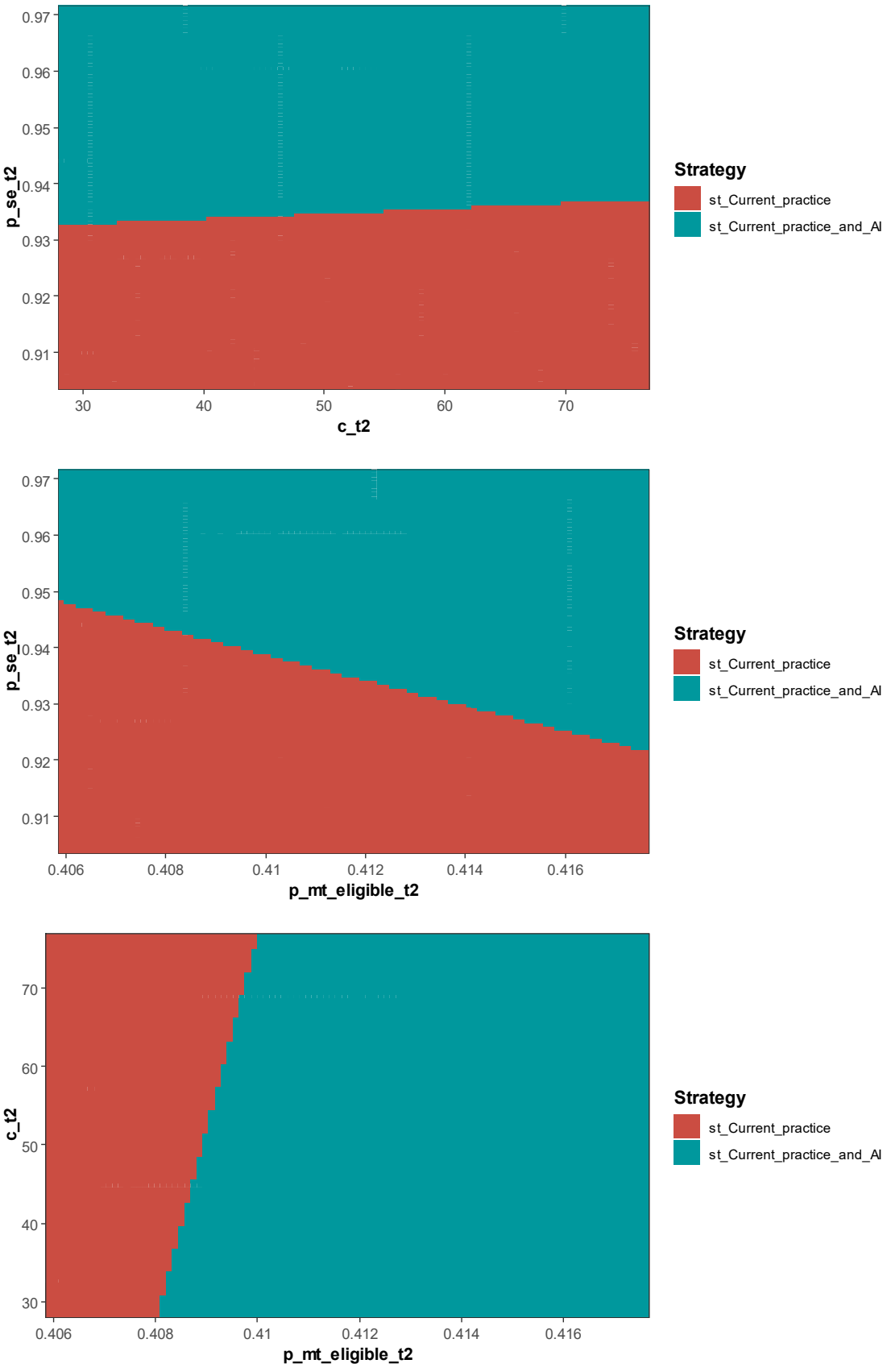


Figure 22: Two-way sensitivity analyses (NMB with willingness to pay of £30,000 per QALY)



4.4.3 Scenario analyses

The results of the deterministic scenario analyses are provided in Table 31. The most influential scenario analyses improving the cost effectiveness of the addition of AI were increasing the AI technology sensitivity to 96%, increasing the proportion of LVO patients eligible for mechanical thrombectomy with AI to 50%, removing the mortality cap and using Seker et al[56] to inform accuracy for current practice without AI (resident graders); in these scenarios the addition of AI was dominant. Decreasing the AI technology sensitivity to 90% and using Seker et al[56] to inform accuracy for current practice without AI (neuroradiologist grader) resulted in current practice without AI being dominant while increasing the AI technology costs to £100 per patient would increase the ICER to £22,072 per QALY gained.

Table 31: Deterministic scenario analyses

Technology	Costs (£)	QALYs	Δ Costs (£)	Δ QALYs	Δ Costs (£) / Δ QALYs
Deterministic base-case					
Current practice without AI	117,267	6.2778	NA	NA	NA
Current practice with AI	117,276	6.2806	10	0.0027	3,490
1 Assuming the AI technology costs are increased to £100 per patient					
Current practice without AI	117,267	6.2778	NA	NA	NA
Current practice with AI	117,327	6.2806	60	0.0027	22,072
2 Assuming the proportion of LVO patients eligible for mechanical thrombectomy with AI is increased to 50%					
Current practice without AI	117,267	6.2778	NA	NA	NA
Current practice with AI	116,551	6.3293	NA	NA	Dominance
3 Assuming the AI technology sensitivity is increased to 96%					
Current practice without AI	117,267	6.2778	NA	NA	NA
Current practice with AI	117,209	6.2851	NA	NA	Dominance
4 Assuming the AI technology sensitivity is decreased to 90%					
Current practice without AI	117,267	6.2778	NA	NA	NA
Current practice with AI	117,425	6.2706	NA	NA	Dominance
5 Assuming the LVO prevalence is increased to 50%					
Current practice without AI	118,899	6.1535	NA	NA	NA
Current practice with AI	118,905	6.1564	6	0.0030	2,016
6 Assuming the LVO prevalence is decreased to 40%					
Current practice without AI	114,760	6.4688	NA	NA	NA
Current practice with AI	114,775	6.4712	15	0.0024	6,318
7 Assuming recurrent strokes are LVOs eligible for thrombectomy (with appropriate mRS distribution)					
Current practice without AI	112,941	6.4604	NA	NA	NA
Current practice with AI	112,948	6.4632	7	0.0028	2,612
8 Assuming recurrent strokes are non-LVOs					
Current practice without AI	108,203	6.6555	NA	NA	NA
Current practice with AI	108,208	6.6585	5	0.0029	1,649
9 Assuming additional FP costs are increased to £2,000					
Current practice without AI	117,313	6.2778	NA	NA	NA

Technology	Costs (£)	QALYs	Δ Costs (£)	Δ QALYs	Δ Costs (£) / Δ QALYs
Current practice with AI	117,324	6.2806	12	0.0027	4,400
10 Assuming the annual recurrent stroke probability is decreased to 2%					
Current practice without AI	112,968	6.4541	NA	NA	NA
Current practice with AI	112,976	6.4569	7	0.0028	2,559
11 Assuming the annual recurrent stroke probability is increased to 4%					
Current practice without AI	121,340	6.1111	NA	NA	NA
Current practice with AI	121,352	6.1138	12	0.0026	4,426
12 Assuming the proportion of patients eligible for thrombectomy is increased to 50% (both strategies)					
Current practice without AI	116,550	6.3260	NA	NA	NA
Current practice with AI	116,551	6.3293	1	0.0033	248
13 Assuming the proportion of patients eligible for thrombectomy is decreased to 35% (both strategies)					
Current practice without AI	117,769	6.2441	NA	NA	NA
Current practice with AI	117,785	6.2464	16	0.0023	6,735
14 Utility values based on Rebchuk et al (0.93, 0.86, 0.68, 0.57, 0.31 and 0.06 for mRS 0-5)					
Current practice without AI	117,267	6.4529	NA	NA	NA
Current practice with AI	117,276	6.4555	10	0.0025	3,763
15 Utility values based on Wang et al (0.97, 0.88, 0.72, 0.54, 0.23 and -0.17 for mRS 0-5)					
Current practice without AI	117,267	6.1980	NA	NA	NA
Current practice with AI	117,276	6.2010	10	0.0030	3,224
16 Assuming no mortality cap (allowing mortality to be potentially lower than general population mortality)					
Current practice without AI	230,687	9.7510	NA	NA	NA
Current practice with AI	230,645	9.7550	NA	NA	Dominance
17 Assuming no utility cap (allowing utility values to be potentially higher than general population utility values)					
Current practice without AI	117,267	6.7299	NA	NA	NA
Current practice with AI	117,276	6.7330	10	0.0030	3,136
18 Assuming both no mortality cap and no utility cap					
Current practice without AI	230,687	10.4390	NA	NA	NA
Current practice with AI	230,645	10.4434	NA	NA	Dominance
19 Assuming accuracy for current practice without AI is based on Seker 2020 (neuroradiologist grader)					
Current practice without AI	117,104	6.2879	NA	NA	NA
Current practice with AI	117,276	6.2806	NA	NA	Dominance
20 Assuming accuracy for current practice without AI is based on Seker 2020 (resident graders)					
Current practice without AI	117,341	6.2729	NA	NA	NA
Current practice with AI	117,276	6.2806	NA	NA	Dominance

5. DISCUSSION

5.1 Statement of principal findings

5.1.1 Clinical effectiveness

The evidence base, to inform assessment of the clinical effectiveness of AI-derived software technologies for analysing CT brain scans in people with suspected stroke, was limited. This assessment focused on evaluating the effectiveness of AI-derived software technologies as adjuncts or aid to human interpretation (i.e., as they would be used in clinical practice and as recommended by the manufacturers). Our assessment included a systematic review to identify evidence to address three specific research questions:

1. Does AI-derived software assisted review of non-enhanced CT brain scans for guiding thrombolysis treatment decisions for people with suspected acute stroke represent a clinically and cost-effective use of NHS resources?

2a. Does AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke represent a clinically and cost-effective use of NHS resources?

2b. Does AI-derived software assisted review of CT perfusion brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke after a CTA brain scan represent a clinically and cost-effective use of NHS resources?

The scope included multiple software products, from 13 manufacturers (described in Section 2.2). For nine of the 13 manufacturers, no studies were identified that met the inclusion criteria (Table 2) for our systematic review. All studies identified concerned AI-derived software technologies from four manufacturers, Avicenna, Brainomix, iSchemaView and Viz, and the majority 18[33-36, 40, 41, 43-46, 49, 51, 52, 55, 56, 59-61] out of 22 studies[33-36, 39-41, 43-46, 48-52, 55, 56, 59-62] reported data to inform research question 2a (i.e., evaluated AI-derived software for the interpretation of CTA). All of the studies identified by our systematic review were either studies assessing the diagnostic accuracy of AI-derived software alone (i.e., **not** as it would be used in clinical practice, as recommended by the manufacturers and as specified in the inclusion criteria for this assessment),[35, 36, 39-41, 43, 48, 50, 51, 55, 56, 59-62] or 'before and after' observational studies reporting information about the effects of implementing AI-derived software technologies for treated patients only.[33, 34, 44-46, 49, 52]

Is the use of AI-derived software to assist review of non-enhanced CT brain scans to guide thrombolysis treatment decisions for people with suspected acute stroke a clinically effective intervention?

Three studies[39, 48, 62] provided information about the accuracy of AI-derived software technologies for the detection ICH, in patients with suspected AIS. The sensitivity and specificity estimates were 90.2% (95% CI: 83.9% to 94.2%) and 100% (95% CI: 97.5% to 100%) for Viz ICH,[39] 91.1% (95% CI: 82.8% to 95.6%) and 88.9 (95% CI: 80.2% to 94.0%) for the un-specified Brainomix AI-derived software technology,[48] [redacted][62] One additional study provided information about the effects on time to treatment of implementing the e-ASPECTS and e-CTA modules of Brainomix e-Stroke in a centre which did not offer thrombectomy (patients requiring thrombectomy were transferred to another unit).[44] This study reported increases in the proportions of patients receiving both intravenous thrombolysis and thrombectomy, following implementation, as well as a reduction in the meantime from first CT to groin puncture (174 minutes to 145 minutes) for transferred thrombectomy patients.[44]

Is the use of AI-derived software to assist review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?

Eleven studies provided information about the accuracy of various AI-derived software technologies for the detection of LVO on CTA scans in patients with AIS. [35, 36, 40, 41, 43, 51, 55, 56, 59-61] The anatomical locations of occlusions included in the definition of the target condition varied across studies. Where the target condition included occlusions of ICA, carotid terminus, or the M1- or M2-segments of the MCA, the sensitivity and specificity estimates were 95.4% (95% CI: 92.7% to 97.1%) and 79.4% (95% CI: 75.8% to 82.6%) for Rapid CTA,[35] 91.2% (95% CI: 77.0% to 97.0%) and 85.0 (95% CI: 64.0% to 94.8%) for Viz LVO,[40] 83.8% (95% CI: 77.3% to 88.7%) and 95.7% (95% CI: 91.0% to 98.0%) for Brainomix e-CTA,[56] and 98.1% (95% CI: 94.5% to 99.3%) and 98.2% (95% CI: 95.5% to 99.3%) for Avicenna CINA LVO.[51] There was some evidence to indicate that where studies included more distal (e.g., M3-segment of the MCA) elements of the anterior circulation or included posterior circulation in their definition of the target condition, this was associated with markedly reduced estimates of sensitivity. One study provided an estimate of the sensitivity of Rapid LVO for detection of occlusions of the ICA, carotid terminus, or M1- or M2/3-segments of the MCA of 63.6% (95% CI: 51.6% to 74.2%),[55] and a further study provided an estimate of the sensitivity of Viz LVO for the detection of occlusions the ICA, carotid terminus, the M1- or M2-segments of the MCA, or posterior circulation occlusions of 66.2% (95% CI: 54.3% to 76.3%).[43] All four studies that provided information about the effects of implementing Viz LVO[43, 45, 46, 52] and one study that provided information about the effects

of implementing Rapid CTA[33] in clinical settings reported that implementation was associated with reductions in time to treatment for thrombectomy patients and where reported, with no significant change in clinical outcomes, as indicated by mRS.[33, 45, 46, 52] Three of these studies concerned the effects of implementing Viz LVO in patients who were transferred between centres for thrombectomy[43, 46, 52] and one concerned the effects of implementing Viz LVO in patients who received thrombectomy within centre (no transfer)[45]; the study concerning the implementation of Rapid CTA was conducted in *'a large multi-hospital network with CSCs and 24-hour neurointerventional coverage,'* but did not state whether data were for patients who received thrombectomy following transfer, patients who received thrombectomy within centre, or a mixture of both.[33] It should be noted that two of these studies[46, 52] evaluated the implementation of Viz LVO in the context of providing an automated alert system (i.e., not as specified in the scope for this assessment) and the remaining two studies[43, 45] were reported as conference abstracts that did not provide sufficient information to determine how Viz LVO had been implemented; where studies have evaluated implementation of an AI-derived software technology in the context of provision of an automated alert system, it is plausible that any observed reductions in time to intervention may be driven by this 'early alert' step.

Is the use of AI-derived software-assisted review of CT perfusion brain scans to guide mechanical thrombectomy treatment decisions for people with an ischaemic stroke, after a CTA brain scan, a clinically effective intervention?

One study provided information to allow the calculation of measures of the diagnostic performance of Rapid CTP for identifying patients who are suitable candidates for thrombectomy.[50] Based on information about the results of Rapid CTP image analysis provided in the paper and using treatment received as the reference standard, the estimated sensitivity was 95.2% (95% CI: 90.0% to 97.8%) and the estimated specificity was 80.0% (95% CI: 67.0% to 88.8%). Two further studies provided information about the effects of implementing Rapid AI (including Rapid CTA and Rapid CTP).[34, 49] These studies reported inconsistent findings. One study reported no significant change in the mean time from door to groin puncture (MD 2.0 (95% CI: -12.9 to 16.9) minutes) or the proportion of patients with a mRS ≤3 (calculated OR 1.34 (95% CI: 0.66 to 2.74)), for thrombectomy patients, following the implementation of RapidAI;[49] it was not clear whether this study concerned patients who were transferred for thrombectomy or patients who were treated within centre. By contrast, the second study reported a reduction in the meantime from door to groin puncture after implementation (MD -33.2 (95% CI: -60.2 to -6.2) minutes) and no change in mean 90 day mRS (2.9 before and after), for thrombectomy patients treated within a CSC (no transfer), following implementation of the RapidAI Mobile Application.[34]

5.1.2 Cost effectiveness

Does AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke represent a clinically and cost-effective use of NHS resources?

Our cost effectiveness results are estimated based on expert elicitation to inform accuracy estimates for both AI-derived software technologies as an adjunct/aid to human readers and human readers without AI-derived software technologies. The probabilistic results indicated that the addition of AI to detect LVO is potentially more effective (QALY gain of 0.003), more costly (increased costs of £8.61) and cost effective for willingness to pay thresholds of £3,380 per QALY and higher. The cost effectiveness analyses indicated that there is a negative correlation between incremental costs and incremental QALYs, i.e., if a technology is more effective it also tends to be associated with fewer costs. Differences between AI-derived software technologies as an adjunct/aid to human readers and human readers without AI-derived software technologies were in general very small. The cost increase for AI was mainly driven by the short-term costs (including the AI technology costs); while overall costs related to the mRS4 and mRS5 health states decrease when AI is added. The increased QALYs for AI were driven by QALY differences in the mRS0 and mRS1 health states. Finally, the estimated life years were very similar.

5.2 Strengths and limitations of assessment

5.2.1 Clinical effectiveness

Extensive literature searches were conducted in an attempt to maximise retrieval of relevant studies. These included electronic searches of a variety of bibliographic databases, as well as screening of clinical trials registers and conference abstracts to identify unpublished studies. Because of the known difficulties in identifying test accuracy studies using study design-related search terms,[110] search strategies were developed to maximise sensitivity at the expense of reduced specificity. Thus, large numbers of citations were identified and screened, relatively few of which met the inclusion criteria of the review.

The possibility of publication bias remains a potential problem for all systematic reviews. Considerations may differ for systematic reviews of test accuracy studies. It is relatively simple to define a positive result for studies of treatment, e.g., a significant difference between the treatment and control groups which favours treatment. This is not the case for test accuracy studies, which measure agreement between index test and reference standard. It would seem likely that studies finding greater agreement (high estimates of sensitivity and specificity) will be published more often. In addition, test accuracy data are often collected as part of routine clinical practice, or by

retrospective review of records; test accuracy studies are not subject to the formal registration procedures applied to randomised controlled trials and are therefore more easily discarded when results appear unfavourable. The extent to which publication bias occurs in studies of test accuracy remains unclear, however, simulation studies have indicated that the effect of publication bias on meta-analytic estimates of test accuracy is minimal.[111] Formal assessment of publication bias in systematic reviews of test accuracy studies remains problematic and reliability is limited.[24] We did not undertake a statistical assessment of publication bias in this review. However, our search strategy included a variety of routes to identify un-published studies and resulted in the inclusion of a number of conference abstracts.

The rapidly evolving nature of research in this topic area presented a particular challenge. In order to be as inclusive as possible we conducted a search of the medRvix the preprint server and asked clinical experts (specialist committee members for this topic) to provide details of any potentially relevant ongoing or un-published studies, of which they were aware. One included study was identified from the medRvix search[55] and a further un-published study was provided AiC by a specialist committee member.[62] Results from these studies should be treated with appropriate caution, as they have not yet undergone peer review. In order to minimise the chances of omitting relevant new articles, published since the original core strategies were run in July 2021, the main Embase and MEDLINE searches and the medRvix search were rerun in their entirety in October 2021 before submission of our draft report.

Clear inclusion criteria were specified in the protocol for this review, the review has been registered on PROSPERO (CRD42021269609) and the protocol is available from https://www.nice.org.uk/guidance/gid-dg10044/documents/final-protocol. The eligibility of studies for inclusion is therefore transparent. In addition, we have provided specific reasons for exclusion for all of the studies which were considered potentially relevant at initial citation screening and were subsequently excluded on assessment of the full publication (Appendix 4). The review process followed recommended methods to minimise the potential for error and/or bias;[22] studies were independently screened for inclusion by two reviewers and data extraction and quality assessment were done by one reviewer and checked by a second. Any disagreements were resolved by consensus.

The main limitations for this assessment were the paucity of evidence, particularly in relation to research questions 1 and 2b, and, where evidence was identified, the applicability of that evidence to the specified questions.

The concerns regarding the applicability of the included studies were common across all three research questions.

The primary applicability concern, for studies that provided test accuracy data, was in relation to the implementation of the index test (AI-derived software technology). In all of these studies,[35, 36, 39-41, 43, 48, 50, 51, 55, 56, 59-62] the AI-derived software technology was evaluated as a stand-alone intervention, rather than as an adjunct or aid to human interpretation (as it would be used in clinical practice, as recommended by the manufacturers and as specified in the inclusion criteria for this assessment (Table 2)).

In addition to diagnostic test accuracy studies, this assessment included some observational 'before and after' studies[33, 34, 44-46, 49, 52] that assessed the effects of implementing AI-derived software technologies in 'real world' clinical settings on time to intervention and in some cases,[33, 45, 46, 52] on clinical outcome. The information provided by studies of this type is limited in that it concerns only treated (i.e., test positive) patients; no information is provided about test negative patients, hence there is no information about the extent to which AI-derived software technologies, as implemented, may miss patients with the target condition(s). In addition, no 'real world' implementation study, included in this assessment, compared clinical outcomes along with time to intervention, in populations that were comparable (with respect to key baseline characteristics) before and after the implementation of the AI-derived software technology, and where the AI-derived software technology was the only change to the care pathway. Differences in the study population (before and after implementation) and/or additional changes in the care pathway (other than implementation of the AI-derived software technology) mean that the extent to which any observed changes in time to intervention or clinical outcome are attributable to the implementation of the AI-derived software technology is highly uncertain. Studies which report only the effects of implementation of AI-derived software technologies on time to intervention are deficient in that they do not provide the information about clinical outcomes needed to inform decision making; a reduction in time to intervention may not always be advantageous, e.g., if the time saving is associated with a detrimental effect on clinical outcomes.

With respect to research question 1, *'Is the use of AI-derived software to assist review of non-enhanced CT brain scans to guide thrombolysis treatment decisions for people with suspected acute stroke a clinically effective intervention?'* we were only able to identify three studies which reported information about the accuracy of AI-derived software technologies for the interpretation of NCCT in people with suspected acute stroke[39, 48, 62] and one further observational 'before and after' study[44] that assessed the combined effects of implementing Brainomix e-ASPECTS and e-CTA. Studies that

evaluated included AI-derived software technologies frequently did not meet the population inclusion criteria for this assessment, e.g., studies that evaluated the accuracy of AI-derived software technologies for the detection of ICH in all head CTs (i.e., including trauma patients and other suspected pathologies), with no separate data for patients with suspected stroke.

During the inclusion screening phase of our systematic review, we noted a number of articles reporting multivariable regression analyses, where good clinical outcome/functional independence (90 day mRS 0-2) was the dependent variable and baseline Brainomix e-ASPECTS score or e-Stroke-derived ischaemic core volume, on NCCT, was evaluated as a potential predictor of clinical outcome following thrombectomy.[112-115] These studies do not meet the inclusion criteria for our assessment because they do not provide a comparison of image interpretation with versus without the assistance of AI-derived software technologies to guide treatment decisions (e.g., whether or not to perform mechanical thrombectomy). In the examples cited, all participants had anterior circulation large vessel occlusion strokes and underwent mechanical thrombectomy.[112-115] One study reported that in a multivariable regression analysis, adjusting for potential confounders including age, sex, hypertension, diabetes mellitus, atrial fibrillation, smoking status, baseline blood glucose, baseline NIHSS score, receipt of intravenous thrombolysis (tissue-type plasminogen activator), and time from last-known-well to imaging low ischaemic core volume, based on Brainomix e-Stroke software interpretation of baseline NCCT, was independently predictive of good outcome (adjusted OR 0.98 (95% CI: 0.97 to 0.99)).[112] Two further studies[113, 115] reported that the results of multivariable regression analyses indicated that e-ASPECTS score, on baseline NCCT, was an independent predictive of good outcome; adjusted OR 1.30 (95% CI: 1.06 to 1.60), adjusted for age, premorbid mRS, baseline NIHSS, hypertension, hypercholesterolemia, diabetes mellitus, and prior stroke,[113] and OR 1.37 (95% CI: 1.01 to 1.84), co-variables not reported.[115] The final study of this type included variables for age, premorbid mRS, atrial fibrillation, previous stroke, baseline blood glucose, and haemoglobin A1c, baseline NIHSS, hyperdense vessel sign, e-ASPECTS, general anaesthesia, recanalisation and secondary ICH following intravenous thrombolysis and reported that e-ASPECTS was not independently predictive of good outcome. [114] Although they do not directly inform the research questions specified for this assessment, studies of this type may be of clinical interest in that they describe the potential of AI-derived parameters, taken from initial NCCT imaging, to predict clinical outcome following thrombectomy.

With respect to research question 2b, *'Is the use of AI-derived software assisted review of CT perfusion brain scans to guide mechanical thrombectomy treatment decisions for people with an ischaemic stroke, after a CTA brain scan, a clinically effective intervention?'* we were only able to

identify one study that reported sufficient information to allow the calculation of measures of the diagnostic accuracy of Rapid CTP for identifying patients who are suitable candidates for thrombectomy, using treatment received as the reference standard[50] and two further observational 'before and after' studies[34, 49] that assessed the effects of implementing RapidAI.

Of further note, two of the multivariable regression analyses described above also reported that low ischaemic core volume, assessed using iSchemaview Rapid CTP, was independently predictive of good clinical outcome (90 day mRS 0-2), adjusted OR 0.98 (95% CI: 0.96 to 1.00),[113] and adjusted OR 0.98 (95% CI: 0.97 to 0.99).[112]

This assessment did not identify sufficient evidence to support modelling of the cost effectiveness of AI-derived software assisted review of CT perfusion brain scans to guide mechanical thrombectomy treatment decisions for people with an ischaemic stroke, after a CTA brain scan (research question 2b). However, although a systematic review of the effectiveness of treatments outside the scope of this assessment, it is notable that a number of key randomised controlled trials conducted in the USA[82, 116, 117] and Australia,[81] supporting the effectiveness of thrombectomy in addition to intravenous thrombolysis, for patients with anterior circulation intra-cranial LVOs, utilised ischemic core volume as a component of the participant selection criteria; in all instances ischemic core volume on CT was assessed using iSchemaview Rapid CTP, which may perhaps indicate iSchemaView Rapid software is already widely used for the interpretation of CT perfusion images.

5.2.2 Cost effectiveness

Our CEA is the most comprehensive analysis to-date focusing on AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke. The de novo probabilistic model was based on a previously developed CEA by van Leeuwen and colleagues[67]. For the present analysis, a number of adjustments were made to the model, but most of the assumptions were maintained. The adjustments included adding probabilistic analyses, discount rates in line with NICE reference, and the choice of alternative input parameters where this was considered appropriate (e.g., for implementing mortality and health state utility values).

Our initial intention was to inform accuracy estimates in the economic model through a comprehensive, high quality systematic review of diagnostic accuracy studies. However, the available evidence was not appropriate to inform of CEA, as the accuracy estimates available were for AI-derived software technologies as stand-alone interventions, rather than as an adjunct or aid to human interpretation (as defined in the scope for this assessment). To be able to perform a CEA, we

obtained accuracy estimates by means of elicitation of expert beliefs. For this, we used an established tool[75] that has been validated and that follows established methodological guidance for expert elicitation.[76-78] We obtained responses from five clinical experts, representing a range of relevant specialties. Additional parameters were, where necessary, based on a pragmatic literature review. Such a review is standard practice in economic modeling given the large number of parameters required.

As in any economic model, a number of major and minor assumptions had to be made. It is important to understand the impact of these assumptions in order to correctly interpret the results of the model. The impact of most assumptions has been explored in sensitivity and scenario analyses. One assumption that might be a matter for discussion is the focus of the AI-derived software assisted review on triage and supporting the thrombectomy decision, considering the claim that AI-derived software assisted review could provide a more accurate diagnosis of LVO. Other potential benefits, such as potential reduced time to treatment through the addition of AI-derived software assisted review were not considered in the base-case analyses. However, in scenario and sensitivity analyses the impact of additional benefits of AI-derived software assisted review were considered, indicating that this might potentially be an influential assumption warranting further studies (see also discussion of uncertainties in the cost effectiveness; Section 5.3.2).

Finally, another strength of this assessment was the use of R (instead of the commonly used Microsoft Excel) to estimate the cost effectiveness. The use of R allows leveraging the benefits of using modern programming languages[70] including improved transparency, reproducibility, modifiability, computational efficiency. The accessibility of R models might be perceived as a barrier for users unfamiliar with programming languages. Therefore, an accessible user interface was provided to the R model through the R Shiny package. Through the R Shiny user interface, users can specify different assumptions, change input parameters values, run underlying R code, and visualise results. With the simple instructions provided in the readme file (included with the submission) this model is accessible to those with no programming knowledge allowing critical inquiry from decision makers and other stakeholders. Moreover, to aid model transparency as well as model credibility and for consistency with suggested good practices and conventions, the technical implementation of the computational model was inspired by recent work by the DARTH group[71, 72] and others.[73]

5.3 Uncertainties

5.3.1 Clinical effectiveness

The key question i.e., whether or not the addition of AI-derived software technologies can improve the performance of human readers at the decision points specified in the three research questions,

and hence improve clinical outcomes for stroke patients, is not adequately addressed by either the diagnostic test accuracy studies or the observational 'before and after' studies included in this assessment.

We did not identify any studies that evaluated the diagnostic accuracy an AI-derived software technology when used as an adjunct to human readers. One study included in this assessment, provided a direct comparison of the accuracy of an AI-derived software technology (Brainomix e-CTA) alone versus individual human readers with different training and experience, for the detection of LVO (Table 14).[56] This study found that the sensitivity of e-CTA alone (84.3% (95% CI: 74.0% to 91.0%)) was similar to (neurology resident 1, 85.7% (95% CI: 75.7% to 92.1%)) or lower than (neurology resident 2, 91.4% (95% CI: 82.5% to 96.0%); radiology resident, 95.7% (95% CI: 88.1% to 98.5); neuroradiologist, 97.1% (95% CI: 90.2% to 99.2%)) that of un-assisted human readers.[56] Based on these results, in order for it to be possible for the AI-derived software technology to improve the performance of human readers, there would need to be a systematic difference in the reasons for a false negative (missed LVO) between the AI-derived software technology and human readers such that some or all of the small proportion of LVOs missed by human readers would be detected by the AI-derived software technology. However, it should be noted that it is unclear whether these unfavourable comparative accuracy results are reproducible or generalisable across different AI-derived software technologies and human readers in UK clinical settings; higher sensitivity estimates have been reported, using other AI-derived software technologies alone (Rapid CTA, Viz LVO and Avicennna CINNA LVO), for the detection of LVO (Section 3.2.4) and we did not identify any UK studies comparing the accuracy of AI-derived software technologies alone to that of human readers.

The 2018 position statement on AI, from the Royal College of Radiologists, includes the following text, under the heading of Regulation: *'A robust regulatory framework for the integration of AI into medical practice needs to be drawn up. Many different companies of varying sizes are developing AI tools for use in radiology and clinical oncology. These companies are making claims about the power of these tools - some of which are unsubstantiated. If tools fail to live up to these claims, public trust in the technology could be damaged.'*[14] The position statement goes on to specify, under the heading of Quality Assurance/Governance/Veracity, that: *'Published results for sensitivity and specificity of AI tools will be necessary prior to the introduction of any technology in the radiology/clinical workflow.'* [14] None of the AI-derived software technologies included in this assessment meet this requirement, in that we have not identified any estimates of the sensitivity and specificity (published or unpublished) of these interventions as they would be used in clinical practice (as an adjunct/aid to human interpretation of CT images). Some sensitivity and specificity estimates have been reported

for the following AI-derived software technologies, evaluated as stand-alone interventions: Viz ICH and Viz LVO; iSchemaview Rapid CTA, Rapid LVO and Rapid CTP; Brainomix e-ASPECTS and e-CTA; Avicenna CINA LVO. These data are provided in Sections 3.2.3 to 3.2.5 of this report. For the remaining AI-derived software technologies, included in the scope for this assessment and described in Section 2.2. of this report, we did not identify any studies that met the inclusion criteria for this assessment.

Seven[33, 34, 43-46, 52] of the eight[33, 34, 43-46, 49, 52] observational 'before and after' studies that assessed the effects of implementing AI-derived software technologies, in patients undergoing thrombectomy, reported results indicating that implementation was associated with a reduction in time to intervention. However, no study reported information to suggest that these reductions in time to intervention were associated with improvements in clinical outcome; all six studies that assessed clinical outcome reported results suggesting that the implementation of an AI-derived software technology had no effect on functional outcome, as indicated by mRS.[33, 34, 45, 46, 49, 52] There is evidence, from an individual-patient-data (IPD) meta-analysis[118] and a multi-centre randomised controlled trial (the MR CLEAN study),[119] to indicate a negative correlation between time to intervention and functional outcome in patients with LVO who undergo thrombectomy. The results of the IPD meta-analysis indicated that earlier treatment with thrombectomy in addition to pharmacological thrombolysis was associated with lower degrees of disability, as indicated by 90 day mRS, than pharmacological thrombolysis alone and that this benefit remained statistically significant up to 7 hours and 18 minutes from onset of symptoms to arterial puncture; each hour of reperfusion delay was associated with a reduction in the proportion of patients achieving function independence (mRS 0 to 2), absolute risk difference (ARD) -5.2% (95% CI: -8.3% to -2.1%).[118] Similarly, the MR CLEAN study reported that thrombectomy remained an effective intervention, with respect to the proportion of patients achieving functional independence, up to 6 hours and 18 minutes from onset of symptoms to arterial puncture and that the ARD for achieving a good functional outcome was reduced by 6% for every hour of delay to reperfusion.[119] However, it remains unclear whether the potential reductions in time to intervention that might be achieved as a result of implementing of AI-derived software technologies would translate into improved clinical outcomes in 'real world' settings. In addition, it should be remembered that the implementation of an AI-derived software technology has the potential to change, not only the outcomes of patients who undergo thrombectomy, but also which patients are selected for thrombectomy. Hence, evidence of a beneficial effect of implementation, for patients undergoing thrombectomy, is insufficient to show clinical effectiveness. This is because it would remain possible for there to be no effect or a detrimental effect on overall clinical outcomes in the scenario where implementation resulted in

more patients who were suitable candidates for thrombectomy being missed (e.g., where an AI-derived software technology misses LVO in the same types of patients as a less experienced human reader and hence provides false reassurance).

The scope for this assessment specified one clinically relevant sub-group: *'People over the age of 80 with small vessel disease and calcification of the cerebrovasculature.'*[120] We did not identify any evidence to inform an assessment of the clinical effectiveness of any of the specified AI-derived software technologies in this population.

The inclusion criteria for this assessment (Table 2) specified an early (last known well within 6 hours) window for research question 2a, on the clinical and cost effectiveness of AI-derived software technologies for the interpretation of CTA, and a later (last known well more than 6 hours previously, but within 24 hours) window for research question 2b, on the clinical and cost effectiveness of AI-derived software technologies for the interpretation of CTP following CTA. However, it remains unclear to what extent patients in the early window may benefit from additional imaging (CTP). Randomised controlled trials conducted in the UK[85] and in the Netherlands,[79] in patients with LVO (detected on CTA, MRA or DSA), who were treated within 6 hours of symptom onset (i.e., the population specified for research question 2a (Table2)), reported absolute differences the proportion of patients who were functionally independent (mRS 0 - 2) at 90 days of 11%[85] and 13.5%[79] in favour of thrombectomy. Of note, trials that additionally used utilised ischemic core volume, assessed using Rapid CTP, as an imaging criterion to select patients for inclusion, within the 6 hour time window specified for research question 2a reported larger absolute differences the proportion of patients who were functionally independent (mRS 0 - 2) at 90 days of 31%[81] and 25%[82] in favour of thrombectomy.

It is unclear to what extent the diagnostic accuracy of AI-derived software technologies may vary according to the precise way in which the target condition is defined (e.g., the extent of the arterial anatomy included in the definition of an LVO). In addition, what constitutes a clinically appropriate definition of the target condition LVO may change over time as thrombectomy techniques improve and the evidence base on the efficacy of thrombectomy evolves.

5.3.2 Cost effectiveness

The CEAC indicated that, at willingness to pay thresholds of £20,000 and £30,000 per QALY gained, the probabilities of current practice with AI being cost effective were 54% and 56% respectively. Moreover, the estimated annual risks associated with the addition of AI were estimated to be £7.0 million and £8.4 million, at willingness to pay thresholds of £20,000 and £30,000 per QALY gained,

respectively. To reduce these risks, further evidence on the sensitivity of both technologies was considered as most important. This is particularly relevant given that the current accuracy estimates were based on expert elicitation (since empirical evidence was lacking for AI-derived software technologies as an adjunct/aid to human readers) that would require confirmation. In addition, sensitivity analyses indicated that in case the addition of AI resulted in a reduced time to treatment thereby increasing the proportion of patients with LVO who are eligible for mechanical thrombectomy, this would be an important outcome to consider in future studies. In that case, the clinical consequences (e.g., in terms of distribution over mRS states) of the reduced time to treatment through the addition of AI are an important consideration. The current base-case assessment did not consider any consequences of potentially reduced time to treatment through AI as this claim was not supported by available evidence. Firstly, it is unclear whether the addition of AI would indeed reduce time to treatment: in the only studies where a reduction in time to treatment was observed, it was unclear whether this was potentially caused by redesign/optimisation of the logistic process. Caution is needed in interpreting these studies, as such findings are likely heavily context dependent and rely on the exact implementation of the addition of AI (e.g., implementation with automated alert system). Hence, the optimal implementation and place of AI is a potentially relevant topic for research. Notably, scenario analyses using alternative accuracy estimates for care as usual without AI, indicated that AI might be especially useful for non-expert graders, but this requires confirmation in future studies. Secondly, it is unclear if indeed the addition of AI would reduce the time to treatment, and what the consequences would be in terms of impact on clinical outcomes such as distribution between mRS states. Moreover, from a cost perspective more evidence regarding the additional costs of the AI technology, and costs related to mRS4 and mRS5 would be informative.

6. CONCLUSIONS

6.1 Implications for service provision

The available evidence is not suitable to determine the clinical effectiveness of using AI-derived software to support the review of CT brain scans in acute stroke, in the NHS setting.

All studies that assessed the diagnostic accuracy of AI-derived software technologies evaluated these technologies as stand-alone interventions, rather than as an adjunct or aid to image interpretation by a healthcare professional (i.e., **not** as AI-derived software technologies would be used in clinical practice, as their use is recommended by the manufacturers and as specified in the inclusion criteria for this assessment).

In addition to diagnostic test accuracy studies, this assessment included some observational 'before and after' studies that assessed the effects of implementing AI-derived software technologies in 'real world' clinical settings. The information provided by studies of this type was limited in that it concerned only treated (i.e., test positive) patients; no information was provided about test negative patients and hence there was no information about the extent to which AI-derived software technologies, as implemented, may miss patients with the target condition(s).

The economic analyses did not provide evidence to prefer the AI-derived software strategy over current clinical practice. However, results indicated that if the addition of AI-derived software assisted review, for guiding mechanical thrombectomy treatment decisions, increased the sensitivity of the diagnostic pathway (i.e., reduced the proportion of undetected LVO's) this may be considered cost effective. Nevertheless, the sensitivity of AI-derived software assisted review when added to current clinical practice is largely uncertain and likely depends on the implementation of AI-derived software assisted review.

6.2 Suggested research priorities

Given the deficiencies in the evidence base, outlined in Section 6.1, studies are needed (for all AI-derived software technologies) that evaluate these technologies as they would be implemented in clinical practice.

Diagnostic cohort studies should evaluate the performance of AI-derived software technologies, when used as an adjunct/aid to human readers. Ideally such studies should compare the performance of the AI-derived software technology in combination with a human reader to that of the human reader alone, where interpretation by an experienced expert or panel of experts provides the reference standard. Studies should be conducted in the population and setting in which the AI-

derived software technology would be applied in practice (e.g., for the interpretation of CTA to select patients for thrombectomy, studies should be conducted in adults with confirmed AIS who were last known to be well within 6 hours). Studies of this type would allow assessment of whether and to what extent the addition of AI-derived software technologies changes the performance of human readers, in the relevant clinical context.

Observational studies, evaluating the effects of implementing AI-derived software technologies in UK clinical settings, may also be of interest. Again, the precise way in which the technologies are implemented is critical to the utility of such studies for UK decision making. Based on the scope defined for this assessment, AI-derived software technologies would need to be implemented as a real time adjunct/aid to human readers and not as e.g., an automated early alert system. Observational comparative studies provide a lower level of evidence with respect to the effects of an intervention than RCTs. Where observational study designs are used to provide estimates of effect, it is therefore important to control, as far as possible, for potential confounding factors (factors other than the AI-derived software technology that may affect the outcome or outcomes being assessed), for example, by matching participants in the intervention and comparator groups on key risk factors. It is also important that the care pathway remains unchanged, other than with respect to the implementation of the AI-derived software technology. Studies of the effects of implementation of AI-derived software technologies should measure clinical outcomes alongside intermediate outcomes such as time to intervention and should report outcomes for test negative as well as test positive patients (e.g., for the interpretation of CTA to select patients for thrombectomy, outcomes should be reported for both patients who received thrombectomy and those who did not).

Cluster-randomised controlled trials, where stroke centres are randomised to implement AI-derived software technologies or to continue with current practice, would offer a more methodologically robust approach to evaluating the effects of implementation.

Finally, implementations of AI-derived software technologies other than as specified in the scope for this assessment (e.g., AI-derived software technologies used as stand-alone early alert systems used to select images/patients for further consideration by a human reader, or the potential of AI-derived parameters taken from initial NCCT imaging to predict clinical outcome following thrombectomy and hence the potential utility of these parameters to select patients for thrombectomy) may warrant consideration and further research.

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APPENDIX 1: LITERATURE SEARCH STRATEGIES

Main clinical effectiveness searches

Database	Dates covered	Hits
Embase	1974-2021/07/07	1,960
MEDLINE + PreMedline	1946-2021/07/07	1,110
CDSR	up to 2021/07/Iss7	135
CENTRAL	up to 2021/07/Iss7	406
DARE + HTA (CRD)	up to 2015/03 & 2018/03	361
Science Citation Index (SCI) + CPCI-S	1988–2021/07/06	857
KSR Evidence	up to 2021/07/07	42
Epistemonikos	up to 2021/07/07	3
NIHR HTA	up to 2021/07/02	5
INAHTA	up to 2021/07/06	265
ARIF	up to 2021/07/02	0
PROSPERO	up to 2021/07/07	23
INPLASY	up to 2021/07/02	1
LILACs	up to 2021/07/02	374
ClinTrials.gov	up to 2021/07/02	39
EUCTR	up to 2021/07/28	16
WHO ICTRP	up to 2021/07/02	14
ScanMedicine	up to 2021/07/02	28
Northern Light	2010–2021/Wk25	64
Total		**5,703**

Embase (Ovid): 1974-2021/07/07
Searched: 8.7.21

Stroke + Diagnostic/Scan + AI (NoA)

1 exp brain ischemia/ (199232)
2 exp brain hemorrhage/ (150355)
3 basal ganglion hemorrhage/ (654)
4 cerebrovascular accident/ (226798)
5 brain infarction/ (55721)
6 blood vessel occlusion/ (11569)
7 (Stroke$ or apople$ or cerebral vasc$ or cerebrovasc$ or cerebro vasc$ or poststroke$ or encephalorrhag$ or hematencephalon$ or large vessel occlusion$).ti,ab,ot. (498658)
8 ((brain or blood flow) adj2 disturb$).ti,ab,ot. (2899)
9 ((sinus or sagittal) adj3 thromb$).ti,ab,ot. (7142)
10 (isch?emi$ adj3 (seizure$ or attack$ or thrombo$ or embolic or encephalopath$ or neural)).ti,ab,ot. (40502)
11 ((Bleed$ or h?emorrhag$) adj2 corpus callosum).ti,ab,ot. (27)
12 ((brain or cerebr$ or cerebell$ or cortical or Intraparenchymal or intracortical or vertebrobasil$ or hemispher$ or intracran$ or intra-cran$ or intracerebral or intratentorial or intra-tentorial or intraventricular or intra-ventricular or periventricular or peri-ventricular or supratentorial or supra-tentorial or anterior circulat$ or posterior circulat$ or basal gangli$ or global or focal or parenchymal

or subarachnoid or sub-arachnoid or putaminal or putamen or posterior fossa or intra-axial or intraaxial or lacunar) adj3 (arrest$ or attack$ or isch?emi$ or infarct$ or insufficien$ or emboli$ or occlus$ or hypox$ or vasospasm or obstruction or vasculopath$ or failure$ or thromb$ or h?emorrhag$ or microh?emorrhag$ or accident$ or h?ematoma$ or bleed$ or microbleed$ or insult$)).ti,ab,ot. (292691)
13 (CVA or CVAS or MCA$ or ICH or ICHs or CVST or CVSTs or CVDST or CVT or CVDSTs or CVTs or LVO or LVOs).ti,ab. (81862)
14 or/1-13 (861830)
15 ((diagnos$ or predict$ or specificity or sensitiv$) adj4 (criteria or criterion or guideline$ or pattern$ or trend$ or utili$ or management or prevalence or initiat$ or distribution$ or coverage or variety or selection or spread or alternative$ or frequen$)).ti,ab,ot. (493299)
16 diagnosis/ or early diagnosis/ (1442538)
17 exp brain scintiscanning/ (9831)
18 Neurologic examination/ (70389)
19 Computer assisted tomography/ (776896)
20 Brain radiography/ (7759)
21 ((Brain or cerebral or neurologic$ or CT or head) adj2 (scan$ or scintigraph$ or examination$ or angiograph$ or image analys$ or perfusion$ or radiograph$)).ti,ab,ot,hw. (388831)
22 (CAT scan$ or CTA or CTP or neuroimag$ or neuro-imag$ or (comput$ adj2 tomograph$)).ti,ab,ot,hw. (1298946)
23 (Gamma encephalograph$ or Gammaencephalograph$ or Radio encephalograph$ or Radioencephalograph$).ti,ab,ot,hw. (48)
24 or/15-23 (3118232)
25 exp artificial intelligence/ (49699)
26 automated pattern recognition/ (16903)
27 decision support system/ (23908)
28 computer assisted diagnosis/ (40299)
29 Convolutional neural network/ (9836)
30 (Artificial intelligence or AI or machine intelligence or computer-aided triage$ or support vector machine$ or relevance vector machine$).ti,ab,ot. (75268)
31 ((automat$ or computer) adj2 (analys$ or diagnos$ or detect$)).ti,ab,ot. (54307)
32 ((deep or machine) adj learning).ti,ab,ot. (65494)
33 (decision support$ adj (software or tool$)).ti,ab,ot. (4658)
34 (CNN or CNNs or convNet or (convolut$ adj2 neural network$) or convolutional ANNs or convolutional ANN or convolutional NNs or convolutional NN).ti,ab. (15300)
35 automat$ hierarch$ evaluat$.ti,ab. (1)
36 (Aidoc or e-CTA or e-ASPECTS or e-stroke or brainomix or brainscan or "brainscan.ai" or icobrain or icometrix or qER or Qure or Zebra$ or e-CTP or briefcase or rapid CTA or rapid LVO or rapid core or rapid ASPECTS or rapid ICH or rapidai or blackford or "viz.ai" or viz or "ct perfusion 4d" or cercare or cina$ or Avicenna or accipio$ or maxQ AI or biomind or "biomind.ai" or ischemaview or rapid CTP or "qure.ai").ti,ab. (125734)
37 or/25-36 (395358)
38 14 and 24 and 37 (2069)
39 (letter or editorial or note).pt. (2732767)
40 38 not 39 (2006)
41 animal/ (1515289)
42 animal experiment/ (2691055)
43 (rat or rats or mouse or mice or murine or rodent or rodents or hamster or hamsters or pig or pigs or porcine or rabbit or rabbits or animal or animals or dogs or dog or cats or cow or bovine or sheep or ovine or monkey or monkeys).ti,ab,ot,hw. (7014819)
44 or/41-43 (7014819)

45 exp human/ (22461462)
46 human experiment/ (549308)
47 or/45-46 (22463344)
48 44 not (44 and 47) (5340409)
49 40 not 48 (1960)

MEDLINE and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations, Daily and Versions (Ovid): 1946-2021/07/07
Searched: 8.7.21

1 exp Brain Ischemia/ (114022)
2 exp Intracranial Hemorrhages/ (74140)
3 Stroke/ (110696)
4 (Stroke$ or apople$ or cerebral vasc$ or cerebrovasc$ or cerebro vasc$ or poststroke$ or encephalorrhag$ or hematencephalon$ or large vessel occlusion$).ti,ab,ot. (321196)
5 ((brain or blood flow) adj2 disturb$).ti,ab,ot. (2094)
6 ((sinus or sagittal) adj3 thromb$).ti,ab,ot. (4982)
7 (isch?emi$ adj3 (seizure$ or attack$ or thrombo$ or embolic or encephalopath$ or neural)).ti,ab,ot. (26336)
8 ((Bleed$ or h?emorrhag$) adj2 corpus callosum).ti,ab,ot. (23)
9 ((brain or cerebr$ or cerebell$ or cortical or Intraparenchymal or intracortical or vertebrobasil$ or hemispher$ or intracran$ or intra-cran$ or intracerebral or intratentorial or intra-tentorial or intraventricular or intra-ventricular or periventricular or peri-ventricular or supratentorial or supra-tentorial or anterior circulat$ or posterior circulat$ or basal gangli$ or global or focal or parenchymal or subarachnoid or sub-arachnoid or putaminal or putamen or posterior fossa or intra-axial or intraaxial or lacunar) adj3 (arrest$ or attack$ or isch?emi$ or infarct$ or insufficien$ or emboli$ or occlus$ or hypox$ or vasospasm or obstruction or vasculopath$ or failure$ or thromb$ or h?emorrhag$ or microh?emorrhag$ or accident$ or h?ematoma$ or bleed$ or microbleed$ or insult$)).ti,ab,ot. (207796)
10 (CVA or CVAS or MCA$ or ICH or ICHs or CVST or CVSTs or CVDST or CVT or CVDSTs or CVTs or LVO or LVOs).ti,ab. (47842)
11 or/1-10 (547945)
12 ((diagnos$ or predict$ or specificity or sensitiv$) adj4 (criteria or criterion or guideline$ or pattern$ or trend$ or utili$ or management or prevalence or initiat$ or distribution$ or coverage or variety or selection or spread or alternative$ or frequen$)).ti,ab,ot. (343809)
13 Diagnosis/ (17448)
14 Early Diagnosis/ (28246)
15 Brain/dg [Diagnostic Imaging] (49771)
16 Stroke/dg [Diagnostic Imaging] (7424)
17 Radiography/ (321804)
18 exp Radionuclide Imaging/ (221021)
19 Neurologic Examination/ (27644)
20 Tomography, X-Ray Computed/ (395500)
21 ((Brain or cerebral or neurologic$ or CT or head) adj2 (scan$ or scintigraph$ or examination$ or angiograph$ or image analys$ or perfusion$ or radiograph$)).ti,ab,ot,hw. (226174)
22 (CAT scan$ or CTA or CTP or neuroimag$ or neuro-imag$ or (comput$ adj2 tomograph$)).ti,ab,ot,hw. (465619)
23 (Gamma encephalograph$ or Gammaencephalograph$ or Radio encephalograph$ or Radioencephalograph$).ti,ab,ot,hw. (155)
24 or/12-23 (1606067)
25 exp Artificial Intelligence/ (117654)
26 Pattern Recognition, Automated/ (25872)

27 Neural Networks, Computer/ (31087)
28 (Artificial intelligence or AI or machine intelligence or computer-aided triage$ or support vector machine$ or relevance vector machine$).ti,ab,ot. (58543)
29 ((automat$ or computer) adj2 (analys$ or diagnos$ or detect$)).ti,ab,ot. (42174)
30 ((deep or machine) adj learning).ti,ab,ot. (54334)
31 (decision support$ adj (software or tool$)).ti,ab,ot. (3372)
32 (CNN or CNNs or convNet or (convolut$ adj2 neural network$) or convolutional ANNs or convolutional ANN or convolutional NNs or convolutional NN).ti,ab. (12557)
33 automat$ hierarch$ evaluat$.ti,ab. (1)
34 (Aidoc or e-CTA or e-ASPECTS or e-stroke or brainomix or brainscan or "brainscan.ai" or icobrain or icometrix or qER or Qure or Zebra$ or e-CTP or briefcase or rapid CTA or rapid LVO or rapid core or rapid ASPECTS or rapid ICH or rapidai or blackford or "viz.ai" or viz or "ct perfusion 4d" or cercare or cina$ or Avicenna or accipio$ or maxQ AI or biomind or "biomind.ai" or ischemaview or rapid CTP or "qure.ai").ti,ab. (102411)
35 or/25-34 (341861)
36 11 and 24 and 35 (1151)
37 (letter or editorial or note).pt. (1715243)
38 exp animals/ not (exp animals/ and humans/) (4857607)
39 36 not (37 or 38) (1110)

Cochrane Database of Systematic Reviews (CDSR)(Wiley): up to 2021/07/Iss7
Cochrane Central Register of Controlled Trials (CENTRAL) (Wiley): up to 2021/07/Iss7
Searched: 8.7.21

#1 MeSH descriptor: [Brain Ischemia] explode all trees 3746
#2 MeSH descriptor: [Intracranial Hemorrhages] explode all trees 2038
#3 (Stroke* or apople* or cerebral-vasc* or cerebrovasc* or cerebro-vasc* or poststroke* or encephalorrhag* or hematencephalon* or large-vessel-occlusion*):ti,ab,kw 67048
#4 ((brain or blood flow) near/2 disturb*):ti,ab,kw 164
#5 ((sinus or sagittal) near/3 thromb*):ti,ab,kw 207
#6 ((ischaemi* or ischemi*) near/3 (seizure* or attack* or thrombo* or embolic or encephalopath* or neural)):ti,ab,kw 4773
#7 ((Bleed* or hemorrhag* or haemorrhag*) near/2 corpus-callosum):ti,ab,kw 0
#8 ((brain or cerebr* or cerebell* or cortical or Intraparenchymal or intracortical or vertebrobasil* or hemispher* or intracran* or intra-cran* or intracerebral or intratentorial or intra-tentorial or intraventricular or intra-ventricular or periventricular or peri-ventricular or supratentorial or supra-tentorial or anterior-circulat* or posterior-circulat* or basal-gangli* or global or focal or parenchymal or subarachnoid or sub-arachnoid or putaminal or putamen or posterior-fossa or intra-axial or intraaxial or lacunar) near/3 (arrest* or attack* or ischaemi* or ischemi* or infarct* or insufficien* or emboli* or occlus* or hypox* or vasospasm or obstruction or vasculopath* or failure* or thromb* or hemorrhag* or haemorrhag* or microhemorrhag* or microhaemorrhad or haemorrhag* or accident* or hematoma* or haemotoma* or bleed* or microbleed* or insult*)):ti,ab,kw 34886
#9 (CVA or CVAS or MCA* or ICH or ICHs or CVST or CVSTs or CVDST or CVT or CVDSTs or CVTs or LVO or LVOs):ti,ab,kw 4959
#10 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 82032
#11 ((diagnos* or predict* or specificity or sensitiv*) near/4 (criteria or criterion or guideline* or pattern* or trend* or utili* or management or prevalence or initiat* or distribution* or coverage or variety or selection or spread or alternative* or frequen*)):ti,ab,kw 30643
#12 MeSH descriptor: [Diagnosis] explode all trees 342030
#13 MeSH descriptor: [Early Diagnosis] explode all trees 1796

#14 MeSH descriptor: [Brain] explode all trees and with qualifier(s): [diagnostic imaging - DG] 1679
#15 MeSH descriptor: [Radiography] explode all trees 21097
#16 MeSH descriptor: [Radionuclide Imaging] explode all trees 4662
#17 MeSH descriptor: [Neurologic Examination] explode all trees 23937
#18 MeSH descriptor: [Tomography, X-Ray Computed] explode all trees 5168
#19 ((Brain or cerebral or neurologic* or CT or head) near/2 (scan* or scintigraph* or examination* or angiograph* or image analys* or perfusion* or radiograph*)):ti,ab,kw 15653
#20 (Gamma-encephalograph* or Gammaencephalograph* or Radio-encephalograph* or Radioencephalograph*):ti,ab,kw 0
#21 (CAT scan* or CTA or CTP or neuroimag* or neuro-imag* or (comput* near/2 tomograph*)):ti,ab,kw 24102
#22 #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 391257
#23 MeSH descriptor: [Artificial Intelligence] explode all trees 1128
#24 MeSH descriptor: [Pattern Recognition, Automated] explode all trees 184
#25 MeSH descriptor: [Diagnosis, Computer-Assisted] explode all trees 1867
#26 MeSH descriptor: [Neural Networks, Computer] explode all trees 129
#27 (Artificial-intelligence or AI or machine-intelligence or computer-aided-triage* or support-vector-machine* or relevance-vector-machine*):ti,ab,kw 5045
#28 ((automat* or computer) near/2 (analys* or diagnos* or detect*)):ti,ab,kw 3064
#29 ((deep or machine) near/1 learning):ti,ab,kw 1791
#30 (decision-support* near/1 (software or tool*)):ti,ab,kw 552
#31 (CNN or CNNs or convNet or (convolut* near/2 neural-network*) or convolutional-ANNs or convolutional-ANN or convolutional-NNs or convolutional-NN):ti,ab,kw 326
#32 "automat* hierarch* evaluat*":ti,ab,kw 0
#33 (Aidoc or e-CTA or e-ASPECTS or e-stroke or brainomix or brainscan or "brainscan.ai" or icobrain or icometrix or qER or Qure or Zebra* or e-CTP or briefcase or rapid-CTA or rapid-LVO or rapid-core or rapidai or rapid-ASPECTS or rapid-LCH or blackford or "viz.ai" or viz or "ct perfusion 4d" or cercare or cina* or Avicenna or accipio* or maxQ-AI or biomind or "biomind.ai" or ischemaview or rapid-CTP or "qure.ai"):ti,ab,kw 4601
#34 #23 or #24 #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 15237
#35 #10 and #22 and #34 541

CDSR = 135
CENTRAL = 406

Science Citation Index Expanded (Web of Science): 1988–2021/07/06
Conference Proceedings Citation Index (Web of Science): 1988–2021/07/06
Searched: 6.7.21

 # 24 857 #22 NOT #23 Indexes=SCI-EXPANDED, CPCI-S Timespan=All years
23 4,041,528 TS=(cat or cats or dog or dogs or animal or animals or rat or rats or hamster or hamster or feline or ovine or canine or bovine or sheep or mice)
22 890 #21 AND #13 AND #8
21 704,777 #20 OR #19 OR #18 OR #17 OR #16 OR #15 OR #14
20 161,375 TS=(Aidoc OR e-CTA OR e-ASPECTS OR e-stroke OR brainomix OR brainscan OR "brainscan.ai" OR icobrain OR icometrix OR qER OR Qure OR Zebra* OR e-CTP OR briefcase OR “rapid CTA” OR “rapid LVO” OR “rapid core” OR “rapid ASPECTS” OR “rapid ICH” OR rapidai OR blackford OR "viz.ai" OR viz OR "ct perfusion 4d" OR cercare OR cina* OR Avicenna OR accipio* OR “maxQ AI” OR biomind OR "biomind.ai" OR ischemaview OR “rapid CTP” OR "qure.ai")
19 2 TS=“automat* hierarch* evaluat*”

18 71,652 TS=(CNN OR CNNs OR convNet OR (convolut* NEAR/2 “neural network*”) OR “convolutional ANNs” OR “convolutional ANN” OR “convolutional NNs” OR “convolutional NN”)
17 9,599 TS=(“decision support*” NEAR/2 (software OR tool*))
16 242,068 TS=((deep OR machine) NEAR/2 learning)
15 124,965 TS=((automat* OR computer) NEAR/2 (analys* OR diagnos* OR detect*))
14 192,179 TS=(“Artificial intelligence” OR AI OR “machine intelligence” OR “computer-aided triage*” OR “support vector machine*” OR “relevance vector machine*”)
13 950,006 #12 OR #11 OR #10 OR #9
12 1 TS=(“Gamma encephalograph*” OR Gammaencephalograph* OR “Radio encephalograph*” OR Radioencephalograph*)
11 404,804 TS=(“CAT scan*” OR CTA OR CTP OR neuroimag* OR neuro-imag* OR (comput* NEAR/2 tomograph*))
10 161,458 TS=((Brain OR cerebral OR neurologic* OR CT OR head) NEAR/2 (scan* OR scintigraph* OR examination* OR angiograph* OR "image analys*" OR perfusion* OR radiograph*))
9 473,469 TS=((diagnos* OR predict* OR specificity OR sensitiv*) NEAR/4 (criteria OR criterion OR guideline* OR pattern* OR trend* OR utili* OR management OR prevalence OR initiat* OR distribution* OR coverage OR variety OR selection OR spread OR alternative* OR frequen*))
8 501,283 #7 OR #6 OR #5 OR #4 OR #3 OR #2 OR #1
7 53,057 TI=(CVA OR CVAS OR MCA* OR ICH OR ICHs OR CVST OR CVSTs OR CVDST OR CVT OR CVDSTs OR CVTs OR LVO OR LVOs) OR AB=(CVA OR CVAS OR MCA* OR ICH OR ICHs OR CVST OR CVSTs OR CVDST OR CVT OR CVDSTs OR CVTs OR LVO OR LVOs)
6 125,500 TS=((brain OR cerebr* OR cerebell* OR cortical OR Intraparenchymal OR intracortical OR vertebrobasil* OR hemispher* OR intracran* OR intra-cran* OR intracerebral OR intratentorial OR intra-tentorial OR intraventricular OR intra-ventricular OR periventricular OR peri-ventricular OR supratentrial OR supra-tentorial OR “anterior circulat*” OR “posterior circulat*” OR “basal gangli*” OR global OR focal OR parenchymal OR subarachnoid OR sub-arachnoid OR putaminal OR putamen OR “posterior fossa” OR intra-axial OR intraaxial OR lacunar) NEAR/3 (arrest* OR attack* OR isch?emi* OR infarct* OR insufficien* OR emboli* OR occlus* OR hypox* OR vasospasm OR obstruction OR vasculopath* OR failure* OR thromb* OR h?emorrhag* OR microh?emorrhag* OR accident* OR h?ematoma* OR bleed* OR microbleed* OR insult*))
5 9 TS=((Bleed* OR h?emorrhag*) NEAR/2 “corpus callosum”)
4 4,227 TS=(isch?emi* NEAR/3 (seizure* OR attack* OR thrombo* OR embolic OR encephalopath* OR neural))
3 5,016 TS=((sinus OR sagittal) NEAR/3 thromb*)
2 2,426 TS=((brain OR “blood flow”) NEAR/2 disturb*)
1 395,490 TS=(Stroke* OR apople* OR “cerebral vasc*” OR cerebrovasc* OR “cerebro vasc*” OR poststroke* OR encephalorrhag* OR hematencephalon* OR “large vessel occlusion*”)

Database of Abstracts of Reviews of Effects (DARE) (Internet) (https://www.crd.york.ac.uk/CRDWeb/): up to 2015/03/31
Health Technology Assessment Database (HTA) (Internet) (https://www.crd.york.ac.uk/CRDWeb/): up to 2018/03/31

Searched: 7.7.21

1	MeSH DESCRIPTOR Brain Ischemia EXPLODE ALL TREES	328
2	MeSH DESCRIPTOR Intracranial Hemorrhages EXPLODE ALL TREES	258
3	MeSH DESCRIPTOR Stroke EXPLODE ALL TREES	1356
4	MeSH DESCRIPTOR Ischemic Stroke EXPLODE ALL TREES	0

5	MeSH DESCRIPTOR Hemorrhagic Stroke EXPLODE ALL TREES	0
6	(Stroke* or apople* or "cerebral vasc*" or cerebrovasc* or "cerebro vasc*" or poststroke* or encephalorrhag* or hematencephalon* or "large vessel occlusion*")	3402
7	(((brain or "blood flow") and disturb*)) OR (((sinus or sagittal) and thromb*)) OR (((ischemi* or ischaemi*) and (seizure* or attack* or thrombo* or embolic or encephalopath* or neural)))	691
8	(((Bleed* or hemorrhag* or haemorrhag*) and "corpus callosum")) OR (((brain or cerebr* or cerebell* or cortical or Intraparenchymal or intracortical or vertebrobasil* or hemispher* or intracran* or intra-cran* or intracerebral or intratentorial or intra-tentorial or intraventricular or intra-ventricular or periventricular or peri-ventricular or supratentorial or supra-tentorial or anterior circulat* or "posterior circulat*" or "basal gangli*" or global or focal or parenchymal or subarachnoid or sub-arachnoid or putaminal or putamen or "posterior fossa" or intra-axial or intraaxial or lacunar) and (arrest* or attack* or ischemi* or ischaemi* or infarct* or insufficien* or emboli* or occlus* or hypox* or vasospasm or obstruction or vasculopath* or failure* or thromb* or hemorrhag* or haemorrhag* or microhemorrhag* or microhaemorrhag* or accident* or hematoma* or haematoma* or bleed* or microbleed* or insult*))) OR (CVA or CVAS or MCA* or ICH or ICHs or CVST or CVSTs or CVDST or CVT or CVDSTs or CVTs or LVO or LVOs)	2618
9	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	5187
10	MeSH DESCRIPTOR Diagnosis EXPLODE ALL TREES	29251
11	MeSH DESCRIPTOR Early Diagnosis EXPLODE ALL TREES	413
12	MeSH DESCRIPTOR brain EXPLODE ALL TREES WITH QUALIFIER DG IN DARE,HTA	0
13	MeSH DESCRIPTOR stroke EXPLODE ALL TREES WITH QUALIFIER DG IN DARE,HTA	0
14	MeSH DESCRIPTOR Radionuclide Imaging EXPLODE ALL TREES	725
15	MeSH DESCRIPTOR Neurologic Examination EXPLODE ALL TREES	772
16	(((Brain or cerebral or neurologic* or CT or head) and (scan* or scintigraph* or examination* or angiograph* or "image analys*" or perfusion* or radiograph*))) OR (((diagnos* or predict* or specificity or sensitiv*) and (criteria or criterion or guideline* or pattern* or trend* or utili* or management or prevalence or initiat* or distribution* or coverage or variety or selection or spread or alternative* or frequen*))) OR (("CAT scan*" or CTA or CTP or neuroimag* or neuro-imag* or (comput* and tomograph*)))	25348
17	("Gamma encephalograph*" or Gammaencephalograph* or "Radio encephalograph*" or Radioencephalograph*)	0
18	#10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17	40752

19	MeSH DESCRIPTOR Artificial Intelligence EXPLODE ALL TREES	290
20	MeSH DESCRIPTOR Pattern Recognition, Automated EXPLODE ALL TREES	3
21	MeSH DESCRIPTOR Neural Networks, Computer EXPLODE ALL TREES	0
22	("Artificial intelligence" or AI or "machine intelligence" or "computer-aided triage*" or "support vector machine*" or "relevance vector machine*") OR (((automat* or computer) and (analys* or diagnos* or detect*))) OR (((deep or machine) and learning))	2249
23	(("decision support*" and (software or tool*))) OR (CNN or CNNs or convNet or (convolut* and "neural network*") or "convolutional ANNs" or "convolutional ANN" or "convolutional NNs" or "convolutional NN") OR ("automat* hierarch* evaluat*")	176
24	(Aidoc OR "e-CTA" OR "e-ASPECTS" OR "e-stroke" OR brainomix OR brainscan OR "brainscan.ai" OR icobrain OR icometrix OR qER OR Qure OR Zebra* OR "e-CTP" OR briefcase OR "rapid CTA" OR "rapid LVO" OR "rapid core" OR "rapid ASPECTS" OR "rapid ICH" OR rapidai OR blackford OR "viz.ai" OR viz OR "ct perfusion 4d" OR cercare OR cina* OR Avicenna OR accipio* OR maxQ AI OR biomind OR "biomind.ai" OR ischemaview OR "rapid CTP" OR "qure.ai")	5365
25	#19 OR #20 OR #21 OR #22 OR #23 OR #24	7756
26	#9 AND #18 AND #25	497
27	* IN DARE, HTA	62769
28	#26 AND #27	361

KSR Evidence (KSR Ltd)(https://ksrevidence.com/): up to 2021/07/07
Searched: 7.7.21

1 (Stroke* or apople* or "cerebral vasc*" or cerebrovasc* or "cerebro vasc*" or poststroke* or encephalorrhag* or hematencephalon* or "large vessel occlusion*") in Title or Abstract 6910 results
2 ((brain or "blood flow") adj2 disturb*) in Title or Abstract 14 results
3 ((sinus or sagittal) adj3 thromb*) in Title or Abstract 34 results
4 ((ischemi* or ischaemi*) adj3 (seizure* or attack* or thrombo* or embolic or encephalopath* or neural)) in Title or Abstract 601 results
5 ((Bleed* or hemorrhag* or haemorrhag*) adj2 "corpus callosum") in Title or Abstract 1 result
6 CVA or CVAS or MCA* or ICH or ICHs or CVST or CVSTs or CVDST or CVT or CVDSTs or CVTs or LVO or LVOs in Title or Abstract 534 results
7 ((brain or cerebr* or cerebell* or cortical or Intraparenchymal or intracortical or vertebrobasil* or hemispher* or intracran* or intra-cran* or intracerebral or intratentorial or intra-tentorial or intraventricular or intra-ventricular or periventricular or peri-ventricular or supratentorial or supra-tentorial or "anterior circulat*" or "posterior circulat*" or "basal gangli*" or global or focal or parenchymal or subarachnoid or sub-arachnoid or putaminal or putamen or "posterior fossa" or intra-axial or intraaxial or lacunar) adj3 (arrest* or attack* or ischemi* or ischaemi* or infarct* or insufficien* or emboli* or occlus* or hypox* or vasospasm or obstruction or

vasculopath* or failure* or thromb* or hemorrhag* or haemorrhag* or microhemorrhag* or microhaemorrhag* or accident* or hematoma* or haematoma* or bleed* or microbleed* or insult*)) in Title or Abstract 2211 results
8 #1 or #2 or #3 or #4 or #5 or #6 or #7 in All text 8102 results
9 ((diagnos* or predict* or specificity or sensitiv*) adj4 (criteria or criterion or guideline* or pattern* or trend* or utili* or management or prevalence or initiat* or distribution* or coverage or variety or selection or spread or alternative* or frequen*)) in Title or Abstract 5140 results
10 ((Brain or cerebral or neurologic* or CT or head) adj2 (scan* or scintigraph* or examination* or angiograph* or "image analys*" or perfusion* or radiograph*)) in Title or Abstract 704 results
11 ("CAT scan*" or CTA or CTP or neuroimag* or neuro-imag* or (comput* adj2 tomograph*)) in Title or Abstract 2625 results
12 "Gamma encephalograph*" or Gammaencephalograph* or "Radio encephalograph*" or Radioencephalograph* in Title or Abstract 0 results
13 #9 or #10 or #11 or #12 in Title or Abstract 7867 results
14 "Artificial intelligence" or AI or "machine intelligence" or "computer-aided triage*" or "support vector machine*" or "relevance vector machine*" in Title or Abstract 421 results
15 ((automat* or computer) adj2 (analys* or diagnos* or detect*)) in Title or Abstract 181 results
16 ((deep or machine) adj learning) in Title or Abstract 354 results
17 ("decision support*" adj (software or tool*)) in Title or Abstract 56 results
18 CNN or CNNs or convNet or (convolut* adj2 "neural network*") or "convolutional ANNs" or "convolutional ANN" or "convolutional NNs" or "convolutional NN" in Title or Abstract 34 results
19 Aidoc OR "e-CTA" OR "e-ASPECTS" OR "e-stroke" OR brainomix OR brainscan OR "brainscan ai" OR icobrain OR icometrix OR qER OR Qure OR Zebra* OR "e-CTP" OR briefcase OR "rapid CTA" OR "rapid LVO" OR "rapid core" OR "rapid ASPECTS" OR "rapid ICH" OR rapidai OR blackford OR "viz ai" OR viz OR "ct perfusion 4d" OR cercare OR cina* OR Avicenna OR accipio* OR maxQ AI OR biomind OR "biomind ai" OR ischemaview OR "rapid CTP" OR "qure ai" in Title or Abstract 16149 results
20 #14 or #15 or #16 or #17 or #18 or #19 in All text 16916 results
21 #20 and #13 and #8 in All text 42 results

Epistemonikos (https://www.epistemonikos.org/): up to 2021/07/07
Searched: 7.7.21

(title:((title:(stroke* OR "brain haemorrhag*" OR "brain hemorrhag*" OR "brain bleed*" OR "cerebr* bleed*") OR abstract:(stroke* OR "brain haemorrhag*" OR "brain hemorrhag*" OR "brain bleed*" OR "cerebr* bleed*")) AND (title:(diagnos* OR "brain scan*" OR "CT scan*" OR "CAT scan*" OR "comput* tomograph*") OR abstract:(diagnos* OR "brain scan*" OR "CT scan*" OR "CAT scan*" OR "comput* tomograph*")) AND (title:("artificial intelligence" OR AI OR "machine intelligence" OR "computer-aided triage*" OR "decision support software") OR abstract:("artificial intelligence" OR AI OR "machine intelligence" OR "computer-aided triage*" OR "decision support software"))) OR abstract:((title:(stroke* OR "brain haemorrhag*" OR "brain hemorrhag*" OR "brain bleed*" OR "cerebr* bleed*") OR abstract:(stroke* OR "brain haemorrhag*" OR "brain hemorrhag*" OR "brain bleed*" OR "cerebr* bleed*")) AND (title:(diagnos* OR "brain scan*" OR "CT scan*" OR "CAT scan*" OR "comput* tomograph*") OR abstract:(diagnos* OR "brain scan*" OR "CT scan*" OR "CAT scan*" OR "comput* tomograph*")) AND (title:("artificial intelligence" OR AI OR "machine intelligence" OR "computer-aided triage*" OR "decision support software") OR abstract:("artificial intelligence" OR AI OR "machine intelligence" OR "computer-aided triage*" OR "decision support software"))))
3 results filtered to systematic review

NIHR Health Technology Assessment (HTA) (Internet) (https://www.nihr.ac.uk/): up to 2021/07/02
Searched: 2.7.21

Search terms	Journal reports	Research Projects
"artificial intelligence"	0	5

INAHTA (http://www.inahta.org/): up to 2021/07/06
Searched: 6.7.21

((((“Artificial intelligence” OR AI OR “machine intelligence” OR “computer-aided triage*” or "automat* analys*" or "computer analys*" or "decision support* software")[abs]) OR (((“Artificial intelligence” OR AI OR “machine intelligence” OR “computer-aided triage*” or "automat* analys*" or "computer analys*" or "decision support* software")[Title]) OR ("Artificial Intelligence"[mhe])) AND (((stroke* or "intracranial haemorrhag*" or "intracranial hemorrhag*" or "brain ischaemi*" or "brain ischemi*")[abs]) OR ((stroke* or "intracranial haemorrhag*" or "intracranial hemorrhag*" or "brain ischaemi*" or "brain ischemi*")[Title]) OR ("Stroke"[mh]) OR ("Intracranial Hemorrhages"[mhe]) OR ("Brain Ischemia"[mhe]))

265 results

Aggressive Research Intelligence Facility (ARIF) (Internet) (https://www.birmingham.ac.uk/research/activity/mds/projects/HaPS/PHEB/ARIF/index.aspx)
Searched: 2.7.21

Unable to search as ARIF databases were unavailable due to ongoing server issues

PROSERO (CRD)(http://www.crd.york.ac.uk/prospero/): up to 2021/07/07
Searched: 7.7.21

#1 MeSH DESCRIPTOR Stroke EXPLODE ALL TREES 1371
#2 MeSH DESCRIPTOR Ischemic Stroke EXPLODE ALL TREES 36
#3 MeSH DESCRIPTOR Hemorrhagic Stroke EXPLODE ALL TREES 1
#4 stroke* OR "brain haemorrhag*" OR "brain hemorrhag*" OR "brain bleed*" OR "cerebr* bleed*" 7515
#5 #4 OR #3 OR #2 OR #1 7530
#6 MeSH DESCRIPTOR Diagnosis EXPLODE ALL TREES 16729
#7 MeSH DESCRIPTOR Early Diagnosis EXPLODE ALL TREES 389
#8 MeSH DESCRIPTOR Tomography, X-Ray Computed EXPLODE ALL TREES 386
#9 "brain scan*" OR "CT scan*" OR "CAT scan*" OR "comput* tomograph*" 2310
#10 #6 OR #7 OR #8 OR #9 18292
#11 MeSH DESCRIPTOR Artificial Intelligence EXPLODE ALL TREES 357
#12 MeSH DESCRIPTOR Pattern Recognition, Automated EXPLODE ALL TREES 1
#13 "artificial intelligence" OR AI OR "machine intelligence" OR "computer-aided triage*" OR "decision support software" 943
#14 #13 OR #12 OR #11 1170
#15 #5 AND #10 AND #14 23

INPLASY (Internet) (https://inplasy.com/): up to 2021/07/02
Searched: 2.7.21

MeSH / Keyword search	Hits
Artificial intelligence	1

LILACS (Internet) (http://regional.bvsalud.org/php/index.php?lang=en): up to 2021/07/02
Searched: 2.7.21

(mh:(stroke or "brain ischaemia" or "brain ischemia" or "intracranial haemorrhage*" or "intracranial hemorrhage*" or "large vessel occlusion*")) AND (diagnosis or "cat scan" or "CT scan" or "brain scan" or "neuroimag*" or "neuro-imag*") AND ("artificial intelligence" or AI or "machine intelligence" or "computer aided triage" or "automat* diagnos*" or "computer diagnos*" or "decision support software")

374 results

ClinicalTrials.gov (Internet) (https://www.who.int/clinical-trials-registry-platform): up to 2021/07/02
Searched: 2.7.21

((stroke OR "brain ischemia" OR "brain ischaemia" or "blood vessel occlusion" OR "cerebral ischemia" or "cerebral ischaemia" or "large vessel occlusion" OR "intracranial haemorrhage" OR "intracranial hemorrhage") AND ("artificial intelligence" OR "automated pattern recognition" OR "computer assisted diagnosis" OR "computer aided triage" OR "decision support software" OR "automated diagnosis"))

39 results

EU Clinical Trials Register (Internet) (https://www.clinicaltrialsregister.eu/ctr-search/search): up to 2021/07/28
Searched: 28.7.21

Search terms	Hits
“artificial intelligence”	2
“machine intelligence”	0
Aidoc	0
e-cta	0
e-aspects	0
e-stroke	0
Brainomix	0
Brainscan*	0
Icobrain	0
Icometrix	0
Qer	0
qure	1
Zebra*	3
c-ctp	0
Briefcase	0
“rapid CTA”	0
“rapid LVO”	0
“rapid core”	0

“rapid aspects”	0
“rapid ICH”	0
Rapidai	0
Blackford	0
Viz.ai	0
Viz	8
“ct perfusion 4d”	0
Cercare	0
Cina* AND stroke	2
Avicenna	0
Accipio*	0
“maxq ai”	0
Biomind*	0
Ischemaview	0
“rapid ctp”	0
Qure.ai	0
Total	**16**

WHO ICTRP (Internet) (https://ictrptest.azurewebsites.net/Default.aspx) : up to 2021/07/02
Searched: 2.7.21

Search terms	Hits
Artificial intelligence AND stroke	14

ScanMedicine (Internet) (https://scanmedicine.com/): up to 2021/07/02
Searched: 2.7.21

Search terms	Hits
"artificial intelligence" + stroke [only]	28

Northern Light Life Sciences Conference Abstracts (Ovid): 2010–2021/Wk25
Searched: 7.7.21

1 exp Brain Ischemia/ (5706)
2 exp Intracranial Hemorrhages/ (12738)
3 Stroke/ (37884)
4 (Stroke$ or apople$ or cerebral vasc$ or cerebrovasc$ or cerebro vasc$ or poststroke$ or encephalorrhag$ or hematencephalon$ or large vessel occlusion$).ti,ab. (50748)
5 (CVA or CVAS or MCA$ or ICH or ICHs or CVST or CVSTs or CVDST or CVT or CVDSTs or CVTs or LVO or LVOs).ti,ab. (7951)
6 ((brain or cerebr$ or cerebell$ or cortical or Intraparenchymal or intracortical or vertebrobasil$ or hemispher$ or intracran$ or intra-cran$ or intracerebral or intratentorial or intra-tentorial or intraventricular or intra-ventricular or periventricular or peri-ventricular or supratentorial or supra-tentorial or anterior circulat$ or posterior circulat$ or basal gangli$ or global or focal or parenchymal or subarachnoid or sub-arachnoid or putaminal or putamen or posterior fossa or intra-axial or intraaxial or lacunar) adj3 (arrest$ or attack$ or isch?emi$ or infarct$ or insufficien$ or emboli$ or occlus$ or hypox$ or vasospasm or obstruction or vasculopath$ or failure$ or thromb$ or

h?emorrhag$ or microh?emorrhag$ or accident$ or h?ematoma$ or bleed$ or microbleed$ or insult$)).ti,ab. (18023)
7 ((brain or blood flow) adj2 disturb$).ti,ab. (104)
8 ((sinus or sagittal) adj3 thromb$).ti,ab. (543)
9 (isch?emi$ adj3 (seizure$ or attack$ or thrombo$ or embolic or encephalopath$ or neural)).ti,ab. (2184)
10 ((Bleed$ or h?emorrhag$) adj2 corpus callosum).ti,ab. (2)
11 or/1-10 (86665)
12 Diagnosis/ (0)
13 Early Diagnosis/ (21707)
14 Radiography/ (0)
15 exp Radionuclide Imaging/ (0)
16 Neurologic Examination/ (0)
17 Tomography, X-Ray Computed/ (0)
18 ((Brain or cerebral or neurologic$ or CT or head) adj2 (scan$ or scintigraph$ or examination$ or angiograph$ or image analys$ or perfusion$ or radiograph$)).ti,ab. (19256)
19 (CAT scan$ or CTA or CTP or neuroimag$ or neuro-imag$ or (comput$ adj2 tomograph$)).ti,ab. (24365)
20 (Gamma encephalograph$ or Gammaencephalograph$ or Radio encephalograph$ or Radioencephalograph$).ti,ab. (0)
21 or/12-20 (61593)
22 exp Artificial Intelligence/ (0)
23 Pattern Recognition, Automated/ (0)
24 Neural Networks, Computer/ (0)
25 (CNN or CNNs or convNet or (convolut$ adj2 neural network$) or convolutional ANNs or convolutional ANN or convolutional NNs or convolutional NN).ti,ab. (1290)
26 (Artificial intelligence or AI or machine intelligence or computer-aided triage$ or support vector machine$ or relevance vector machine$).ti,ab. (6547)
27 ((automat$ or computer) adj2 (analys$ or diagnos$ or detect$)).ti,ab. (4358)
28 ((deep or machine) adj learning).ti,ab. (8611)
29 automat$ hierarch$ evaluat$.ti,ab. (0)
30 (decision support$ adj (software or tool$)).ti,ab. (775)
31 (Aidoc or e-CTA or e-ASPECTS or e-stroke or brainomix or brainscan or "brainscan.ai" or icobrain or icometrix or qER or Qure or Zebra$ or e-CTP or briefcase or rapid CTA or rapid LVO or rapid core or rapid ASPECTS or rapid ICH or rapidai or blackford or "viz.ai" or viz or "ct perfusion 4d" or cercare or cina$ or Avicenna or accipio$ or maxQ AI or biomind or "biomind.ai" or ischemaview or rapid CTP or "qure.ai").ti,ab. (7552)
32 or/22-31 (27321)
33 11 and 21 and 32 (64)

Named technologies

Database	**Dates covered**	**Hits**
Embase	2017-2021/09/03	1,361
MEDLINE + PreMedline	2017-2021/09/03	915
Northern Light	2017–2021/Wk34	46
Total		**2,322**

Embase (Ovid): 2017–2021/09/03
Date searched: 7.9.21

Stroke + named tech + (Limits: NoA/2017-C)

1 exp brain ischemia/ (200071)
2 exp brain hemorrhage/ (152081)
3 basal ganglion hemorrhage/ (662)
4 cerebrovascular accident/ (230100)
5 brain infarction/ (56277)
6 blood vessel occlusion/ (11766)
7 (Stroke$ or apople$ or cerebral vasc$ or cerebrovasc$ or cerebro vasc$ or poststroke$ or encephalorrhag$ or hematencephalon$ or large vessel occlusion$).ti,ab,ot. (503730)
8 ((brain or blood flow) adj2 disturb$).ti,ab,ot. (2924)
9 ((sinus or sagittal) adj3 thromb$).ti,ab,ot. (7228)
10 (isch?emi$ adj3 (seizure$ or attack$ or thrombo$ or embolic or encephalopath$ or neural)).ti,ab,ot. (40907)
11 ((Bleed$ or h?emorrhag$) adj2 corpus callosum).ti,ab,ot. (27)
12 ((brain or cerebr$ or cerebell$ or cortical or Intraparenchymal or intracortical or vertebrobasil$ or hemispher$ or intracran$ or intra-cran$ or intracerebral or intratentorial or intra-tentorial or intraventricular or intra-ventricular or periventricular or peri-ventricular or supratentorial or supra-tentorial or anterior circulat$ or posterior circulat$ or basal gangli$ or global or focal or parenchymal or subarachnoid or sub-arachnoid or putaminal or putamen or posterior fossa or intra-axial or intraaxial or lacunar) adj3 (arrest$ or attack$ or isch?emi$ or infarct$ or insufficien$ or emboli$ or occlus$ or hypox$ or vasospasm or obstruction or vasculopath$ or failure$ or thromb$ or h?emorrhag$ or microh?emorrhag$ or accident$ or h?ematoma$ or bleed$ or microbleed$ or insult$)).ti,ab,ot. (295196)
13 (CVA or CVAS or MCA$ or ICH or ICHs or CVST or CVSTs or CVDST or CVT or CVDSTs or CVTs or LVO or LVOs).ti,ab. (82820)
14 or/1-13 (870499)
15 (Aidoc or e-CTA or e-ASPECTS or e-stroke or brainomix or brainscan or "brainscan.ai" or icobrain or icometrix or qER or Qure or Zebra$ or e-CTP or briefcase or rapid CTA or rapid LVO or rapid core or rapid ASPECTS or rapid ICH or rapidai or blackford or "viz.ai" or viz or "ct perfusion 4d" or cercare or cina$ or Avicenna or accipio$ or maxQ AI or biomind or "biomind.ai" or ischemaview or rapid CTP or "qure.ai").ti,ab. (127715)
16 14 and 15 (3409)
17 (letter or editorial or note).pt. (2753204)
18 16 not 17 (3392)
19 animal/ (1525609)
20 animal experiment/ (2713339)
21 (rat or rats or mouse or mice or murine or rodent or rodents or hamster or hamsters or pig or pigs or porcine or rabbit or rabbits or animal or animals or dogs or dog or cats or cow or bovine or sheep or ovine or monkey or monkeys).ti,ab,ot,hw. (7057425)
22 or/19-21 (7057425)
23 exp human/ (22670126)
24 human experiment/ (552250)
25 or/23-24 (22672045)
26 22 not (22 and 25) (5366393)
27 18 not 26 (3030)
28 limit 27 to yr="2017 -Current" (1361)

MEDLINE and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations, Daily and Versions (Ovid): 2017–2021/09/03
Searched: 7.9.21

1 exp Brain Ischemia/ (114939)
2 exp Intracranial Hemorrhages/ (74704)
3 Stroke/ (112246)
4 (Stroke$ or apople$ or cerebral vasc$ or cerebrovasc$ or cerebro vasc$ or poststroke$ or encephalorrhag$ or hematencephalon$ or large vessel occlusion$).ti,ab,ot. (325118)
5 ((brain or blood flow) adj2 disturb$).ti,ab,ot. (2108)
6 ((sinus or sagittal) adj3 thromb$).ti,ab,ot. (5061)
7 (isch?emi$ adj3 (seizure$ or attack$ or thrombo$ or embolic or encephalopath$ or neural)).ti,ab,ot. (26633)
8 ((Bleed$ or h?emorrhag$) adj2 corpus callosum).ti,ab,ot. (23)
9 ((brain or cerebr$ or cerebell$ or cortical or Intraparenchymal or intracortical or vertebrobasil$ or hemispher$ or intracran$ or intra-cran$ or intracerebral or intratentorial or intra-tentorial or intraventricular or intra-ventricular or periventricular or peri-ventricular or supratentorial or supra-tentorial or anterior circulat$ or posterior circulat$ or basal gangli$ or global or focal or parenchymal or subarachnoid or sub-arachnoid or putaminal or putamen or posterior fossa or intra-axial or intraaxial or lacunar) adj3 (arrest$ or attack$ or isch?emi$ or infarct$ or insufficien$ or emboli$ or occlus$ or hypox$ or vasospasm or obstruction or vasculopath$ or failure$ or thromb$ or h?emorrhag$ or microh?emorrhag$ or accident$ or h?ematoma$ or bleed$ or microbleed$ or insult$)).ti,ab,ot. (209642)
10 (CVA or CVAS or MCA$ or ICH or ICHs or CVST or CVSTs or CVDST or CVT or CVDSTs or CVTs or LVO or LVOs).ti,ab. (48496)
11 or/1-10 (553497)
12 (Aidoc or e-CTA or e-ASPECTS or e-stroke or brainomix or brainscan or "brainscan.ai" or icobrain or icometrix or qER or Qure or Zebra$ or e-CTP or briefcase or rapid CTA or rapid LVO or rapid core or rapid ASPECTS or rapid ICH or rapidai or blackford or "viz.ai" or viz or "ct perfusion 4d" or cercare or cina$ or Avicenna or accipio$ or maxQ AI or biomind or "biomind.ai" or ischemaview or rapid CTP or "qure.ai").ti,ab. (104207)
13 11 and 12 (2182)
14 (letter or editorial or note).pt. (1729571)
15 exp animals/ not (exp animals/ and humans/) (4881960)
16 13 not (14 or 15) (1953)
17 limit 16 to yr="2017 -Current" (915)

Northern Light Life Sciences Conference Abstracts (Ovid): 2017–2021/Wk34
Searched: 7.9.21

1 exp Brain Ischemia/ (6060)
2 exp Intracranial Hemorrhages/ (13588)
3 Stroke/ (40328)
4 (Stroke$ or apople$ or cerebral vasc$ or cerebrovasc$ or cerebro vasc$ or poststroke$ or encephalorrhag$ or hematencephalon$ or large vessel occlusion$).ti,ab. (54065)
5 (CVA or CVAS or MCA$ or ICH or ICHs or CVST or CVSTs or CVDST or CVT or CVDSTs or CVTs or LVO or LVOs).ti,ab. (8472)
6 ((brain or cerebr$ or cerebell$ or cortical or Intraparenchymal or intracortical or vertebrobasil$ or hemispher$ or intracran$ or intra-cran$ or intracerebral or intratentorial or intra-tentorial or intraventricular or intra-ventricular or periventricular or peri-ventricular or supratentorial or supra-tentorial or anterior circulat$ or posterior circulat$ or basal gangli$ or global or focal or parenchymal

or subarachnoid or sub-arachnoid or putaminal or putamen or posterior fossa or intra-axial or intraaxial or lacunar) adj3 (arrest$ or attack$ or isch?emi$ or infarct$ or insufficien$ or emboli$ or occlus$ or hypox$ or vasospasm or obstruction or vasculopath$ or failure$ or thromb$ or h?emorrhag$ or microh?emorrhag$ or accident$ or h?ematoma$ or bleed$ or microbleed$ or insult$)).ti,ab. (19017)
7 ((brain or blood flow) adj2 disturb$).ti,ab. (113)
8 ((sinus or sagittal) adj3 thromb$).ti,ab. (576)
9 (isch?emi$ adj3 (seizure$ or attack$ or thrombo$ or embolic or encephalopath$ or neural)).ti,ab. (2281)
10 ((Bleed$ or h?emorrhag$) adj2 corpus callosum).ti,ab. (2)
11 or/1-10 (92032)
12 (Aidoc or e-CTA or e-ASPECTS or e-stroke or brainomix or brainscan or "brainscan.ai" or icobrain or icometrix or qER or Qure or Zebra$ or e-CTP or briefcase or rapid CTA or rapid LVO or rapid core or rapid ASPECTS or rapid ICH or rapidai or blackford or "viz.ai" or viz or "ct perfusion 4d" or cercare or cina$ or Avicenna or accipio$ or maxQ AI or biomind or "biomind.ai" or ischemaview or rapid CTP or "qure.ai").ti,ab. (7830)
13 11 and 12 (86)
14 limit 13 to yr="2017 -Current" (46)

Preprints Search

Database	Dates covered	Hits
MedRxiv	up to 2021/09/29	538
Total		**538**

MedRxiv: the preprint server for Health Sciences (https://www.medrxiv.org/): up to 2021/09/29 Searched 29.9.21

Advanced search

Full text or abstract or title (match whole all)	Hits
stroke* Aidoc	1
Stroke* e-CTA	0
Stroke* e-ASPECTS	0
e-stroke	14
Stroke* brainomix	0
Stroke* brainscan	1
Stroke* brainscan.ai	0
stroke icobrain	1
Stroke* icometrix	2
Stroke* qER	0
Stroke* Qure	3
Stroke* Zebra*	1
Stroke* e-CTP	0
Stroke* briefcase	0
Stroke* rapid CTA	14
Stroke* rapid LVO	8

Stroke* rapid core	247
Stroke* rapid ASPECTS	331
Stroke* rapid ICH	27
Stroke* rapidai	1
Stroke* blackford	1
Stroke* viz.ai	2
Stroke* viz	23
Stroke* ct perfusion 4d	15
Stroke* cercare	0
Stroke* cina*	2
Stroke* Avicenna	2
Stroke* accipio*	0
Stroke* maxQ AI	0
Stroke* biomind	0
Stroke* biomind.ai	0
Stroke* ischemaview	1
Stroke* rapid CTP	5
Stroke* qure.ai	0
Total	**702**
Total without dupes	**538**

Guidelines

Database	**Dates covered**	**Hits**
TRIP	2017-2021/10/26	59
GIN	2017-2021/10/20	7
HTA	2017-2018/03	17
NICE	2017-2021/10/20	1
NIHR HTA	2017-2021/10/20	8
ECRI	2017-2021/10/20	39
NHS Evidence	2017-2021/10/20	358
INAHTA	2017-2021/10/20	64
Total		**553**

TRIP database (https://www.tripdatabase.com/): 2017–2021/10/26
Date searched: 26.10.21

Limits: All of these words in Title
Publication year - 2017-2021

Search term (in Title)	**Results**
Stroke	59
TIA	59
transient ischaemic attack	2
transient ischemic attack	2
brain ischaemia	0
brain ischemia	0
intracranial haemorrhage	0
intracranial hemorrhage	0

vessel occlusion	1
Total	**123**
TOTAL (after deduplication)	**59**

Guidelines International Network (GIN) (https://g-i-n.net/international-guidelines-library/): 2017–2021/10/20
Searched: 20.10.21

Limits:
Publication year - 2017-2021
Guideline publication status - Published

Search term	Results
Stroke	7
TIA	0
TOTAL	**7**

Health Technology Assessment Database (HTA) (CRD): 2017-2018/03
Searched 20.10.21

1 MeSH DESCRIPTOR Brain Ischemia EXPLODE ALL TREES 328 Delete
2 MeSH DESCRIPTOR Intracranial Hemorrhages EXPLODE ALL TREES 258 Delete
3 ((Stroke* or apople* or cerebral-vasc* or cerebrovasc* or cerebro-vasc* or poststroke* or encephalorrhag* or hematencephalon* or large-vessel-occlusion*)) 3402 Delete
4 (((brain or blood flow) NEAR2 disturb*)) 1 Delete
5 (((sinus or sagittal) NEAR3 thromb*)) 5 Delete
6 (((ischaemi* or ischemi*) NEAR3 (seizure* or attack* or thrombo* or embolic or encephalopath* or neural))) 342 Delete
7 (((Bleed* or hemorrhag* or haemorrhag*) NEAR2 corpus-callosum)) 0 Delete
8 (((brain or cerebr* or cerebell* or cortical or Intraparenchymal or intracortical or vertebrobasil* or hemispher* or intracran* or intra-cran* or intracerebral or intratentorial or intra-tentorial or intraventricular or intra-ventricular or periventricular or peri-ventricular or supratentorial or supra-tentorial or anterior-circulat* or posterior-circulat* or basal-gangli* or global or focal or parenchymal or subarachnoid or sub-arachnoid or putaminal or putamen or posterior-fossa or intra-axial or intraaxial or lacunar) NEAR3 (arrest* or attack* or ischaemi* or ischemi* or infarct* or insufficien* or emboli* or occlus* or hypox* or vasospasm or obstruction or vasculopath* or failure* or thromb* or hemorrhag* or haemorrhag* or microhemorrhag* or microhaemorrhad or haemorrhag* or accident* or hematoma* or haemotoma* or bleed* or microbleed* or insult*))) 1054 Delete
9 ((CVA or CVAS or MCA* or ICH or ICHs or CVST or CVSTs or CVDST or CVT or CVDSTs or CVTs or LVO or LVOs)) 309 Delete
10 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 4155 Delete
11 (#10) IN HTA 515 Delete
12 (#10) IN HTA FROM 2017 TO 2021 17 Delete

National Institute for Health and Care Excellence (NICE) (https://www.nice.org.uk/guidance/): 2017-2021/10/20
Searched: 20.10.21

Browsed 'Stroke and transient ischaemic attack' section at:

https://www.nice.org.uk/guidance/conditions-and-diseases/cardiovascular-conditions/stroke-and-transient-ischaemic-attack/products?Status=Published

Limited to publication date 2017-2021

Records found: 1

NIHR Health Technology Assessment (HTA) (https://www.nihr.ac.uk/): 2017-2021/10/20
Searched 20.10.21

Home/Researchers/Data and publications
2017-C: limited PDF

Search term	Results
Stroke	8
TIA	0/1 (dupe)
'transient ischaemic attack'	0
'transient ischemic attack'	0
'brain ischaemia'	0
'brain ischemia'	0
'intracranial haemorrhage'	0/1
'intracranial hemorrhage'	0
'vessel occlusion'	0
Total	**10**
TOTAL (after deduplication)	**8**

ECRI Guidelines Trust (https://guidelines.ecri.org/): 2017-2021/10/20
Searched: 20.10.21

Limits:
Publication year - 2017-2021

Search term	Results
Stroke	39
TIA	1
'transient ischaemic attack'	3
'transient ischemic attack'	2
'brain ischaemia'	0
'brain ischemia'	0
'intracranial haemorrhage'	0
'intracranial hemorrhage'	0
'vessel occlusion'	0
TOTAL (after deduplication)	**39**

NHS Evidence (https://www.evidence.nhs.uk/): 2017-2021/10/20
Searched 20.10.21

Limited to Guidance and HTAs (2017-C)

Terms searched	Hits
(stroke or "brain ischemia" or "brain ischaemia" or "blood vessel occlusion" or "cerebral ischemia" or "cerebral ischaemia" or "large vessel occlusion" or "intracranial haemorrhage" or "intracranial hemorrhage") AND (scan* or scintigraph* or examination* or angiograph* or image analys* or perfusion* or radiograph* or CTA or CTP or CTAs or CTPs or neuroimag* or neuro-imag*)	358
Total	**358**

International HTA Database (INAHTA)(https://database.inahta.org/): 2017-2021/10/20
Searched: 20.10.21

Records found: 64

14 #13 OR #12 OR #11 OR #10 OR #9 OR #8 OR #7 OR #6 OR #5 OR #4 OR #3 OR #2 OR #1 435
13 "blood vessel occlusion" 0
12 "intracranial hemorrhage" 6
11 "intracranial haemorrhage" 4
10 "large vessel occlusion" 2
9 "cerebral ischaemia" 2
8 "cerebral ischemia" 1
7 "brain ischaemia" 0
6 "brain ischemia" 2
5 TIA 16
4 "transient ischaemic attack" 9
3 "transient ischemic attack" 7
2 stroke* 409
1 "Stroke"[mhe] 225

Limits: Publication year - 2017-2021
Project status - Completed

October Update searches

Database	Dates covered	Hits
EMBASE	1974-2021/10/18	2,098
MEDLINE + PreMedline	1946-2021/10/15	1,192
medRxiv	Up to 2021/10/20	37
Total		**3,327**

Embase (Ovid): 1974-2021/10/18
Searched: 19.10.21

1 exp brain ischemia/ (200949)
2 exp brain hemorrhage/ (153883)
3 basal ganglion hemorrhage/ (672)
4 cerebrovascular accident/ (232943)
5 brain infarction/ (56774)
6 blood vessel occlusion/ (12030)
7 (Stroke$ or apople$ or cerebral vasc$ or cerebrovasc$ or cerebro vasc$ or poststroke$ or encephalorrhag$ or hematencephalon$ or large vessel occlusion$).ti,ab,ot. (509763)
8 ((brain or blood flow) adj2 disturb$).ti,ab,ot. (2932)
9 ((sinus or sagittal) adj3 thromb$).ti,ab,ot. (7391)
10 (isch?emi$ adj3 (seizure$ or attack$ or thrombo$ or embolic or encephalopath$ or neural)).ti,ab,ot. (41377)
11 ((Bleed$ or h?emorrhag$) adj2 corpus callosum).ti,ab,ot. (27)
12 ((brain or cerebr$ or cerebell$ or cortical or Intraparenchymal or intracortical or vertebrobasil$ or hemispher$ or intracran$ or intra-cran$ or intracerebral or intratentorial or intra-tentorial or intraventricular or intra-ventricular or periventricular or peri-ventricular or supratentorial or supra-tentorial or anterior circulat$ or posterior circulat$ or basal gangli$ or global or focal or parenchymal or subarachnoid or sub-arachnoid or putaminal or putamen or posterior fossa or intra-axial or intraaxial or lacunar) adj3 (arrest$ or attack$ or isch?emi$ or infarct$ or insufficien$ or emboli$ or occlus$ or hypox$ or vasospasm or obstruction or vasculopath$ or failure$ or thromb$ or h?emorrhag$ or microh?emorrhag$ or accident$ or h?ematoma$ or bleed$ or microbleed$ or insult$)).ti,ab,ot. (298073)
13 (CVA or CVAS or MCA$ or ICH or ICHs or CVST or CVSTs or CVDST or CVT or CVDSTs or CVTs or LVO or LVOs).ti,ab. (83973)
14 or/1-13 (879622)
15 ((diagnos$ or predict$ or specificity or sensitiv$) adj4 (criteria or criterion or guideline$ or pattern$ or trend$ or utili$ or management or prevalence or initiat$ or distribution$ or coverage or variety or selection or spread or alternative$ or frequen$)).ti,ab,ot. (504238)
16 diagnosis/ or early diagnosis/ (1452121)
17 exp brain scintiscanning/ (9890)
18 Neurologic examination/ (71955)
19 Computer assisted tomography/ (791392)
20 Brain radiography/ (7979)
21 ((Brain or cerebral or neurologic$ or CT or head) adj2 (scan$ or scintigraph$ or examination$ or angiograph$ or image analys$ or perfusion$ or radiograph$)).ti,ab,ot,hw. (397707)
22 (CAT scan$ or CTA or CTP or CTAs or CTPs or neuroimag$ or neuro-imag$ or (comput$ adj2 tomograph$)).ti,ab,ot,hw. (1331476)
23 (Gamma encephalograph$ or Gammaencephalograph$ or Radio encephalograph$ or Radioencephalograph$).ti,ab,ot,hw. (48)
24 or/15-23 (3169335)
25 exp artificial intelligence/ (53172)
26 automated pattern recognition/ (16993)
27 decision support system/ (24298)
28 computer assisted diagnosis/ (40643)
29 Convolutional neural network/ (11478)
30 (Artificial intelligence or AI or machine intelligence or computer-aided triage$ or support vector machine$ or relevance vector machine$).ti,ab,ot. (79275)
31 ((automat$ or computer) adj2 (analys$ or diagnos$ or detect$)).ti,ab,ot. (55546)
32 ((deep or machine) adj learning).ti,ab,ot. (72859)

33 (decision support$ adj (software or tool$)).ti,ab,ot. (4842)
34 (CNN or CNNs or convNet or (convolut$ adj2 neural network$) or convolutional ANNs or convolutional ANN or convolutional NNs or convolutional NN).ti,ab. (17172)
35 automat$ hierarch$ evaluat$.ti,ab. (1)
36 (Aidoc or e-CTA or e-ASPECTS or e-stroke or brainomix or brainscan or "brainscan.ai" or icobrain or icometrix or qER or Qure or Zebra$ or e-CTP or briefcase or rapid CTA or rapid LVO or rapid core or rapid ASPECTS or rapid ICH or rapidai or blackford or "viz.ai" or viz or "ct perfusion 4d" or cercare or cina$ or Avicenna or accipio$ or maxQ AI or biomind or "biomind.ai" or ischemaview or rapid CTP or "qure.ai").ti,ab. (129176)
37 or/25-36 (411932)
38 14 and 24 and 37 (2210)
39 (letter or editorial or note).pt. (2769185)
40 38 not 39 (2145)
41 animal/ (1534498)
42 animal experiment/ (2730003)
43 (rat or rats or mouse or mice or murine or rodent or rodents or hamster or hamsters or pig or pigs or porcine or rabbit or rabbits or animal or animals or dogs or dog or cats or cow or bovine or sheep or ovine or monkey or monkeys).ti,ab,ot,hw. (7090039)
44 or/41-43 (7090039)
45 exp human/ (22842436)
46 human experiment/ (556748)
47 or/45-46 (22844369)
48 44 not (44 and 47) (5387198)
49 40 not 48 (2098)

MEDLINE and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations, Daily and Versions (Ovid): 1946–2021/10/15
Searched: 19.10.21

1 exp Brain Ischemia/ (115589)
2 exp Intracranial Hemorrhages/ (75053)
3 Stroke/ (113288)
4 (Stroke$ or apople$ or cerebral vasc$ or cerebrovasc$ or cerebro vasc$ or poststroke$ or encephalorrhag$ or hematencephalon$ or large vessel occlusion$).ti,ab,ot. (327818)
5 ((brain or blood flow) adj2 disturb$).ti,ab,ot. (2117)
6 ((sinus or sagittal) adj3 thromb$).ti,ab,ot. (5117)
7 (isch?emi$ adj3 (seizure$ or attack$ or thrombo$ or embolic or encephalopath$ or neural)).ti,ab,ot. (26850)
8 ((Bleed$ or h?emorrhag$) adj2 corpus callosum).ti,ab,ot. (23)
9 ((brain or cerebr$ or cerebell$ or cortical or Intraparenchymal or intracortical or vertebrobasil$ or hemispher$ or intracran$ or intra-cran$ or intracerebral or intratentorial or intra-tentorial or intraventricular or intra-ventricular or periventricular or peri-ventricular or supratentorial or supra-tentorial or anterior circulat$ or posterior circulat$ or basal gangli$ or global or focal or parenchymal or subarachnoid or sub-arachnoid or putaminal or putamen or posterior fossa or intra-axial or intraaxial or lacunar) adj3 (arrest$ or attack$ or isch?emi$ or infarct$ or insufficien$ or emboli$ or occlus$ or hypox$ or vasospasm or obstruction or vasculopath$ or failure$ or thromb$ or h?emorrhag$ or microh?emorrhag$ or accident$ or h?ematoma$ or bleed$ or microbleed$ or insult$)).ti,ab,ot. (210934)
10 (CVA or CVAS or MCA$ or ICH or ICHs or CVST or CVSTs or CVDST or CVT or CVDSTs or CVTs or LVO or LVOs).ti,ab. (48905)
11 or/1-10 (557308)

12 ((diagnos$ or predict$ or specificity or sensitiv$) adj4 (criteria or criterion or guideline$ or pattern$ or trend$ or utili$ or management or prevalence or initiat$ or distribution$ or coverage or variety or selection or spread or alternative$ or frequen$)).ti,ab,ot. (350992)
13 Diagnosis/ (17472)
14 Early Diagnosis/ (28758)
15 Brain/dg [Diagnostic Imaging] (51780)
16 Stroke/dg [Diagnostic Imaging] (7712)
17 Radiography/ (322703)
18 exp Radionuclide Imaging/ (223371)
19 Neurologic Examination/ (27754)
20 Tomography, X-Ray Computed/ (399785)
21 ((Brain or cerebral or neurologic$ or CT or head) adj2 (scan$ or scintigraph$ or examination$ or angiograph$ or image analys$ or perfusion$ or radiograph$)).ti,ab,ot,hw. (229398)
22 (CAT scan$ or CTA or CTP or CTAs or CTPs or neuroimag$ or neuro-imag$ or (comput$ adj2 tomograph$)).ti,ab,ot,hw. (475578)
23 (Gamma encephalograph$ or Gammaencephalograph$ or Radio encephalograph$ or Radioencephalograph$).ti,ab,ot,hw. (155)
24 or/12-23 (1629565)
25 exp Artificial Intelligence/ (125230)
26 Pattern Recognition, Automated/ (25989)
27 Neural Networks, Computer/ (33266)
28 (Artificial intelligence or AI or machine intelligence or computer-aided triage$ or support vector machine$ or relevance vector machine$).ti,ab,ot. (61743)
29 ((automat$ or computer) adj2 (analys$ or diagnos$ or detect$)).ti,ab,ot. (43089)
30 ((deep or machine) adj learning).ti,ab,ot. (60757)
31 (decision support$ adj (software or tool$)).ti,ab,ot. (3515)
32 (CNN or CNNs or convNet or (convolut$ adj2 neural network$) or convolutional ANNs or convolutional ANN or convolutional NNs or convolutional NN).ti,ab. (14199)
33 automat$ hierarch$ evaluat$.ti,ab. (1)
34 (Aidoc or e-CTA or e-ASPECTS or e-stroke or brainomix or brainscan or "brainscan.ai" or icobrain or icometrix or qER or Qure or Zebra$ or e-CTP or briefcase or rapid CTA or rapid LVO or rapid core or rapid ASPECTS or rapid ICH or rapidai or blackford or "viz.ai" or viz or "ct perfusion 4d" or cercare or cina$ or Avicenna or accipio$ or maxQ AI or biomind or "biomind.ai" or ischemaview or rapid CTP or "qure.ai").ti,ab. (105422)
35 or/25-34 (356783)
36 11 and 24 and 35 (1237)
37 (letter or editorial or note).pt. (1738660)
38 exp animals/ not (exp animals/ and humans/) (4898472)
39 36 not (37 or 38) (1192)

medRxiv: the preprint server for Health Sciences (https://www.medrxiv.org/): up to 2021/10/20 Searched 20.10.21

Advanced search

Full text or abstract or title (match whole all)	Update (20.10.21) Hits
stroke* Aidoc	0
Stroke* e-CTA	0
Stroke* e-ASPECTS	0
e-stroke	0
Stroke* brainomix	0

Stroke* brainscan	1
Stroke* brainscan.ai	0
stroke icobrain	0
Stroke* icometrix	0
Stroke* qER	0
Stroke* Qure	0
Stroke* Zebra*	0
Stroke* e-CTP	0
Stroke* briefcase	0
Stroke* rapid CTA	0
Stroke* rapid LVO	0
Stroke* rapid core	22
Stroke* rapid ASPECTS	23
Stroke* rapid ICH	1
Stroke* rapidai	0
Stroke* blackford	0
Stroke* viz.ai	0
Stroke* viz	1
Stroke* ct perfusion 4d	0
Stroke* cercare	0
Stroke* cina*	0
Stroke* Avicenna	0
Stroke* accipio*	0
Stroke* maxQ AI	0
Stroke* biomind	0
Stroke* biomind.ai	0
Stroke* ischemaview	1
Stroke* rapid CTP	1
Stroke* qure.ai	0
Total	**50**
Total without dupes	**37**

Cost Effectiveness Searches

Database	**Dates covered**	**Hits**
Embase	2005-2021/09/15	988
MEDLINE + PreMedline	2005-2021/09/15	1,233
NHS EED	2005-2015/03	559
EconLit	2005-2021/09/21	82
Science Citation Index (SCI) + CPCI-S	2005–2021/09/21	1,007
RePeC (Ideas)	2005-2021/09/21	79
Total		**3,948**

Embase (Ovid): 2005-2021/09/15

Searched: 16.9.21

Stroke + (Cat Scan/diagnostics) + NHSEED SD filter (20015-C)

1 exp brain ischemia/ (200456)
2 exp brain hemorrhage/ (152656)
3 basal ganglion hemorrhage/ (669)
4 cerebrovascular accident/ (230904)
5 brain infarction/ (56442)
6 blood vessel occlusion/ (11828)
7 (Stroke$ or apople$ or cerebral vasc$ or cerebrovasc$ or cerebro vasc$ or poststroke$ or encephalorrhag$ or hematencephalon$ or large vessel occlusion$).ti,ab,ot. (505578)
8 ((brain or blood flow) adj2 disturb$).ti,ab,ot. (2928)
9 ((sinus or sagittal) adj3 thromb$).ti,ab,ot. (7285)
10 (isch?emi$ adj3 (seizure$ or attack$ or thrombo$ or embolic or encephalopath$ or neural)).ti,ab,ot. (41063)
11 ((Bleed$ or h?emorrhag$) adj2 corpus callosum).ti,ab,ot. (27)
12 ((brain or cerebr$ or cerebell$ or cortical or Intraparenchymal or intracortical or vertebrobasil$ or hemispher$ or intracran$ or intra-cran$ or intracerebral or intratentorial or intra-tentorial or intraventricular or intra-ventricular or periventricular or peri-ventricular or supratentorial or supra-tentorial or anterior circulat$ or posterior circulat$ or basal gangli$ or global or focal or parenchymal or subarachnoid or sub-arachnoid or putaminal or putamen or posterior fossa or intra-axial or intraaxial or lacunar) adj3 (arrest$ or attack$ or isch?emi$ or infarct$ or insufficien$ or emboli$ or occlus$ or hypox$ or vasospasm or obstruction or vasculopath$ or failure$ or thromb$ or h?emorrhag$ or microh?emorrhag$ or accident$ or h?ematoma$ or bleed$ or microbleed$ or insult$)).ti,ab,ot. (296096)
13 (CVA or CVAS or MCA$ or ICH or ICHs or CVST or CVSTs or CVDST or CVT or CVDSTs or CVTs or LVO or LVOs).ti,ab. (83193)
14 or/1-13 (873429)
15 ((diagnos$ or predict$ or specificity or sensitiv$) adj4 (criteria or criterion or guideline$ or pattern$ or trend$ or utili$ or management or prevalence or initiat$ or distribution$ or coverage or variety or selection or spread or alternative$ or frequen$)).ti,ab,ot. (500975)
16 diagnosis/ or early diagnosis/ (1447537)
17 exp brain scintiscanning/ (9877)
18 Neurologic examination/ (71424)
19 Computer assisted tomography/ (787646)
20 Brain radiography/ (7923)
21 ((Brain or cerebral or neurologic$ or CT or head) adj2 (scan$ or scintigraph$ or examination$ or angiograph$ or image analys$ or perfusion$ or radiograph$)).ti,ab,ot,hw. (394865)
22 (CAT scan$ or CTA or CTP or CTAs or CTPs or neuroimag$ or neuro-imag$ or (comput$ adj2 tomograph$)).ti,ab,ot,hw. (1322884)
23 (Gamma encephalograph$ or Gammaencephalograph$ or Radio encephalograph$ or Radioencephalograph$).ti,ab,ot,hw. (48)

24 or/15-23 (3154111)
25 14 and 15 (18433)
26 health-economics/ (33663)
27 exp economic-evaluation/ (323525)
28 exp health-care-cost/ (307833)
29 exp pharmacoeconomics/ (212823)
30 or/26-29 (684070)
31 (econom$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$).ti,ab. (1186225)
32 (expenditure$ not energy).ti,ab. (44234)
33 (value adj2 money).ti,ab. (2638)
34 budget$.ti,ab. (41819)
35 or/31-34 (1225642)
36 30 or 35 (1565097)
37 letter.pt. (1190591)
38 editorial.pt. (702926)
39 note.pt. (865546)
40 or/37-39 (2759063)
41 36 not 40 (1440016)
42 (metabolic adj cost).ti,ab. (1642)
43 ((energy or oxygen) adj cost).ti,ab. (4612)
44 ((energy or oxygen) adj expenditure).ti,ab. (33824)
45 or/42-44 (38934)
46 41 not 45 (1432035)
47 exp animal/ (27569658)
48 exp animal-experiment/ (2743270)
49 nonhuman/ (6663210)
50 (rat or rats or mouse or mice or hamster or hamsters or animal or animals or dog or dogs or cat or cats or bovine or sheep).ti,ab,sh. (5992658)
51 or/47-50 (29634110)
52 exp human/ (22733515)
53 exp human-experiment/ (554891)
54 52 or 53 (22735496)
55 51 not (51 and 54) (6899644)
56 46 not 55 (1300585)
57 25 and 56 (1126)
58 limit 57 to yr="2005 -Current" (988)

Economics terms based on Costs filter:
Centre for Reviews and Dissemination. Search strategies: NHS EED EMBASE using OvidSP (economics filter) [Internet]. York: Centre for Reviews and Dissemination; 2014 [accessed 2.6.14]. Available from: http://www.crd.york.ac.uk/crdweb/searchstrategies.asp#nhseedembase

MEDLINE(Ovid) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations and Daily: 2005-2021/09/15
Searched 16.9.21

1 exp Brain Ischemia/ (115093)
2 exp Intracranial Hemorrhages/ (74784)
3 Stroke/ (112477)
4 (Stroke$ or apople$ or cerebral vasc$ or cerebrovasc$ or cerebro vasc$ or poststroke$ or encephalorrhag$ or hematencephalon$ or large vessel occlusion$).ti,ab,ot. (325891)
5 ((brain or blood flow) adj2 disturb$).ti,ab,ot. (2108)
6 ((sinus or sagittal) adj3 thromb$).ti,ab,ot. (5069)
7 (isch?emi$ adj3 (seizure$ or attack$ or thrombo$ or embolic or encephalopath$ or neural)).ti,ab,ot. (26691)
8 ((Bleed$ or h?emorrhag$) adj2 corpus callosum).ti,ab,ot. (23)
9 ((brain or cerebr$ or cerebell$ or cortical or Intraparenchymal or intracortical or vertebrobasil$ or hemispher$ or intracran$ or intra-cran$ or intracerebral or intratentorial or intra-tentorial or intraventricular or intra-ventricular or periventricular or peri-ventricular or supratentorial or supra-tentorial or anterior circulat$ or posterior circulat$ or basal gangli$ or global or focal or parenchymal or subarachnoid or sub-arachnoid or putaminal or putamen or posterior fossa or intra-axial or intraaxial or lacunar) adj3 (arrest$ or attack$ or isch?emi$ or infarct$ or insufficien$ or emboli$ or occlus$ or hypox$ or vasospasm or obstruction or vasculopath$ or failure$ or thromb$ or h?emorrhag$ or microh?emorrhag$ or accident$ or h?ematoma$ or bleed$ or microbleed$ or insult$)).ti,ab,ot. (209964)
10 (CVA or CVAS or MCA$ or ICH or ICHs or CVST or CVSTs or CVDST or CVT or CVDSTs or CVTs or LVO or LVOs).ti,ab. (48598)
11 or/1-10 (554564)
12 ((diagnos$ or predict$ or specificity or sensitiv$) adj4 (criteria or criterion or guideline$ or pattern$ or trend$ or utili$ or management or prevalence or initiat$ or distribution$ or coverage or variety or selection or spread or alternative$ or frequen$)).ti,ab,ot. (348884)
13 Diagnosis/ (17470)
14 Early Diagnosis/ (28588)
15 Brain/dg [Diagnostic Imaging] (51013)
16 Stroke/dg [Diagnostic Imaging] (7589)
17 Radiography/ (322399)
18 exp Radionuclide Imaging/ (222597)
19 Neurologic Examination/ (27713)
20 Tomography, X-Ray Computed/ (398463)
21 ((Brain or cerebral or neurologic$ or CT or head) adj2 (scan$ or scintigraph$ or examination$ or angiograph$ or image analys$ or perfusion$ or radiograph$)).ti,ab,ot,hw. (228460)
22 (CAT scan$ or CTA or CTP or CTAs or CTPs or neuroimag$ or neuro-imag$ or (comput$ adj2 tomograph$)).ti,ab,ot,hw. (472827)
23 (Gamma encephalograph$ or Gammaencephalograph$ or Radio encephalograph$ or Radioencephalograph$).ti,ab,ot,hw. (155)
24 or/12-23 (1622669)
25 11 and 24 (99863)
26 economics/ (27366)
27 exp "costs and cost analysis"/ (249120)
28 economics, dental/ (1919)
29 exp "economics, hospital"/ (25299)
30 economics, medical/ (9153)
31 economics, nursing/ (4006)
32 economics, pharmaceutical/ (3018)

33 (economic$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$).ti,ab. (888235)
34 (expenditure$ not energy).ti,ab. (32593)
35 (value adj1 money).ti,ab. (36)
36 budget$.ti,ab. (31710)
37 or/26-36 (1045094)
38 ((energy or oxygen) adj cost).ti,ab. (4365)
39 (metabolic adj cost).ti,ab. (1538)
40 ((energy or oxygen) adj expenditure).ti,ab. (26701)
41 or/38-40 (31589)
42 37 not 41 (1037831)
43 letter.pt. (1151819)
44 editorial.pt. (580627)
45 historical article.pt. (365432)
46 or/43-45 (2077389)
47 42 not 46 (999755)
48 25 and 47 (1716)
49 exp animals/ not (exp animals/ and humans/) (4885879)
50 48 not 49 (1684)
51 limit 50 to yr="2005 -Current" (1233)

Costs filter:
Centre for Reviews and Dissemination. NHS EED Economics Filter: Medline (Ovid) monthly search [Internet]. York: Centre for Reviews and Dissemination; 2010 [cited 28.9.10]. Available from: http://www.york.ac.uk/inst/crd/intertasc/nhs_eed_strategies.html

NHS Economic Evaluation Database (NHS EED) (Internet)

(https://www.crd.york.ac.uk/CRDWeb/): 2005-2015/03
Searched: 16.9.2

1 MeSH DESCRIPTOR Brain Ischemia EXPLODE ALL TREES 328 Delete
2 MeSH DESCRIPTOR Intracranial Hemorrhages EXPLODE ALL TREES 258 Delete
3 MeSH DESCRIPTOR Stroke EXPLODE ALL TREES 1356 Delete
4 MeSH DESCRIPTOR Ischemic Stroke EXPLODE ALL TREES 0 Delete
5 MeSH DESCRIPTOR Hemorrhagic Stroke EXPLODE ALL TREES 0 Delete
6 ((Stroke* or apople* or "cerebral vasc*" or cerebrovasc* or "cerebro vasc*" or poststroke* or encephalorrhag* or hematencephalon* or "large vessel occlusion*")) 3402 Delete
7 ((((brain or "blood flow") and disturb*)) OR (((sinus or sagittal) and thromb*)) OR (((ischemi* or ischaemi*) and (seizure* or attack* or thrombo* or embolic or encephalopath* or neural)))) 691 Delete
8 ((((Bleed* or hemorrhag* or haemorrhag*) and "corpus callosum")) OR (((brain or cerebr* or cerebell* or cortical or Intraparenchymal or intracortical or vertebrobasil* or hemispher* or intracran* or intra-cran* or intracerebral or intratentorial or intra-tentorial or intraventricular or intra-ventricular or periventricular or peri-ventricular or supratentorial or supra-tentorial or anterior circulat* or "posterior circulat*" or "basal gangli*" or global or focal or parenchymal or subarachnoid or sub-arachnoid or putaminal or putamen or "posterior fossa" or intra-axial or intraaxial or lacunar) and (arrest* or attack* or ischemi* or ischaemi* or infarct* or insufficien* or emboli* or occlus* or

hypox* or vasospasm or obstruction or vasculopath* or failure* or thromb* or hemorrhag* or haemorrhag* or microhemorrhag* or microhaemorrhag* or accident* or hematoma* or haematoma* or bleed* or microbleed* or insult*))) OR (CVA or CVAS or MCA* or ICH or ICHs or CVST or CVSTs or CVDST or CVT or CVDSTs or CVTs or LVO or LVOs)) 2618 Delete

9 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8) 5187 Delete

10 MeSH DESCRIPTOR Diagnosis EXPLODE ALL TREES 29251 Delete

11 MeSH DESCRIPTOR Early Diagnosis EXPLODE ALL TREES 413 Delete

12 MeSH DESCRIPTOR brain EXPLODE ALL TREES WITH QUALIFIER DG IN NHSEED 0 Delete

13 MeSH DESCRIPTOR stroke EXPLODE ALL TREES WITH QUALIFIER DG IN NHSEED 0 Delete

14 MeSH DESCRIPTOR Radionuclide Imaging EXPLODE ALL TREES 725 Delete

15 MeSH DESCRIPTOR Neurologic Examination EXPLODE ALL TREES 772 Delete

16 ((((Brain or cerebral or neurologic* or CT or head) and (scan* or scintigraph* or examination* or angiograph* or "image analys*" or perfusion* or radiograph*))) OR (((diagnos* or predict* or specificity or sensitiv*) and (criteria or criterion or guideline* or pattern* or trend* or utili* or management or prevalence or initiat* or distribution* or coverage or variety or selection or spread or alternative* or frequen*))) OR (("CAT scan*" or CTA or CTP or neuroimag* or neuro-imag* or (comput* and tomograph*)))) 25348 Delete

17 (("Gamma encephalograph*" or Gammaencephalograph* or "Radio encephalograph*" or Radioencephalograph*)) 0 Delete

18 (#10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17) 40752 Delete

19 #9 AND #18 3280 Delete

20 (#19) IN NHSEED 1081 Delete

21 (#19) IN NHSEED FROM 2005 TO 2021 559 Delete

Econlit (EBSCO): 2005-2021/09/21
Searched: 21.9.21

S16 S13 AND S14 Limiters - Published Date: 20050101-20211231 82

S15 S13 AND S14 93

S14 S8 OR S9 OR S10 OR S11 OR S12 94,023

S13 S1 OR S2 OR S3 OR S4 OR S5 OR S6 430

S12 “Gamma encephalograph*” OR Gammaencephalograph* OR “Radio encephalograph*” OR Radioencephalograph* 0

S11 comput* N2 tomograph* 36

S10 “CAT scan*” OR CTA OR CTP OR neuroimag* OR neuro-imag* 174

S9 scan* OR scintigraph* OR examination* OR angiograph* OR "image analys*" OR perfusion* OR radiograph* 20,848

S8 diagnos* OR predict* 74,198

S7 TI (CVA OR CVAS OR MCA* OR ICH OR ICHs OR CVST OR CVSTs OR CVDST OR CVT OR CVDSTs OR CVTs OR LVO OR LVOs) OR AB (CVA OR CVAS OR MCA* OR ICH OR ICHs OR CVST OR CVSTs OR CVDST OR CVT OR CVDSTs OR CVTs OR LVO OR LVOs) 516

S6 TI (brain OR cerebr* OR cerebell* OR cortical OR Intraparenchymal OR intracortical OR vertebrobasil* OR hemispher* OR intracran* OR intra-cran* OR intracerebral OR intratentorial OR intra-tentorial OR intraventricular OR intra-ventricular OR periventricular OR peri-ventricular OR supratentrial OR supra-tentorial OR “anterior circulat*” OR “posterior circulat*” OR “basal gangli*”

OR global OR focal OR parenchymal OR subarachnoid OR sub-arachnoid OR putaminal OR putamen OR “posterior fossa” OR intra-axial OR intraaxial OR lacunar) AND TI(arrest* OR attack* OR isch?emi* OR infarct* OR insufficien* OR emboli* OR occlus* OR hypox* OR vasospasm OR obstruction OR vasculopath* OR failure* OR thromb* OR h?emorrhag* OR microh?emorrhag* OR accident* OR h?ematoma* OR bleed* OR microbleed* OR insult*) 68
S5 (Bleed N4 “corpus callosum”) or (h?emorrhag* n4 “corpus callosum”) 0
S4 TX isch?emi* 14
S3 TX (sinus N3 thromb*) or (sagittal N3 thromb*) 0
S2 TX (brain N2 disturb*) or (“blood flow” N2 disturb*) 1
S1 TX Stroke* OR apople* OR “cerebral vasc*” OR cerebrovasc* OR “cerebro vasc*” OR poststroke* OR encephalorrhag* OR hematencephalon* OR “large vessel occlusion*” 353

Science Citation Index Expanded (Web of Science): 2005-2021/09/21
Conference Proceedings Citation Index (Web of Science): 2005-2021/09/21
Searched: 21.9.21

27 #26 results from Science Citation Index Expanded (SCI-EXPANDED), Conference Proceedings Citation Index – Science (CPCI-S) 1,007
26 #14 AND 24 and 2005 or 2006 or 2007 or 2008 or 2009 or 2010 or 2011 or 2012 or 2013 or 2014 or 2015 or 2016 or 2017 or 2018 or 2019 or 2020 or 2021 (Publication Years) 1,106
25 #14 AND #24 1,350
24 #19 NOT #23 2,887,051
23 #20 OR #21 OR #22 319,156
22 TS=((energy or oxygen) SAME expenditure) 49,598
21 TS=(metabolic SAME cost) 17,108
20 TS=((energy or oxygen) SAME cost) 266,150
19 #15 OR #16 OR #17 OR #18 3,165,727
18 TS=(budget*) 146,577
17 TS=(value NEAR/1 money) 3,953
16 TS=(expenditure* not energy) 67,519
15 TS=(economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic*) 3,030,437
14 #8 AND #13 48,914
13 #12 OR #11 OR #10 OR #9 1,063,103
12 TS=(“Gamma encephalograph*” OR Gammaencephalograph* OR “Radio encephalograph*” OR Radioencephalograph*) 1
11 TS=(“CAT scan*” OR CTA OR CTP OR CTAs OR CTPs OR neuroimag* OR neuro-imag* OR (comput* NEAR/2 tomograph*)) 447,821
10 TS=((Brain OR cerebral OR neurologic* OR CT OR head) NEAR/2 (scan* OR scintigraph* OR examination* OR angiograph* OR "image analys*" OR perfusion* OR radiograph*)) 177,922
9 TS=((diagnos* OR predict* OR specificity OR sensitiv*) NEAR/4 (criteria OR criterion OR guideline* OR pattern* OR trend* OR utili* OR management OR prevalence OR initiat* OR distribution* OR coverage OR variety OR selection OR spread OR alternative* OR frequen*)) 537,076
8 #7 OR #6 OR #5 OR #4 OR #3 OR #2 OR #1 541,925
7 TI=(CVA OR CVAS OR MCA* OR ICH OR ICHs OR CVST OR CVSTs OR CVDST OR CVT OR CVDSTs OR CVTs OR LVO OR LVOs) OR AB=(CVA OR CVAS OR MCA* OR ICH OR ICHs OR CVST OR CVSTs OR CVDST OR CVT OR CVDSTs OR CVTs OR LVO OR LVOs) 60,217
6 TS=((brain OR cerebr* OR cerebell* OR cortical OR Intraparenchymal OR intracortical OR vertebrobasil* OR hemispher* OR intracran* OR intra-cran* OR intracerebral OR intratentorial OR intra-tentorial OR intraventricular OR intra-ventricular OR periventricular OR peri-ventricular OR

supratentrial OR supra-tentorial OR “anterior circulat*” OR “posterior circulat*” OR “basal gangli*” OR global OR focal OR parenchymal OR subarachnoid OR sub-arachnoid OR putaminal OR putamen OR “posterior fossa” OR intra-axial OR intraaxial OR lacunar) NEAR/3 (arrest* OR attack* OR isch?emi* OR infarct* OR insufficien* OR emboli* OR occlus* OR hypox* OR vasospasm OR obstruction OR vasculopath* OR failure* OR thromb* OR h?emorrhag* OR microh?emorrhag* OR accident* OR h?ematoma* OR bleed* OR microbleed* OR insult*)) 133,540
5 TS=((Bleed* OR h?emorrhag*) NEAR/2 “corpus callosum”) 10
4 TS=(isch?emi* NEAR/3 (seizure* OR attack* OR thrombo* OR embolic OR encephalopath* OR neural)) 4,529
3 TS=((sinus OR sagittal) NEAR/3 thromb*) 5,630
2 TS=((brain OR “blood flow”) NEAR/2 disturb*) 2,569
1 TS=((Stroke* OR apople* OR “cerebral vasc*” OR cerebrovasc* OR “cerebro vasc*” OR poststroke* OR encephalorrhag* OR hematencephalon* OR “large vessel occlusion*”)) 426,003

RePEc: Research Papers in Economics http://repec.org/): 2005-2021/09/21
Searched 21.9.21

Keywords in whole record

((stroke | "brain ischemia" | "brain ischaemia" | "blood vessel occlusion" | "cerebral ischemia" | "cerebral ischaemia" | "large vessel occlusion" | "intracranial haemorrhage" | "intracranial hemorrhage") + (diagnose | diagnostic | diagnostics | scan | scans | scintigraph | angiograph | radiograph | CTA | CTP | CTAs | CTPs | neuroimaging | neuro-imaging))
Limit: 2005-2021

Found 79 records

HRQoL and Utilities

Database	Dates covered	Hits
Embase	1974-2021/11/01	1,254
CEA Registry	up to 2021/07/14	788
Total		**2,042**

Embase (Ovid): 1974-2021/11/01
Searched: 12.8.21

Stroke + EQ5D only

1 exp brain ischemia/ (201252)
2 exp brain hemorrhage/ (154320)
3 basal ganglion hemorrhage/ (674)
4 cerebrovascular accident/ (233847)
5 brain infarction/ (56899)
6 blood vessel occlusion/ (12067)
7 (Stroke$ or apople$ or cerebral vasc$ or cerebrovasc$ or cerebro vasc$ or poststroke$ or encephalorrhag$ or hematencephalon$ or large vessel occlusion$).ti,ab,ot. (511132)

8 ((brain or blood flow) adj2 disturb$).ti,ab,ot. (2937)
9 ((sinus or sagittal) adj3 thromb$).ti,ab,ot. (7415)
10 (isch?emi$ adj3 (seizure$ or attack$ or thrombo$ or embolic or encephalopath$ or neural)).ti,ab,ot. (41482)
11 ((Bleed$ or h?emorrhag$) adj2 corpus callosum).ti,ab,ot. (27)
12 ((brain or cerebr$ or cerebell$ or cortical or Intraparenchymal or intracortical or vertebrobasil$ or hemispher$ or intracran$ or intra-cran$ or intracerebral or intratentorial or intra-tentorial or intraventricular or intra-ventricular or periventricular or peri-ventricular or supratentorial or supra-tentorial or anterior circulat$ or posterior circulat$ or basal gangli$ or global or focal or parenchymal or subarachnoid or sub-arachnoid or putaminal or putamen or posterior fossa or intra-axial or intraaxial or lacunar) adj3 (arrest$ or attack$ or isch?emi$ or infarct$ or insufficien$ or emboli$ or occlus$ or hypox$ or vasospasm or obstruction or vasculopath$ or failure$ or thromb$ or h?emorrhag$ or microh?emorrhag$ or accident$ or h?ematoma$ or bleed$ or microbleed$ or insult$)).ti,ab,ot. (298685)
13 (CVA or CVAS or MCA$ or ICH or ICHs or CVST or CVSTs or CVDST or CVT or CVDSTs or CVTs or LVO or LVOs).ti,ab. (84175)
14 or/1-13 (881919)
15 (eq-5d or eq5d or eq-5 or eq5 or euro qual or euroqual or euro qual5d or euroqual5d or euro qol or euroqol or euro qol5d or euroqol5d or euro quol or euroquol or euro quol5d or euroquol5d or eur qol or eurqol or eur qol5d or eur qol5d or eur?qul or eur?qul5d or euro$ quality of life or european qol).ti,ab. (25202)
16 (euro$ adj3 (5 d or 5d or 5 dimension$ or 5dimension$ or 5 domain$ or 5domain$)).ti,ab. (7370)
17 or/15-16 (25235)
18 14 and 17 (1510)
19 (letter or editorial or note).pt. (2774277)
20 conference.so. (589741)
21 18 not (19 or 20) (1254)

CEA Registry (http://www.cearegistry.org): up to 2021/07/14
Searched: 14.7.21

Keywords	Ratios	Utility weights
Ischaemic stroke	44	100/130
Ischemic stroke	100/243	100/502
haemorrhagic stroke	9	57
large vessel occlusion	9	13
hemorrhagic stroke	31	100/136
intracranial haemorrhage	8	98
intracranial hemorrhage	49	100/228
Total	**220/250 (dupes removed)**	**568/1,164**

Review of reviews

Database	Dates covered	Hits
CDSR	up to 2021/10/Iss10	404
KSR Evidence	up to 2021/10/14	498
Total		**902**

CDSR (Wiley): up to 2021/10/Iss10
Searched: 14.10.21

Stroke + CTscan/Diagnostics

#1 MeSH descriptor: [Brain Ischemia] explode all trees 3805
#2 MeSH descriptor: [Intracranial Hemorrhages] explode all trees 2064
#3 (Stroke* or apople* or cerebral-vasc* or cerebrovasc* or cerebro-vasc* or poststroke* or encephalorrhag* or hematencephalon* or large-vessel-occlusion*):ti,ab,kw 68306
#4 ((brain or blood flow) near/2 disturb*):ti,ab,kw 168
#5 ((sinus or sagittal) near/3 thromb*):ti,ab,kw 216
#6 ((ischaemi* or ischemi*) near/3 (seizure* or attack* or thrombo* or embolic or encephalopath* or neural)):ti,ab,kw 4859
#7 ((Bleed* or hemorrhag* or haemorrhag*) near/2 corpus-callosum):ti,ab,kw 0
#8 ((brain or cerebr* or cerebell* or cortical or Intraparenchymal or intracortical or vertebrobasil* or hemispher* or intracran* or intra-cran* or intracerebral or intratentorial or intra-tentorial or intraventricular or intra-ventricular or periventricular or peri-ventricular or supratentorial or supra-tentorial or anterior-circulat* or posterior-circulat* or basal-gangli* or global or focal or parenchymal or subarachnoid or sub-arachnoid or putaminal or putamen or posterior-fossa or intra-axial or intraaxial or lacunar) near/3 (arrest* or attack* or ischaemi* or ischemi* or infarct* or insufficien* or emboli* or occlus* or hypox* or vasospasm or obstruction or vasculopath* or failure* or thromb* or hemorrhag* or haemorrhag* or microhemorrhag* or microhaemorrhad or haemorrhag* or accident* or hematoma* or haemotoma* or bleed* or microbleed* or insult*)):ti,ab,kw 35512
#9 (CVA or CVAS or MCA* or ICH or ICHs or CVST or CVSTs or CVDST or CVT or CVDSTs or CVTs or LVO or LVOs):ti,ab,kw 5080
#10 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 83530
#11 ((diagnos* or predict* or specificity or sensitiv*) near/4 (criteria or criterion or guideline* or pattern* or trend* or utili* or management or prevalence or initiat* or distribution* or coverage or variety or selection or spread or alternative* or frequen*)):ti,ab,kw 31376
#12 MeSH descriptor: [Diagnosis] explode all trees 347283
#13 MeSH descriptor: [Early Diagnosis] explode all trees 1859
#14 MeSH descriptor: [Brain] explode all trees and with qualifier(s): [diagnostic imaging - DG] 1750
#15 MeSH descriptor: [Radiography] explode all trees 21297
#16 MeSH descriptor: [Radionuclide Imaging] explode all trees 4690
#17 MeSH descriptor: [Neurologic Examination] explode all trees 24248
#18 MeSH descriptor: [Tomography, X-Ray Computed] explode all trees 5244
#19 ((Brain or cerebral or neurologic* or CT or head) near/2 (scan* or scintigraph* or examination* or angiograph* or image analys* or perfusion* or radiograph*)):ti,ab,kw 16002
#20 (Gamma-encephalograph* or Gammaencephalograph* or Radio-encephalograph* or Radioencephalograph*):ti,ab,kw 0
#21 (CAT scan* or CTA or CTP or neuroimag* or neuro-imag* or (comput* near/2 tomograph*)):ti,ab,kw 24745
#22 #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 397794
#23 #10 and #22 23138

CDSR retrieved = 404

KSR Evidence (KSR Ltd): up to 2021/10/14
Searched: 14.10.21

Query Results
1 (Stroke* or apople* or "cerebral vasc*" or cerebrovasc* or "cerebro vasc*" or poststroke* or encephalorrhag* or hematencephalon* or "large vessel occlusion*") in Title or Abstract 7315 results
2 ((brain or "blood flow") adj2 disturb*) in Title or Abstract 14 results
3 ((sinus or sagittal) adj3 thromb*) in Title or Abstract 37 results
4 ((ischemi* or ischaemi*) adj3 (seizure* or attack* or thrombo* or embolic or encephalopath* or neural)) in Title or Abstract 639 results
5 ((Bleed* or hemorrhag* or haemorrhag*) adj2 "corpus callosum") in Title or Abstract 1 result
6 CVA or CVAS or MCA* or ICH or ICHs or CVST or CVSTs or CVDST or CVT or CVDSTs or CVTs or LVO or LVOs in Title or Abstract 582 results
7 ((brain or cerebr* or cerebell* or cortical or Intraparenchymal or intracortical or vertebrobasil* or hemispher* or intracran* or intra-cran* or intracerebral or intratentorial or intra-tentorial or intraventricular or intra-ventricular or periventricular or peri-ventricular or supratentorial or supra-tentorial or "anterior circulat*" or "posterior circulat*" or "basal gangli*" or global or focal or parenchymal or subarachnoid or sub-arachnoid or putaminal or putamen or "posterior fossa" or intra-axial or intraaxial or lacunar) adj3 (arrest* or attack* or ischemi* or ischaemi* or infarct* or insufficien* or emboli* or occlus* or hypox* or vasospasm or obstruction or vasculopath* or failure* or thromb* or hemorrhag* or haemorrhag* or microhemorrhag* or microhaemorrhag* or accident* or hematoma* or haematoma* or bleed* or microbleed* or insult*)) in Title or Abstract 2368 results
8 #1 or #2 or #3 or #4 or #5 or #6 or #7 in All text 8597 results
9 ((diagnos* or predict* or specificity or sensitiv*) adj4 (criteria or criterion or guideline* or pattern* or trend* or utili* or management or prevalence or initiat* or distribution* or coverage or variety or selection or spread or alternative* or frequen*)) in Title or Abstract 5493 results
10 ((Brain or cerebral or neurologic* or CT or head) adj2 (scan* or scintigraph* or examination* or angiograph* or "image analys*" or perfusion* or radiograph*)) in Title or Abstract 759 results
11 ("CAT scan*" or CTA or CTP or neuroimag* or neuro-imag* or (comput* adj2 tomograph*)) in Title or Abstract 2808 results
12 "Gamma encephalograph*" or Gammaencephalograph* or "Radio encephalograph*" or Radioencephalograph* in Title or Abstract 0 results
13 #9 or #10 or #11 or #12 in All text 8410 results
14 #8 and #13 in All text 498 results

Accuracy of human readers

Database	**Dates covered**	**Hits**
Medline + PreMedline	2017-2021/10/15	2,726
Total		**2,726**

MEDLINE and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations, Daily and Versions (Ovid): 2017-2021/10/15
Searched 19.10.21

Stroke + CTscan/Diagnostics + reader (Limits 2017-C, Not Covid)

1 exp Brain Ischemia/ (115589)
2 exp Intracranial Hemorrhages/ (75053)
3 Stroke/ (113288)
4 (Stroke$ or apople$ or cerebral vasc$ or cerebrovasc$ or cerebro vasc$ or poststroke$ or encephalorrhag$ or hematencephalon$ or large vessel occlusion$).ti,ab,ot. (327818)
5 ((brain or blood flow) adj2 disturb$).ti,ab,ot. (2117)
6 ((sinus or sagittal) adj3 thromb$).ti,ab,ot. (5117)
7 (isch?emi$ adj3 (seizure$ or attack$ or thrombo$ or embolic or encephalopath$ or neural)).ti,ab,ot. (26850)
8 ((Bleed$ or h?emorrhag$) adj2 corpus callosum).ti,ab,ot. (23)
9 ((brain or cerebr$ or cerebell$ or cortical or Intraparenchymal or intracortical or vertebrobasil$ or hemispher$ or intracran$ or intra-cran$ or intracerebral or intratentorial or intra-tentorial or intraventricular or intra-ventricular or periventricular or peri-ventricular or supratentorial or supra-tentorial or anterior circulat$ or posterior circulat$ or basal gangli$ or global or focal or parenchymal or subarachnoid or sub-arachnoid or putaminal or putamen or posterior fossa or intra-axial or intraaxial or lacunar) adj3 (arrest$ or attack$ or isch?emi$ or infarct$ or insufficien$ or emboli$ or occlus$ or hypox$ or vasospasm or obstruction or vasculopath$ or failure$ or thromb$ or h?emorrhag$ or microh?emorrhag$ or accident$ or h?ematoma$ or bleed$ or microbleed$ or insult$)).ti,ab,ot. (210934)
10 (CVA or CVAS or MCA$ or ICH or ICHs or CVST or CVSTs or CVDST or CVT or CVDSTs or CVTs or LVO or LVOs).ti,ab. (48905)
11 or/1-10 (557308)
12 ((diagnos$ or predict$ or specificity or sensitiv$) adj4 (criteria or criterion or guideline$ or pattern$ or trend$ or utili$ or management or prevalence or initiat$ or distribution$ or coverage or variety or selection or spread or alternative$ or frequen$)).ti,ab,ot. (350992)
13 Diagnosis/ (17472)
14 Early Diagnosis/ (28758)
15 Brain/dg [Diagnostic Imaging] (51780)
16 Stroke/dg [Diagnostic Imaging] (7712)
17 Radiography/ (322703)
18 exp Radionuclide Imaging/ (223371)
19 Neurologic Examination/ (27754)
20 Tomography, X-Ray Computed/ (399785)
21 ((Brain or cerebral or neurologic$ or CT or head) adj2 (scan$ or scintigraph$ or examination$ or angiograph$ or image analys$ or perfusion$ or radiograph$)).ti,ab,ot,hw. (229398)
22 (CAT scan$ or CTA or CTP or CTAs or CTPs or neuroimag$ or neuro-imag$ or (comput$ adj2 tomograph$)).ti,ab,ot,hw. (475578)
23 (Gamma encephalograph$ or Gammaencephalograph$ or Radio encephalograph$ or Radioencephalograph$).ti,ab,ot,hw. (155)
24 or/12-23 (1629565)
25 11 and 24 (100335)
26 (rater$ or reader$ or inter-rater$ or inter-reader$ or radiologist$ or resident$ or consultant$ or expert$ or experience$).ti,ab,ot. (1674641)
27 25 and 26 (9582)

28 limit 27 to yr="2017 -Current" (2790)
29 coronavirus/ or betacoronavirus/ or coronavirus infections/ (46824)
30 (Betacoronavirus$ or Sars-cov-2 or sars-cov2 or sarscov-2 or SARSCOV2 or Coronavirus$ or corona virus$ or covid-19 or covid19$ or 2019-ncov or corona-virus$ or wuhan-2019-ncov or cov19 or cov-19 or coronavirinae or Coronaviridae or CV19 or 2019nCoV or 19nCoV or nCoV$ or COVID).ti,ab,ot,hw,kw. (203858)
31 ((new or novel or "19" or "2019" or Wuhan or Hubei or China or Chinese) adj5 (virus$ or pneumonia$ or outbreak$ or epidemic$ or pandemic$ or influenza or flu or CoV or HCoV)).ti,ab,ot,hw,kw. (129317)
32 or/29-31 (243973)
33 28 not 32 (2726)

Review of reviews: Alteplase

Database	Dates covered	Hits
CDSR	up to 2021/11/Iss11	15
KSR Evidence	up to 2021/11/11	191
Total		**206**

Cochrane Database of Systematic Reviews (CDSR)(Wiley): up to 2021/11/Iss11
Searched 11.11.21
ID Search Hits
#1 MeSH descriptor: [Tissue Plasminogen Activator] explode all trees 1729
#2 (Alteplase or Activase or Actilyse or activacin or atlepase or Cathflo Activase or g 11021 or g 11035 or g 11044 or g11021 or g11035 or g11044 or gmk 527 or gmk527 or grtpa or ly 210825 or ly210825 or mmr 701 or mmr701 or td 2061 or td2061 or tisokinase):ti,ab 1158
#3 (t-PA or rt-PA or rtpa or ttpa):ti,ab 2903
#4 (tissue* near/3 plasminogen near/3 activator):ti,ab 2485
#5 (tissue* near/3 activator near/3 plasminogen):ti,ab 2480
#6 (plasminogen near/3 activator near/3 tissue*):ti,ab 2486
#7 (plasminogen near/3 tissue* near/3 activator):ti,ab 2485
#8 #1 or #2 or #3 or #4 or #5 or #6 or #7 5068

CDSR retrieved 15 results

KSR evidence: up to 2021/11/11
Searched 11.11.21
1 (Alteplase or Activase or Actilyse or activacin or atlepase or Cathflo Activase or g 11021 or g 11035 or g 11044 or g11021 or g11035 or g11044 or gmk 527 or gmk527 or grtpa or ly 210825 or ly210825 or mmr 701 or mmr701 or td 2061 or td2061 or tisokinase) in All text 79 results
2 (t-PA or rt-PA or rtpa or ttpa) in Title or Abstract 50 results
3 (tissue* near/3 plasminogen near/3 activator) in Title or Abstract 118 results
4 (tissue* near/3 activator near/3 plasminogen) in Title or Abstract 118 results
5 (plasminogen near/3 activator near/3 tissue*) in Title or Abstract 118 results
6 (plasminogen near/3 tissue* near/3 activator) in Title or Abstract 118 results
7 #1 or #2 or #3 or #4 or #5 or #6 in All text 191 results

APPENDIX 2: DATA EXTRACTION TABLES

Table 32: Baseline study details

Study Details	Selection criteria	Participant details	AI intervention
Adhya 2021[33] **Publication type:** Full paper **Country:** USA **Funding:** None: 'The author(s) received no financial support for the research, authorship, and/or publication of this article.' **Recruitment:** November 2019 to November 2020 (retrospective) **Number of participants:** 310	**Inclusion criteria:** All patients who received CTA for the evaluation of AIS or neurological deficit that included RAPID-CTA with relative vessel density of 60% or less **Exclusion criteria:** NR **Research Question:** (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?	**Mean (SD) age, years:** 70 (NR) **Male (%):** 145 (47) **No further participant characteristics were reported**	Rapid CTA

Study Details	Selection criteria	Participant details	AI intervention
Al-Kawaz 2021[34] **Publication type:** Full paper **Country:** USA **Funding:** None: 'The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.' **Recruitment:** June 2019 to October 2020 (retrospective) **Number of participants:** 64	**Inclusion criteria:** Patients presenting with LVO **Exclusion criteria:** NR **Research Question:** (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention? (Q2b) Is AI-derived software assisted review of CT perfusion brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke after a CTA brain scan a clinically effective intervention?	***Intervention:*** **Median (IQR) age, years:** 67 (57, 81) **Male (%):** 17 (51.5) **Diabetes (%):** 11 (33.3) **Hypertension (%):** 27 (81.8) **Baseline NIHSS, median (IQR):** 15 (10, 22) ***Comparator:*** **Median (IQR) age, years:** 69.5 (60, 77) **Male (%):**16 (48.5) **Diabetes (%):** 11 (33.3) **Hypertension (%):** 25 (80.6) **Baseline NIHSS, median (IQR):** 11 (9, 18) **There were no significant differences, in baseline characteristics, between groups**	RapidAI

Study Details	Selection criteria	Participant details	AI intervention
Amukotuwa 2019a,[35] DEFUSE 2 and 3, plus three additional cohorts (one of which was the Amukotwa 2019b cohort) **Publication type:** Full paper **Country:** NR **Funding:** Public: 'This study was funded by grants from the National Institutes of Health: 1R01EB002711, 1R01NS039325, and 1U10NS086487.' Individual study authors disclosed shareholdings in or fees from iScemaView. **Recruitment:** July 2008 to December 2018 (retrospective) **Number of participants:** 926	**Inclusion criteria:** NR **Exclusion criteria:** Screen failure; CTA not included in the acute CT protocol; inadequate data format; CTA deemed, by an experienced neuroradiologist, to be technically inadequate to allow accurate interpretation by a human reader **Research Question:** (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?	**Median (IQR) age, years:** 70 (58, 80) **Male (%):** 504 (54.4) **Baseline NIHSS, median (IQR):** 14 (9, 19) **No further participant characteristics were reported**	Rapid CTA

Study Details	Selection criteria	Participant details	AI intervention
Amukotuwa 2019b[36] **Publication type:** Full paper **Country:** Australia **Funding:** None; individual study authors disclosed receipt of support and/or consulting fees from iScemaView **Recruitment:** January 2017 to December 2018 (retrospective) **Number of participants:** 477	**Inclusion criteria:** Consecutive adult (≥18 years) patients who had undergone multimodal brain CT for suspected AIS within 24 hours of symptom onset or last seen well **Exclusion criteria:** Technically inadequate CTA (poor contrast bolus or substantial motion or metal artifact that precluded accurate assessment of the intracranial arteries to the level of the distal M2 segments of the middle cerebral arteries by an experienced neuroradiologist); thin slice CTA images unavailable **Research Question:** (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?	**Median (IQR) age, years:** 70(60, 80) **Male (%):** 271 (56.8) **Baseline NIHSS, median (IQR):** 6 (2, 9) **No further participant characteristics were reported**	Rapid CTA
Barreira 2018a,[60] **ALADIN** Barreira 2018b[37] Rodrigues 2019a[38] **Publication type:** Conference abstract **Country:** USA **Funding:** NR **Recruitment:** NR 201 to NR 2017 (retrospective) **Number of participants:** 875	**Inclusion criteria:** Random sample from a retrospective cohort of AIS patients with and without anterior circulation LVOs **Exclusion criteria:** NR **Research Question:** (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?	**Male (%):**433 (49.5) **Baseline NIHSS, median (IQR):** 15 (10, 20) **No further participant characteristics were reported**	Viz LVO

Study Details	Selection criteria	Participant details	AI intervention
Barreira 2018d,[39] ADVANCE **Publication type:** Conference abstract **Country:** USA **Funding:** NR **Recruitment:** NR 201 to NR 2017 (retrospective) **Number of participants:** 284	**Inclusion criteria:** Random sample from a cohort of stroke patients with and without ICH **Exclusion criteria:** NR **Research Question:** (Q1) Is AI-derived software assisted review of non-enhanced CT brain scans for guiding thrombolysis treatment decisions for people with suspected acute stroke a clinically effective intervention?	**No participant characteristics were reported**	Viz ICH
Chatterjee 2018[40] **Publication type:** Conference abstract **Country:** USA **Funding:** NR **Recruitment:** NR (retrospective) **Number of participants:** 54	**Inclusion criteria:** Patients with acute stroke CTA studies **Exclusion criteria:** NR **Research Question:** (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?	**No participant characteristics were reported**	Viz LVO

Study Details	Selection criteria	Participant details	AI intervention
Dehkharghani 2021[41] Dehkharghani 2021[42] **Publication type:** Full paper **Country:** USA; Switzerland; Brazil **Funding:** Industry: 'Supported by iSchemaView.' **Recruitment:** NR (retrospective) **Number of participants:** 217	**Inclusion criteria**: Individuals undergoing cerebrovascular CTA, from the CRISP and DASH trials and from institutional registries of participating hospitals; technically adequate, thin section (≤2 mm) contiguous cerebrovascular CTA sources axial images, free of artifacts that would degrade interpretation by human readers (e.g., those related to severe metallic streak or beam hardening) **Exclusion criteria:** Age <18 years **Research Question:** (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?	**Mean (SD) age, years:** 64 (16) **Male (%):** 116 (54) **No further participant characteristics were reported**	Rapid CTA
Dornbos 2020[43] **Publication type:** Conference abstract **Country:** USA **Funding:** NR **Recruitment:** May 2019 to December 2019 (retrospective) **Number of participants:** 680	**Inclusion criteria:** Consecutive stroke cases **Exclusion criteria:** NR **Research Question:** (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?	**No participant characteristics were reported**	Viz LVO

Study Details	Selection criteria	Participant details	AI intervention
Gunda 2020[44] **Publication type:** Conference abstract **Country:** Hungary **Funding:** NR **Recruitment:** 'Two identical 7-month periods in 2017 and 2108' (retrospective) **Number of participants:** 797	**Inclusion criteria**: Stroke patients (no further details reported) **Exclusion criteria:** NR **Research Question:** (Q1) Is AI-derived software assisted review of non-enhanced CT brain scans for guiding thrombolysis treatment decisions for people with suspected acute stroke a clinically effective intervention? (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?	**No participant characteristics were reported**	Brainomix eASPECTS and eCTA

Study Details	Selection criteria	Participant details	AI intervention
Hassan 2021a[45] **Publication type:** Conference abstract **Country:** USA **Funding:** NR **Recruitment:** November 2016 to November 2020 (retrospective) **Number of participants:** 188	**Inclusion criteria:** LVO transfer patients who arrived at a comprehensive care centre for two years prior to and after implementation of AI software in November 2018 **Exclusion criteria:** NR **Research Question:** (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?	***Intervention:*** **Mean (SD) age, years:** 69.9 (15.8) **Male (%):** 58 (56.9) **Ethnicity (%):** White 26 (25.5); Hispanic 78 (76.5); African American 0 (0); Asian 0 (0) **AF (%):** 21 (20.6) **Diabetes (%):** 51 (50) **Smoking (%):** 9 (8.8) **Hypertension (%):** 81 (79.4) **Previous TIA/stroke (%):** 24 (23.5) **Baseline NIHSS, mean (SD):** 15.9 (7.1) ***Comparator:*** **Mean (SD) age, years:** 68.5 (13.1) **Male (%):** 51 (59.3) **Ethnicity:** White 16 (18.6); Hispanic 68 (79.1); African American 1 (1.2); Asian 1 (1.2) **AF (%):** 19 (22.1) **Diabetes (%):** 45 (52.3) **Smoking (%):** 7 (8.1) **Hypertension (%):** 69 (80.2) **Previous TIA/stroke (%):** 23 (26.7) **Baseline NIHSS, mean (SD):** 16.1 (8.3) **There were no significant differences, in baseline characteristics, between groups**	Viz LVO

Study Details	Selection criteria	Participant details	AI intervention
Hassan 2020[46] Hassan 2021b[47] **Publication type:** Full paper **Country:** USA **Funding:** None: 'The author(s) received no financial support for the research, authorship, and/or publication of this article.' One study author disclosed receipt of fees from Viz.ai. **Recruitment:** February 2017 to May 2019 (retrospective) **Number of participants:** 43	**Inclusion criteria:** LVO transfer patients from a single primary care centre, transferred to a comprehensive care centre **Exclusion criteria:** NR **Research Question:** (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?	***Intervention:*** **Mean (SD) age, years:** 69.1 (13.3) **Male (%):** 6 (40.0) **Ethnicity:** White 5 (30); Hispanic 10 (70); African American 0 (0); Asian 0 (0) **AF (%):** 1 (6.7) **Diabetes (%):** 7 (46.7) **Smoking (%):** 2 (13.3) **Hypertension (%):** 13 (86.7) **Baseline NIHSS, mean (SD):** 14.1 (6.8) ***Comparator:*** **Mean (SD) age, years:** 71.6 (12.3) **Male (%):** 15 (53.4) **Ethnicity:** White 5 (17.9); Hispanic 23 (82.1); African American 0 (0); Asian 0 (0) **AF (%):** 10 (35.7) **Diabetes (%):** 12 (42.9) **Smoking (%):** 2 (7.1) **Hypertension (%):** 25 (89.3) **Baseline NIHSS, mean (SD):** 18.3 (7.4) **There were no significant differences, in baseline characteristics, between groups**	Viz LVO

Study Details	Selection criteria	Participant details	AI intervention
Herweh 2020[48] **Publication type:** Conference abstract **Country:** NR **Funding:** NR **Recruitment:** NR (retrospective) **Number of participants:** 160	**Inclusion criteria:** Patients with suspected AIS **Exclusion criteria:** NR **Research Question:** (Q1) Is AI-derived software assisted review of non-enhanced CT brain scans for guiding thrombolysis treatment decisions for people with suspected acute stroke a clinically effective intervention?	**No participant characteristics were reported**	Brainomix
Kamal 2017[49] **Publication type:** Conference abstract **Country:** NR **Funding:** NR **Recruitment:** January 2014-July 2016 (retrospective) **Number of participants:** 186	**Inclusion criteria:** Patients undergoing thrombectomy (no further details reported) **Exclusion criteria:** NR **Research Question:** (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention? (Q2b) Is AI-derived software assisted review of CT perfusion brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke after a CTA brain scan a clinically effective intervention?	***Intervention:*** **Mean (SD) age, years:** 63.0 (16.0) **Male (%):** 24 (48.0) **Diabetes (%):** 12/43 (27.9) **Smoking (%):** 15/43 (24.9) **Baseline NIHSS, Mean (SD):** 20.0 (7.0) ***Comparator:*** **Mean (SD) age, years:** 61.0 (15.0) **Male (%):** 89(65.4) **Diabetes (%):** 26/100 (26) **Smoking (%):** 21/101 (20.8) **Baseline NIHSS, Mean (SD):** 17.0 (6.0) **There were no significant differences, in baseline characteristics, between groups**	RapidAI

Study Details	Selection criteria	Participant details	AI intervention
Kauw 2020[50] **Publication type:** Full paper **Country:** Netherlands; USA **Funding:** Public: 'Dutch Heart Foundation and the Netherlands Organization for Scientific Research, domain Applied and Engineering Sciences, as part of their joint strategic research program: Earlier Recognition of Cardiovascular Disease (grant number 14732).' **Recruitment:** NR 2012 to NR 2018 (retrospective) **Number of participants:** 176	**Inclusion criteria:** Consecutive patients with AIS undergoing CTP for thrombectomy triage **Exclusion criteria:** NR **Research Question:** (Q2b) Is AI-derived software assisted review of CT perfusion brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke after a CTA brain scan a clinically effective intervention?	**Mean (SD) age, years:** 72 (15) **Male (%):** 86 (49) **No further participant characteristics were reported**	Rapid CTP

Study Details	Selection criteria	Participant details	AI intervention
Mair 2021,[62] **RITeS** **Publication type:** Full paper (pre-publication) **Funding:** [redacted] **Recruitment:** [redacted] **Number of participants:** [redacted]	**Inclusion criteria:** [redacted] **Exclusion criteria:** [redacted] **Research Question:** (Q1) Is AI-derived software assisted review of non-enhanced CT brain scans for guiding thrombolysis treatment decisions for people with suspected acute stroke a clinically effective intervention?	[redacted]	[redacted]

Study Details	Selection criteria	Participant details	AI intervention
McLouth 2021[51] **Publication type:** Full paper **Country:** USA **Funding:** NR; individual study authors declared employment by or stockholding in Avicenna.ai **Recruitment:** NR 2017 to NR 2019 (retrospective) **Number of participants:** 378	**Inclusion criteria:** Patients with suspected LVO, on clinical grounds, in whom CTA studies had been performed, identified from University of California, Irvine (UCI) and a teleradiology service, vRAD (Minneapolis, USA) databases using key words such as "CTA", "head" and "large vessel occlusion". **Exclusion criteria:** NR **Research Question:** (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?	**Male (%):** 185 (40.9) **No further participant characteristics were reported**	CINA LVO

Study Details	Selection criteria	Participant details	AI intervention
Morey 2020a[52] Morey 2020b[53] Morey 2021[54] **Publication type:** Full paper **Country:** USA **Funding:** None: 'This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.' **Recruitment:** July 2018 to March 2020 (retrospective) **Number of participants:** 55	**Inclusion criteria:** Consecutive patients who presented to a primary stroke centre that used Viz LVO and who were transferred to a thrombectomy capable stroke centre or comprehensive stroke centre for LVO stroke and underwent thrombectomy **Exclusion criteria:** Inpatient at the time of stroke; thrombectomy decision delayed due to fluctuating symptoms **Research Question:** (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?	***Intervention:*** **Mean (SD) age, years:** 72.8 (15.4) **Male (%):** 13 (50) **AF (%):** 14 (53.8) **Diabetes (%):** 8 (30.8) **Hypertension (%):** 14 (53.8) **Previous TIA/stroke (%):** 2 (7.7) **Baseline NIHSS, median (IQR):** 14 (NR, NR) ***Comparator:*** **Mean (SD) age, years:** 76.2 (13.9) **Male (%):** 14 (48.3) **AF (%):** 15 (55.6) **Diabetes (%):** 12 (42.9) **Hypertension (%):** 23 (82.1) **Previous TIA/stroke (%):** 6 (20.7) **Baseline NIHSS, median (IQR):** 17 (NR, NR) **The proportion of patients with hypertension significantly lower in the intervention than in the comparator group**	Viz LVO

Study Details	Selection criteria	Participant details	AI intervention
Paz 2021[55] **Publication type:** Full paper **Country:** Canada **Funding:** NR **Recruitment:** Retrospective (July 2020 to December 2020) **Number of participants:** 151	**Inclusion criteria:** Patients who presented with suspected acute stroke symptoms and whose imaging studies were processed by RAPID LVO. **Exclusion criteria:** NR **Research Question:** (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?	**Mean (SD) age, years:** 70.6 (15.9) **Male (%):** 69 (45.7) **No further participant characteristics were reported**	Rapid LVO
Seker 2020[56] Seker 2019a[57] Seker 2019b[58] **Publication type:** Full paper **Country:** Germany **Funding:** None: 'The author(s) received no financial support for the research, authorship, and/or publication of this article' Individual study authors declared receipt of support and/or fees from Brainomix. **Recruitment:** January 2014 to December 2017 (retrospective) **Number of participants:** 301	**Inclusion criteria:** Case-control validation study: Cases comprised patients with LVO of the terminal carotid artery or middle cerebral artery up to the proximal M2 level who had CTA images of sufficient quality (CT scan primarily in the arterial phase without severe motion artifacts and with a slice thickness of ≤1 mm); controls comprised CTA examinations from 141 consecutive AIS patients without LVO. **Exclusion criteria:** NR **Research Question:** (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?	**No participant characteristics were reported**	Brainomix eCTA

Study Details	Selection criteria	Participant details	AI intervention
Shalitin 2020[61] **Publication type:** Full paper (pre-publication) **Country:** USA **Funding:** NR; individual study authors appear to have been employees of Viz.ai **Recruitment:** NR **Number of participants:** 2544	**Inclusion criteria:** NR **Exclusion criteria:** NR **Research Question:** (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?	**Mean (SD) age, years:** 66.0 (17.4) **Male (%):** 1186 (46.6) **No further participant characteristics were reported**	Viz LVO
Yahav-Dovrat 2021[59] **Publication type:** Full paper **Country:** USA **Funding:** NR; individual study authors disclosed receipt of support and/or consulting fees from Viz.ai **Recruitment:** January 2018 to March 2019 (retrospective) **Number of participants:** 1167	**Inclusion criteria:** All CTA scans including non-acute ischemic stroke cases (subgroup data for stroke protocol patients) **Exclusion criteria:** Examinations with metal artifact, severe motion, or incomplete skull scanning **Research Question:** (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?	**Mean (SD) age, years:** 62.2 (19.6) **Male (%):** 689 (59) **No further participant characteristics were reported**	Viz LVO

AF: atrial fibrillation; AI: artificial intelligence; AIS: acute ischemic stroke; CT: computed tomography; CTA: computed tomography angiography; CTP computed tomography perfusion; DM: diabetes mellitus; IQR: inter-quartile range LVO: large vessel occlusion; NHS: National Health Service; NR: not reported; NIHSS: National Institute of Health Stroke Scale; SD: standard deviation TIA: transient ischemic attack

Table 33: Details of AI-derived software technology and references standard/comparator

Study details	Imaging details	AI-derived software technology	Reference standard/Comparator
Adhya 2021[33] **Research Question:** (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?	**No details were reported**	**AI-derived software technology:** Rapid CTA, version not reported (iSchemaView, Menlo Park, CA) **Analysis:** Unclear (routine practice, post-implementation of Rapid CTA)	**Comparator image interpretation:** Unclear (routine practice, pre-implementation of Rapid CTA)
Al-Kawaz 2021[34] **Research Question:** (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention? (Q2b) Is AI-derived software assisted review of CT perfusion brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke after a CTA brain scan a clinically effective intervention?	**No details were reported**	**AI-derived software technology:** RapidAI Mobile Application (iSchemaView, Menlo Park, CA) **Analysis:** Unclear (routine practice, post-implementation of RapidAI Mobile App)	**Comparator image interpretation:** Unclear (routine practice, pre-implementation of RapidAI Mobile App)
Amukotuwa 2019a,[35] **DEFUSE 2 and 3, plus three additional cohorts (one of which was the Amukotwa 2019b cohort)** **Research Question:** (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding	**No details were reported** The article stated that study sites used a *'representative sample of scanner models from all major CT vendors'*	**AI-derived software technology:** Rapid CTA, version 4.9.1 (iSchemaView, Menlo Park, CA) **Analysis:** AI alone	**Reference standard image interpretation:** For patients from DEFUSE 2 and 3, the presence and location of occlusive lesion had already been determined by the study investigators and was verified by a neuroradiologist with 8 years post-fellowship experience. For the remaining cohorts, two neuroradiologists with 9

Study details	Imaging details	AI-derived software technology	Reference standard/Comparator
mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?			years post-fellowship experience determined the presence and site of occlusive lesions, in consensus, based on multimodal CT including CTA and with access to all clinical and imaging data (including perfusion); any disagreements were resolved by review of all available imaging, including perfusion.
Amukotuwa 2019b[36] **Research Question:** (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?	**CT scanner:** 256-slice multi-detector CT (iCT 256, Philips Healthcare, Cleveland, OH) **CTA image acquisition:** 80 mL of non-ionic contrast (Omnipaque 350, GE Healthcare, WI) intravenous at 5 mL/s followed by a 40 mL saline flush at 6 mL/s; helical acquisition; tube voltage 100 kV; slice collimation width 0.625 mm; image matrix 512x512; spiral pitch factor 0.518; slice thickness 4mm	**AI-derived software technology:** Rapid CTA, version 4.9 (iSchemaView, Menlo Park, CA) **Analysis:** AI alone	**Reference standard image interpretation:** Two diagnostic neuroradiologists with 8- and 9-years post-fellowship experience and access to the complete multimodal CT (NCCT, CTP and CTA) and details of the clinical presentation. Consensus was recorded and verified by an interventional neuroradiologist with 7 years' experience.
Barreira 2018a,[60] **Research Question:** (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?	**No details were reported**	**AI-derived software technology:** Viz LVO, version 3.04 (Viz.ai Inc., San Francisco CA) **Analysis:** AI alone	**Reference standard image interpretation:** CTAs were analysed and graded by experienced stroke neuroradiologists (no further details were reported)
Barreira 2018d,[39] **Research Question:** (Q1) Is AI-derived software assisted review of non-enhanced CT brain scans for guiding thrombolysis treatment	**No details were reported**	**AI-derived software technology:** Viz ICH, version 2.0 (Viz.ai Inc., San Francisco CA) **Analysis:** AI alone	**Reference standard image interpretation:** Experienced stroke neurologists grading the same NCCTs with a semi-automated tool (OsiriX MD version 9.0.1)

Study details	Imaging details	AI-derived software technology	Reference standard/Comparator
decisions for people with suspected acute stroke a clinically effective intervention?			
Chatterjee 2018[40] **Research Question:** (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?	**No details were reported**	**AI-derived software technology:** Viz LVO, version not reported (Viz.ai Inc., San Francisco CA) **Analysis:** AI alone	**Reference standard image interpretation:** No details were reported.
Dehkharghani 2021[41] **Research Question:** (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?	**CT scanner:** GE Medical, Philips, Siemens or Toshiba (no further details reported) **CTA image acquisition:** No details were reported	**AI-derived software technology:** Rapid LVO, version 1.0 (iSchemaView, Menlo Park, CA) **Analysis:** AI alone	**Reference standard image interpretation:** Two board-certified neuroradiologists, with 11- and 7-years' experience, blinded to clinical history and imaging outcome, independently scored all examinations for LVO. An LVO was defined as occlusion or near occlusion by a focal stenosis >80%. Discrepancies between the two readers were adjudicated by a third board-certified neuroradiologist with 7 years' experience. For examinations classified as positive, readers were subsequently presented with the automated output and asked to assess it for presence of LVO, LVO side and inclusion of compromised vessel segment within the region of interest; All three criteria had to be met in order for an automated image to be classified as true positive.
Dornbos 2020[43]	**No details were reported**	**AI-derived software technology:** Viz LVO, version not reported (Viz.ai Inc.,	**Reference standard image interpretation:**

Study details	Imaging details	AI-derived software technology	Reference standard/Comparator
Research Question: (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?		San Francisco CA) **Analysis:** AI alone	Blinded neuroradiologists, (no further details were reported)
Gunda 2020[44] **Research Question:** (Q1) Is AI-derived software assisted review of non-enhanced CT brain scans for guiding thrombolysis treatment decisions for people with suspected acute stroke a clinically effective intervention? (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?	**No details were reported**	**AI-derived software technology:** e-ASPECTS and e-CTA, version not reported (Brainomix, Oxford, UK) **Analysis:** Unclear, *'AI decision support software was implemented in 2018 and delivery of stroke care was otherwise unchanged'*	**Comparator image interpretation:** Unclear (standard stroke care before implementation of AI decision support software)
Hassan 2021a[45] **Research Question:** (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?	**No details were reported**	**AI-derived software technology:** Viz LVO, version not reported (Viz.ai Inc., San Francisco CA) **Analysis:** Unclear (routine practice, post-implementation of Viz LVO)	**Comparator image interpretation:** Unclear (routine practice, pre-implementation of Viz LVO)
Hassan 2020[46] **Research Question:** (Q2a) Is AI-derived software assisted	**No details were reported**	**AI-derived software technology:** Viz LVO, version not reported (Viz.ai Inc., San Francisco CA)	**Comparator image interpretation:** Unclear (routine practice, pre-implementation of Viz LVO)

Study details	Imaging details	AI-derived software technology	Reference standard/Comparator
review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?		**Analysis:** Unclear (routine practice, post-implementation of Viz LVO)	
Herweh 2020[48] **Research Question:** (Q1) Is AI-derived software assisted review of non-enhanced CT brain scans for guiding thrombolysis treatment decisions for people with suspected acute stroke a clinically effective intervention?	**No details were reported**	**AI-derived software technology:** BrainomixVR (Brainomix, Oxford, UK) **Analysis:** AI alone	**Reference standard image interpretation:** Image interpretation by a board-certified neuroradiologist
Kamal 2017[49] **Research Question:** (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention? (Q2b) Is AI-derived software assisted review of CT perfusion brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke after a CTA brain scan a clinically effective intervention?	**No details were reported**	**AI-derived software technology:** RapidAI (iSchemaView, Menlo Park, CA) **Analysis:** Unclear, *'implementation of automated software analysis with instant e-mail distribution to treating clinicians'*	**Comparator image interpretation:** Unclear (routine practice, pre-implementation of RapidAI)
Kauw 2020[50] **Research Question:** (Q2b) Is AI-derived software assisted review of CT perfusion brain scans for guiding mechanical thrombectomy	**CT scanner:** No details were reported **CTA and CTP image acquisition:** CTP and CTA were performed as part of routine stroke work-up. The CTP was	**AI-derived software technology:** Rapid CTP, version not reported (iSchemaView, Menlo Park, CA) **Analysis:** AI alone	**Reference standard image interpretation:** Images were reviewed, for potential causes of post-processing failure, by two clinicians (experience not specified) in consensus, who were blinded to clinical

Study details	Imaging details	AI-derived software technology	Reference standard/Comparator
treatment decisions for people with an ischaemic stroke after a CTA brain scan a clinically effective intervention?	performed with cine mode on 80 kV and 100 mAs with 37 phases at 1 sec interval, followed by 33 phases at 3 sec interval, on a 128-slice scanner. Either 1 or 2 runs with 5 mm slices were performed, covering at least Alberta stroke program early CT score levels 1 and 2 of the brain. The CTA was performed on 120 kV and 225 mAs and covered the aortic arch to the brain apex. Slice thickness was 0.625 mm. Iodinated contrast dose was 40 mL for CTP and 70 mL for CTA, injected at 4-5 mL/sec.		data but had access to all imaging data available at the time of patient evaluation. RAPID CTP post-processing failures were re-processed manually using IntelliSpace software (Philips, Best, The Netherlands). For this assessment, treatment received was used as the reference standard.
Mair 2021[62] **Research Question:** (Q1) Is AI-derived software assisted review of non-enhanced CT brain scans for guiding thrombolysis treatment decisions for people with suspected acute stroke a clinically effective intervention?	**CT scanner:** [redacted] **CTA image acquisition:** [redacted]	**AI-derived software technology:** [redacted] **Analysis:** [redacted]	**Reference/Comparator standard image interpretation:** [redacted]

Study details	Imaging details	AI-derived software technology	Reference standard/Comparator
			[redacted]
McLouth 2021[51] **Research Question:** (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?	**CT scanner:** GE Medica Systems, Philips, Siemens, Canon (formerly Toshiba), or NMS. No further details reported. **CTA image acquisition:** Inclusion criteria for CTA scans: strict axial acquisition; 512x512 matrix; slice thickness ≤1.25 mm; kVp range 80-140; arterial phase timing of contrast bolus confirmed by mini test bolus or automatic bolus tracking software; arterial (or other sharp) reconstruction kernel.	**AI-derived software technology:** CINA LVO, version 1.0 (Avicenna.ai, La Ciotat, France) **Analysis:** AI alone	**Reference standard image interpretation:** CTA interpreted by two U.S. board-certified neuroradiologists, with consensus determined by a third board-certified neuroradiologist.
Morey 2020a[52] **Research Question:** (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding	**No details were reported**	**AI-derived software technology:** Viz LVO, version not reported (Viz.ai Inc., San Francisco CA) **Analysis:**	**Comparator image interpretation:** Unclear (routine practice, pre-implementation of Viz LVO)

Study details	Imaging details	AI-derived software technology	Reference standard/Comparator
mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?		Unclear (routine practice, post-implementation of Viz LVO)	
Paz 2021[55] **Research Question:** (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?	**CT scanner:** No details were reported **CTA image acquisition:** Institutional stroke protocol performed on all patients, comprising NCCT acquisition of the head followed by CTA (section thickness 0.8-1.0 mm) of the head; Toshiba Aquilion One 320 slices scanner; 80 kV, 310 mA for the mask, 150 mA for the pre-arterial phase, 300 mA for the arterial phase and 150 mA for the remainder of the acquisition; contrast IOSVUE 370; total scan time 60 sec; axial thickness 1 mm, with interval of 0.8 mm; MIP on all 19 volumes coronal and sagittal 2 m, with 2 mm interval; DSA movie and perfusion maps.	**AI-derived software technology:** Rapid LVO, version not reported (iSchemaView, Menlo Park, CA) **Analysis:** AI alone	**Reference standard image interpretation:** No details were reported
Seker 2020[56] **Research Question:** (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?	**CT scanner:** The article stated that: *'CTA imaging was performed using a variety of multi-slice CT scanners at stroke centres participating in a regional network.'* **CTA image acquisition:** CT acquisition protocols varied, reflecting real world practice. In general, a single contrast bolus was given intravenous, followed by a saline flush. Aortic contrast opacification was monitored using bolus tracking. CT scans	**AI-derived software technology:** e-CTA, version not reported (Brainomix, Oxford, UK) **Analysis:** AI alone	**Reference standard image interpretation:** CTA interpreted by a board-certified neuroradiologist with >10 years' experience and access to all clinical and imaging data, including data on interventional therapy and follow-up **Comparator image interpretation:** For a sub-group of the study population, diagnostic accuracy data were reported for four comparators (one board-certified Neuroradiologist, one

Study details	Imaging details	AI-derived software technology	Reference standard/Comparator
	were from the aortic arch to the vertex. Only axial reformations with a slice thickness between 0.6 and 1 mm were included.		Radiology resident and two Neurology residents)
Shalitin 2020[61] **Research Question:** (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?	**CT scanner:** GE Medical, Philips, Siemens, Toshiba or 'other' (no further details reported) **CTA image acquisition:** No details were reported	**AI-derived software technology:** Viz LVO, version not reported (Viz.ai Inc., San Francisco CA) **Analysis:** AI alone	**Reference standard image interpretation:** Image interpretation by *'a team of radiology trained annotators'* (no further details were reported)
Yahav-Dovrat 2021[59] **Research Question:** (Q2a) Is AI-derived software assisted review of CTA brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke a clinically effective intervention?	**No details were reported**	**AI-derived software technology:** Viz LVO, version not reported (Viz.ai Inc., San Francisco CA) **Analysis:** AI alone	**Reference standard image interpretation:** Interpretation of CTA by one of four senior neuroradiologists with 7-25 years of experience
CT: computed tomography; CTA: CT angiography; CTP: CT perfusion; ICH: intracranial haemorrhage; LVO: large vessel occlusion; NCCT: non-contrast CT			

APPENDIX 3: STUDY QUALITY

QUADAS-2 Assessments

Study: DEFUSE 2 and DEFUSE 3, Amukotuwa 2019a[35]

DOMAIN 1: PATIENT SELECTION
A. RISK OF BIAS

The study population comprised five cohorts, DEFUSE 2 and 3, plus three additional cohorts (one of which was the Amukotwa 2019b[36] cohort), of patients who had undergone acute CTA. CTA deemed, by an experienced neuroradiologist, to be technically inadequate to allow accurate interpretation by a human reader, were excluded.

Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	**RISK: Unclear**

B. APPLICABILITY

Retrospective analysis of five cohorts of patients from stroke studies, with no clear inclusion criteria reported for this study.

Do the included patients match the question?	**Concerns: Unclear**

DOMAIN 2: INDEX TEST(S)
A. RISK OF BIAS

RAPID CTA: The study reports the diagnostic performance of the AI technology alone (hence, blinding to reference standard results NA), for the target condition LVO (subgroups for various anatomical locations reported), using various thresholds.

Were the index test results interpreted without knowledge of the results of the reference standard?	NA
If a threshold was used, was it pre-specified?	Yes
Could the conduct or interpretation of the index test have introduced bias?	**RISK: Low**

B. APPLICABILITY

The AI technology was evaluated as a stand-alone intervention, rather than as an adjunct to human interpretation.

Are there concerns that the index test, its conduct, or interpretation differ from the review question?	**Concerns: High**

DOMAIN 3: REFERENCE STANDARD
A. RISK OF BIAS

For patients from DEFUSE 2 and 3, the presence and location of occlusive lesion had already been determined by the study investigators and was verified by a neuroradiologist with 8 years post-fellowship experience. For the remaining cohorts, two neuroradiologists with 9 years post-fellowship experience determined the presence and site of occlusive lesions, in consensus, based on multimodal CT including CTA and with access to all clinical and imaging data (including perfusion); any disagreements were resolved by review of all available imaging, including perfusion. The reference standard determination was made before application of the AI intervention.

Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index test?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	**RISK: Low**

B. APPLICABILITY

Is there concern that the target condition as defined by the reference standard does not match the review question?	**Concerns: Low**

DOMAIN 4: FLOW AND TIMING
A. RISK OF BIAS

The study utilised CTA images from patients for whom a reference standard diagnosis had already been established. All patients appear to have been included in the analysis.	
Was there an appropriate time interval between index test and reference standard?	Yes
Did patients receive the same or a similar reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	**RISK: Low**

Study: Amukotuwa 2019b[36]

DOMAIN 1: PATIENT SELECTION
A. RISK OF BIAS

Retrospective analysis of consecutive adult (≥18 years) patients who had undergone multimodal brain CT for suspected AIS within 24 hours of symptom onset or last seen well. Technically inadequate CTAs (poor contrast bolus or substantial motion or metal artifact that precluded accurate assessment of the intracranial arteries to the level of the distal M2 segments of the middle cerebral arteries by an experienced neuroradiologist) were excluded.

Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	**RISK: Low**
B. APPLICABILITY	
Do the included patients match the question?	**Concerns: Low**

DOMAIN 2: INDEX TEST(S)
A. RISK OF BIAS

RAPID CTA: The study reports the diagnostic performance of the AI technology alone (hence, blinding to reference standard results NA), for the target condition LVO (subgroups for various anatomical locations reported), using a pre-specified threshold.

Were the index test results interpreted without knowledge of the results of the reference standard?	NA
If a threshold was used, was it pre-specified?	Yes
Could the conduct or interpretation of the index test have introduced bias?	**RISK: Low**
B. APPLICABILITY	

The AI technology was evaluated as a stand-alone intervention, rather than as an adjunct to human interpretation.

Are there concerns that the index test, its conduct, or interpretation differ from the review question?	**Concerns: High**

DOMAIN 3: REFERENCE STANDARD
A. RISK OF BIAS

Two diagnostic neuroradiologists with 8- and 9-years post-fellowship experience who had access to the complete multimodal CT (NCCT, CTP and CTA) and details of the clinical presentation. Consensus was recorded and verified by an interventional neuroradiologist with 7 years' experience. The reference standard determination was made before application of the AI intervention.

Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index test?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	**RISK: Low**
B. APPLICABILITY	
Is there concern that the target condition as defined by the reference standard does not match the review question?	**Concerns: Low**

DOMAIN 4: FLOW AND TIMING
A. RISK OF BIAS

The study utilised CTA images from patients for whom a reference standard diagnosis had already been established. All patients appear to have been included in the analysis.

Was there an appropriate time interval between index test and reference standard?	Yes
Did patients receive the same or a similar reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	**RISK: Low**

Study: ALADIN, Barreira 2018a[60]

DOMAIN 1: PATIENT SELECTION
A. RISK OF BIAS

A random sample from a retrospective cohort of AIS patients with and without anterior circulation LVOs. No exclusion criteria were reported.

Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	**RISK: Unclear**

B. APPLICABILITY

Time from symptom onset or 'last seen well' not reported

Do the included patients match the question?	**Concerns: Unclear**

DOMAIN 2: INDEX TEST(S)
A. RISK OF BIAS

Viz LVO: The study reports the diagnostic performance of the AI technology alone (hence, blinding to reference standard results NA), for the target condition LVO. No threshold was specified.

Were the index test results interpreted without knowledge of the results of the reference standard?	NA
If a threshold was used, was it pre-specified?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	**RISK: Unclear**

B. APPLICABILITY

The AI technology was evaluated as a stand-alone intervention, rather than as an adjunct to human interpretation.

Are there concerns that the index test, its conduct, or interpretation differ from the review question?	**Concerns: High**

DOMAIN 3: REFERENCE STANDARD
A. RISK OF BIAS

CTAs analysed and graded by experienced stroke neuroradiologists (no further details reported).

Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index test?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	**RISK: Unclear**

B. APPLICABILITY

Is there concern that the target condition as defined by the reference standard does not match the review question?	**Concerns: Low**

DOMAIN 4: FLOW AND TIMING
A. RISK OF BIAS

The index test and reference standard utilised the same CTA images. All patients appear to have been included in the analysis.

Was there an appropriate time interval between index test and reference standard?	Yes
Did patients receive the same or a similar reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	**RISK: Low**

Study: Barreira 2018d[39]

DOMAIN 1: PATIENT SELECTION
A. RISK OF BIAS

Retrospective analysis of a random sample from a cohort of stroke patients with and without ICH (cases and controls). No exclusion criteria reported.

Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	No
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	**RISK: High**

B. APPLICABILITY

Not patients with suspected AIS (case-control design)

Do the included patients match the question?	**Concerns: High**

DOMAIN 2: INDEX TEST(S)
A. RISK OF BIAS

Viz ICH: The study reports the diagnostic performance of the AI technology alone (hence, blinding to reference standard results NA), for the target condition ICH. No threshold was specified.

Were the index test results interpreted without knowledge of the results of the reference standard?	NA
If a threshold was used, was it pre-specified?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	**RISK: Unclear**

B. APPLICABILITY

The AI technology was evaluated as a stand-alone intervention, rather than as an adjunct to human interpretation.

Are there concerns that the index test, its conduct, or interpretation differ from the review question?	**Concerns: High**

DOMAIN 3: REFERENCE STANDARD
A. RISK OF BIAS

Experienced stroke neurologists grading the same NCCTs with a semi-automated tool (OsiriX MD v.9.0.1)

Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index test?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	**RISK: Unclear**

B. APPLICABILITY

Is there concern that the target condition as defined by the reference standard does not match the review question?	**Concerns: Low**

DOMAIN 4: FLOW AND TIMING
A. RISK OF BIAS

The index test and reference standard utilised the same CTA images. All patients appear to have been include in the analysis.

Was there an appropriate time interval between index test and reference standard?	Yes
Did patients receive the same or a similar reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	**RISK: Low**

Study: Chatterjee 2018[40]

DOMAIN 1: PATIENT SELECTION
A. RISK OF BIAS

Retrospective analysis of images from patients with stroke CTA studies. No exclusion criteria specified.

Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	**RISK: Unclear**

B. APPLICABILITY

Time from symptom onset or 'last seen well' not reported

Do the included patients match the question?	**Concerns: Unclear**

DOMAIN 2: INDEX TEST(S)
A. RISK OF BIAS

Viz LVO: The study reports the diagnostic performance of the AI technology alone (hence, blinding to reference standard results NA), for the target condition LVO. No threshold was specified.

Were the index test results interpreted without knowledge of the results of the reference standard?	NA
If a threshold was used, was it pre-specified?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	**RISK: Unclear**

B. APPLICABILITY

The AI technology was evaluated as a stand-alone intervention, rather than as an adjunct to human interpretation.

Are there concerns that the index test, its conduct, or interpretation differ from the review question?	**Concerns: High**

DOMAIN 3: REFERENCE STANDARD
A. RISK OF BIAS

'Conventional angiography' (no further details reported).

Is the reference standard likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index test?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	**RISK: Unclear**

B. APPLICABILITY

Is there concern that the target condition as defined by the reference standard does not match the review question?	**Concerns: Unclear**

DOMAIN 4: FLOW AND TIMING
A. RISK OF BIAS

The index test and reference standard utilised the same CTA images. All patients appear to have been include in the analysis.

Was there an appropriate time interval between index test and reference standard?	Yes
Did patients receive the same or a similar reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	**RISK: Low**

Study: CRISP and DASH, Dehkharghani 2021[41]

DOMAIN 1: PATIENT SELECTION
A. RISK OF BIAS

Retrospective analysis of adult (≥18 years) individuals undergoing cerebrovascular CTA, from the CRISP and DASH trials and from institutional registries of participating hospitals; technically adequate, thin section (≤2 mm) contiguous cerebrovascular CTA sources axial images, free of artifacts that would degrade interpretation by human readers (e.g., those related to severe metallic streak or beam hardening). The study used a random selection of at least 100 LVO positive and 100 LVO negative patients, with enrichment to balance subgroup imbalances in age groupings and scanner manufacturer.

Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	No
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	**RISK: High**

B. APPLICABILITY

Not patients with AIS and suspected LVO (case-control type design).

Do the included patients match the question? **Concerns: High**

DOMAIN 2: INDEX TEST(S)
A. RISK OF BIAS

RAPID CTA: The study reports the diagnostic performance of the AI technology alone (hence, blinding to reference standard results NA), for the target condition LVO (subgroups for age and scanner manufacturer reported), using a pre-specified threshold.

Were the index test results interpreted without knowledge of the results of the reference standard?	NA
If a threshold was used, was it pre-specified?	Yes
Could the conduct or interpretation of the index test have introduced bias?	**RISK: Low**

B. APPLICABILITY

The AI technology was evaluated as a stand-alone intervention, rather than as an adjunct to human interpretation.

Are there concerns that the index test, its conduct, or interpretation differ from the review question? **Concerns: High**

DOMAIN 3: REFERENCE STANDARD
A. RISK OF BIAS

Two board-certified neuroradiologists, with 11- and 7-years' experience, blinded to clinical history and imaging outcome, independently scored all examinations for LVO. An LVO was defined as occlusion or near occlusion by a focal stenosis >80%. Discrepancies between the two readers were adjudicated by a third board-certified neuroradiologist with 7 years' experience. For examinations classified as positive, readers were subsequently presented with the automated output and asked to assess it for presence of LVO, LVO side and inclusion of compromised vessel segment within the region of interest; All three criteria had to be met in order for an automated image to be classified as true positive.

Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index test?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	**RISK: Low**

B. APPLICABILITY

Is there concern that the target condition as defined by the reference standard does not match the review question? **Concerns: Low**

DOMAIN 4: FLOW AND TIMING
A. RISK OF BIAS

The study utilised CTA images from patients for whom a reference standard diagnosis had already been

established. All patients appear to have been include in the analysis.	
Was there an appropriate time interval between index test and reference standard?	Yes
Did patients receive the same or a similar reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	**RISK: Low**

Study: Dornbos 2020[43]

DOMAIN 1: PATIENT SELECTION
A. RISK OF BIAS

A retrospective chart review of consecutive code stroke cases at a comprehensive stroke centre and two spoke hospitals. No exclusion criteria were reported.

Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	**RISK: Unclear**

B. APPLICABILITY

Time from symptom onset or 'last seen well' not reported

Do the included patients match the question?	**Concerns: Unclear**

DOMAIN 2: INDEX TEST(S)
A. RISK OF BIAS

Viz LVO: The study reports the diagnostic performance of the AI technology alone (hence, blinding to reference standard results NA), for the target condition LVO. No threshold was specified.

Were the index test results interpreted without knowledge of the results of the reference standard?	NA
If a threshold was used, was it pre-specified?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	**RISK: Unclear**

B. APPLICABILITY

The AI technology was evaluated as a stand-alone intervention, rather than as an adjunct to human interpretation.

Are there concerns that the index test, its conduct, or interpretation differ from the review question?	**Concerns: High**

DOMAIN 3: REFERENCE STANDARD
A. RISK OF BIAS

CT/CTA interpretation by 'blinded neuroradiologists' (no further details reported).

Is the reference standard likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index test?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	**RISK: Unclear**

B. APPLICABILITY

Is there concern that the target condition as defined by the reference standard does not match the review question?	**Concerns: Unclear**

DOMAIN 4: FLOW AND TIMING
A. RISK OF BIAS

The index test and reference standard utilised the same CTA images. All patients appear to have been included in the analysis.

Was there an appropriate time interval between index test and reference standard?	Yes
Did patients receive the same or a similar reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	**RISK: Low**

Study: Herweh 2020[48]

DOMAIN 1: PATIENT SELECTION
A. RISK OF BIAS

'Selected' NCCT scans (slice thickness 1mm) from patients with suspected AIS. No exclusion criteria were reported.

Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	**RISK: High**

B. APPLICABILITY

Time from symptom onset or 'last seen well' not reported

Do the included patients match the question?	**Concerns: Unclear**

DOMAIN 2: INDEX TEST(S)
A. RISK OF BIAS

Brainomix: The study reports the diagnostic performance of the AI technology alone (hence, blinding to reference standard results NA), for the target condition ICH. No threshold was specified.

Were the index test results interpreted without knowledge of the results of the reference standard?	NA
If a threshold was used, was it pre-specified?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	**RISK: Unclear**

B. APPLICABILITY

The AI technology was evaluated as a stand-alone intervention, rather than as an adjunct to human interpretation.

Are there concerns that the index test, its conduct, or interpretation differ from the review question?	**Concerns: High**

DOMAIN 3: REFERENCE STANDARD
A. RISK OF BIAS

Image interpretation by a board-certified neuroradiologist (no further details reported).

Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index test?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	**RISK: Unclear**

B. APPLICABILITY

Is there concern that the target condition as defined by the reference standard does not match the review question?	**Concerns: Low**

DOMAIN 4: FLOW AND TIMING
A. RISK OF BIAS

The index test and reference standard utilised the same CTA images. All patients appear to have been included in the analysis.

Was there an appropriate time interval between index test and reference standard?	Yes
Did patients receive the same or a similar reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	**RISK: Low**

Study: Kauw 2020[50]

DOMAIN 1: PATIENT SELECTION
A. RISK OF BIAS

Retrospective analysis of images from a database of consecutive patients with AIS undergoing CTP for thrombectomy triage. No exclusion criteria were reported.

Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	**RISK: Unclear**

B. APPLICABILITY

Time from symptom onset or 'last seen well' not reported

Do the included patients match the question?	**Concerns: Unclear**

DOMAIN 2: INDEX TEST(S)
A. RISK OF BIAS

Rapid CTP: The study reports the diagnostic performance of the AI technology alone (hence, blinding to reference standard results NA) to determine the suitability of patients for thrombectomy. No threshold was specified.

Were the index test results interpreted without knowledge of the results of the reference standard?	NA
If a threshold was used, was it pre-specified?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	**RISK: Unclear**

B. APPLICABILITY

The AI technology was evaluated as a stand-alone intervention, rather than as an adjunct to human interpretation.

Are there concerns that the index test, its conduct, or interpretation differ from the review question?	**Concerns: High**

DOMAIN 3: REFERENCE STANDARD
A. RISK OF BIAS

Images were reviewed, for potential causes of post-processing failure, by two clinicians (experience not specified) in consensus, who were blinded to clinical data but had access to all imaging data available at the time of patient evaluation. RAPID CTP post-processing failures were re-processed manually using IntelliSpace software (Philips, Best, The Netherlands). 2x2 Data have could only be derived for the performance of the AI intervention by using treatment received as the reference standard.

Is the reference standard likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index test?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	**RISK: High**

B. APPLICABILITY

Is there concern that the target condition as defined by the reference standard does not match the review question?	**Concerns: High**

DOMAIN 4: FLOW AND TIMING
A. RISK OF BIAS

The index test and reference standard utilised the same CTA images. All patients appear to have been included in the analysis.

Was there an appropriate time interval between index test and reference standard?	Yes
Did patients receive the same or a similar reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	**RISK: Low**

Study: RITeS, Mair 2021[62]

DOMAIN 1: PATIENT SELECTION
A. RISK OF BIAS

[redacted]

Was a consecutive or random sample of patients enrolled? [redacted]
Was a case-control design avoided?
Did the study avoid inappropriate exclusions?

Could the selection of patients have introduced bias? **RISK: Unclear**

B. APPLICABILITY

[redacted]

Do the included patients match the question? **Concerns: Low**

DOMAIN 2: INDEX TEST(S)
A. RISK OF BIAS

[redacted]

Were the index test results interpreted without knowledge of the results of the reference standard? [redacted]
If a threshold was used, was it pre-specified? [redacted]

Could the conduct or interpretation of the index test have introduced bias? **RISK: Low**

B. APPLICABILITY

[redacted]

Are there concerns that the index test, its conduct, or interpretation differ from the review question? **Concerns: High**

DOMAIN 3: REFERENCE STANDARD
A. RISK OF BIAS

[redacted]

Is the reference standard likely to correctly classify the target condition? [redacted]
Were the reference standard results interpreted without knowledge of the results of the index test?

Could the reference standard, its conduct, or its interpretation have introduced bias? **RISK: Low**

B. APPLICABILITY

Is there concern that the target condition as defined by the reference standard does not match the review question? **Concerns: High**

DOMAIN 4: FLOW AND TIMING
A. RISK OF BIAS

[redacted]

Was there an appropriate time interval between index test and reference standard? [redacted]

Did patients receive the same or a similar reference standard? [redacted]

Were all patients included in the analysis?

Could the patient flow have introduced bias? **RISK: Low**

Study: McLouth 2021[51]

DOMAIN 1: PATIENT SELECTION
A. RISK OF BIAS

Retrospective study using images from patients with suspected LVO, on clinical grounds, in whom CTA studies had been performed, identified from University of California, Irvine (UCI) and a teleradiology service, vRAD (Minneapolis, USA) databases using key words such as "CTA", "head" and "large vessel occlusion". No exclusion criteria were reported.

Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	**RISK: High**

B. APPLICABILITY

Time from symptom onset or 'last seen well' not reported

Do the included patients match the question?	**Concerns: Unclear**

DOMAIN 2: INDEX TEST(S)
A. RISK OF BIAS

CINA LVO: The study reports the diagnostic performance of the AI technology alone (hence, blinding to reference standard results NA) for the target condition LVO (subgroups for age and scanner manufacturer). No threshold was specified.

Were the index test results interpreted without knowledge of the results of the reference standard?	NA
If a threshold was used, was it pre-specified?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	**RISK: Unclear**

B. APPLICABILITY

The AI technology was evaluated as a stand-alone intervention, rather than as an adjunct to human interpretation.

Are there concerns that the index test, its conduct, or interpretation differ from the review question?	**Concerns: High**

DOMAIN 3: REFERENCE STANDARD
A. RISK OF BIAS

CTA interpreted by two U.S. board-certified neuroradiologists, with consensus determined by a third board-certified neuroradiologist.

Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index test?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	**RISK: Unclear**

B. APPLICABILITY

Is there concern that the target condition as defined by the reference standard does not match the review question?	**Concerns: Low**

DOMAIN 4: FLOW AND TIMING
A. RISK OF BIAS

The index test and reference standard utilised the same CTA images. All patients appear to have been included in the analysis.

Was there an appropriate time interval between index test and reference standard?	Yes
Did patients receive the same or a similar reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	**RISK: Low**

Study: Paz 2021[55]

DOMAIN 1: PATIENT SELECTION
A. RISK OF BIAS

Retrospective study of all patients with suspected acute stroke symptoms whose images had been analysed using Rapid LVO. No exclusion criteria were reported.

Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	**RISK: Unclear**

B. APPLICABILITY

Time from symptom onset or 'last seen well' not reported

Do the included patients match the question?	**Concerns: Unclear**

DOMAIN 2: INDEX TEST(S)
A. RISK OF BIAS

Rapid LVO: The study reports the diagnostic performance of the AI technology alone (hence, blinding to reference standard results NA) for the target condition LVO. No threshold was specified.

Were the index test results interpreted without knowledge of the results of the reference standard?	NA
If a threshold was used, was it pre-specified?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	**RISK: Unclear**

B. APPLICABILITY

The AI technology was evaluated as a stand-alone intervention, rather than as an adjunct to human interpretation.

Are there concerns that the index test, its conduct, or interpretation differ from the review question?	**Concerns: High**

DOMAIN 3: REFERENCE STANDARD
A. RISK OF BIAS

No details were reported regarding how the reference standard diagnosis was determined.

Is the reference standard likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index test?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	**RISK: Unclear**

B. APPLICABILITY

Is there concern that the target condition as defined by the reference standard does not match the review question?	**Concerns: Unclear**

DOMAIN 4: FLOW AND TIMING
A. RISK OF BIAS

The index test and reference standard utilised the same CTA images, however, no details of the reference standard for interpretation of images were reported. All patients appear to have been included in the analysis.

Was there an appropriate time interval between index test and reference standard?	Yes
Did patients receive the same or a similar reference standard?	Unclear
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	**RISK: Unclear**

Study: Seker 2020[56]

DOMAIN 1: PATIENT SELECTION
A. RISK OF BIAS

Case-control validation study: Cases comprised patients with LVO of the terminal carotid artery or middle cerebral artery up to the proximal M2 level who had CTA images of sufficient quality (CT scan primarily in the arterial phase without severe motion artifacts and with a slice thickness of ≤1 mm); controls comprised CTA examinations from 141 consecutive AIS patients without LVO. No exclusion criteria were reported.

Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	No
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	**RISK: High**

B. APPLICABILITY

Case-control type study; not patients with AIS and suspected LVO.

Do the included patients match the question?	**Concerns: High**

DOMAIN 2: INDEX TEST(S)
A. RISK OF BIAS

Brainomix eCTA: The study reports the diagnostic performance of the AI technology alone (hence, blinding to reference standard results NA) for the target condition LVO (subgroups for anatomical location). No threshold was specified.

Were the index test results interpreted without knowledge of the results of the reference standard?	NA
If a threshold was used, was it pre-specified?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	**RISK: Unclear**

B. APPLICABILITY

The AI technology was evaluated as a stand-alone intervention, rather than as an adjunct to human interpretation.

Are there concerns that the index test, its conduct, or interpretation differ from the review question?	**Concerns: High**

DOMAIN 3: REFERENCE STANDARD
A. RISK OF BIAS

CTA interpreted by a board-certified neuroradiologist with >10 years' experience and access to all clinical and imaging data, including data on interventional therapy and follow-up. The study utilised CTA images from patients for whom a reference standard diagnosis had already been established (case-control).

Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index test?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	**RISK: Low**

B. APPLICABILITY

Is there concern that the target condition as defined by the reference standard does not match the review question?	**Concerns: Low**

DOMAIN 4: FLOW AND TIMING
A. RISK OF BIAS

The study utilised CTA images from patients for whom a reference standard diagnosis had already been established. All patients appear to have been included in the analysis.

Was there an appropriate time interval between index test and reference standard?	Yes
Did patients receive the same or a similar reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	**RISK: Low**

Study: Shalitin 2020[61]

DOMAIN 1: PATIENT SELECTION
A. RISK OF BIAS

Patients with CTA analysed using Viz LVO. No inclusion or exclusion criteria were reported. 'All sequential scans within a defined date range were reviewed and analysed.'

Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	**RISK: Unclear**

B. APPLICABILITY

No inclusion or exclusion criteria were reported. Time from symptom onset or 'last seen well' not reported

Do the included patients match the question?	**Concerns: Unclear**

DOMAIN 2: INDEX TEST(S)
A. RISK OF BIAS

Viz LVO: The study reports the diagnostic performance of the AI technology alone (hence, blinding to reference standard results NA), for the target condition LVO. No threshold was specified.

Were the index test results interpreted without knowledge of the results of the reference standard?	NA
If a threshold was used, was it pre-specified?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	**RISK: Unclear**

B. APPLICABILITY

The AI technology was evaluated as a stand-alone intervention, rather than as an adjunct to human interpretation.

Are there concerns that the index test, its conduct, or interpretation differ from the review question?	**Concerns: High**

DOMAIN 3: REFERENCE STANDARD
A. RISK OF BIAS

'Image interpretation by 'a team of radiology trained annotators' (no further details reported).

Is the reference standard likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index test?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	**RISK: Unclear**

B. APPLICABILITY

Is there concern that the target condition as defined by the reference standard does not match the review question?	**Concerns: Unclear**

DOMAIN 4: FLOW AND TIMING
A. RISK OF BIAS

The index test and reference standard utilised the same CTA images. All patients appear to have been included in the analysis.

Was there an appropriate time interval between index test and reference standard?	Yes
Did patients receive the same or a similar reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	**RISK: Low**

Study: Yahav-Dovrat 2021[59]

DOMAIN 1: PATIENT SELECTION
A. RISK OF BIAS

All consecutive head and neck CTA scans in a comprehensive stroke centre. Examinations with metal artifact, severe motion, or incomplete skull scanning were excluded from the analysis.

Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	**RISK: Low**

B. APPLICABILITY

Time from symptom onset or 'last seen well' not reported

Do the included patients match the question?	**Concerns: Unclear**

DOMAIN 2: INDEX TEST(S)
A. RISK OF BIAS

Viz LVO: The study reports the diagnostic performance of the AI technology alone (hence, blinding to reference standard results NA), for the target condition LVO (subgroup data for 'stroke protocol' patients). No threshold was specified.

Were the index test results interpreted without knowledge of the results of the reference standard?	NA
If a threshold was used, was it pre-specified?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	**RISK: Unclear**

B. APPLICABILITY

The AI technology was evaluated as a stand-alone intervention, rather than as an adjunct to human interpretation.

Are there concerns that the index test, its conduct, or interpretation differ from the review question?	**Concerns: High**

DOMAIN 3: REFERENCE STANDARD
A. RISK OF BIAS

Interpretation of CTA by one of four senior neuroradiologists with 7-25 years of experience. The reference standard interpretation was taken from the patients' files, i.e., determined before application of Viz LVO.

Is the reference standard likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index test?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	**RISK: Low**

B. APPLICABILITY

Is there concern that the target condition as defined by the reference standard does not match the review question?	**Concerns: Low**

DOMAIN 4: FLOW AND TIMING
A. RISK OF BIAS

The index test and reference standard utilised the same CTA images. All patients appear to have been include in the analysis.

Was there an appropriate time interval between index test and reference standard?	Yes
Did patients receive the same or a similar reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	**RISK: Low**

Quality Assessment of observational 'before and after' studies

Adhya 2021[33]

Q1. Did the study have a prospective design?	**No**
Retrospective study reporting one-year real world experience of rapid CTA.	

Q2. Did the study population include an appropriate spectrum of patients?	**Unclear**
No information was reported about the time from symptom onset or 'last known well' for included participants.	

Q3. Were the criteria used to select patients for CT imaging similar, before and after the introduction of the AI intervention?	**Yes**
All patients at the emergency department for stroke or neurological deficit, during two time periods, before and after implementation of Rapid CTA.	

Q4. Were the study populations, before and after the introduction of the AI intervention, similar with respect to baseline demographic characteristics (e.g., age, male/female), co-morbid conditions (e.g., hypertension, diabetes, atrial fibrillation) and risk factors (e.g., smoking status, previous history)??	**Unclear**
Insufficient comparative baseline characteristics reported.	

Q5. Other than the availability of AI software, was the care pathway similar before and after the introduction of the AI intervention?	**Yes**
All interventional equipment, endovascular therapists, neuroradiology staff, and hospitals serviced were identical during the study period, and the only significant change was the installation of RAPID-CTA.	

Q6. Was the implementation of the AI intervention clearly described? (e.g.,, how and when it was used to assist human readers and what was the level of training and experience of the human readers)	**No**
No information reported.	

Q7. Were the CT imaging criteria used to select patients for treatment (e.g.,, thrombectomy) clearly reported for both the periods before and after the introduction of the AI intervention?	**No**
No information reported.	

Q8. In addition to time to intervention outcomes, did the study report the proportion of patients who received treatment (e.g.,, thrombectomy) before and after the introduction of the AI intervention?	**No**
Total number of patients evaluated in each time period not reported.	

Q9. In addition to time to intervention outcomes, did the study report clinical outcomes (e.g.,, 90-day mRS) before and after the introduction of the AI intervention?	**Yes**
Mean 90-day mRS and number of participants with mRS ≤2 reported.	

Al-Kawaz 2021[34]

Q1. Did the study have a prospective design?	**No**
Retrospective analysis of prospectively collected data of patients presenting with LVOs between June 2019 and October 2020.	

Q2. Did the study population include an appropriate spectrum of patients?	**Unclear**
Patients with LVOs. No information was reported about the time from symptom onset or 'last known well' for included participants.	

Q3. Were the criteria used to select patients for CT imaging similar, before and after the introduction of the AI intervention?	**Unclear**
No information reported.	

Q4. Were the study populations, before and after the introduction of the AI intervention, similar with respect to baseline demographic characteristics (e.g., age, male/female), co-morbid conditions (e.g., hypertension, diabetes, atrial fibrillation) and risk factors (e.g., smoking status, previous history)?	**Yes**
There were no significant differences in baseline demographic characteristics (age and proportion male), co-morbid conditions (hypertension or DM) or NIHSS.	

Q5. Other than the availability of AI software, was the care pathway similar before and after the introduction of the AI intervention?	**Unclear**
No information reported.	

Q6. Was the implementation of the AI intervention clearly described? (e.g., how and when it was used to assist human readers and what was the level of training and experience of the human readers)	**Yes**
The inter-hospital treatment times analysis included patients presenting from a PSC affiliated with the CSC that used the RapidAI mobile application. Stroke Neurologists provided tele-stroke services to the PSC and had remote access to imaging. All remaining patients in the analyses presented from the CSC emergency room.	

Q7. Were the CT imaging criteria used to select patients for treatment (e.g., thrombectomy) clearly reported for both the periods before and after the introduction of the AI intervention?	**No**
No information reported.	

Q8. In addition to time to intervention outcomes, did the study report the proportion of patients who received treatment (e.g., thrombectomy) before and after the introduction of the AI intervention?	**NA**
All included participants received thrombectomy.	

Q9. In addition to time to intervention outcomes, did the study report clinical outcomes (e.g., 90-day mRS) before and after the introduction of the AI intervention?	**No**
Study reports time from door to groin puncture only.	

Gunda 2020[44]

Q1. Did the study have a prospective design?	**No**
Two identical seven-month periods, in 2017 and 2018, were retrospectively evaluated.	

Q2. Did the study population include an appropriate spectrum of patients?	**Unclear**
Insufficient information (study includes admitted stroke patients with no further details reported).	

Q3. Were the criteria used to select patients for CT imaging similar, before and after the introduction of the AI intervention?	**Yes**
The AI-derived software technology was implemented in 2018 and delivery of stroke care was otherwise unchanged over the two years.	

Q4. Were the study populations, before and after the introduction of the AI intervention, similar with respect to baseline demographic characteristics (e.g., age, male/female), co-morbid conditions (e.g., hypertension, diabetes, atrial fibrillation) and risk factors (e.g., smoking status, previous history)?	**Unclear**
No information reported.	

Q5. Other than the availability of AI software, was the care pathway similar before and after the introduction of the AI intervention?	**Yes**
The AI-derived software technology was implemented in 2018 and delivery of stroke care was otherwise unchanged over the two years.	

Q6. Was the implementation of the AI intervention clearly described? (e.g., how and when it was used to assist human readers and what was the level of training and experience of the human readers)	**No**
No information reported.	

Q7. Were the CT imaging criteria used to select patients for treatment (e.g., thrombectomy) clearly reported for both the periods before and after the introduction of the AI intervention?	**No**
No information reported.	

Q8. In addition to time to intervention outcomes, did the study report the proportion of patients who received treatment (e.g., thrombectomy) before and after the introduction of the AI intervention?	**Yes**
The proportion of patients transferred for thrombectomy increased from 2.8% to 4.8% and the proportion receiving thrombolysis increased from 11.5% to 18.1% after implementation of the AI-derived software technology.	

Q9. In addition to time to intervention outcomes, did the study report clinical outcomes (e.g., 90-day mRS) before and after the introduction of the AI intervention?	**No**
No clinical outcomes were reported (treatment rates and time to treatment only).	

Hassan 2020[46]

Q1. Did the study have a prospective design?	**No**
A retrospective study of LVO patients who presented to a PSC and were transferred to a CSC.	

Q2. Did the study population include an appropriate spectrum of patients?	**Yes**
Patients who presented at the PSC with an LVO on CTA and were transferred to the CSC with the intent of having endovascular treatment.	

Q3. Were the criteria used to select patients for CT imaging similar, before and after the introduction of the AI intervention?	**Yes**
The selection criteria were the same for both populations.	

Q4. Were the study populations, before and after the introduction of the AI intervention, similar with respect to baseline demographic characteristics (e.g., age, male/female) co-morbid conditions (e.g., hypertension, diabetes, atrial fibrillation) and risk factors (e.g., smoking status, previous history)?	**No**
There were no significant differences in baseline demographic characteristics (age, proportion male or ethnicity), co-morbid conditions (DM or hypertension) and risk factors (smoking status). The proportion of patients with AF and the mean baseline NIHSS were higher in the before implementation population.	

Q5. Other than the availability of AI software, was the care pathway similar before and after the introduction of the AI intervention?	**Yes**
The article includes a flow chart showing the care pathway before and after the introduction of the AI-derived software technology; only the imaging interpretation steps differ.	

Q6. Was the implementation of the AI intervention clearly described? (e.g., how and when it was used to assist human readers and what was the level of training and experience of the human readers)	**Yes**
After the implementation of the AI-derived technology, the physician at the CSC sees CTA results and confirms LVO on the app, before accepting the patient for transfer.	

Q7. Were the CT imaging criteria used to select patients for treatment (e.g., thrombectomy) clearly reported for both the periods before and after the introduction of the AI intervention?	**No**
Insufficient information reported.	

Q8. In addition to time to intervention outcomes, did the study report the proportion of patients who received treatment (e.g., thrombectomy) before and after the introduction of the AI intervention?	**Yes**
Before implementation of the AI-derived software technology, all 28 transferred patients received thrombectomy. After implementation, thrombectomy was withheld from four of the 15 transferred patients due to thrombolytic recanalisation following IV thrombolysis, or extensive infarction.	

Q9. In addition to time to intervention outcomes, did the study report clinical outcomes (e.g., 90-day mRS) before and after the introduction of the AI intervention?	**Yes**
Number of patients with mRS at discharge ≤2, length of hospital stay, in-hospital complications and in-hospital mortality reported for all patients (including those who did not receive thrombectomy).	

Hassan 2021a[45]

Q1. Did the study have a prospective design?	**No**
The study used information from a 'prospectively collected database'.	

Q2. Did the study population include an appropriate spectrum of patients?	**Yes**
All LVO transfer patients arriving at a CSC.	

Q3. Were the criteria used to select patients for CT imaging similar, before and after the introduction of the AI intervention?	**Yes**
All LVO transfer patients arriving at a CSC for approximately two years prior to and following implementation of the AI-derived software technology.	

Q4. Were the study populations, before and after the introduction of the AI intervention, similar with respect to baseline demographic characteristics (e.g., age, male/female), co-morbid conditions (e.g., hypertension, diabetes, atrial fibrillation) and risk factors (e.g., smoking status, previous history)?	**Yes**
There were no significant differences in baseline demographic characteristics (age, proportion male or ethnicity), co-morbid conditions (DM, hypertension, AF), risk factors (history of stroke/TIA or smoking status), or NIHSS.	

Q5. Other than the availability of AI software, was the care pathway similar before and after the introduction of the AI intervention?	**Unclear**
No information reported.	

Q6. Was the implementation of the AI intervention clearly described? (e.g., how and when it was used to assist human readers and what was the level of training and experience of the human readers)	**No**
No information reported.	

Q7. Were the CT imaging criteria used to select patients for treatment (e.g., thrombectomy) clearly reported for both the periods before and after the introduction of the AI intervention?	**No**
No information reported.	

Q8. In addition to time to intervention outcomes, did the study report the proportion of patients who received treatment (e.g., thrombectomy) before and after the introduction of the AI intervention?	**NA**
All included participants received thrombectomy.	

Q9. In addition to time to intervention outcomes, did the study report clinical outcomes (e.g., 90-day mRS) before and after the introduction of the AI intervention?	**Yes**
Number of patients with mRS at discharge ≤2, length of hospital stay and in-hospital mortality reported.	

Kamal 2017[49]

Q1. Did the study have a prospective design?	**No**
A retrospective cohort study of AIS patients undergoing thrombectomy.	

Q2. Did the study population include an appropriate spectrum of patients?	**Unclear**
Insufficient information reported (AIS patients undergoing thrombectomy, no further details reported).	

Q3. Were the criteria used to select patients for CT imaging similar, before and after the introduction of the AI intervention?	**Unclear**
No information reported.	

Q4. Were the study populations, before and after the introduction of the AI intervention, similar with respect to baseline demographic characteristics (e.g., age, male/female), co-morbid conditions (e.g., hypertension, diabetes, atrial fibrillation) and risk factors (e.g., smoking status, previous history)?	**Yes**
There were no significant differences in baseline demographic characteristics (age or proportion male), co-morbid conditions (DM or hypertension), risk factors (smoking status), or NIHSS.	

Q5. Other than the availability of AI software, was the care pathway similar before and after the introduction of the AI intervention?	**Unclear**
No information reported.	

Q6. Was the implementation of the AI intervention clearly described? (e.g., how and when it was used to assist human readers and what was the level of training and experience of the human readers)	**No**
No information reported.	

Q7. Were the CT imaging criteria used to select patients for treatment (e.g., thrombectomy) clearly reported for both the periods before and after the introduction of the AI intervention?	**No**
No information reported.	

Q8. In addition to time to intervention outcomes, did the study report the proportion of patients who received treatment (e.g., thrombectomy) before and after the introduction of the AI intervention?	**NA**
All included patients received thrombectomy.	

Q9. In addition to time to intervention outcomes, did the study report clinical outcomes (e.g., 90-day mRS) before and after the introduction of the AI intervention?	**Unclear**
Proportion of patients with mRS ≤3 reported (no time point specified)	

Morey 2020a[52]

Q1. Did the study have a prospective design?	**No**
A retrospective analysis of a prospectively maintained database.	

Q2. Did the study population include an appropriate spectrum of patients?	**Yes**
Consecutive patients who were transferred to a TSC or CSC with LVO and who underwent thrombectomy. In-patients and patients in whom the thrombectomy decision was delayed due to fluctuating symptoms were excluded.	

Q3. Were the criteria used to select patients for CT imaging similar, before and after the introduction of the AI intervention?	**Unclear**
No information reported.	

Q4. Were the study populations, before and after the introduction of the AI intervention, similar with respect to baseline demographic characteristics (e.g., age, male/female), co-morbid conditions (e.g., hypertension, diabetes, atrial fibrillation) and risk factors (e.g., smoking status, previous history)?	**No**
There were no significant differences in baseline demographic characteristics (age or proportion male), co-morbid conditions (DM or hypertension), risk factors (previous stroke/TIA), or NIHSS. The proportion or patients with hypertension was higher in the before implementation population.	

Q5. Other than the availability of AI software, was the care pathway similar before and after the introduction of the AI intervention?	**Unclear**
No information reported.	

Q6. Was the implementation of the AI intervention clearly described? (e.g., how and when it was used to assist human readers and what was the level of training and experience of the human readers)	**No**
No information reported.	

Q7. Were the CT imaging criteria used to select patients for treatment (e.g., thrombectomy) clearly reported for both the periods before and after the introduction of the AI intervention?	**No**
No information reported.	

Q8. In addition to time to intervention outcomes, did the study report the proportion of patients who received treatment (e.g., thrombectomy) before and after the introduction of the AI intervention?	**NA**
All included participants received thrombectomy.	

Q9. In addition to time to intervention outcomes, did the study report clinical outcomes (e.g., 90-day mRS) before and after the introduction of the AI intervention?	**Yes**
Median 90-day mRS and number of participants with 90-day mRS ≤2 were reported.	

APPENDIX 4: DETAILS OF EXCLUDED STUDIES WITH RATIONALE

To be included in the review studies had to fulfil the following criteria:

Population:	Adults (≥18 years old) attending a secondary care stroke centre with: (Q1) suspected acute stroke and who were last known to be well within 24 hours; (Q2a) AIS, who were last known to be well within 6 hours; (Q2b) suspected acute stroke, who were last known to be well more than 6 hours previously, but within 24 hours, and in whom ischaemic stroke has been confirmed on plain CT
Index Test:	AI-derived software: Aidoc ICH, Aidoc LVO, Aidoc mobile (Aidoc); Accipio (MaxQ AI); e-ASPECTS, e-CTP, e-CTA (Brainomix); icobrain ct (Icometrix); Biomind (Biomind.ai); Brainscan; Cercare stroke (Cercare Medical); CINA ICH, CINA LVO, CINA ASPECTS (Avicenna); CT Perfusion 4D (GE Healthcare); qER (Qure.ai); Rapid ASPECTS, Rapid ICH, Rapid CTA, Rapid LVO, Rapid CTP), RapidAI (iSchemaView); Viv ICH, Viz LVO, Viz CTP (Viz.ai); Zebra-Med (Zebra Medical Vision) (Q1) AI-derived software assisted review of plain CT by a healthcare professional other than a neuroradiologist (Q2a) AI-derived software assisted CTA by a healthcare professional other than a neuroradiologist (Q2b) AI-derived software assisted CTA and CTP review by a healthcare professional other than a neuroradiologist
Reference Standard:	Unassisted, (Q1) plain CT, (Q2a) CTA, (Q2b) CTP, review by a neuroradiologist, or by a consensus panel
Comparator:	(Q1) Unassisted plain CT review by a neuroradiologist or other healthcare professional (Q2a) Unassisted CTA review by a neuroradiologist or other healthcare professional (Q2b) AI-derived software assisted CTA and AI-derived software assisted CT perfusion brain scan review by a neuroradiologist or other healthcare professional **OR** Unassisted CTA and AI-derived software assisted CT perfusion brain scan review by a neuroradiologist or other healthcare professional
Outcome:	Test accuracy (the numbers of true positive, false negative, false positive and true negative test results), for the target condition: (Q1) ICH or ischaemic stroke; (Q2a) LVO/occlusion of the proximal anterior circulation; (Q2b)

LVO/occlusion of the proximal anterior circulation for CTA and presence of salvageable tissue for CTP

Clinical/patient-perceived outcomes: mortality, function (e.g., modified Rankin score), health-related quality of life, procedure-related adverse events (e.g., bleed subsequent to thrombolysis), length of hospital stay

The table below summarises studies which were screened for inclusion based on full text publication but did not fulfil one or more of the above criteria. Studies were assessed sequentially against criteria; as soon as a study had failed based on one of the criteria it was not assessed against subsequent criteria. The table shows which of the criteria each study fulfilled ("Y") and on which item it failed ("N") or was unclear.

Study Details	Study Design	Population	Index Test	Reference Standard OR Comparator	Outcome
Abdelkhaleq, 2021[121]	Y	N	Y	N	N
Aboutaleb, 2020[122]	Y	Y	N		
Aghaebrahim, 2020[123]	N	N			
Aktar, 2020[124]	Y	N	Y	N	
Albers, 2019[125]	Y	Y	Y	N	N
Alderson, 2020a[126]	Y	Y	Y	N	N
Alderson, 2020b[127]	N				
Apterbach, 2021[128]	Y	Y	N		
Austein, 2018[129]	Y	Y	Y	Y	N
Austein, 2019a[130]	Y	Y	Y	Y	N
Austein, 2019b[131]	Y	N			
Austein, 2020[132]	Y	Y	Y	Y	N
Bacchi, 2020[133]	Y	Y	N		
Bar, 2019[134]	Y	Y	Y	N	N
Barman, 2019[135]	Y	Y	N		
Barros, 2019[136]	Y	Y	N		
Beijing Tiantan, 2022[137]	Y	Y	N		
Bentley, 2013[138]	Y	N			
Bentley, 2014[139]	Y	N			
Bhagat, 2021[140]	Y	N			
Biswas, 2020[141]	N				

Study Details	Study Design	Population	Index Test	Reference Standard OR Comparator	Outcome
Bouslama, 2019[142]	Y	Y	Y	N	
Bouslama, 2021[112]	Y	Y	Y	N	
Bouvy, 2020[143]	Y	N			
Brinjikji, 2020[144]	Y	Y	Y	Y	N
Brinjikji, 2021a[145]	Y	Y	Y	Y	N
Brinjikji, 2021b[146]	N				
Bruggeman, 2021[147]	Y	Y	N		
Brugnara, 2020[148]	Y	Y	N		
Buls, 2021[149]	Y	N			
Bulwa 2019[150]	Y	Y	Y	Y	N
Campbell, 2015[151]	Y	Y	N		
Capasso, 2021[152]	Y	Y	Y	N	
Chatterjee 2019[153]	Y	Y	Y	Y	N
Chilamkurthy, 2018[154]	Y	N			
Chriashkova, 2019a[155]	Y	Y	Y	Y	N
Chriashkova, 2019b[156]	Y	Y	Y	Y	N
Chung, 2019[157]	Y	Y	Y	Y	N
Chung, 2020[158]	Y	N			
Cimflova, 2020a[159]	Y	Y	Y	N	
Cimflova, 2020b[160]	Y	Y	Y	N	
Copelan, 2020[161]	Y	Y	Y	Y	N
D'Esterre, 2014[162]	Y	Y	N		
Davidovic, 2017[163]	Y	Y	N		
Davis, 2020[164]	Y	N			
Dehkharghani, 2015[165]	N				
Delio, 2021a[166]	Y	Y	Y	Y	N
Delio, 2021b[167]	Y	Y	Y	Y	N
Demeestere, 2018a[168]	N				
Demeestere, 2018b[113]	N				
Desai, 2019[169]	Y	Y	Y	Y	N
Devlin, 2019 [170]	Y	Y	Y	Y	N
Docema, 2021[171]	Y	Y	N		

Study Details	Study Design	Population	Index Test	Reference Standard OR Comparator	Outcome
Elijovich, 2021 [172]	Y	Y	Y	N	N
Ferreti, 2020a[173]	Y	Y	Y	N	
Ferreti, 2020b[174]	Y	Y	Y	Y	N
Fischer 2018[175]	Y	Y	Y	Y	N
Ford 2020[176]	Y	Y	Y	Y	N
Ginat, 2020[177]	Y	N			
Ginat, 2021[178]	Y	N			
Goebel, 2018a[179]	Y	Y	Y	Y	N
Goebel, 2018b[180]	Y	Y	Y	Y	N
Goebel, 2018c[181]	Y	Y	Y	Y	N
Goncalves, 2017[182]	Y	Unclear	Y	Y	N
Grunwald, 2015[183]	Y	Y	Y	Y	N
Grunwald, 2016a[184]	N				
Grunwald, 2016b[185]	N				
Grunwald, 2016c[186]	N				
Grunwald, 2019[187]	Y	Y	Y	Y	N
Guberina, 2018[188]	Y	Y	Y	N	
Heit, 2021[189]	Y	N			
Herweh, 2014[190]	Y	Y	Y	N	
Herweh, 2016[191]	Y	Y	Y	N	
Herweh 2020[192]	Y	Y	N		
Hoelter, 2020[193]	Y	Y	Y	Y	N
Hoffmann 2019[194]	Y	N			
Hokkinen, 2021[195]	Y	Y	Y	Y	N
Hoving, 2018[196]	Y	Y	Y	Y	N
Hoyte, 2017[197]	Y	Y	Y	Y	N
Jankowitz, 2021[198]	Y	N			
John, 2019[199]	Y	Y	Y	Y	N
John, 2020[200]	Y	Y	Y	Y	N
Katramados, 2021[201]	Y	Y	N		
Kelavkar, 2017[202]	Y	Y	N		
Kettenberger, 2018[203]	Y	Y	N		

Study Details	Study Design	Population	Index Test	Reference Standard OR Comparator	Outcome
Kettenberger, 2019[204]	Y	Y	N		
Kim, 2021[205]	Y	Y	N		
Kniep, 2020[206]	Y	Y	N		
Knight-Greenfield, 2018[207]	Y	Y	N		
Kral, 2020[208]	Y	Y	Y	N	
Kuang, 2018[209]	Y	Y	Y	Y	N
Kuang, 2019[210]	Y	Y	Y	N	N
Kuang, 2020[211]	Y	Y	Y	Y	N
Kuo, 2019[212]	Y	Y	N		
Lasocha, 2020[213]	Y	Y	Y	Y	N
Lee, 2020[214]	Y	Y	N		
Liu, 2021[215]	Y	Y	Y	N	
Lo, 2021[216]	Y	Y	N		
Loffler, 2021[217]	Y	Y	Y	Y	N
Maegerlein, 2019[218]	Y	Y	Y	Y	N
Mair, 2020[219]	Y	Y	Y	Y	N
Mansour, 2020[220]	Y	Y	Y	Y	N
Meijs, 2017[221]	Y	Y	Y	Y	N
Meijs, 2020[222]	Y	Y	N		
Modak, 2019[223]	Y	Y	Y	Y	N
Morey, 2021[224]	Y	Y	Y	Y	N
Murray, 2019 [225]	N				
Nagel, 2017[226]	Y	Y	Y	Y	N
Nagel, 2018[227]	N				
Nagel, 2019[228]	Y	Y	Y	Y	N
Nagel, 2020[229]	Y	Y	Y	Y	N
Neuberger, 2019[230]	Y	Y	Y	Y	N
Neuberger, 2020[231]	Y	Y	Y	Y	N
Neuhaus, 2020[232]	Y	Y	Y	Y	N
Nishio, 2020[233]	Y	Y	N		
Ojeda, 2019[234]	Y	N			
Olive-Gadea, 2018a[235]	Y	Y	Y	Y	N

Study Details	Study Design	Population	Index Test	Reference Standard OR Comparator	Outcome
Olive-Gadea, 2018b[236]	Y	Y	Y	Y	N
Olive-Gadea, 2019[115]	Y	Y	Y	Y	N
Olive-Gadea, 2020a[237]	Y	Y	N		
Olive-Gadea, 2020b[238]	Y	Y	N		
Pfaff, 2017a[239]	Y	Y	Y	Y	N
Pfaff, 2017b[114]	Y	Y	Y	Y	N
Pisani, 2020[240]	Y	Y	Y	Y	N
Pisani, 2021[241]	Y	Y	Y	Y	N
Prokhorikhin, 2020[242]	Y	Y	N		
Providence Little Company of, 2020[243]	N				
Psychogios, 2021[244]	Y	Y	Y	Y	N
Purrucker, 2018[245]	Y	Y	Y	Y	N
Purrucker, 2020[246]	Y	Y	Y	Y	N
Qiu, 2021[247]	Y	Y	N		
Rao, 2021[248]	Y	Y	N		
Rava, 2021[249]	Y	Y	Y	Y	N
Reidler, 2020[250]	Y	Y	N		
Sachdev, 2015[251]	Y	Y	Y	Y	N
Seo, 2019[252]	Y	Y	Y	Y	N
Shah, 2017 [253]	Y	Y	Y	Y	N
Sheth, 2019a[254]	Y	Y	Y	Y	N
Sheth, 2019b[255]	Y	Y	N		
Shinohara, 2020a[256]	Y	Y	N		
Shinohara, 2020b[257]	Y	Y	N		
Siegler, 2020[258]	Y	Y	Y	Y	N
Sundaram, 2019[259]	Y	Y	Y	Y	N
Suomalainen, 2019[260]	Y	Y	Y	Y	N
Suomalainen, 2020[261]	Y	Y	Y	Y	N
Timaran, 2021[262]	Y	Y	Y	N	
Tolhuisen, 2019a[263]	Y	Y	N		
Tolhuisen, 2019b[263]	Y	Y	N		

Study Details	Study Design	Population	Index Test	Reference Standard OR Comparator	Outcome
Tsang, 2020[264]	Y	Y	Y	Y	N
Tyan, 2014[265]	Y	Y	N		
University of Guadalajara, 2019[266]	Y	Y	N		
Vargas, 2021 [267]	Y	Y	Y	N	N
Voter, 2021a[268]	Y	N			
Voter, 2021b[269]	Y	N			
Vyas, 2019[270]	N				
Wang C, 2021[271]	Y	Y	N		
Wang TG, 2021[272]	Y	Y	Y	N	
Weiss, 2020[273]	Y	Y	Y	Y	N
Weiss, 2021[274]	Y	Y	Y	Y	N
Yang L, 2020[275]	Y	Y	N		
Yang W, 2020[276]	Y	Y	N		
Zamarro Parra, 2019[277]	Y	Y	Y	Y	N

APPENDIX 5: PRISMA CHECKLIST

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Title page
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Preceding table of contents
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Section 2
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Section 1
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Sections 3.1.2 and 3.1.5
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Section 3.1.1
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Appendix 1
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Section 3.1.3
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Section 3.1.3
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g., for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Sections 3.1.2 and 3.1.3
	10b	List and define all other variables for which data were sought (e.g., participant and intervention characteristics, funding	Section 3.1.3

Section and Topic	Item #	Checklist item	Location where item is reported
		sources). Describe any assumptions made about any missing or unclear information.	
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Section 3.1.4
Effect measures	12	Specify for each outcome the effect measure(s) (e.g., risk ratio, mean difference) used in the synthesis or presentation of results.	Section 3.1.3
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g., tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Section 3.1.5
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	NA
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Section 3.1.5
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Section 3.1.5
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g., subgroup analysis, meta-regression).	NA
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	NA
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	NA
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	NA
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Figure 3 and section 3.2.1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Appendix 4

Section and Topic	Item #	Checklist item	Location where item is reported
Study characteristics	17	Cite each included study and present its characteristics.	Section 3.2.1, Table 3 and Appendix 2
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Section 3.2.2 and Appendix 3
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g., confidence/credible interval), ideally using structured tables or plots.	Sections 3.2.3, 3.2.4 and 3.2.5
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Section 3.2.2
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g., confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Section 3.2.4, Table 11 and Figures 4 and 5
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Table 11 and Figure 5
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Table 11 and Figure 5
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	NA
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Section 3.2.4, Table 11 and Figures 4 and 5
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Section 5.1.1
	23b	Discuss any limitations of the evidence included in the review.	Sections 5.2.1 and 5.3.1
	23c	Discuss any limitations of the review processes used.	Section 5.2.1

Section and Topic	Item #	Checklist item	Location where item is reported
	23d	Discuss implications of the results for practice, policy, and future research.	Section 6
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	PROSPERO registration: CRD42021269609
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	PROSPERO
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	NA (no amendments)
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Funded by NIHR
Competing interests	26	Declare any competing interests of review authors.	None
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	None

APPENDIX 6: NICE GUIDANCE RELEVANT TO THE MANAGEMENT OF SUPECTED ACUTE STROKE

Stroke and transient ischaemic attack in over 16s: diagnosis and initial management. NICE guideline (NG128), published 1st May 2019.
https://www.nice.org.uk/guidance/ng128

Alteplase for treating acute ischaemic stroke. Technology appraisal guidance (TA264), published 26th September 2012.
https://www.nice.org.uk/guidance/ta264/chapter/1-Guidance

Mechanical clot retrieval for treating acute ischaemic stroke. Interventional procedures guidance (IPG548), published 24th February 2016.
https://www.nice.org.uk/guidance/ipg548

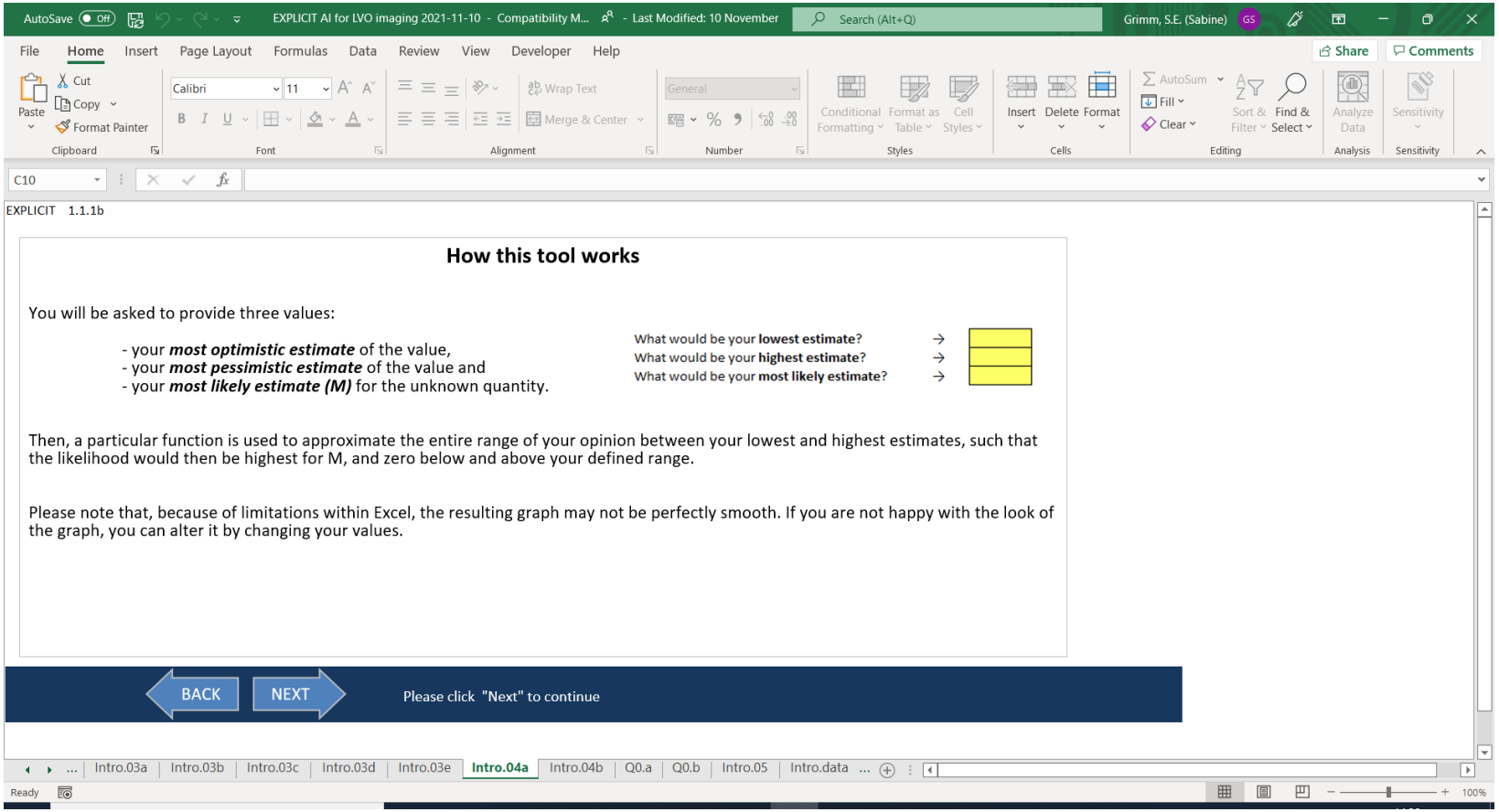
Stroke in adults. Quality standard (QS2), published 29th June 2010, last updated 12th April 2016.
https://www.nice.org.uk/guidance/qs2

Mechanical thrombectomy devices for acute ischaemic stroke. Medtech innovation briefing (MIB153), published 30th July 2018.
https://www.nice.org.uk/advice/mib153

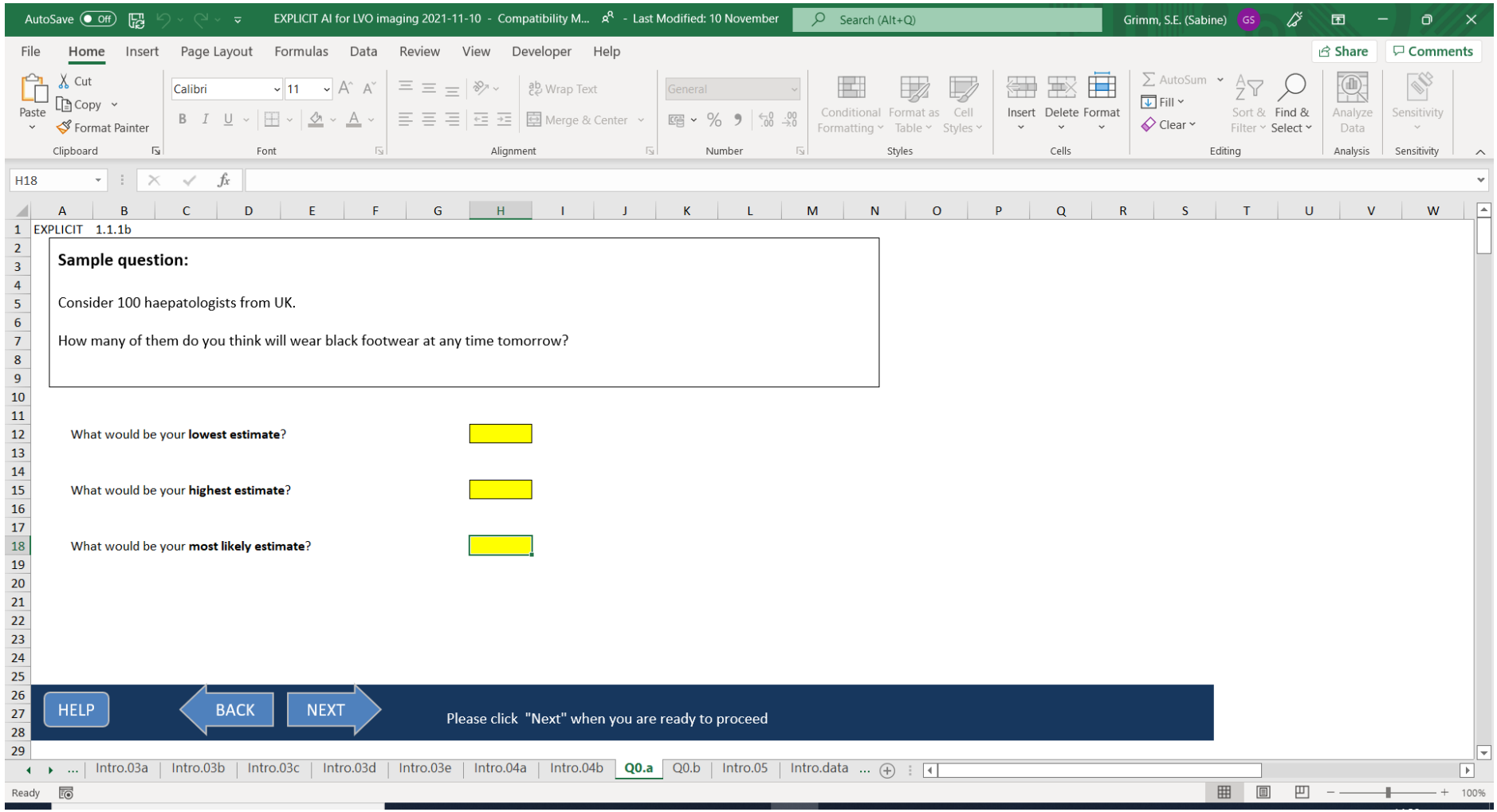
RapidAI for analysing CT/MRI brain scans in people with suspected acute stroke. Medtech innovation briefing (MIB262), published 1st June 2021.
https://www.nice.org.uk/advice/mib262

APPENDIX 7: EXPLICIT TOOL SCREENSHOTS

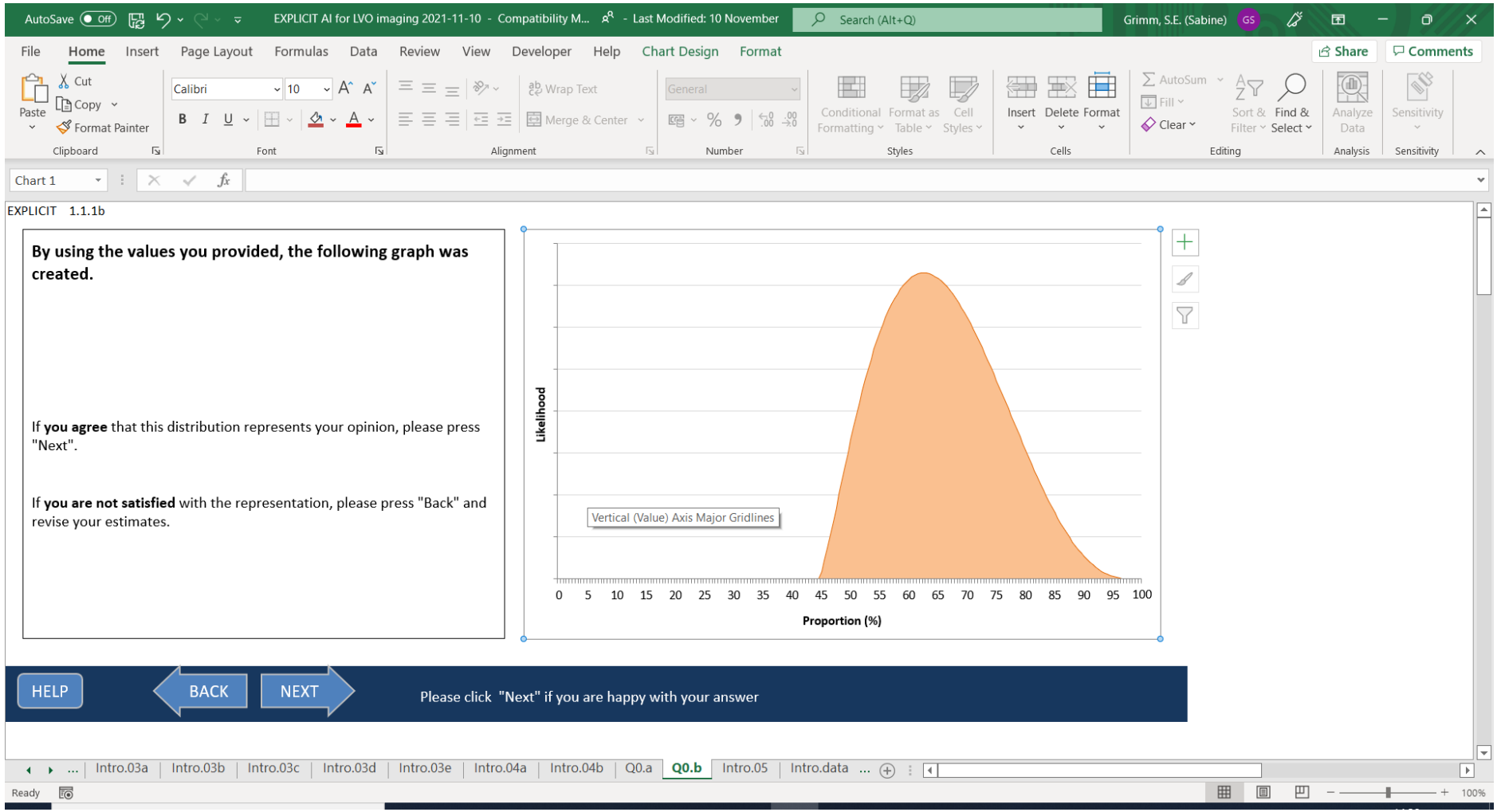
Explanations on how to use the tool



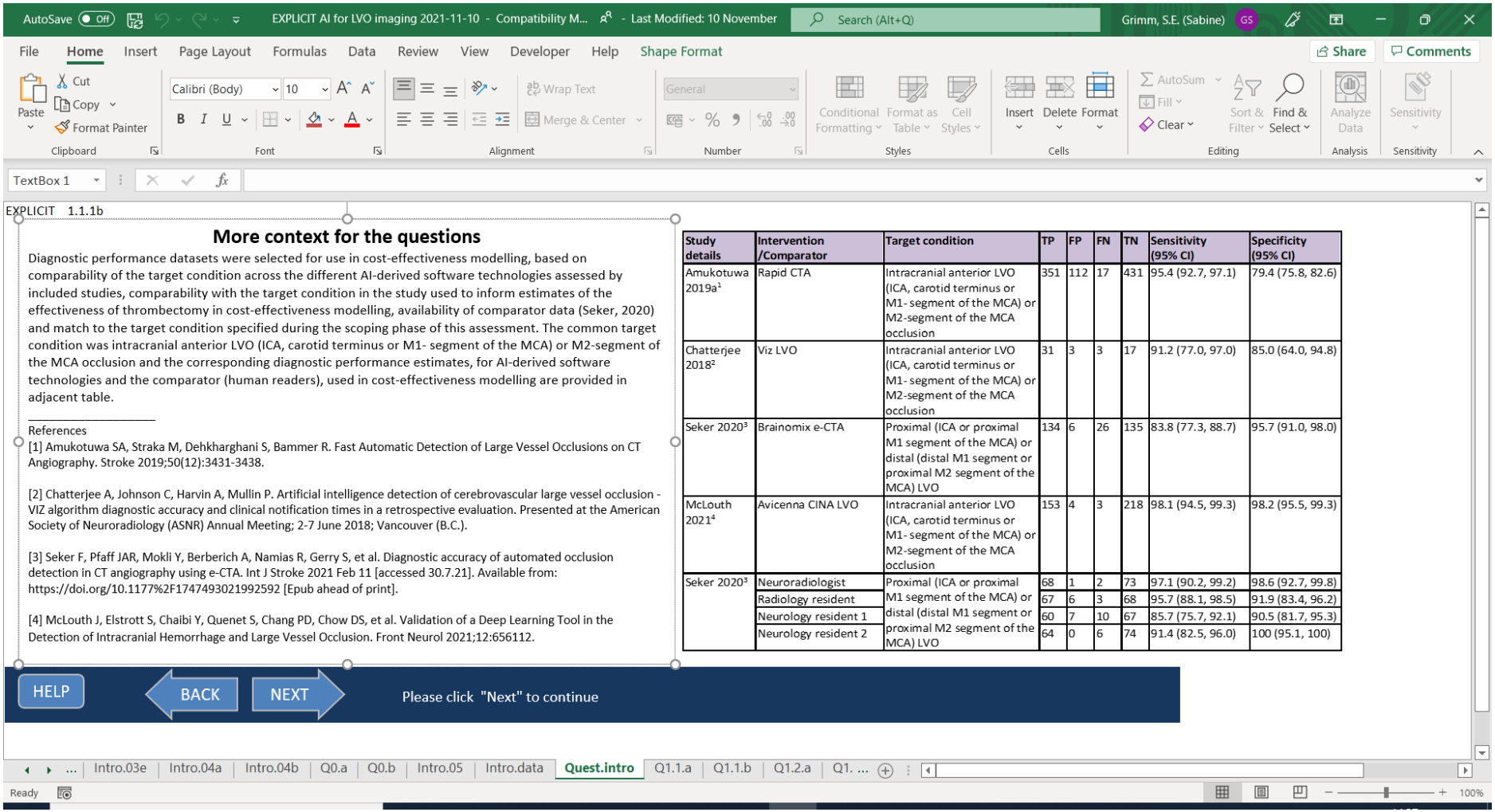
Example training exercise



Example training exercise results screen



Background information provided to experts



EXPLICIT 1.1.1b

More context for the questions

Diagnostic performance datasets were selected for use in cost-effectiveness modelling, based on comparability of the target condition across the different AI-derived software technologies assessed by included studies, comparability with the target condition in the study used to inform estimates of the effectiveness of thrombectomy in cost-effectiveness modelling, availability of comparator data (Seker, 2020) and match to the target condition specified during the scoping phase of this assessment. The common target condition was intracranial anterior LVO (ICA, carotid terminus or M1- segment of the MCA) or M2-segment of the MCA occlusion and the corresponding diagnostic performance estimates, for AI-derived software technologies and the comparator (human readers), used in cost-effectiveness modelling are provided in adjacent table.

References

[1] Amukotuwa SA, Straka M, Dehkharghani S, Bammer R. Fast Automatic Detection of Large Vessel Occlusions on CT Angiography. Stroke 2019;50(12):3431-3438.

[2] Chatterjee A, Johnson C, Harvin A, Mullin P. Artificial intelligence detection of cerebrovascular large vessel occlusion - VIZ algorithm diagnostic accuracy and clinical notification times in a retrospective evaluation. Presented at the American Society of Neuroradiology (ASNR) Annual Meeting; 2-7 June 2018; Vancouver (B.C.).

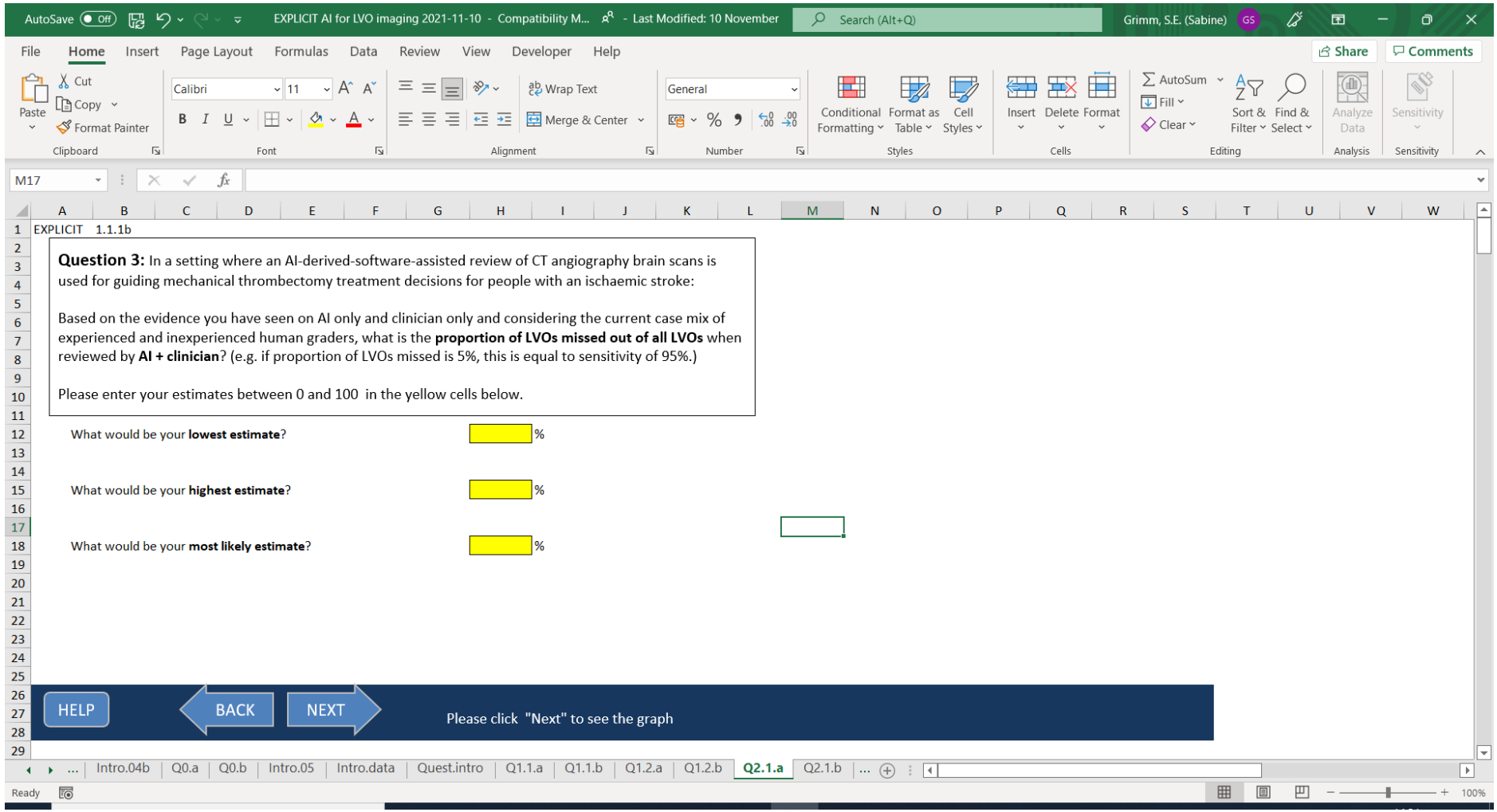
[3] Seker F, Pfaff JAR, Mokli Y, Berberich A, Namias R, Gerry S, et al. Diagnostic accuracy of automated occlusion detection in CT angiography using e-CTA. Int J Stroke 2021 Feb 11 [accessed 30.7.21]. Available from: https://doi.org/10.1177%2F1747493021992592 [Epub ahead of print].

[4] McLouth J, Elstrott S, Chaibi Y, Quenet S, Chang PD, Chow DS, et al. Validation of a Deep Learning Tool in the Detection of Intracranial Hemorrhage and Large Vessel Occlusion. Front Neurol 2021;12:656112.

Study details	Intervention /Comparator	Target condition	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Amukotuwa 2019a[1]	Rapid CTA	Intracranial anterior LVO (ICA, carotid terminus or M1- segment of the MCA) or M2-segment of the MCA occlusion	351	112	17	431	95.4 (92.7, 97.1)	79.4 (75.8, 82.6)
Chatterjee 2018[2]	Viz LVO	Intracranial anterior LVO (ICA, carotid terminus or M1- segment of the MCA) or M2-segment of the MCA occlusion	31	3	3	17	91.2 (77.0, 97.0)	85.0 (64.0, 94.8)
Seker 2020[3]	Brainomix e-CTA	Proximal (ICA or proximal M1 segment of the MCA) or distal (distal M1 segment or proximal M2 segment of the MCA) LVO	134	6	26	135	83.8 (77.3, 88.7)	95.7 (91.0, 98.0)
McLouth 2021[4]	Avicenna CINA LVO	Intracranial anterior LVO (ICA, carotid terminus or M1- segment of the MCA) or M2-segment of the MCA occlusion	153	4	3	218	98.1 (94.5, 99.3)	98.2 (95.5, 99.3)
Seker 2020[3]	Neuroradiologist	Proximal (ICA or proximal M1 segment of the MCA) or distal (distal M1 segment or proximal M2 segment of the MCA) LVO	68	1	2	73	97.1 (90.2, 99.2)	98.6 (92.7, 99.8)
	Radiology resident		67	6	3	68	95.7 (88.1, 98.5)	91.9 (83.4, 96.2)
	Neurology resident 1		60	7	10	67	85.7 (75.7, 92.1)	90.5 (81.7, 95.3)
	Neurology resident 2		64	0	6	74	91.4 (82.5, 96.0)	100 (95.1, 100)

HELP BACK NEXT Please click "Next" to continue

Sensitivity question AI + human



Specificity question AI + human