National Institute for Health and Care Excellence

Guideline version (Consultation)

Subarachnoid haemorrhage

[K] Evidence review for diagnostic imaging strategies

NICE guideline <number>

Evidence review underpinning

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Draft for consultation

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1 Diagnostic imaging strategies

Evidence review underpinning recommendations 1.1.14 to 1.1.19 in the NICE guideline.

1.1 Review question: What is the accuracy of different imaging strategies to detect a culprit aneurysm in adults with confirmed subarachnoid haemorrhage?

1.2 Introduction

People with a confirmed diagnosis of subarachnoid haemorrhage require further investigation to establish the cause of the haemorrhage. In around 80% of cases vascular imaging demonstrates a culprit intracranial arterial aneurysm, which is thought to have ruptured into the subarachnoid space.

Digital subtraction angiography (DSA) has been used to detect intracranial arterial aneurysm for many years and is thought to have high diagnostic accuracy. DSA is an invasive radiographic procedure, requires administration of radiographic contrast, and is associated with a small risk of stroke (<0.1%).

In current practice CT angiography (CTA) is used widely to detect intracranial arterial aneurysm and if an aneurysm is detected, aneurysmal SAH is confirmed and the patient will be referred to a neuroscience centre for further management. CTA is a non-invasive investigation but exposes people to ionising radiation and requires administration of intravenous radiographic contrast.

MR angiography has also been used to detect intracranial arterial aneurysm in people with subarachnoid haemorrhage but may require general anaesthesia and is difficult in unstable patients.

The consequence of overlooking a ruptured brain aneurysm may be an early re-bleeding event, which could result in disability or death. Due to this possibility, investigation strategies have evolved to maximise the prospect of aneurysm detection. A negative test result on the investigation pathway is interpreted in the context of the clinical and imaging level of suspicion of aneurysmal bleeding. Good quality tests that are clearly negative are reassuring and suggest that investigation for other causes of the presentation should be considered.

This review assesses the diagnostic accuracy of CT angiography and MR angiography for the detection of cerebral arterial aneurysm, with digital subtraction angiography as the reference standard.

1.3 PICO table

For full details see the review protocol in Appendix A:.

Table 1: PICO characteristics of review question

Population	Adults (16 and older) with a confirmed subarachnoid haemorrhage caused by a suspected ruptured aneurysm.
Target condition	Aneurysmal subarachnoid haemorrhage
Index tests	• MR Angiography • CT angiography
Reference standard	Direct angiography (DSA)

Statistical measures	Statistical measure to detecting aSAH: • Sensitivity • Specificity • Positive Predictive Value (PPV) • Negative Predictive Value (NPV) • Receiver Operating Characteristic (ROC) curve or area under curve)
Study design	• Cross-sectional studies • Cohort studies.

1.4 Clinical evidence

1.4.1 Included studies

Sixty-four studies were included in the review,[1, 4, 5, 7, 29, 31, 33, 35, 37, 38, 43, 50, 54, 55, 58, 61, 64, 67, 77, 82, 90, 95, 99, 105, 113, 120, 123, 124, 129, 131, 132, 134, 139, 144, 145, 157, 163, 170, 172, 174, 176, 177, 179, 182, 184, 185, 188, 189, 196, 199, 200, 202, 209, 211, 215, 219, 225, 227, 232, 234, 248, 253, 258, 263] these are summarised in Table 2 below. Evidence from these studies is summarised in the clinical evidence summary below (Table 3).

Studies reporting the diagnostic accuracy of CTA or MRA against a reference standard of a DSA were included. Where studies provided insufficient information to conduct a meta-analysis (true positives, true negatives, false positives, false negatives), or too few common studies were included (≤2 studies for the same diagnostic outcome) diagnostic accuracy results were reported individually on a per-study basis.

See also the study selection flow chart in Appendix C:, sensitivity and specificity forest plots and summary receiver operating characteristics (SROC) curves in Appendix E:, and study evidence tables in Appendix D:.

1.4.2 Excluded studies

See the excluded studies list in Appendix H:.

1.4.3 Summary of clinical studies included in the evidence review

Table 2: Summary of studies included in the evidence review

Study	Population	Target condition	Index test	Reference standard	Comments
CTA					
Agid 2006[1]	Patients with subarachnoid haemorrhage who underwent CTA and DSA (n=73) Cross-sectional study	Intracranial aneurysms	CTA	DSA	The diagnosis of acute SAH was confirmed by either neurosurgical exploration or by catheter based intra-arterial DSA
Anderson 1997[3]	Patients with suspected intracranial aneurysms examined by both CTA and DSA. 32 of the 40 patients presented with acute SAH. N=40 Cross-sectional study	Intracranial aneurysms	CTA	DSA	
Aulbach 2016[7]	Patients with acute SAH. N=116 Cross-sectional study	Intracranial aneurysms	CTA	DSA	
Chen 2009[29]	Patients who successively underwent unenhanced CT of the head, 16 slice CTA and 2d-DSA no more than 3 days apart N=152	Intracranial aneurysms	CTA	DSA	Mixed population with large proportion of patients not SAH

Study	Population	Target condition	Index test	Reference standard	Comments
	Cross-sectional study				
Chen 2010[33]	Patients with symptoms and signs suggestive of intracranial aneurysm. N=388 Cross-sectional study	Intracranial aneurysms	CTA	DSA	315 of these 388 patients had SAH, 39 patients had SAH and intraventricular haemorrhage (IVH), 20 patients had SAH and intraparenchymal haemorrhage (IPH), and 14 patients had SAH, IVH and IPH.
Chen 2013[31]	Consecutive patients suspected of having cerebral aneurysms. N=282 Cross-sectional study	Intracranial aneurysms	CTA	DSA	Of the 282 patients, 179 (63.5%) patients had subarachnoid haemorrhage, 31 (11.0%) had subarachnoid and intraventricular haemorrhage, 15 (5.3%) had subarachnoid and intraparenchymal haemorrhage
Colen 2007[38]	Patients who underwent CTA of the head and intracranial DSA within 48 hours for SAH between July 2003 – January 2005 (n=211) Cross-sectional study	Intracranial aneurysms	CTA	DSA	
Dammert 2004[43]	Patients admitted for SAH (41) or atypical ICH (9) requiring further	Intracranial aneurysms	CTA	DSA	Mean accuracy from 3 observers.

Study	Population	Target condition	Index test	Reference standard	Comments
	investigation in the form of angiography. N=50 Cross-sectional study				
Donmez 2011[50]	Patients with the diagnosis of non-traumatic acute SAH established by either non enhanced cerebral CT examination or by xanthochromia at lumbar puncture (n=134) Cross-sectional study	Intracranial aneurysms	CTA	DSA	
Ergun 2011[54]	Patients who underwent CTA and DSA due to the detection of subarachnoid haemorrhage by non-enhanced cranial CT (n=37) Cross-sectional study	Intracranial aneurysms	CTA	DSA	
Feng 2020[58]	Patients suspected of having intracranial aneurysms were considered for inclusion. Patients with intracranial aneurysms confirmed during DSA or surgery were included. Cross-sectional study	Intracranial aneurysms	CTA	DSA/surgery	

Study	Population	Target condition	Index test	Reference standard	Comments
Fluss 2020[61]	Nontraumatic intracranial haemorrhage cases managed by the senior author over a 15-month. (n=59) Cross-sectional study	Intracranial aneurysms	CTA	DSA	Data on patients with aSAH included for analysis. (n=37)
Gamal 2015[64]	Adult patients who had clinical symptoms of non-traumatic SAH or cerebral aneurysm diagnosed by CT (n=25) Cross-sectional study	Intracranial aneurysms	CTA	DSA	
Gerardin 2009[67]	Patients with SAH confirmed by CT scan or lumbar puncture over a 10 month period (n=20) Cross-sectional study	Intracranial aneurysms	CTA	DSA	
Haghighatkhah 2008[77]	Patients were admitted under clinical symptoms and signs suggestive of harbouring an intracranial aneurysm and all had non-traumatic SAH according to brain CT scan or lumbar puncture. N=85 Cross-sectional study	Intracranial aneurysms	CTA	DSA	
Hashemi 2011[82]	consecutive patients with the initial diagnosis	Intracranial aneurysms	CTA	DSA	

Study	Population	Target condition	Index test	Reference standard	Comments
	of subarachnoid haemorrhage were enrolled into the study and screened for aneurysms with CTA followed by conventional DSA who were considered for diagnostic accuracy of CTA in comparison with the first DSA for the detection of aneurysm (n=99) Cross-sectional study				
Jayaraman 2004[95]	patients undergoing DSA for non-traumatic SAH indicated either by imaging findings at non enhanced CT of by xanthochromia at lumbar puncture (n=35) Cross-sectional study	Intracranial aneurysms	CTA	DSA	
Kangasniemi 2004[99]	Patients who underwent both CTA and DSA for suspected SAH (n=179) Cross-sectional study	Intracranial aneurysms	CTA	DSA	
Kelliny 2011[105]	Patients who underwent both technically adequate catheter angiography and CTA for a suspicion of a	Intracranial aneurysms	CTA	DSA	

Study	Population	Target condition	Index test	Reference standard	Comments
	ruptured aneurysm (n=241) Cross-sectional study				
Kouskouras 2004[113]	Patients who presented with SAH or neurological symptoms (cranial nerve palsy) who underwent helical CTA and DSA (n=32) Cross-sectional study	Intracranial aneurysms	CTA	DSA	
Lenhart 1997[120]	patients suffering with acute non traumatic SAH who underwent CTA after non enhanced CT and DSA examination (n=53) Cross-sectional study	Intracranial aneurysms	CTA	DSA	
Li 2014[123]	Patients were enrolled into the study if they had signs and symptoms suggestive of SAH or presented with SAH on non enhanced CT scan and completed both CTA and DSA (n=88) Cross-sectional study	Intracranial aneurysms	CTA	DSA	
Lu 2012[129]	patients who first underwent dual-source CT angiography and then 3D DSA, with a	Intracranial aneurysms	CTA	DSA	

Study	Population	Target condition	Index test	Reference standard	Comments
	time interval of 1 day (n=525) Cross-sectional study				
Luo 2012[131]	Patients with spontaneous SAH and suspected intracranial aneurysms. N=56 Cross-sectional study	Intracranial aneurysms	CTA	DSA	
Lv 2011[132]	Patients were eligible if they had undergone both dual energy subtraction CTA and DSA for suspected intracranial aneurysms. (n=97) Cross-sectional study	Intracranial aneurysms	CTA	DSA	
MacKinnon 2013[134]	Consecutive patients who underwent CTA for SAH. N=176 Cross-sectional study	Intracranial aneurysms	CTA	DSA	
McKinney 2008[139]	Patients who had clinical histories requesting urgent evaluation for intracranial aneurysm via 64 multi-slice CTA (n=66) Cross-sectional study	Intracranial aneurysms	CTA	DSA	Not all patients had DSA and some may have had surgery (as a reference test) due to their clinical condition

Study	Population	Target condition	Index test	Reference standard	Comments
Milosevic 1999[145]	Patients with acute SAH. Confirmation of the haemorrhage by a conventional CT scan was immediately followed by intracranial CTA. N=52 Cross-sectional study	Intracranial aneurysms	CTA	DSA	In 7 patients who underwent surgery on the basis of CTA findings, results were compared with neurological findings.
Milosevic Medenica 2010[144]	Patients referred for angiography, presenting with clinical symptomatology of SAH (28), SAH and ICH (12), IVH (2), headache (2), seizures (1), hemiparesis (1), the or incidentally found aneurysm (1). N=47 Cross-sectional study	Intracranial aneurysms	CTA	DSA	Subset with DSA comparison included for analysis (n=21)
Ni 2016[157]	Patients were enrolled if they were clinically suspected subarachnoid haemorrhage or aneurysms. N=105 Cross-sectional study	Intracranial aneurysms	CTA	DSA	58 patients had bleeding: 11 patients with subarachnoid haemorrhage, 32 with subarachnoid haemorrhage combined with other bleeding focus (i.e., intracerebral hematoma, ventricular hematoma and others),

Study	Population	Target condition	Index test	Reference standard	Comments
					15 with other intracranial hematoma.
Papke 2007[163]	Patients with clinical symptoms of SAH and be able to undergo both CTA and DSA. N=87 Cross-sectional study	Intracranial aneurysms	CTA	DSA	
Pedersen 2001[170]	Patients admitted to the participating hospital with acute SAH confirmed by the patient history and subarachnoid blood demonstrated at plain CT or by lumbar puncture. N=162 Cross-sectional study	Intracranial aneurysms	CTA	DSA	
Philipp 2017[172]	Patients who were consecutively admitted with a diagnosis of acute, nontraumatic SAH. N=401 Cross-sectional study	Intracranial aneurysms	CTA	DSA	
Poon 2006[176]	Patients with ruptured cerebral aneurysms had undergone surgical interventions who had both CTA and DSA performed as	Intracranial aneurysms	CTA	DSA	There were two aneurysms (18%) missed in DSA which were detected in CTA

Study	Population	Target condition	Index test	Reference standard	Comments
	preoperative diagnostic imaging. Subarachnoid haemorrhage (SAH) was confirmed in all the CT scans of the brain. N=11 Cross-sectional study				
Pozzi-Mucelli 2007[177]	Patients with clinical and imaging findings strongly suggesting the presence of SAH. N=29 Cross-sectional study	Intracranial aneurysms	CTA	DSA	Those without CT confirmation but with strong clinical suspicion of SAH were still included.
Preda 1998[179]	Patients examined with CTA for suspected intracranial malformations. N=28 Cross-sectional study	Intracranial aneurysms	CTA	DSA	The diagnosis on admission was SAH in 19 cases, third cranial nerve palsy in 2 cases, and persistent headache in 5 cases.
Ramasundara 2010[182]	Patients with suspected subarachnoid haemorrhage who had CTA scans that had matching DSA studies. N=36 Cross-sectional study	Intracranial aneurysms	CTA	DSA	
Ramgren 2015[184]	Patients in whom non-traumatic SAH was suspected and later confirmed by either non-	Intracranial aneurysms	CTA	DSA	

Study	Population	Target condition	Index test	Reference standard	Comments
	enhanced CT (NECT) or lumbar puncture. N=326 Cross-sectional study				
Romijn 2008[185]	patients who presented with clinically suspected SAH underwent both CTA and DSA for diagnosis of an intracranial aneurysm (n=108) Cross-sectional study	Intracranial aneurysms	CTA	DSA	
Rotim 2007[188]	Patients with suspected SAH, confirmed by CT scan who underwent CTA and DSA examinations (n=29) Cross-sectional study	Intracranial aneurysms	CTA	DSA	
Saboori 2011[189]	Patients with a confirmatory CT scan of SAH and underwent CTA and DSA (n=19) Cross-sectional study	Intracranial aneurysms	CTA	DSA	
Seruga 2001[199]	Patients with confirmed SAH on CT scan or lumbar puncture, including further CTA (n=30) Cross-sectional study	Intracranial aneurysms	CTA	DSA	

Study	Population	Target condition	Index test	Reference standard	Comments
Strayle-Batra 1998[202]	Patients examined by CT angiography and DSA for the detection of aneurysms or for planning interventional procedures (n=17) Cross-sectional study	Intracranial aneurysms	CTA	DSA	
Taschner 2007[209]	Patients admitted with non-traumatic SAH. Diagnosis made by CT (25) or LP (2). N=27 Cross-sectional study	Intracranial aneurysms	CTA	DSA	
Teksam 2005[211]	Consecutive patients who underwent MSCTA and DSA N=103 Cross-sectional study	Intracranial aneurysms	CTA	DSA	large proportion of patients had other medical conditions aside from SAH
Tipper 2005[215]	Patients with positive findings for SAH on initial examination indicated for DSA and further imaging (n=57) Cross-sectional study	Intracranial aneurysms	CTA	DSA	
Uysal 2005[219]	Patients who had CTAs and DSAs with suspicion of aneurysm due to SAH detected by non-enhanced cranial CT (n=32)	Intracranial aneurysms	CTA	DSA	2x2 table completed from narrative within paper and results reported differ

Study	Population	Target condition	Index test	Reference standard	Comments
	Cross-sectional study				
Van Zwam 2012[225]	Patients admitted with a diagnosis of non-traumatic SAH established by CT or lumbar puncture. N=75 Cross-sectional study	Intracranial aneurysms	CTA	DSA	
Vieco 1995[227]	Patients with Unenhanced CT scan showing SAH blood or spinal tap showing recent intrathecal bleeding (n=30) Cross-sectional study	Intracranial aneurysms	CTA	DSA	
Wang 2010[234]	Patients with clinical symptoms of SAH and the ability to undergo multidetector. CTA. N=121 Cross-sectional study	Intracranial aneurysms	CTA	DSA and surgery	
Wang 2013[232]	Patients with diagnosis of spontaneous SAH established by either unenhanced CT examination or xanthochromia at lumbar puncture who underwent CTA and DSA (n=52)	Intracranial aneurysms	CTA	DSA	

Study	Population	Target condition	Index test	Reference standard	Comments
	Cross-sectional study				
Wintermark 2003[248]	Patients with clinical suspicion of SAH undergoing successive performance of multi-slice CT angiography and DS angiography. N=50 Cross-sectional study	Intracranial aneurysms	CTA	DSA	
Yoon 2007[258]	Patients with suspected intracranial aneurysms were referred to the participating hospital's institution. N=85 Cross-sectional study	Intracranial aneurysms	CTA	DSA	Patients selected on the basis of clinical or radiologic findings, including presentation with acute SAH confirmed by nonenhanced CT or lumbar puncture (n=75); symptoms and signs suggestive of aneurysm, such as headache or cranial neuropathy (n=6); or a previous routine CT scan or MR angiogram suggesting the presence of an intracranial aneurysm (n=4).
Zhang 2010[263]	Patients who have clinical evidence of intracranial aneurysm and be able to undergo both CTA and DSA. The	Intracranial aneurysms	CTA	DSA	

Study	Population	Target condition	Index test	Reference standard	Comments
	indication for CTA and DSA was established on the basis of the clinical findings (n=46) Cross-sectional study				
MRA					
Anzalone 1995[5]	patients with CT positive acute SAH who underwent DSA and MRA within 5 hours of admission (n=27) Cross-sectional study	Intracranial aneurysms	MRA	DSA	
Chen 2012[35]	Patients with a Glasgow Coma Scale (GCS) score of 15 and SAH confirmed by a plain CT N=165 Cross-sectional study	Intracranial aneurysms	MRA	DSA	
Chung 1999[37]	Patients who underwent screening with brain MR angiography and DSA for the detection of intracranial aneurysms were included within the consecutive study (n=30) Cross-sectional study	Intracranial aneurysms	MRA	DSA	
Farahmand 2013[55]	Patients admitted to hospital with non-traumatic SAH or	Intracranial aneurysms	MRA	DSA	

Study	Population	Target condition	Index test	Reference standard	Comments
	intracranial haemorrhage, intraventricular haemorrhage or infarction. N=55 Cross-sectional study				
Feng 2020[58]	Patients suspected of having intracranial aneurysms were considered for inclusion. Patients with intracranial aneurysms confirmed during DSA or surgery were included. Cross-sectional study	Intracranial aneurysms	MRA	DSA/surgery	
Gamal 2015[64]	all consecutive adult patients who had clinical symptoms of non-traumatic SAH or cerebral aneurysm diagnosed by CT (n=25) Cross-sectional study	Intracranial aneurysms	MRA	DSA	
Ida 1997[90]	Patients with acute subarachnoid haemorrhage receiving emergency intracranial MRA. N=28 Cross-sectional study	Intracranial aneurysms	MRA	DSA	

Study	Population	Target condition	Index test	Reference standard	Comments
Li 2017[124]	patients who had non-traumatic subarachnoid haemorrhage that was confirmed with non-enhanced CT scan and underwent MRA and DSA (n=277) Cross-sectional study	Intracranial aneurysms	MRA	DSA	
Pierot 2013[174]	All consecutive adult patients admitted with acute non traumatic SAH, confirmed by non-enhanced CT or lumbar puncture. (n=84) Cross-sectional study	Intracranial aneurysms	MRA	DSA	
Schmieder 1999[196]	Patients with acute SAH or with CT scans showing anomalies being suspicious of aneurysms. N=54 Cross-sectional study	Intracranial aneurysms	MRA	DSA	
Shahzad 2011[200]	Patients with non-traumatic SAH. N=30 Cross-sectional study	Intracranial aneurysms	MRA	DSA	
Van Zwam 2012[225]	Patients admitted with a diagnosis of non-traumatic SAH	Intracranial aneurysms	MRA	DSA	

Study	Population	Target condition	Index test	Reference standard	Comments
	established by CT or lumbar puncture. N=75 Cross-sectional study				
Yan 2018[253]	Consecutive patients with SAH (GCS=15) confirmed by a non-contrast head computed tomographic scan. N=183 Cross-sectional study	Intracranial aneurysms	MRA	DSA	Subset of patients with non-SAH not included in analysis.

See Appendix D: for full evidence tables.

1.4.4 Quality assessment of clinical studies included in the evidence review

Table 3: Clinical evidence summary: Diagnostic test accuracy for CTA and MRA

Index Test	Number of patients (studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Effect size (95%CI)	Quality
CTA							
CTA (per patient)	3174 (24)	Serious[a]	Not serious	Not serious	Not serious	Sensitivity=97.6% [c] (96.3%-98.6%)	MODERATE
		Serious[a]	Not serious	Not serious	Not serious	Specificity= 94% [c] (90.9%-96.4%)	MODERATE

Index Test	Number of patients (studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Effect size (95%CI)	Quality
CTA (per aneurysm)	3926 (31)	Serious[a]	Not serious	Not serious	Not serious	Sensitivity= 95.4% [c] (94%-97%)	MODERATE
		Serious[a]	Not serious	Not serious	Serious[b]	Specificity= 93.4% [c] (88.3-96.3%)	LOW
MRA							
MRA (per patient)	738 (6)	Serious[a]	Not serious	Not serious	Not serious	Sensitivity= 96.4% [c] (90%-99%)	MODERATE
		Serious[a]	Not serious	Not serious	Serious[b]	Specificity= 94% [c] (82.2%-98.01%)	LOW
MRA (per aneurysm)	(712 (7)	Serious[a]	Not serious	Not serious	Not serious	Sensitivity=97.3% [c] (94%-99%)	MODERATE
		Serious[a]	Not serious	Not serious	Serious[b]	Specificity=88% [c] (74.1%-95%)	LOW

(a) Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the majority of studies were rated at high risk of bias, and downgraded by 2 increments if the majority of studies were rated at very high risk of bias.
(b) Imprecision was assessed based on inspection of the confidence region in the diagnostic meta-analysis or, where diagnostic meta-analysis has not been conducted, assessed according to the range of confidence intervals in the individual studies. Two clinical decision thresholds were determined at the value above which a test would be recommended (90%), and a second below which a test would be considered of no clinical use (60%).The evidence was downgraded by 1 increment when the range of the confidence interval around the point estimate crossed one threshold, and downgraded by 2 increments when the range covered two thresholds
(c) Pooled sensitivity/specificity from diagnostic meta-analysis

1 **Table 4: Clinical evidence summary: Diagnostic test accuracy for CTA and MRA - evidence not suitable for meta-analysis**

Index Test (Threshold)	Number of patients (studies)	Risk of bias	Sensitivity % (range)	Specificity % (range)
Index Test CTA				
CTA (per patient)	703 (9)	Very high	Median: 95% (86% to 100%)[a]	Median: 98.5% (80% to 100%)
Agid 2006[1]	*73*	*Very high*	*94%*	*100%*
Anzalone 1995[5]	*27*	*High*	*91.3%*	*100%*
Colen 2007[38]	*211*	*Very high*	*95%*	*97%*
Li 2014[123]	*88*	*High*	*100%*	*100%*
McKinney 2008[139]	*66*	*Very high*	*96%*	*90%*
Milosevic Medenica 2010[144]	*47*	*Very high*	*87.5%*	-
Pierot 2013[174]	*84*	*High*	*86%*	*80%*
Tipper 2005[215]	*57*	*High*	*97.7%*	*100%*
Wintermark 2003[248]	*50*	*High*	*99%*	*95.2%*
CTA (per aneurysm)	936 (11)	High	Median: 94% (83% to 100%)[a]	Median: 94.7% (66.7% to 100%)
Colen 2007[38]	*211*	*Very high*	*83%*	*93%*
Donmez 2011[50]	*134*	*High*	*95.1%*	*94.1%*
Ergun 2011[54]	*37*	*Very high*	*92.8%*	*83.3%*
Feng 2020[58]	*79*	*Very high*	*91%*	*66.7%*
Li 2014[123]	*88*	*High*	*100%*	*100%*
Rotim 2007[188]	*29*	*High*	*96.6%*	*100%*
Seruga 2001[199]	*30*	*Very high*	*94%*	-
Strayle-Batra 1998[202]	*17*	*High*	*85%*	-
Tipper 2005[215]	*57*	*High*	*96.2%*	*100%*
Wintermark 2003[248]	*50*	*High*	*94.8%*	*95.2%*
Index Test MRA				
MRA (per patient) Pierot 2013[174]	84 (1)	High	95%	80%

Index Test (Threshold)	Number of patients (studies)	Risk of bias	Sensitivity % (range)	Specificity % (range)
MRA (per aneurysm) Feng 2020[58]	79 (1)	Very high	83.1%	66.7%

(a) Studies providing insufficient information to conduct a meta-analysis (true positives, true negatives, false positives, false negatives). Diagnostic accuracy results reported individually on a per-study basis and median values taken as summary statistics. Overall median was calculated using Excel.

1.5 Economic evidence

1.5.1 Included studies

One health economic study with the relevant comparison was included in this review[191]. This is summarised in the health economic evidence profile below (Table 5) and the health economic evidence table in Appendix G:.

1.5.2 Excluded studies

One health economic study was excluded due to limited applicability and methodological limitations[93]. This is listed in Appendix H, with reasons for exclusion given.

See also the health economic study selection flow chart in Appendix F:.

1.5.3 Summary of studies included in the economic evidence review

Table 5: Health economic evidence profile: DSA vs CTA vs MRA

<table>
<tr><th>Study</th><th>Applicability</th><th>Limitations</th><th>Other comments</th><th>Incremental Cost</th><th>Incremental Effects</th><th>Cost effectiveness</th><th>Uncertainty</th></tr>
<tr><td>Sailer 2013[191] (Dutch)</td><td>Partially applicable [(a)]</td><td>Potentially serious limitations[(b)]</td><td>• Probabilistic model based on diagnostic accuracy data from one study (van Zwam[225])
• Cost-utility analysis (QALYs)
• Population: Patients with acute non-traumatic subarachnoid haemorrhage
• Comparators:
1. DSA
2. CTA
3. MRA
• Time horizon:1 year</td><td colspan="4">Full incremental analysis (pa):[(c) (d)]
<table>
<tr><th>Int</th><th>Cost[(e)]</th><th>QALY</th><th>Inc cost</th><th>Inc QALY</th><th>ICER</th></tr>
<tr><td>3</td><td>£34,382</td><td>0.5947</td><td colspan="3">Baseline</td></tr>
<tr><td>2</td><td>£33,505</td><td>0.5983</td><td>Saves £773</td><td>0.006</td><td>Extendedly dominated by 1</td></tr>
<tr><td>1</td><td>£32,732</td><td>0.6039</td><td>Saves £1,650</td><td>0.009</td><td>Dominant</td></tr>
</table>
DSA is dominant (lowest costs and highest QALYs)
Prob. 1 CE (£20/30K) threshold: NR

A scenario analysis conducted with additional strategies of DSA if aneurysm deemed not suitable for coiling on CTA or MRA found that CTA + DSA was dominant.</td></tr>
</table>

Abbreviations: ICER= incremental cost-effectiveness ratio; QALY= quality-adjusted life years; RCT= randomised controlled trial

(a) Dutch 2010 unit costs may not reflect current NHS context – current UK NHS cost of DSA much higher than that used in the economic evaluation. Discounting of costs and outcomes is not in line with NICE reference case; however as the analysis only assess a one year time horizon this may only have a small effect on the results. The calculation of QALYs is not in line with the NICE reference case, as utility values were not derived from EQ-5D.

(b) Diagnostic accuracy data taken from one study and therefore may not reflect the full body of available evidence. One year time horizon may not capture full costs and health benefits.

(c) Intervention number in order of least to most effective (in terms of QALYs).

(d) Full incremental analysis of available strategies: first strategies are ruled out that are dominated (another strategy is more effective and has lower costs) or subject to extended dominance (the strategy is more effective and more costly but the incremental cost effectiveness ratio is higher than the next most effective option and so it would never be the most cost effective option); incremental costs, incremental effects and incremental cost effectiveness ratios are calculated for the remaining strategies by comparing each to the next most effective option.

(e) 2010 Dutch Euro converted to UK pounds.[162] Cost components incorporated: diagnostic tests, personnel, equipment, materials, maintenance, housing, cleaning, administration and overheads. One year costs of surgical clipping or endovascular coiling.

(f)

1.5.4 Unit costs

Relevant unit costs are provided below to aid consideration of cost effectiveness.

Table 6: UK costs of diagnostic angiography

Drug	Description	Average cost
Computerised Tomography Angiography	Computerised Tomography Scan of One Area, with Post-Contrast Only, 19 years and over [NHS Reference Cost code: RD21A]	£101
Magnetic Resonance Angiography	Magnetic Resonance Imaging Scan of One Area, with Pre and Post-Contrast, 19 years and over [NHS Reference Cost code: RD03Z]	£190
Digital Subtraction Angiography	Percutaneous Transluminal Arteriography, of Intracranial or Extracranial Blood Vessel [NHS Reference Cost code: YA11Z]	£1,448

Source: NHS Reference Cost 2018/19 [156]

1.6 Evidence statements

1.6.1 Clinical evidence statements

- Nine studies reported the diagnostic test accuracy of CTA at detecting aneurysmal SAH (per patient). These studies reported a median sensitivity of 95% (with a range of 86 to 100%) and a median specificity of 95.5% (with a range of 80 to 100%). 9 studies, n=703, very high risk of bias.
- Eleven studies reported the diagnostic test accuracy of CTA at detecting aneurysmal SAH (per aneurysm). These studies reported a median sensitivity of 94% (with a range of 83 to 100%) and a median specificity of 94.7% (with a range of 66.7 to 100%). 11 studies, n=936, high risk of bias.
- One study reported the diagnostic test accuracy of MRA at detecting aneurysmal SAH (per patient). This study reported a sensitivity of 95% and a specificity of 80%. 1 study, n=84, high risk of bias.
- One study reported the diagnostic test accuracy of MRA at detecting aneurysmal SAH (per aneurysm). This study reported a sensitivity of 83.1% and a specificity of 66.7%. 1 study, n=79, very high risk of bias.

1.6.2 Health economic evidence statements

- One cost-utility analysis found that digital subtraction angiography was dominant compared to computerised tomography angiography and magnetic resonance angiography. This was assessed as partially applicable with potentially serious limitations.

1.7 The committee's discussion of the evidence

1.7.1 Interpreting the evidence

1.7.1.1 The diagnostic measures that matter most

The committee considered both sensitivity and specificity measures to be critical outcomes in this review. Sensitivity is important to identify the presence of an aneurysm as being the possible cause of a bleed, ruling out aSAH in test negative patients. A high specificity can rule in an aneurysm being the cause of SAH in test positive patients, identifying a high proportion of those without an intracranial aneurysm. The committee agreed that a diagnostic accuracy with sensitivity of ≥90% and specificity of ≥90% would provide value in clinical practice. The committee noted that the sensitivity and specificity of CTA and MRA was reported either per patient (in correctly diagnosing the participants with a presence or absence of aneurysm(s)) or per aneurysm (in correctly diagnosing the presence or absence of each individual aneurysm). The committee agreed that there was value in reviewing both measures of diagnostic accuracy.

The important outcomes were positive predictive value, negative predictive value and receiver operating characteristic (ROC) curve or area under the curve. Where outcome data permitted the calculation of NPV and PPV, these were calculated and are included in the clinical evidence tables in 75. The committee noted these values but also the potential for variable prevalence to affect PPV and NPV and so considered sensitivity and specificity better indicators of diagnostic test accuracy.75

1.7.1.2 The quality of the evidence

The evidence was moderate to low quality due to the risk of bias and imprecision. The majority of the evidence was of moderate quality, downgraded due to the risk of bias. Where evidence was considered to be at a high risk of bias, this was typically due to uncertainty as to whether the index test results were known at the point of the reference standard investigation, or vice versa. There was also a lack of detail in the outcome data reported in a number of trials, presenting further bias and preventing meta-analysis of a large proportion of the evidence identified. The committee noted imprecision for some of the outcomes reported but agreed that most of the data reviewed demonstrated a high level of precision. This overall moderate quality and the large number of studies contributing data to the diagnostic test accuracy outcomes gave the committee confidence in the evidence presented, enabling it to make a set of strong recommendations.

1.7.1.3 Benefits and harms

The committee noted that the benefit of accurately identifying an aneurysm in people with suspected SAH is to confirm the diagnosis of aSAH and an indication of the cause of a bleed. This aids decisions for subsequent intervention to manage the bleed and limit subsequent sequelae.

The diagnostic accuracy of CT angiography (CTA) showed a pooled sensitivity of 97.6% and a specificity of 94% (per patient) for detecting cerebral aneurysms. Those studies which could not be included in the meta-analysis had a range of 86-100% sensitivity and 80-100% specificity. The accuracy of CTA (per aneurysm) had a sensitivity of 95.4% and specificity of 93.4%. The sensitivity and specificity varied from 83-100% and 83.3-100%, respectively, for those studies not within the pooled analysis. The committee noted that the sensitivity and specificity of CTA (per patient and per aneurysm) showed a high diagnostic test accuracy and were above the 90% thresholds to demonstrate clinical utility. The committee also highlighted that the CTA can be completed in a few minutes, is non-invasive, has few associated risks and is highly accurate. The evidence showed that magnetic resonance angiography (MRA) had a pooled sensitivity of 96.4% and specificity of 94% (per patient) for detecting cerebral aneurysms. One study, which could not be included in the pooled analysis, showed a sensitivity of 95% and specificity of 80% for MRA. When assessing the diagnostic accuracy of MRA (per aneurysm), the pooled sensitivity and specificity were 97.3% and 88%, respectively. The committee agreed that the sensitivity and specificity of MRA (per patient and per aneurysm) also showed a high diagnostic test accuracy, although slightly lower than CTA. The committee noted that the sensitivity (per patient and per aneurysm) and specificity (per aneurysm) of MRA was above the 90% thresholds to demonstrate clinical utility, and the specificity (per aneurysm) was marginally below this point at 88%. The committee agreed that the complexities in getting a high quality MRA make this investigation less beneficial. The problems relate to availability of scanners, time (MRA can take around 45 minutes), patient discomfort or tolerance, artefacts due to movement, and need for sedation and in some cases general anaesthesia.

DSA is recognised to be the ‘gold standard’ investigation but is a resource-intensive and invasive procedure. DSA carries a low risk of procedural complications including stroke and arterial access site haematoma, and need for sedation or general anaesthesia. DSA is currently commonly carried out when a CTA is negative but there is still a high suspicion of aSAH. In rare cases there may be a need to repeat a DSA when the initial DSA is negative but a high degree of clinical suspicion remains.

The committee agreed the evidence demonstrated that CTA has a slightly higher diagnostic accuracy than MRA in identifying intracranial arterial aneurysms. The committee confirmed it was usual practice to use CTA in the first instance because it has high diagnostic accuracy and is the quickest and least invasive test. These advantages allowed the committee to make a strong recommendation to offer CT angiography of the head to people with a confirmed diagnosis of SAH to identify the cause of bleeding and guide treatment.

The committee agreed that the significance of intracranial arterial aneurysm(s) demonstrated by CTA in a person with SAH should be interpreted in the context of the pattern of subarachnoid blood seen on the diagnostic CT head scan. On the basis of their experience the committee made a consensus recommendation that aneurysmal SAH can be diagnosed if the CTA shows intracranial arterial aneurysm(s) and the pattern of subarachnoid blood is compatible with rupture of (one of) the aneurysm(s).

The committee agreed that a diagnosis of aneurysmal SAH cannot be confirmed if the location of an intracranial arterial aneurysm is not compatible with the distribution of subarachnoid blood and that specialist multidisciplinary review of the neuroimaging would be required to determine further management options. On the basis of their experience the committee made a consensus recommendation that clinicians seek the opinion of the multidisciplinary team without delay if CTA shows intracranial arterial aneurysm(s), and the pattern of subarachnoid blood is not compatible with rupture of (one of) the aneurysm(s).

The committee acknowledged that a CTA in a person with suspected SAH that does not demonstrate intracranial arterial aneurysm(s) also requires careful interpretation, and agreed that further investigation could be considered if an aneurysm is still suspected. The committee were aware from their experience that DSA is a resource-intensive and invasive procedure but is readily available in neurosurgical centres and has a high diagnostic accuracy. MRA can also be used as a second line investigation but has lower diagnostic accuracy and is logistically difficult and time-consuming in people with SAH. The committee acknowledged uncertainty in the economic evidence comparing imaging modalities for the detection of intracranial arterial aneurysm and that DSA is used as a second line investigation in current clinical practice. On the basis of their experience the committee made a consensus recommendation to consider DSA (or MRA if DSA is contraindicated) if CTA does not identify the cause of the SAH and an aneurysm is still suspected. The committee also recommended that aneurysmal subarachnoid haemorrhage can be diagnosed if DSA or MRA shows an intracranial arterial aneurysm(s) and the pattern of subarachnoid blood is compatible with rupture of (one of) the aneurysm(s).

The committee recognised that this diagnostic pathway recommended may not lead to a definitive diagnosis and so made a consensus recommendation that alternative diagnoses should be considered if CTA and DSA or MRA do not show an intracranial arterial aneurysm.

1.7.2 Cost effectiveness and resource use

One cost-utility analysis was included in this review which compared CTA, MRA and DSA. This is a decision tree model from a Dutch perspective, which incorporated the diagnostic accuracy data from 1 study included in the clinical review. This analysis suggests that DSA is the most cost effective imaging modality in people with subarachnoid haemorrhage caused by a suspected aneurysm, accruing both higher QALYs and lower costs than CTA or MRA. This was assessed as partially applicable with very serious limitations.

The committee discussed the difference in diagnostic accuracy data used in the model to that in the clinical review, noting in particular the lower sensitivity of CTA, and the lower specificity of MRA used in the model compared to the pooled results from the clinical review. Given the high costs associated with a false negative result and both the high costs and QALY detriment associated with a false positive result in the model, the committee considered that the model results could be quite different with different diagnostic accuracy data inputs.

The committee noted that the diagnostic accuracy data used to model the feasibility of clipping or coiling in the model does not reflect expectations of current practice. In particular, the committee considered that imaging has improved over time, and the sensitivity and specificity of CTA and MRA in determining the feasibility of coiling and clipping are likely to be higher in contemporary practice.

There are also significant differences between unit costs of imaging used in the model and those of the current UK NHS. In particular, the committee noted the cost of both CTA and MRA in current practice are slightly lower than the costs used in the model, whereas the current UK cost of DSA is around double the cost used in the model.

It is difficult to assess how these differences in diagnostic accuracy data and cost would affect the model results overall. Nevertheless, the committee considered it less likely that DSA would be the most cost effective option in current UK practice, and did not put much weight on the model results when making recommendations.

The committee noted that CTA is often used as the first test in current practice and has been shown to be highly accurate as well as the least costly imaging strategy. Overall, the committee did not consider that there would be a significant resource impact of the recommendations as they reflect current practice in the NHS.

1.7.3 Other factors the committee took into account

The committee highlighted that CTA may be carried out at the same time as a diagnostic CT head scan and part of a 2-stage investigation, thereby saving time and resource. This supported the recommendation made by the committee to offer CT angiography of the head to people with a confirmed diagnosis of subarachnoid haemorrhage to identify the cause of bleeding and guide treatment.

The committee considered that CT and MR technologies have improved significantly and it is likely that the sensitivity and specificity for detection of aneurysms will be greater than suggested by some older evidence. This further supported the recommendation made.

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Appendices

Appendix A: Review protocols

Table 7: Review protocol: Diagnostic imaging strategies

ID	Field	Content
0.	PROSPERO registration number	CRD42019146789
1.	Review title	What is the accuracy of different imaging strategies to detect a culprit aneurysm in adults with confirmed subarachnoid haemorrhage?
2.	Review question	What is the accuracy of different imaging strategies to detect a culprit aneurysm in adults with confirmed subarachnoid haemorrhage?
3.	Objective	To determine which imaging strategy for aneurysmal subarachnoid haemorrhage is the most accurate.
4.	Searches	The following databases will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE Searches will be restricted by: • English language only The searches may be re-run 6 weeks before the final committee meeting and further studies retrieved for inclusion if relevant. The full search strategies will be published in the final review
5.	Condition or domain being studied	Aneurysmal subarachnoid haemorrhage
6.	Population	Inclusion: Adults (16 and older) with a confirmed subarachnoid haemorrhage caused by a suspected ruptured aneurysm. Exclusion: • Adults (16 and older) with subarachnoid haemorrhage caused by head injury, ischaemic stroke or an arteriovenous malformation. • Children and young people aged 15 years and younger.
7.	Intervention/Exposure/Test	• MR Angiography • CT angiography
8.	Comparator/Reference standard/Confounding factors	Reference standard: • Direct angiography (DSA)

9.	Types of study to be included	Cross-sectional studies Cohort studies.
10.	Other exclusion criteria	Exclusions: • Adults with subarachnoid haemorrhage caused by head injury, ischaemic stroke or an arteriovenous malformation. • Children and young people aged 15 years and younger. • Non- English language studies • Abstracts will be excluded as it is expected there will be sufficient full text published studies available.
11.	Context	
12.	Primary outcomes (critical outcomes)	Statistical measure to detecting aSAH: • Sensitivity • Specificity • Positive Predictive Value (PPV) • Negative Predictive Value (NPV) • Receiver Operating Characteristic (ROC) curve or area under curve)
13.	Secondary outcomes (important outcomes)	
14.	Data extraction (selection and coding)	EndNote will be used for reference management, sifting, citations and bibliographies. All references identified by the searches and from other sources will be screened for inclusion. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract data from studies (see [Developing NICE guidelines: the manual](#) section 6.4).
15.	Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual. Diagnostic test accuracy studies risk of bias was assessed using QUADAS-2. 10% of all evidence reviews are quality assured by a senior research fellow. This includes checking: • papers were included /excluded appropriately • a sample of the data extractions • correct methods are used to synthesise data • a sample of the risk of bias assessments Disagreements between the review authors over the risk of bias in particular studies will be

		resolved by discussion, with involvement of a third review author where necessary.
16.	Strategy for data synthesis	• Aggregate data on diagnostic accuracy of investigations will be collected and synthesized in a quantitative data analysis. • Endnote will be used for bibliography, citations, sifting and reference management. • WinBUGS will be used for meta-analysis of diagnostic accuracy studies if included studies are sufficiently homogeneous. • Data synthesis will be completed by two reviewers, with any disagreements resolved by discussion, or if necessary a third independent reviewer.
17.	Analysis of sub-groups	Strata: • n/a Subgroups: • n/a
18.	Type and method of review	☐ Intervention ☒ Diagnostic ☐ Prognostic ☐ Qualitative ☐ Epidemiologic ☐ Service Delivery ☐ Other (please specify)
19.	Language	English
20.	Country	England
21.	Anticipated or actual start date	
22.	Anticipated completion date	3 February 2021
23.	Stage of review at time of this submission	Review stage / Started / Completed: Preliminary searches ☑ ☑ Piloting of the study selection process ☑ ☑ Formal screening of search results against eligibility criteria ☑ ☑ Data extraction ☑ ☑ Risk of bias (quality) assessment ☑ ☑ Data analysis ☑ ☑
24.	Named contact	5a. Named contact

		National Guideline Centre 5b Named contact e-mail SAH@nice.org.uk 5e Organisational affiliation of the review National Institute for Health and Care Excellence (NICE) and the National Guideline Centre
25.	Review team members	From the National Guideline Centre: • Ms Gill Ritchie • Mr Ben Mayer • Mr Audrius Stonkus • Mr Vimal Bedia • Ms Emma Cowles • Ms Jill Cobb • Ms Amelia Unsworth
26.	Funding sources/sponsor	This systematic review is being completed by the National Guideline Centre which receives funding from NICE.
27.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
28.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website.
29.	Other registration details	
30.	Reference/URL for published protocol	
31.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as:

		• notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.
32.	Keywords	Subarachnoid haemorrhage; imaging strategies
33.	Details of existing review of same topic by same authors	None
34.	Current review status	☐ Ongoing
		☐ Completed but not published
		☐ Completed and published
		☐ Completed, published and being updated
		☐ Discontinued
35..	Additional information	
36.	Details of final publication	www.nice.org.uk

Test and treat protocol

ID	Field	Content
0.	PROSPERO registration number	CRD42019146806
1.	Review title	What is the clinical and cost effectiveness of different imaging strategies to guide the choice of intervention to prevent rebleeding in people with confirmed subarachnoid haemorrhage?
2.	Review question	What is the clinical and cost effectiveness of different imaging strategies to guide the choice of intervention to prevent rebleeding in people with confirmed subarachnoid haemorrhage?
3.	Objective	To determine which imaging strategy for subarachnoid haemorrhage is the most clinically and cost-effective.
4.	Searches	The following databases will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE Searches will be restricted by: • English language only

		The searches may be re-run 6 weeks before final submission of the review and further studies retrieved for inclusion if relevant. The full search strategies for MEDLINE database will be published in the final review.
5.	Condition or domain being studied	Aneurysmal subarachnoid haemorrhage
6.	Population	Inclusion: Adults (16 and older) with a confirmed subarachnoid haemorrhage caused by a suspected or confirmed ruptured aneurysm. Exclusion: • Adults (16 and older) with subarachnoid haemorrhage caused by head injury, ischaemic stroke or an arteriovenous malformation. • Children and young people aged 15 years and younger.
7.	Intervention/Exposure/Test	• Direct angiography • CT angiography • MRA Negative test results must receive no SAH treatment and positive test results should receive some form of SAH treatment (including neurosurgical or endovascular intervention, or conservative management - directness to be assessed against results of intervention reviews elsewhere in the guideline).
8.	Comparator/Reference standard/Confounding factors	Comparator: • To each other
9.	Types of study to be included	Randomised controlled trials (RCTs), systematic reviews of RCTs. If insufficient RCT evidence is available, search for non-randomised studies will be considered if they adjust for key confounders (age), starting with prospective cohort studies.
10.	Other exclusion criteria	Exclusions: • Adults with subarachnoid haemorrhage caused by head injury, ischaemic stroke or an arteriovenous malformation. • Children and young people aged 15 years and younger. • Non- English language studies • Abstracts will be excluded as it is expected there will be sufficient full text published studies available.
11.	Context	
12.	Primary outcomes (critical outcomes)	• Mortality • Health and social-related quality of life (any validated measure)

		• Degree of disability or dependence in daily activities, (any validated measure e.g. Modified Rankin Scale and patient-reported outcome measures) • Adequate information for therapeutic decision making (clear and conclusive diagnosis) • Complications of diagnostic test (e.g. stroke, vascular injury)
13.	Secondary outcomes (important outcomes)	• Subsequent subarachnoid haemorrhage • Return to daily activity (e.g. work) • Length of hospital stay • Complications of intervention (any) • Need for retreatment Outcomes will be grouped at <30 days, 30days-6 months, 6-12 months, and at yearly time-points thereafter.
14.	Data extraction (selection and coding)	• EndNote will be used for reference management, sifting, citations and bibliographies. All references identified by the searches and from other sources will be screened for inclusion. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. • EviBASE will be used for data extraction.
15.	Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual. • Systematic reviews: Risk of Bias in Systematic Reviews (ROBIS) • Randomised Controlled Trial: Cochrane RoB (2.0) • Non randomised study, including cohort studies: Cochrane ROBINS-I 10% of all evidence reviews are quality assured by a senior research fellow. This includes checking: • papers were included /excluded appropriately • a sample of the data extractions • correct methods are used to synthesise data • a sample of the risk of bias assessments Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary.

16.	Strategy for data synthesis	• Pairwise meta-analyses will be performed using Cochrane Review Manager (RevMan5). • GRADEpro will be used to assess the quality of evidence for each outcome, taking into account individual study quality and the meta-analysis results. The 4 main quality elements (risk of bias, indirectness, inconsistency and imprecision) will be appraised for each outcome. Publication bias is tested for when there are more than 5 studies for an outcome. • The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/ • Where meta-analysis is not possible, data will be presented and quality assessed individually per outcome. • Subgroups will be investigated separately if meta-analysed results show heterogeneity.
17.	Analysis of sub-groups	Strata: n/a Subgroups: • Subsequent management o Endovascular management o Neurosurgical management o Conservative (medical management)
18.	Type and method of review	☒ Intervention ☐ Diagnostic ☐ Prognostic ☐ Qualitative ☐ Epidemiologic ☐ Service Delivery ☐ Other (please specify)
19.	Language	English
20.	Country	England
21.	Anticipated or actual start date	
22.	Anticipated completion date	3 February 2021
23.	Stage of review at time of this submission	Review stage | Started | Completed Preliminary searches | ☑ | ☑ Piloting of the study selection process | ☑ | ☑

		Formal screening of search results against eligibility criteria	☑	☑
		Data extraction	☑	☑
		Risk of bias (quality) assessment	☑	☑
		Data analysis	☑	☑
24.	Named contact	5a. Named contact National Guideline Centre 5b Named contact e-mail SAH@nice.org.uk 5e Organisational affiliation of the review National Institute for Health and Care Excellence (NICE) and the National Guideline Centre		
25.	Review team members	From the National Guideline Centre: • Ms Gill Ritchie • Mr Ben Mayer • Mr Audrius Stonkus • Mr Vimal Bedia • Ms Emma Cowles • Ms Jill Cobb • Ms Amelia Unsworth		
26.	Funding sources/sponsor	This systematic review is being completed by the National Guideline Centre which receives funding from NICE.		
27.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.		

28.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website.	
29.	Other registration details		
30.	Reference/URL for published protocol		
31.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.	
32.	Keywords	Subarachnoid haemorrhage; imaging strategies	
33.	Details of existing review of same topic by same authors	None	
34.	Current review status	☐	Ongoing
		☐	Completed but not published
		☐	Completed and published
		☐	Completed, published and being updated
		☐	Discontinued
35..	Additional information		
36.	Details of final publication	www.nice.org.uk	

1 **Table 8: Health economic review protocol**

Review question	All questions where health economic evidence applicable
Objectives	To identify health economic studies relevant to any of the review questions.
Search criteria	• Populations, interventions and comparators must be as specified in the clinical review protocol above. • Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Search strategy	A health economic study search will be undertaken using population-specific terms and a health economic study filter.
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2003, abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual.[155] **Inclusion and exclusion criteria** • If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile. • If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile. • If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included. **Where there is discretion** The health economist will decide based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded based on applicability or methodological limitations will be listed with explanation in the excluded health economic studies appendix below. The health economist will be guided by the following hierarchies. *Setting:* • UK NHS (most applicable). • OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden). • OECD countries with predominantly private health insurance systems (for example, Switzerland).

	• Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations. *Health economic study type:* • Cost–utility analysis (most applicable). • Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis). • Comparative cost analysis. • Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations. *Year of analysis:* • The more recent the study, the more applicable it will be. • Studies published in 2003 or later but that depend on unit costs and resource data entirely or predominantly from before 2003 will be rated as 'Not applicable'. • Studies published before 2003 will be excluded before being assessed for applicability and methodological limitations. *Quality and relevance of effectiveness data used in the health economic analysis:* • The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

Appendix B: Literature search strategies

This literature search strategy was used for the following review;

- What is the accuracy of different imaging strategies to detect a culprit aneurysm in adults with confirmed subarachnoid haemorrhage?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual[155]

For more information, please see the Methods Report published as part of the accompanying documents for this guideline.

B.1 Clinical search literature search strategy

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

Table 9: Database date parameters and filters used

base	s searched	ch filter used
ine (OVID)	– 24 June 2020	isions omised controlled trials ematic review studies rvational studies nostic tests studies
ase (OVID)	– 24 June 2020	isions omised controlled trials ematic review studies rvational studies

base	s searched	ch filter used
		ıostic tests studies
Cochrane Library (Wiley)	rane Reviews to 2020 Issue 6 of 12 TRAL to 2020 Issue 6 of 12	

1 **Medline (Ovid) search terms**

1.	exp Subarachnoid Hemorrhage/
2.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial) adj3 (hemorrhag* or haemorrhag* or bleed* or blood*)).ti,ab.
3.	(SAH or aSAH).ti,ab.
4.	exp Intracranial Aneurysm/
5.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial or brain) adj3 (aneurysm* or aneurism* or hematoma* or haematoma*)).ti,ab.
6.	or/1-5
7.	letter/
8.	editorial/
9.	news/
10.	exp historical article/
11.	Anecdotes as Topic/
12.	comment/
13.	case report/
14.	(letter or comment*).ti.
15.	or/7-14
16.	randomized controlled trial/ or random*.ti,ab.
17.	15 not 16
18.	animals/ not humans/
19.	exp Animals, Laboratory/
20.	exp Animal Experimentation/
21.	exp Models, Animal/
22.	exp Rodentia/
23.	(rat or rats or mouse or mice).ti.
24.	or/17-23
25.	6 not 24
26.	(exp child/ or exp pediatrics/ or exp infant/) not (exp adolescent/ or exp adult/ or exp middle age/ or exp aged/)
27.	25 not 26
28.	limit 27 to English language
29.	Epidemiologic studies/
30.	Observational study/
31.	exp Cohort studies/
32.	(cohort adj (study or studies or analys* or data)).ti,ab.
33.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
34.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
35.	Controlled Before-After Studies/
36.	Historically Controlled Study/

37.	Interrupted Time Series Analysis/
38.	(before adj2 after adj2 (study or studies or data)).ti,ab.
39.	or/29-38
40.	exp case control study/
41.	case control*.ti,ab.
42.	or/40-41
43.	39 or 42
44.	Cross-sectional studies/
45.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
46.	or/44-45
47.	39 or 46
48.	39 or 42 or 46
49.	Meta-Analysis/
50.	exp Meta-Analysis as Topic/
51.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
52.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
53.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
54.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
55.	(search* adj4 literature).ab.
56.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
57.	cochrane.jw.
58.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
59.	or/49-57
60.	randomized controlled trial.pt.
61.	controlled clinical trial.pt.
62.	randomi#ed.ti,ab.
63.	placebo.ab.
64.	randomly.ti,ab.
65.	Clinical Trials as topic.sh.
66.	trial.ti.
67.	or/60-66
68.	exp "Sensitivity and Specificity"/
69.	(sensitivity or specificity).ti,ab.
70.	((pre test or pretest or post test) adj probability).ti,ab.
71.	(predictive value* or PPV or NPV).ti,ab.
72.	likelihood ratio*.ti,ab.
73.	likelihood function/
74.	((area under adj4 curve) or AUC).ti,ab.
75.	(receive* operat* characteristic* or receive* operat* curve* or ROC curve*).ti,ab.
76.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness)).ti,ab.
77.	gold standard.ab.
78.	or/68-77

79.	Magnetic Resonance Angiography/ or Angiography, Digital Subtraction/ or Computed Tomography Angiography/
80.	((magnetic resonance or digital subtraction or computed tomograph*) adj3 angiograph*).ti,ab.
81.	((MR or DS or CT) adj3 (angiograph* or angiogram*)).ti,ab.
82.	(MRA or DSA or CTA).ti,ab.
83.	or/79-82
84.	28 and 83 and (48 or 59 or 67 or 78)

1 **Embase (Ovid) search terms**

1.	*subarachnoid hemorrhage/
2.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial) adj3 (hemorrhag* or haemorrhag* or bleed* or blood*)).ti,ab.
3.	(SAH or aSAH).ti,ab.
4.	exp intracranial aneurysm/
5.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial or brain or saccular or berry or wide-neck*) adj3 (aneurysm* or aneurism* or hematoma* or haematoma*)).ti,ab.
6.	or/1-5
7.	letter.pt. or letter/
8.	note.pt.
9.	editorial.pt.
10.	Case report/ or Case study/
11.	(letter or comment*).ti.
12.	or/7-11
13.	randomized controlled trial/ or random*.ti,ab.
14.	12 not 13
15.	animal/ not human/
16.	Nonhuman/
17.	exp Animal Experiment/
18.	exp Experimental animal/
19.	Animal model/
20.	exp Rodent/
21.	(rat or rats or mouse or mice).ti.
22.	or/14-21
23.	6 not 22
24.	(exp child/ or exp pediatrics/) not (exp adult/ or exp adolescent/)
25.	23 not 24
26.	limit 25 to English language
27.	Clinical study/
28.	Observational study/
29.	family study/
30.	longitudinal study/
31.	retrospective study/
32.	prospective study/
33.	cohort analysis/
34.	follow-up/

35.	cohort*.ti,ab.
36.	34 and 35
37.	(cohort adj (study or studies or analys* or data)).ti,ab.
38.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
39.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
40.	(before adj2 after adj2 (study or studies or data)).ti,ab.
41.	or/27-33,36-40
42.	exp case control study/
43.	case control*.ti,ab.
44.	or/42-43
45.	41 or 44
46.	cross-sectional study/
47.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
48.	or/46-47
49.	41 or 48
50.	41 or 44 or 48
51.	random*.ti,ab.
52.	factorial*.ti,ab.
53.	(crossover* or cross over*).ti,ab.
54.	((doubl* or singl*) adj blind*).ti,ab.
55.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
56.	crossover procedure/
57.	single blind procedure/
58.	randomized controlled trial/
59.	double blind procedure/
60.	or/51-59
61.	systematic review/
62.	meta-analysis/
63.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
64.	((systematic or evidence) adj3 (review* or overview*)).ti,ab.
65.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
66.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
67.	(search* adj4 literature).ab.
68.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
69.	((pool* or combined) adj2 (data or trials or studies or results)).ab.
70.	cochrane.jw.
71.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
72.	or/61-70
73.	exp "sensitivity and specificity"/
74.	(sensitivity or specificity).ti,ab.
75.	((pre test or pretest or post test) adj probability).ti,ab.
76.	(predictive value* or PPV or NPV).ti,ab.

77.	likelihood ratio*.ti,ab.
78.	((area under adj4 curve) or AUC).ti,ab.
79.	(receive* operat* characteristic* or receive* operat* curve* or ROC curve*).ti,ab.
80.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness)).ti,ab.
81.	diagnostic accuracy/
82.	diagnostic test accuracy study/
83.	gold standard.ab.
84.	or/73-83
85.	magnetic resonance angiography/ or computed tomographic angiography/ or digital subtraction angiography/
86.	((magnetic resonance or digital subtraction or computed tomograph*) adj3 angiograph*).ti,ab.
87.	((MR or DS or CT) adj3 (angiograph* or angiogram*)).ti,ab.
88.	(MRA or DSA or CTA).ti,ab.
89.	or/85-88
90.	26 and 89 and (50 or 60 or 72 or 84)

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Subarachnoid Hemorrhage] explode all trees
#2.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial) near/3 (hemorrhag* or haemorrhag* or bleed* or blood*)):ti,ab
#3.	(SAH or aSAH):ti,ab
#4.	MeSH descriptor: [Intracranial Aneurysm] explode all trees
#5.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial or brain or saccular or berry or wide-neck*) near/3 (aneurysm* or aneurism* or hematoma* or haematoma*)):ti,ab
#6.	(or #1-#5)
#7.	MeSH descriptor: [Magnetic Resonance Angiography] this term only
#8.	MeSH descriptor: [Angiography, Digital Subtraction] this term only
#9.	MeSH descriptor: [Computed Tomography Angiography] this term only
#10.	((magnetic resonance or digital subtraction or computed tomograph*) near/3 angiograph*):ti,ab
#11.	((MR or DS or CT) near/3 (angiograph* or angiogram*)):ti,ab
#12.	(MRA or DSA or CTA):ti,ab
#13.	(or #7-#12)
#14.	#6 and #13

B.2 Health Economics literature search strategy

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

1 **Table 10: Database date parameters and filters used**

base	s searched	ch filter used
ine	– 23 June 2020	isions h economics studies
ase	– 23 June 2020	isions h economics studies
e for Research and Dissemination (CRD)	- Inception – 23 June 2020 EED - Inception to March 2015	

2 **Medline (Ovid) search terms**

1.	exp Subarachnoid Hemorrhage/
2.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial) adj3 (hemorrhag* or haemorrhag* or bleed* or blood*)).ti,ab.
3.	(SAH or aSAH).ti,ab.
4.	exp Intracranial Aneurysm/
5.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial or brain or saccular or berry or wide-neck*) adj3 (aneurysm* or aneurism* or hematoma* or haematoma*)).ti,ab.
6.	or/1-5
7.	letter/
8.	editorial/
9.	news/
10.	exp historical article/
11.	Anecdotes as Topic/
12.	comment/
13.	case report/
14.	(letter or comment*).ti.
15.	or/7-14
16.	randomized controlled trial/ or random*.ti,ab.
17.	15 not 16
18.	animals/ not humans/
19.	exp Animals, Laboratory/
20.	exp Animal Experimentation/
21.	exp Models, Animal/
22.	exp Rodentia/
23.	(rat or rats or mouse or mice).ti.
24.	or/17-23
25.	6 not 24
26.	limit 25 to English language
27.	Economics/
28.	Value of life/
29.	exp "Costs and Cost Analysis"/
30.	exp Economics, Hospital/
31.	exp Economics, Medical/
32.	Economics, Nursing/
33.	Economics, Pharmaceutical/

34.	exp "Fees and Charges"/
35.	exp Budgets/
36.	budget*.ti,ab.
37.	cost*.ti.
38.	(economic* or pharmaco?economic*).ti.
39.	(price* or pricing*).ti,ab.
40.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
41.	(financ* or fee or fees).ti,ab.
42.	(value adj2 (money or monetary)).ti,ab.
43.	or/27-42
44.	26 and 43

1 **Embase (Ovid) search terms**

1.	subarachnoid hemorrhage/
2.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial) adj3 (hemorrhag* or haemorrhag* or bleed* or blood*)).ti,ab.
3.	(SAH or aSAH).ti,ab.
4.	exp intracranial aneurysm/
5.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial or brain or saccular or berry or wide-neck*) adj3 (aneurysm* or aneurism* or hematoma* or haematoma*)).ti,ab.
6.	or/1-5
7.	letter.pt. or letter/
8.	note.pt.
9.	editorial.pt.
10.	case report/ or case study/
11.	(letter or comment*).ti.
12.	or/7-11
13.	randomized controlled trial/ or random*.ti,ab.
14.	12 not 13
15.	animal/ not human/
16.	nonhuman/
17.	exp Animal Experiment/
18.	exp Experimental Animal/
19.	animal model/
20.	exp Rodent/
21.	(rat or rats or mouse or mice).ti.
22.	or/14-21
23.	6 not 22
24.	limit 23 to English language
25.	health economics/
26.	exp economic evaluation/
27.	exp health care cost/
28.	exp fee/
29.	budget/

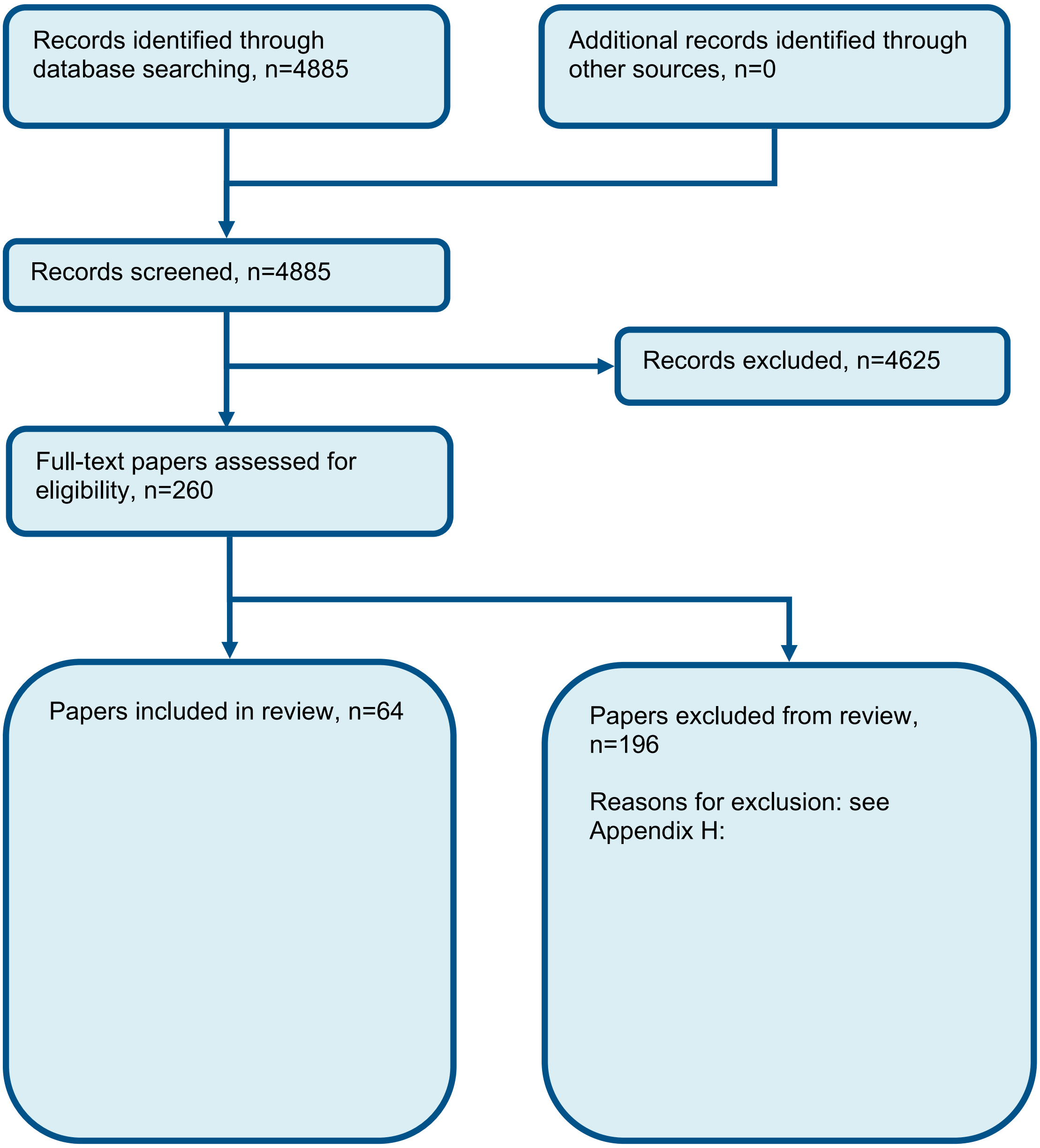
30.	funding/
31.	budget*.ti,ab.
32.	cost*.ti.
33.	(economic* or pharmaco?economic*).ti.
34.	(price* or pricing*).ti,ab.
35.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
36.	(financ* or fee or fees).ti,ab.
37.	(value adj2 (money or monetary)).ti,ab.
38.	or/25-37
39.	24 and 38

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Subarachnoid Hemorrhage EXPLODE ALL TREES
#2.	MeSH DESCRIPTOR Intracranial Hemorrhages EXPLODE ALL TREES
#3.	(((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial) adj3 (hemorrhag* or haemorrhag* or bleed* or blood*)))
#4.	((SAH or aSAH))
#5.	#1 OR #2 OR #3 OR #4
#6.	MeSH DESCRIPTOR Aneurysm EXPLODE ALL TREES
#7.	((aneurysm* or hematoma* or haematoma*))
#8.	#6 OR #7
#9.	MeSH DESCRIPTOR Intracranial Aneurysm EXPLODE ALL TREES
#10.	(((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial) adj3 (aneurysm* or hematoma* or haematoma*)))
#11.	#9 OR #10
#12.	MeSH DESCRIPTOR Aneurysm, ruptured
#13.	(((ruptur* or weak* or brain or trauma*) adj3 (aneurysm* or hematoma* or haematoma*)))
#14.	#12 OR #13
#15.	(#5 or #8 or #11 or #14)

Appendix C: Clinical evidence selection

Figure 1: Flow chart of clinical study selection for the review of diagnostic imaging strategies



Appendix D: Clinical evidence tables

Reference	Agid 2006[1]
Study type	Cross-sectional study
Study methodology	Data source: Division of Neuroradiology, Department of medical imaging, Toronto Western Hospital, Toronto, Canada Recruitment: January 2005 – November 2005, consecutive patients with acute SAH
Number of patients	n = 73
Patient characteristics	Age, mean (SD): 55.8 ± 12.8 Gender (male to female ratio): 27 / 38 Setting: Toronto Western Hospital Country: Canada Inclusion criteria: Patients with subarachnoid haemorrhage who underwent CTA and DSA Exclusion criteria: Not specified
Target condition(s)	aSAH
Index test(s) and reference standard	Index test - CTA All patients had a CTA from the aortic arch to the vertex using 64 slice multidetector CT scanner. CTA images were acquired following intravenous timed injection of contrast agent using an auto-triggered mechanical injector. The injection rate was 4ml/s to a total injection volume of 40ml of contrast agent followed by injection of 20ml of contrast agent at 3ml/s. Reference standard – DSA DSA was performed using a dedicated biplane neuro-angiography suite and included three or four vessel studies with standard frontal and lateral views as well as rotational spin angiograms with 3D reconstruction. In each patient, the same neuroradiologist who originally interpreted the CTA was later responsible for performing and interpreting the DSA, and eventually for endovascular coiling if performed.

Reference	Agid 2006[1]
	CTAs were interpreted in a prospective fashion prior to performing digital subtraction angiography (DSA) and without knowledge of the findings on DSA or open surgery. Time between measurement of index test and reference standard: Not specified

2×2 table

	Reference standard +	Reference standard −	Total	Insufficient data reported to calculate full 2x2 table
Index test +				
Index test −				
Total				

Statistical measures	<u>Index text</u> Per patient: Sensitivity 94% Specificity 100% PPV NPV
Source of funding	<u>Not reported</u>
Limitations	Risk of bias: Very serious Indirectness: No indirectness
Comments	The diagnosis of acute SAH was confirmed by either neurosurgical exploration or by catheter based intra-arterial DSA. These two options were regarded as the gold standard. Only patients who received either DSA or surgery were included in the statistical analysis.

Reference	Anderson 1997[3]
Study type	Cross-sectional
Study methodology	Data source: Patients attending the participating hospital between July 1996 and October 1996. Recruitment: Consecutive eligible patients were included
Number of patients	n = 40
Patient characteristics	Age, mean (SD): Not reported

<table>
<tr><th>Reference</th><th>Anderson 1997[3]</th></tr>
<tr><td></td><td>Gender (male to female ratio): Not reported

Setting: Tertiary care, hospital setting

Country: Canada

Inclusion criteria: Patients with suspected intracranial aneurysms examined by both CTA and DSA. 32 of the 40 patients presented with acute SAH.
Exclusion criteria: Not reported</td></tr>
<tr><td>Target condition(s)</td><td>aSAH</td></tr>
<tr><td>Index test(s) and reference standard</td><td><u>Index test</u>
CTA
General Electric High Speed Spiral CT scanner was used for CTA examination. The reconstructed images were processed at the work station into both shaded surface display and maximum intensity projection.

<u>Reference standard</u>
DSA

CTA and DSA images were interpreted separately and in a blinded fashion by a neuroradiologist.

Time between measurement of index test and reference standard: All patients underwent DSA after several hours of undergoing CTA.</td></tr>
<tr><td>2×2 table
Per aneurysm</td><td><table>
<tr><td></td><td>Reference standard +</td><td>Reference standard −</td><td>Total</td></tr>
<tr><td>Index test +</td><td><u>37</u></td><td><u>1</u></td><td></td></tr>
<tr><td>Index test −</td><td><u>6</u></td><td><u>9</u></td><td></td></tr>
<tr><td>Total</td><td><u>43</u></td><td><u>10</u></td><td></td></tr>
</table></td></tr>
<tr><td>Statistical measures</td><td><u>Index text</u>
Per aneurysm:
Sensitivity 86%
Specificity 90%
PPV 97%
NPV 60%</td></tr>
</table>

Reference	**Anderson 1997**[3]
Source of funding	Not reported
Limitations	Risk of bias: None Indirectness: No indirectness
Comments	

Reference	**Anzalone 1995**[5]
Study type	Cross-sectional study
Study methodology	Data source: Department of neuroradiology, Scientific institute H.S. Raffaele, Milan Italy Recruitment: From May 1991 to March 1993, patients with CT positive acute SAH
Number of patients	n = 27
Patient characteristics	Age, mean (range): 50 (range 27-82) Gender (male to female ratio): 12/15 Setting: Scientific institute H.S. Raffaele, Milan Country: Italy Inclusion criteria: CT positive for SAH with DSA within 5 hours of admission Exclusion criteria: Early surgery or no MRA performed
Target condition(s)	aSAH
Index test(s) and reference standard	Index test - MRA MRA examinations were performed with a 1.5T MR imaginer with a circular polarized head coiled operating in both the transit and receive modes. In the first 21 patients a 3D time of flight sequence was performed, while in the remaining 6, to optimize contrast resolution and minimise saturation effect, a magnetisation transfer gradient and variable flip angle were added to the traditional 3DTOF sequence. Reference standard - DSA DSA was performed via the femoral arteries with selective catherization of both carotid and vertebral arteries. All studies included anteroposterior, lateral and oblique projections. A 1024 x 1024 matrix was used in all cases.

<table>
<tr><th>Reference</th><th>Anzalone 1995[5]</th></tr>
<tr><td></td><td>MRA and DSA examinations were independently scrutinized by two expert neuroradiologists, without knowledge of the history or CT findings.

Time between measurement of index test and reference standard: Within 3 hours or MRA was performed immediately before DSA</td></tr>
<tr><td>2×2 table</td><td><table>
<tr><td></td><td>Reference standard +</td><td>Reference standard −</td><td>Total</td><td rowspan="4">Unable to calculate as numbers given in paper are mixed between per patient and per aneurysm</td></tr>
<tr><td>Index test +</td><td></td><td></td><td></td></tr>
<tr><td>Index test −</td><td></td><td></td><td></td></tr>
<tr><td>Total</td><td></td><td></td><td></td></tr>
</table></td></tr>
<tr><td>Statistical measures</td><td><u>Index text</u>

Sensitivity 91.3%
Specificity 100%
PPV
NPV
PLR
NLR
AUC</td></tr>
<tr><td>Source of funding</td><td>Not specified</td></tr>
<tr><td>Limitations</td><td>Risk of bias: Serious
Indirectness: No indirectness</td></tr>
<tr><td>Comments</td><td></td></tr>
</table>

Reference	Aulbach 2016[7]
Study type	Prospective Cross-sectional
Study methodology	Data source: Patients admitted with aSAH Recruitment: Neuroradiologists or neurosurgeons familiar with the protocol prospectively enrolled patients
Number of patients	n = 116

Reference	Aulbach 2016[7]
Patient characteristics	Age, mean (SD): 53.9 (13.6 years) Gender (male to female ratio): 58/58 Setting: hospital, primary care Country: Germany Inclusion criteria: Patients with acute SAH Exclusion criteria: Patients with typical exclusion criteria for CTA or previous coiling or clipping were excluded. Patients with perimesencephalic SAH were not followed further.
Target condition(s)	aSAH
Index test(s) and reference standard	Index test CTA Examinations were performed on a 16–detector row spiral CT. Reference standard DSA Rotational biplane DSA unit Time between measurement of index test and reference standard: Unclear

2×2 table (per patient)		Reference standard +	Reference standard −	Total
	Index test +	70	0	70
	Index test −	1	45	46
	Total	71	45	

2×2 table (per aneurysm)		Reference standard +	Reference standard −	Total
	Index test +	73	1	73
	Index test −	1	45	46
	Total	74	46	

Reference	**Aulbach 2016[7]**
Statistical measures	Index text per patient Sensitivity: 99 (92-100%) Specificity: 100 (92-100%) PPV: 100 (95-100%) NPV: 98 (89-100%) per aneurysm Sensitivity: 99 (93-100%) Specificity: 98 (89-100%) PPV: 99 (93-100%) NPV: 98 (89-100%) *per patient
Source of funding	Not reported
Limitations	Risk of bias: Very serious Indirectness: No indirectness
Comments	

1

Reference	**Chen 2009[29]**
Study type	Cross-sectional study
Study methodology	Data source: Department of Radiology, The First Affiliated Hospital of Nanjiang Medical University, Nanjing, China Recruitment: Between January 2005 and October 2006, consecutive patients with suspected intracranial aneurysms
Number of patients	n = 152
Patient characteristics	Age, mean (range): 52 years (15-84) Gender (male to female ratio): 6[/86 Setting: The First Affiliated Hospital of Nanjiang Medical University Country: China Inclusion criteria: Patients who successively underwent unenhanced CT of the head, 16 slice CTA and 2d-DSA no more than 3 days apart

Reference	Chen 2009[29]
	Exclusion criteria: Not specified
Target condition(s)	aSAH
Index test(s) and reference standard	Index test - CTA CTA with a 16 row multi-slice CT machine. The CTA was initiated 15 to 22 seconds after the start of an IV infusion of non-ionic iodinated contrast material. The CTA data acquisition was performed according to the following protocol: 120kV, 250mA, slice thickness of 0.75mm and reconstruction interval of 0.40mm Reference standard - DSA Two dimensional DSA was performed within 3 days after CTA study. Standard intra-arterial DSA was performed with a femoral catheterization by the Seldinger technique with a biplane DSA unit. Non-ionic contrast material was used in all cases. The angiographic procedure was routinely accomplished with a standard diagnostic catheter. Selective carotid angiograms were obtained bilaterally in the anteroposterior, lateral and bilateral oblique and additional different projections depending on the location of the aneurysm as needed for each patient. Images were reviewed by 3 neuroradiologists independently. The 16 slice CTA studies were independently assessed by the 2 readers blinded to the 2D-DSA and surgical findings. Time between measurement of index test and reference standard: 3 days
2×2 table Per aneurysm	see table below
Statistical measures	Index text Per aneurysm: Sensitivity 98% Specificity 100% PPV 100% NPV 99%
Source of funding	Not reported
Limitations	Risk of bias: Serious Indirectness: Serious indirectness

2×2 table Per aneurysm

	Reference standard +	Reference standard −	Total
Index test +	90	0	90
Index test −	2	198	200
Total	92	198	290

Reference	Chen 2009[29]
Comments	90 (59.2%) of the patients had SAH

Reference	Chen 2010[33]
Study type	Retrospective Cross-sectional
Study methodology	Data source: Between January 2005 and October 2008, consecutive patients underwent unenhanced CT scan and 16-slice CTA. 315 of these 388 patients had SAH, 39 patients had SAH and intraventricular haemorrhage (IVH), 20 patients had SAH and intraparenchymal haemorrhage (IPH), and 14 patients had SAH, IVH and IPH. Recruitment: Patients were selected by the referring physicians for CTA on the basis of clinical history, including symptoms and signs suggestive of intracranial aneurysm.
Number of patients	n = 388
Patient characteristics	Age, mean (range): 53 years (14-86) Gender (male to female ratio): 190/198 Setting: The Third Affiliated Hospital of Suzhou University Country: China Inclusion criteria: Patients were selected by the referring physicians for CTA on the basis of clinical history, including symptoms and signs suggestive of intracranial aneurysm. Exclusion criteria: Not reported
Target condition(s)	aSAH
Index test(s) and reference standard	<u>Index test</u> CTA All CTA examinations were performed with a 16-slice CT scanner. <u>Reference standard</u> DSA All DSA was performed transfemorally with 5F catheters by using a biplane DSA unit

Reference	**Chen 2010[33]**				
	Time between measurement of index test and reference standard: Intra-arterial DSA was performed within 3 days after CTA study.				
2×2 table Per patient		Reference standard +	Reference standard −	Total	
	Index test +				
	Index test −				
	Total	256	132		
2×2 table Per aneurysm		Reference standard +	Reference standard −	Total	* Study reports 10 false positives (does not match reported calculations)
	Index test +	282	4*	286	
	Index test −	5	128		
	Total	287	132		
Statistical measures	Per aneurysm: Sensitivity 98.3 (96-99.4) Specificity 97 (92.6-99.2) PPV 98.6 (96.5-99.6) NPV 96.3 (91.6-98.8)				
Source of funding	Not reported				
Limitations	Risk of bias: None Indirectness: No indirectness				
Comments	Diagnosis of intracranial aneurysms				

Reference	**Chen 2012[35]**
Study type	Prospective Cross-sectional
Study methodology	Data source: Patients with a Glasgow Coma Scale (GCS) score of 15 and SAH confirmed by a plain CT Recruitment: Consecutive patients included
Number of patients	n = 165

Reference	Chen 2012[35]			
Patient characteristics	Age, mean (SD): 52.32±12.81 Gender (male to female ratio): 74/91 Setting: The Sixth Affiliated People's Hospital Country: China Inclusion criteria: all patients with SAH confirmed by a plain CT and all patients with symptomatic suspected ruptured aneurysms revealed by MRA. Exclusion criteria: patients who had undergone a previous DSA and patients with a severe contrast medium allergy or who had renal failure rendering them unable to tolerate the contrast medium load associated with DSA.			
Target condition(s)	aSAH			
Index test(s) and reference standard	Index test MRA The 3D-TOF-MRA was performed on a 3.0-T system. Reference standard DSA Conventional 2D-DSAwas performed on a monoplanar unit. Time between measurement of index test and reference standard: DSA was performed by an interventional neuroradiologist within 14 days of the MRA (median 2.2 days, range 2 h to 14 days).			
2×2 table Per patient		Reference standard +	Reference standard −	Total
	Index test +	132	1	
	Index test −	4	28	
	Total			165
2×2 table Per aneurysm		Reference standard +	Reference standard −	Total
	Index test +	162	2	
	Index test −	1	27	
	Total			195

Reference	Chen 2012[35]
Statistical measures	<u>Index text</u> Per patient Sensitivity 97.1% (94.2-99.9) Specificity 96.6% (89.5-103.6) PPV 99.2% (97.8-100.7) NPV 87.5% (75.4-99.6) Per aneurysm Sensitivity 97.6% (95.2-99.9) Specificity 93.1% (83.3-102.9) PPV 98.8% (97.1-100.5) NPV 87.1% (74.6-99.6)
Source of funding	This study has been supported by the National Natural Scientific Fund of China, Shanghai Important Subject Fund of Medicine and Program for Shanghai Outstanding Medical Academic Leader.
Limitations	Risk of bias: None Indirectness: No indirectness
Comments	

1

Reference	Chen 2013[31]
Study type	Retrospective Cross-sectional
Study methodology	Data source: Consecutive patients of participating hospital suspected of having cerebral aneurysms. Of the 282 patients, 179 (63.5%) patients had subarachnoid haemorrhage, 31 (11.0%) had subarachnoid and intraventricular haemorrhage, 15 (5.3%) had subarachnoid and intraparenchymal haemorrhage, 10 (3.6%) had intraparenchymal haemorrhage, 15 (5.3%) had subarachnoid, intraventricular, and intraparenchymal haemorrhage, and the remaining 32 (11.3%) patients had a variety of indications, including headache, oculomotor paralysis, tumour, and hydrocephalus. Recruitment: Consecutive patients recruited to study
Number of patients	n = 282
Patient characteristics	Age, mean (range): 58 (21-91) Gender (male to female ratio): 138/144 Setting: Third Affiliated Hospital of Suzhou University

Reference	Chen 2013[31]
	Country: China Inclusion criteria: Between February 2011 and October 2012, 315 patients suspected of having cerebral aneurysms were enrolled Exclusion criteria: Eighteen (5.7%) patients who had undergone prior surgical clipping or endovascular coiling for their cerebral aneurysms were excluded from the study.
Target condition(s)	aSAH
Index test(s) and reference standard	Index test Subtracted volumetric CT angiography The subtracted CT angiographic volumetric data were obtained by subtracting the mask image volumetric data from the conventional non-subtracted CT angiographic volumetric data. The subtraction process was started by loading both the non-enhanced and the contrast enhanced imaging data in the console’s software. Bone tissue data were automatically removed, and these data were used for 3D visualization by means of direct volume-rendering techniques or maximum-intensity projections. Reference standard DSA Invasive selective angiography was performed by means of the transfemoral approach with a biplane DSA unit with rotational capabilities Time between measurement of index test and reference standard: Unclear

2×2 table Per patient		Reference standard +	Reference standard −	Total
	Index test +	197	0	
	Index test −	1	84	
	Total	198	84	282

2×2 table Per aneurysm		Reference standard +	Reference standard −	Total
	Index test +	237	0	
	Index test −	2	84	
	Total	239	84	

Reference	**Chen 2013[31]**
Statistical measures	Index text Per patient: Sensitivity 99 (96.4-99.9) Specificity 100 (95.7-100) PPV 100 (98.1-100) NPV 97.7 (91.9-99.7) Per aneurysm: Sensitivity 99.2 (97-99.9) Specificity 100 (95.7-100) PPV 100 (98.5-100) NPV 97.7 (91.9-99.7)
Source of funding	Supported by the National Natural Science Foundation of China (grant 81370035) and Shanghai Pujiang Talent Programme (grant 15PJD002).
Limitations	Risk of bias: Serious Indirectness: No indirectness
Comments	Non-subtracted and subtracted results reported. Subtracted CTA results extracted

1

Reference	**Chung 1999[37]**
Study type	Cross-sectional study
Study methodology	Data source: Department of Diagnostic Radiology and Neurosurgery, Yong Dong Severance Hospital, Yonsei University College of Medicine, Seoul, South Korea Recruitment: From January 1997 to January 1998, 218 patients underwent screening with brain MR angiography
Number of patients	n = 30
Patient characteristics	Age, mean (SD): Gender (male to female ratio): 14 / 16 Setting: Yong Dong Severance Hospital, Yonsei University College of Medicine Country: South Korea Inclusion criteria: Patients who underwent screening with brain MR angiography and DSA were included within the consecutive study

Reference	Chung 1999[37]
	Exclusion criteria: Not specified
Target condition(s)	aSAH
Index test(s) and reference standard	<u>Index test- MRA</u> Standard MR head imaging was performed with axial T1-weighted (600/14/2 [TR/TE/acquisitions]), axial and coronal turbo spin-echo T2-weighted (4500/120/2), and contrast-enhanced axial and coronal turbo spin-echo T1-weighted (600/14/2) sequences. All MR angiographic studies were performed using a 1.5-T MR system with 25 mT/m gradient capability (Siemens AG, Vision, Erlangen, Germany). A 3D time-of-flight (TOF) technique was used with imaging parameters of 30/6.4 and ramped pulses from 15 to 25 with a centre flip angle of 20. In standard implementation, the scan time for this protocol is 15 minutes 22 seconds. For this particular study, only half the phase-encoded steps were measured, and the rest were set to zero. Diagnoses of aneurysms were performed after evaluating the maximum intensity projection (MIP) images and individual axial sections. The following five vessel segments were analysed separately in each case: the axial and coronal rotations of whole intracranial arteries, the axial rotation of both internal cerebral arteries (ICAs) (including the ICA, the middle cerebral arteries [MCAs] on each side, and the posterior communicating artery origins), and the basilar artery. Target MIP was tried when necessary. <u>Reference standard - DSA</u> DSA was performed within 2 hours after MR angiography to minimize any image discrepancy caused by thrombosis in the aneurysm or spasm in the cases of SAH. Until the start of DSA, one radiologist reported blinded interpretations to another radiologist regarding the character of aneurysmal features (including the size, shape, neck, and parent vessels). In all patients, three- or four-vessel angiography was used, including both ICAs and vertebral arteries. With each injection, antero-posterior and lateral views were obtained, with additional views (oblique, trans-facial, and contralateral carotid artery compression) acquired when necessary. After DSA, the interpretation of MR angiography and DSA was performed blind by two radiologists, with consensus. Of 30 patients, 23 had surgery and one had a detachable coil inserted into the aneurysmal sac. After DSA, the interpretation of MR angiography and DSA was performed blind by two radiologists, with consensus. Time between measurement of index test and reference standard: DSA was performed within 2 hours after MR angiography

2×2 table Per patient

	Reference standard +	Reference standard −	Total
Index test +	38	0	38
Index test −	1	0	1
Total	39	0	39

Reference	**Chung 1999**[37]
Statistical measures	<u>Index text MRA</u> Sensitivity: 97%
Source of funding	Not specified
Limitations	Risk of bias: Serious Indirectness: No indirectness
Comments	Unable to calculate the specificity, PPV and NPV from the numbers reported within the paper

Reference	**Colen 2007**[38]
Study type	Cross-sectional study
Study methodology	Data source: Department of Radiology, University of Washington Medical Centre, Seattle, USA Recruitment: Patients who underwent CTA of the head and intracranial DSA within 48 hours for SAH between July 2003 – January 2005
Number of patients	n = 336
Patient characteristics	Age, Median (range): 55 (13-92) Gender (male to female ratio): 133/78 Setting: University of Washington Medical Centre, Seattle Country: USA Inclusion criteria: Patients who underwent CTA of the head and intracranial DSA within 48 hours for SAH Exclusion criteria: history of trauma, known condition causing SAH, or no aneurysm present on further imaging.
Target condition(s)	aSAH

Reference	Colen 2007[38]				
Index test(s) and reference standard	Index test - CTA Patients were evaluated using 4,8 or 16 slice MDCT. Each CTA examination included unenhanced and contrast enhanced head imaging. The protocol for the CTA portion of the examination was as follows: 110ml of Iodixanol for 4 and 8 MDCT or 80ml of Iohexol for 16 MDCT followed by 30ml of saline infused at 3.0ml for 4 and 14 MDCT and 4ml for 8 MDCT. Slice thickness was 1.25mm for 4 and 8 MDCT and 0.625 for 16 MDCT. Reference standard – DSA DSA imaging was performed using 3D rotational angiography. Images were acquired in the standard projections (AP, lateral and AP / lateral obliques). The three dimensional rotational angiography was routinely performed when an aneurysm was found, this uses a mode over an angle of 180 at a frame rate of 12.5 frames per second. During the run, iodinated contrast agent was injected to provide continuous filling of the vasculature. Ten attending neuroradiologists with various degrees of experience and expertise in cerebral aneurysms generated CTA and DSA reports. In most cases the CTA preceded the DSA Time between measurement of index test and reference standard: not specified				
2×2 table Per patient		Reference standard +	Reference standard −	Total	Patients without aneurysms were treated as negative cases. TN/FP values not reported
	Index test +	200			
	Index test −	11			
	Total	211			
2×2 table Per aneurysm		Reference standard +	Reference standard −	Total	
	Index test +	235			
	Index test −	49			
	Total	284			
Statistical measures	Index text Per patient: Sensitivity 95% Specificity 97% PPV 98% NPV 91.2% PLR NLR AUC Per aneurysm: Sensitivity 83%				

Reference	Colen 2007[38]
	Specificity 93% PPV 96% NPV 72% PLR NLR AUC
Source of funding	Not specified
Limitations	Risk of bias: Very serious Indirectness: No indirectness
Comments	

1

2

Reference	Dammert 2004[43]
Study type	Cross-sectional
Study methodology	Data source: Patients admitted from April 2002 to February 2003 for SAH (41) or atypical intracranial haemorrhage (ICH) (9) requiring further investigation in the form of angiography. Recruitment: Consecutive patients
Number of patients	n = 50
Patient characteristics	Age, mean (range): 46.7 years, range 8–79 years Gender (male to female ratio): 18:32 Setting: University Hospital of the Technical University Aachen Country: Germany Inclusion criteria: patients who underwent both MSCT and DSA to find the cause for bleeding and to assess whether any aneurysms present were suitable for surgery or endovascular treatment.

Reference	Dammert 2004[43]				
	Exclusion criteria: Not reported				
Target condition(s)	aSAH				
Index test(s) and reference standard	<u>Index test</u> CTA The conventional angiography and the CT-data sets were reviewed by three trained neuroradiologists blinded to clinical presentation, angiographic and surgical findings. <u>Reference standard</u> Four-vessel DSA was performed via a femoral approach on a biplanar angiography suite in at least two planes. Time between measurement of index test and reference standard: Not reported				
2×2 table Per aneurysm		Reference standard +	Reference standard −	Total	*values calculated from narrative information. Calculated SP and NPV values differ slightly from reported values.
	Index test +	45.67	1.33	47	
	Index test −	5.33	7.67	13	
	Total	51	9	60	
Statistical measures	<u>Index text</u> Per aneurysm: Sensitivity 89.5% Specificity 83.3% PPV 97.2% NPV 56.1%				
Source of funding	Not reported				
Limitations	Risk of bias: Serious Indirectness: No indirectness				
Comments					

Reference	Donmez 2011[50]
Study type	Cross-sectional study

Reference	Donmez 2011[50]
Study methodology	Data source: University of Erciyes, School of Medicine, Department of Radiology, Kayseri, Turkey Recruitment: Consecutive patients with acute nontraumatic SAH between September 2006 and December 2009
Number of patients	n = 134
Patient characteristics	Age, mean (range): 52 (range 11 – 97) Gender (male to female ratio): 47/81 Setting: University of Erciyes, School of Medicine Country: Turkey Inclusion criteria: Patients with the diagnosis of non-traumatic acute SAH established by either non enhanced cerebral CT examination or by xanthochromia at lumbar puncture. Exclusion criteria: Patients who had undergone prior surgical clipping or endovascular coiling were excluded
Target condition(s)	aSAH
Index test(s) and reference standard	<u>Index test - CTA</u> All cerebral CTA studies were performed with a 16-row MDCT system. CTA was obtained from the level of the foramen magnum up to the vertex in a cranio-caudal direction. Parameters for the CTA acquisition were 0.625mm section thickness; 5.6mm table feed per rotation, 0.6s gantry rotation time; pitch of 0.562; 140kV; and 200 – 280 mA, 512x512 matrix and 25cm field of view. A total of 100mL of contrast agent was injected via the antecubital vein through an 18 or 20 gauge needle by a power injector at a rate of 4 – 5 mL/s. <u>Reference standard – DSA</u> Standard cerebral DSA was performed by using a single plane DSA unit with bilateral selective internal carotid artery injections and either bilateral or unilateral vertebral injections as necessary. Two experienced radiologists who had 7 and 10 years of extensive experience in CT vascular imaging and angiography performed their readings independently, each being blinded to the results of the others readings and in particular to the findings on images acquired with the other modality. Time between measurement of index test and reference standard: All patients underwent cerebral DSA within 12 – 48 hours after CTA examination

Reference	**Donmez 2011[50]**			
2×2 table Per patient		Reference standard +	Reference standard −	Total
	Index test +	112		
	Index test −		16	
	Total			
2×2 table Per aneurysm		Reference standard +	Reference standard −	Total
	Index test +	156		
	Index test −	8		
	Total	164		
Statistical measures	<u>Index text</u> Per aneurysm: Sensitivity 95.1% Specificity 94.1% PPV NPV			
Source of funding	Not specified			
Limitations	Risk of bias: Serious Indirectness: No indirectness			
Comments				

Reference	**Ergun 2011[54]**
Study type	Cross-sectional study
Study methodology	Data source: Department of radiology, Ankara training and research hospital, Ankara, Turkey Recruitment: Patients who underwent CTA and DSA due to the detection of subarachnoid haemorrhage by non-enhanced cranial CT
Number of patients	n = 37
Patient characteristics	Age, mean (range): 57.4 (27-80) Gender (male to female ratio): 14/23 Setting: Ankara training and research hospital

Reference	Ergun 2011[54]				
	Country: Turkey Inclusion criteria: Patients who underwent CTA and DSA due to the detection of subarachnoid haemorrhage by non enhanced cranial CT were included within the study Exclusion criteria: not specified				
Target condition(s)	aSAH				
Index test(s) and reference standard	<u>Index test - CTA</u> 64 slice CTA; Tube voltage – 120kV; tube current 250 mAs; section thickness 0.5mm; increment 2mm; scan time 6 – 9 seconds; scan volume from the first cervical vertebrae to the vertex; <u>Reference standard – DSA</u> No information provided CTA analysis was performed by two radiologists experienced in CT vascular imaging. The reviewers of the CTA were aware of the results of the non-enhanced CT scan and they were informed about the clinical status of the patient from the clinical details written on the request. Time between measurement of index test and reference standard: within 24 – 48 hours post CTA				
2×2 table Per patient		Reference standard +	Reference standard −	Total	2x2 cannot be completed due to incomplete data and mix between per patient and per aneurysm information.
	Index test +				
	Index test −				
	Total				
Statistical measures	<u>Index text</u> Per aneurysm: Sensitivity 92.8 % Specificity 83.3 % PPV 96.2 % NPV 71.4 %				

Reference	Ergun 2011[54]
Source of funding	Not specified
Limitations	Risk of bias: Very serious Indirectness: No indirectness
Comments	Not all patients went on to have DSA as a reference test therefore the surgical findings were used as a gold standard reference

Reference	Farahmand 2013[55]
Study type	Cross-sectional
Study methodology	Data source: Patients who presented to the study centre with the diagnosis of acute SAH Recruitment: Unclear
Number of patients	n = 55
Patient characteristics	Age, mean (SD): 46.3 years ± 7.9 years Gender (male to female ratio): 26:29 Setting: Nemazee Hospital in Shiraz, ICU Country: Iran Inclusion criteria: Patients admitted to hospital with non-traumatic SAH or intracranial haemorrhage, intraventricular haemorrhage or infarction. Exclusion criteria: Poor grade of subarachnoid haemorrhage, absolute contraindication for one of the modalities, and age more than 75 years. If only MRA or DSA was done, these patients were excluded from our analysis.
Target condition(s)	<u>aSAH</u>
Index test(s) and reference standard	<u>Index test</u> MRA Three-dimensional time of flight MR angiograms (3D-TOF MRA) were obtained at 1.5 Tesla with a repetition time (TR) = 23 and echo time (TE) = 6.9, flip angle 20°, a 512 × 256 matrix, magnetization transfer (MT) prepulse, and field of view 18 cm over 24 slices with 1.7 mm effective thickness. No contrast was used. Post-processing consisted of 60° maximum intensity projections (MIP) at six increments for 360° around the head, in both left-to-right and head-to-foot rotations. Images were reconstructed from the whole data set without editing. Source images were viewed on a routine basis.

<table>
<tr><td>Reference</td><td colspan="5">Farahmand 2013[55]</td></tr>
<tr><td></td><td colspan="5"><u>Reference standard</u>
<u>DSA</u>
<u>Intra-arterial DSA studies were done on a digital angiography system (Philips Arcu 48). Elective three- or four-vessel angiography with a standard projection format (anteroposterior, lateral and reverse-oblique) were used, and additional views were obtained, if required, to identify</u>
<u>the parent vessel and aneurysm neck more clearly.</u>

Time between measurement of index test and reference standard: In most patients MRA was done before DSA, or within a maximum of 1 week after DSA.</td></tr>
<tr><td rowspan="4">2×2 table
Per aneurysm</td><td></td><td>Reference standard +</td><td>Reference standard −</td><td>Total</td><td></td></tr>
<tr><td>Index test +</td><td>42</td><td>1</td><td>43</td><td></td></tr>
<tr><td>Index test −</td><td>9</td><td>8</td><td>17</td><td></td></tr>
<tr><td>Total</td><td>51</td><td>9</td><td>60</td><td></td></tr>
<tr><td>Statistical measures</td><td colspan="5"><u>Index text</u>
Sensitivity: 0.82
Specificity: 0.89
PPV: 0.93
NPV: 0.47*

NPV values from study differ to those calculated with 2x2</td></tr>
<tr><td>Source of funding</td><td colspan="5"><u>Shiraz University of Medical Sciences, Shiraz, Iran</u></td></tr>
<tr><td>Limitations</td><td colspan="5">Risk of bias: Very serious
Indirectness: No indirectness</td></tr>
<tr><td>Comments</td><td colspan="5"></td></tr>
</table>

1

Reference	**Feng 2020[58]**
Study type	Cross-sectional study
Study methodology	Data source: Records from the Second Affiliated Hospital of Harbin Medical University Recruitment: Patients retrospectively identified through patient records.

Reference	Feng 2020[58]
Number of patients	n = 79
Patient characteristics	Age, mean (SD): 42.8 (7.9) Gender (male to female ratio): 41/38 Setting: Second Affiliated Hospital of Harbin Medical University Country: China Inclusion criteria: Patients with cerebral aneurysm Exclusion criteria: patients are as follows: (1) allergic to contrast media; (2) with history of vascular interventional embolization; (3) with severe diabetes mellitus or hypertension; (4) with severe abnormal liver or kidney function; (5) with other malignant tumours; (6) who were breast-feeding or with pregnancy; (7) with mental disorders; and (8) with history of craniotomy.
Target condition(s)	aSAH
Index test(s) and reference standard	<u>Index test - CTA</u> The CTA examination was performed in a 256-row GE Revolution CT with the following scanning parameters: voltage 80KV, automatic milliampere, scanning layer thickness 0.625mm, pitch 0.969: 1, rotational speed 0.4 s/circle, and bed speed 19.37 mm/s. <u>Index test - MRA</u> The equipment for the MRA examination was the GE Discovery MR 7503.0T nuclear magnetic resonance scanner. Time-lapse magnetic resonance angiography (TOF-MRA) and the standard head coil were selected. <u>Reference standard – DSA</u> 3D-DSA was performed using a Philips Allura Xper FD 20 X-ray system, and the contrast agent was iohexol (300mgI/ml). Time between measurement of index test and reference standard: unclear

2×2 table Per patient		Reference standard +	Reference standard −	Total	2x2 cannot be completed due to incomplete data and mix between per patient and per aneurysm information.
	Index test +				
	Index test −				
	Total				

<table>
<tr><td>Reference</td><td>Feng 2020[58]</td></tr>
<tr><td>2×2 table
Per aneurysm</td><td><table>
<tr><td></td><td>Reference standard +</td><td>Reference standard −</td><td>Total</td></tr>
<tr><td>Index test +</td><td></td><td></td><td></td></tr>
<tr><td>Index test −</td><td></td><td></td><td></td></tr>
<tr><td>Total</td><td></td><td></td><td></td></tr>
</table></td></tr>
<tr><td>Statistical measures</td><td><u>Index text</u>

CTA
Per aneurysm:
Sensitivity 91.0 %
Specificity 66.7 %

MRA
Per aneurysm:
Sensitivity 83.1 %
Specificity 66.7 %</td></tr>
<tr><td>Source of funding</td><td>Not specified</td></tr>
<tr><td>Limitations</td><td>Risk of bias: Very serious
Indirectness: No indirectness</td></tr>
<tr><td>Comments</td><td>Only patients with aneurysms confirmed were included</td></tr>
</table>

Reference	**Fluss 2020[61]**
Study type	Cross-sectional study
Study methodology	Data source: Nontraumatic intracranial haemorrhage cases managed by the senior author over a 15-month. Data on patients with aSAH included for analysis Recruitment: Data retrieved from a prospectively maintained database
Number of patients	n = 59
Patient characteristics	Age, mean (range): 50 (18-83) Gender (male to female ratio): 27/32 Setting: Medical centre

Reference	Fluss 2020[61]
	Country: USA Inclusion criteria: all nontraumatic intracranial haemorrhage cases managed by the senior author. Cases where both CTA and DSA were obtained were included in the analysis. Exclusion criteria: absolute contraindication for one of the modalities, patients with previous surgical clipping or endovascular coiling of intracranial aneurysms, poor general condition and patients who refused to undergo the procedures.
Target condition(s)	aSAH
Index test(s) and reference standard	Index test – CTA All CTA studies were obtained on a 64-slice multidetector CT, using 2-mm thin cuts. Maximal intensity projection (MIP) images were produced in the axial plane, followed by coronal plane and sagittal plane reconstructions. MRA - MRA was performed on a 1.5 T Toshiba using head coil(Avanto Tokyo, Japan). The scan parameters were: parallel imaging TR 5.4/TE 1.68 ms, flip angle 35, FOV 256 mm, matrix 512, slice thickness 0.4 mm coronal orientation (parallel to basilar artery). Contrast material used was gadopentetatedimeglumine (Magnevist, Bayer Schering, Germany) given intravenously of 0.1 mmol/kg and it is followed by flush of25 ml isotonic saline at 3 ml/s. Reference standard – DSA DSA studies were performed and interpreted by the senior author using a biplane angiography table. CTA and DSA study results were compared. Time between measurement of index test and reference standard: Unclear

2×2 table Per patient

	Reference standard +	Reference standard −	Total
Index test +	29	0	29
Index test −	1	7	8
Total	30	7	37

Reference	**Fluss 2020[61]**
Statistical measures	Index text Per patient Sensitivity 96.7% Specificity 100% PPV 100% NPV 87.5%
Source of funding	Not specified
Limitations	Risk of bias: Serious Indirectness: No indirectness
Comments	

Reference	**Gamal 2015[64]**
Study type	Cross-sectional study
Study methodology	Data source: from a medical centre in Egypt Recruitment: March 2013 to February 2014 all adult patients diagnosed with nontraumatic SAH
Number of patients	n = 25
Patient characteristics	Age, mean (SD): 58.7 ± 15.3 Gender (male to female ratio): 7 /18 Setting: Medical centre Country: Egypt Inclusion criteria: all consecutive adult patients who had clinical symptoms of non traumatic SAH or cerebral aneurysm diagnosed by CT Exclusion criteria: absolute contraindication for one of the modalities, patients with previous surgical clipping or endovascular coiling of intracranial aneurysms, poor general condition and patients who refused to undergo the procedures.

Reference	Gamal 2015[64]
Target condition(s)	aSAH
Index test(s) and reference standard	Index test – CTA/ CEMRA CTA was performed on a 4 slice multi-detector row spiral CT scanner. Scan parameters were 120kV; 200mAs, collimation with 0.9mm, pitch 0.67, field of view 230mm, matrix 512x512, 0.5mm slice; reconstruction was used. A non-ionic iodinated contrast medium; Iopromide 350 mg/ml (Ultravist) was administrated via 20–22 gauge needle intravenously in the antecubital fossaat 4 ml/s with volume 100 ml. The contrast medium was administrated with an automated injector and it is followed by flush of 40 ml isotonic saline at 4 ml/s. MRA - MRA was performed on a 1.5 T Toshiba using head coil(Avanto Tokyo, Japan). The scan parameters were: parallel imaging TR 5.4/TE 1.68 ms, flip angle 35, FOV 256 mm, matrix 512, slice thickness 0.4 mm coronal orientation (parallel to basilar artery). Contrast material used was gadopentetatedimeglumine (Magnevist, Bayer Schering, Germany) given intravenously of 0.1 mmol/kg and it is followed by flush of25 ml isotonic saline at 3 ml/s. Reference standard – DSA All DSA were performed transfemorally with 5 F catheter by using a DSA unit (Siemens, Netherlands) with image intensifier matrix of 1024·1024 pixels. DSA was performed with bilateral selective internal carotid artery injections, unilateral vertebral artery injections and bilateral as necessary. Flush autography was performed by an automatic power injector. All 4 brain feeding arteries were catheterized and imaged.10 ml of non-ionic contrast material (320 mg of Iopromide) was used at a rate of 4–8 ml/s for each injection. Standard anteroposterior, lateral projections and oblique for intracranial aneurysm and anteroposterior and lateral for verte-bral arteries were routinely acquired. Additional angiographic projections were obtained to better visualize an aneurysm. Time between measurement of index test and reference standard: All patients who met the study inclusion criteria underwent CTA and an additional CEMRA study before endovascular therapy and within 48 h after CTA, however the CEMRA study did not delay the treatment.

2×2 table Per CTA		Reference standard +	Reference standard −	Total
	Index test +	19	2	21
	Index test −	1	0	1
	Total	20	2	22

2×2 table Per CEMRA		Reference standard +	Reference standard −	Total
	Index test +	18	2	20
	Index test −	2	0	2
	Total	20	2	22

Reference	**Gamal 2015[64]**
Statistical measures	Index text Per CTA: Sensitivity 95% Specificity - PPV 90.5% NPV - Per CEMRA: Sensitivity 90% Specificity - PPV 90% NPV -
Source of funding	Not specified
Limitations	Risk of bias: Serious Indirectness: No indirectness
Comments	

1

Reference	**Gerardin 2009[67]**
Study type	Cross-sectional study
Study methodology	Data source: Department of Neuroradiology, Hospital Charles Nicolle, University of Rouen, France Recruitment: Patients with SAH confirmed by CT scan or lumbar puncture over a 10 month period
Number of patients	n = 20
Patient characteristics	Age, mean (SD): Gender (male to female ratio): Setting: Hospital Charles Nicolle, University of Rouen Country: France Inclusion criteria: Patients with SAH confirmed by CT scan or lumbar puncture over a 10 month period; MSCTA carried out at admission; diagnostic confirmation established by pre procedural angiography with at least four axis acquisition

Reference	Gerardin 2009[67]
	Exclusion criteria: Death of the patient before performing MSCTA or DSA; patients without pre-procedural four axis DSA.
Target condition(s)	aSAH
Index test(s) and reference standard	Index test All CT examinations were performed using a 16 detector rot CT unit with: axial plane scanning extending from the body of the C2 vertebra to the vertex, 0.5s gantry rotation time, 16x0.625mm collimation, 0.625 pitch, 0.625mm slice thickness, 0.4mm reconstruction interval and 140kV / 300mA/ The contrast agent was injected into an antecubital vein using a power injector. 80mL of contrast agent was pulsed by 80ml of Saline. Reference standard – DSA The DSA was performed via a transfemoral approach after induction o analgesia or under general anesthesia with a DSA unit Multi-star TOP. Four vessel angiograms were obtained in anteroposterior and lateral projections for vertebral artery, completed by bilateral oblique projections for carotid artery only. DSA was performed with 1024x1024 matrix and a field of view of 20cm and 28cm for anteroposterior and lateral view of carotid artery and 14cm for the vertebrobasilar examination. Two neuroradiologists who interpreted first the MSCTA blinded to DSA. DSA were independently reinterpreted by the same physician from the hard copy films. Additional clarity was sought through a neuroradiologist. Time between measurement of index test and reference standard:

2×2 table Per aneurysm

	Reference standard +	Reference standard −	Total
Index test +	37	0	37
Index test −	1	8	9
Total	38	8	45

Statistical measures	Index text Per aneurysm: Sensitivity 97.4% Specificity 100% PPV 100% NPV 88.9%
Source of funding	Not specified

Reference	Gerardin 2009[67]
Limitations	Risk of bias: serious Indirectness: No indirectness
Comments	

Reference	Haghighatkhah 2008[77]
Study type	Cross sectional
Study methodology	Data source: Patient records and diagnostic imaging from participating hospital reviewed. Recruitment: Consecutive patients selected for study inclusion.
Number of patients	n = 85
Patient characteristics	Age, mean (SD): 49.1±13.6 Gender (male to female ratio): 44/69 Setting: Shohada-e-Tajrish Hospital Country: Iran Inclusion criteria: Patients were admitted under clinical symptoms and signs suggestive of harbouring an intracranial aneurysm (acute headache, nausea, vomiting, or stiff neck) and all of them had non-traumatic SAH according to brain CT scan or lumbar puncture. Exclusion criteria: Not reported
Target condition(s)	aSAH
Index test(s) and reference standard	Index test CTA The MSCT angiography examinations were performed with a four detector row CT unit based on a standardized protocol. All CT images were diagnostic and there were no technical failures or complications during scanning. MSCT angiography images were interpreted by one radiologist. Reference standard

Reference	**Haghighatkhah 2008[77]**			
	DSA Standard four-vessel angiography of the brain with DSA biplane system was done via a transfemoral approach. DSA was studied by another radiologist who was blinded to the interpretation of the MSCT angiograms. Time between measurement of index test and reference standard: The maximum interval between MSCT and DSA or surgery was three weeks.			
2×2 table Per patient		Reference standard +	Reference standard −	Total
	Index test +	35	5	40
	Index test −	0	45	45
	Total	35	50	85
Statistical measures	<u>Index text</u> Sensitivity 100% (87.7-99.9) Specificity 90% (77.4-96.3) PPV 87.5 (72-95.3) NPV 100 (90.2-100)			
Source of funding	<u>Not reported</u>			
Limitations	Risk of bias: None Indirectness: No indirectness			
Comments				

Reference	**Hashemi 2011[82]**
Study type	Cross-sectional study
Study methodology	Data source: Department of Neurosurgery, Brain and Spinal Cord Injuries Repair Research Centre, Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, Iran Recruitment: consecutive patients with an initial diagnosis of subarachnoid haemorrhage from 2005 to 2007
Number of patients	n = 99
Patient characteristics	Age, mean (SD): 49.06 ± 13.6 (range, 20-85 years) Gender (male to female ratio): 51/48

Reference	Hashemi 2011[82]
	Setting: Department of Neurosurgery, Imam Khomeini Hospital, Country: Iran Inclusion criteria: consecutive patients with the initial diagnosis of subarachnoid haemorrhage were enrolled into the study and screened for aneurysms with CTA followed by conventional DSA who were considered for diagnostic accuracy of CTA in comparison with the first DSA for the detection of aneurysm Exclusion criteria: Patients without an informed consent and those accomplishing only one of the studies and patients in an emergency situation and/or medical contraindication for high dose iodine administration were excluded. In addition, patients having documented coagulopathy were excluded from the study.
Target condition(s)	aSAH
Index test(s) and reference standard	<u>Index test - CTA</u> CTA was obtained with GE 2004 light speed QXI 4-row D system. Initially an axial brain CT was obtained as baseline information. Then 100 mL of non-ionic contrast (Visipaque or Ultravist) was administered through a gauge 20 intravenous line with the speed of 5 mL/s. The scanning started with the bolus triggering technique at the level of the aortic arch. Axial slices were taken with 1.25 mm thickness and overlapping of 0.625 mm. <u>Reference standard - </u>DSA DSA study was performed with Innova 4100 flat panel system. An anaesthesiologist visited all the cases and sedation was performed if necessary. Trans-femoral catheterization of both common carotid and bilateral vertebral arteries was performed. Ultra-vist 300 was employed as the contrast agent. Images were obtained from arterial to the venous phase and a maximum of 9 mL of contrast was used for each view The obtained images were reported by two independent neuroradiologists. In the presence of documented studies the patients were scheduled for clipping. During cerebral arterial dissection, the number, location and projection of the aneurysms were examined and documented by the operating neurosurgeon. Finally, the diagnostic accuracy of CTA for determination of the number, location and projection of the aneurysms were compared with DSA and intra-operative findings as the gold standard. Time between measurement of index test and reference standard: Not specified

2×2 table Per patient		Reference standard +	Reference standard −	Total
	Index test +	81	0	81

Reference	**Hashemi 2011[82]**				
	Index test −	1	17	18	
	Total	82	17	99	
Statistical measures	<u>Index text</u> Per aneurysm: Sensitivity 98.1% (reported as 98.8% CI 0.934 - 0.998 within summary table within paper) Specificity 91.3% (reported as 100% CI 0.816 - 1 within summary table within paper) PPV 92.8% (reported as 100% CI 0.955 - 1 within summary table within paper) NPV 97.7% (reported as 94.4% CI 0.742 - 0.99 within summary table within paper)				
Source of funding	The study has been a neurosurgery dissertation conducted on the authors own expenses				
Limitations	Risk of bias: Serious Indirectness: No indirectness				
Comments					

1

Reference	**Ida 1997[90]**
Study type	Cross-sectional
Study methodology	Data source: patients with acute subarachnoid haemorrhage from October 1994 through April 1996 Recruitment: consecutive patients included
Number of patients	n = 28
Patient characteristics	Age, mean (SD): 53 (14-75) Gender (male to female ratio): 7/21 Setting: Metropolitan Ebara Hospital. Country: Japan Inclusion criteria: emergency intracranial MR angiography in 28 patients with acute subarachnoid haemorrhage Exclusion criteria: Not reported

Reference	**Ida 1997[90]**
Target condition(s)	aSAH
Index test(s) and reference standard	Index test MRA MR angiography was performed within 24 hours (day 1) after the onset of subarachnoid haemorrhage in 27 patients and within 48 hours (day 2) in one patient. A 1.5-T system with 25 mT/m gradient strength was used, with a circularly polarized head coil. Three-dimensional TOF sequences were acquired with fast imaging with steady-state precession (FISP). Reference standard DSA Intraarterial digital subtraction angiography (IA-DSA) was performed by femoral artery catheterization and a digital subtraction angiographic system. Neurosurgeons were provided with the results of the CT and MR angiographic examinations before IA-DSA was carried out. Routine IA-DSA included anteroposterior Towne and lateral views of both internal carotid arteries and the vertebrobasilar arteries, plus bilateral oblique views of the vessel(s) of interest. Various oblique and/or submentovertex views optimal for depiction of the aneurysm were additionally obtained, depending on the results of MR angiography. Time between measurement of index test and reference standard: In 26 patients, IA-DSA was carried out between days 1 and 3; in one patient, it was done on day 6. The remaining patient (case 10) did not undergo IA-DSA in the acute stage because of renal dysfunction; instead, it was performed on day 21 after hydration and diuresis.

2×2 table Per patient

	Reference standard +	Reference standard −	Total
Index test +	25	0	25
Index test −	1	2	3
Total	26	2	28

2×2 table Per aneurysm

	Reference standard +	Reference standard −	Total
Index test +	35	0	35
Index test −	4	2	6
Total	39	2	41

Statistical measures

Index text
Per patient:
Sensitivity 96.2%
Specificity 100%
PPV 100%
NPV 66.7%

Per aneurysm:
Sensitivity 89.7%

Reference	**Ida 1997[90]**
	Specificity 100% PPV 100% NPV 33.3%
Source of funding	Not reported
Limitations	Risk of bias: None Indirectness: No indirectness
Comments	

Reference	**Jayaraman 2004[95]**
Study type	Cross-sectional study
Study methodology	Data source: Department of diagnostic imaging and Neurosurgery, Rhode Island Hospital / Brown Medical School, Providence, USA Recruitment: Between January and September 2002, patients undergoing DSA for non-traumatic SAH indicated either by imaging findings at nonenhanced CT of by xanthochromia at lumbar puncture.
Number of patients	n = 35
Patient characteristics	Age, mean (range): 54 years (26-79) Gender (male to female ratio): 8 /27 Setting: Rhode Island Hospital / Brown Medical School Country: USA Inclusion criteria: patients undergoing DSA for non-traumatic SAH indicated either by imaging findings at non enhanced CT of by xanthochromia at lumbar puncture. Exclusion criteria: Patients who had undergone prior surgical clipping or coiling for treatment of an aneurysm were excluded
Target condition(s)	aSAH

Reference	Jayaraman 2004[95]
Index test(s) and reference standard	Index test - CTA CT with a multi-detector row scanner. Parameters of the CT angiographic acquisition were 1.25mm section thickness, 0.5mm section interval, pitch of 3, 140kVp, 200mAs, and 14.0cm field of view. The scanning volume extended from the superior aspect of the ring of the first cervical vertebra to a point of 1cm above the level of the lateral ventricles. A total of 120ml of Iohexol a low osmolar iodinated contrast material was administered intravenously with a power injector at a rate of 4ml/s via an 18 or 20 gauge catheter positioned in a peripheral vein. Reference standard - DSA Standard DSA was performed by using a biplane DSA unit with a matrix of 1024x1024 pixels. DSA was performed with bilateral selective common carotid artery injections and either unilateral or bilateral vertebral injections. Four radiologists reviewed the images which were blinded to the results of the others readings and to the findings from the other modalities. Time between measurement of index test and reference standard: not specified

2×2 table Per patient

	Reference standard +	Reference standard −	Total
Index test +	19	1	20
Index test −	2	13	15
Total	21	14	35

Statistical measures	Index text Per patient: Sensitivity 90% Specificity 93% PPV 95% NPV 86%
Source of funding	Not specified
Limitations	Risk of bias: Serious Indirectness: No indirectness
Comments	

Reference	Kangasniemi 2004[99]
Study type	Cross-sectional study

Reference	Kangasniemi 2004[99]
Study methodology	Data source: Department of Radiology, Toolo Hospital, Hus, Finland Recruitment: Patients who underwent both CTA and DSA for suspected SAH between august 2000 and December 2000
Number of patients	n = 179
Patient characteristics	Age, mean (SD): Not specified Gender (male to female ratio): Not specified Setting: Toolo Hospital Country: Finland Inclusion criteria: Undergoing investigation for suspected SAH Exclusion criteria: not specified
Target condition(s)	aSAH
Index test(s) and reference standard	Index test - CTA A multi-slice helical CT scanner with four detector rows was used for CTA. The raw images were acquired with the following parameters: slice thickness 1.25mm, 120kV, 230mA, field of view 23cm; table speed 3.75mm/s; rotational speed 0.8seconds. a total of 120 ml of contrast medium was injected into cubital vein with an automated injector at a speed of 4ml/s. Reference standard – DSA A standard single plane DSA unit with a matrix resolution of 1024x1024 was used. For each imaged vessel at least three projections including anteroposterior, lateral and oblique views were obtained. Time between measurement of index test and reference standard: not specified

2×2 table Per aneurysm

	Reference standard +	Reference standard −	Total
Index test +	170	8	178
Index test −	8	260	268
Total	178	268	446

Reference	**Kangasniemi 2004**[99]
Statistical measures	Index text Per aneurysm: Sensitivity 96% Specificity 97% PPV 96% NPV 97%
Source of funding	Not specified
Limitations	Risk of bias: Serious Indirectness: No indirectness
Comments	

1

Reference	**Kelliny 2011**[105]
Study type	Cross-sectional study
Study methodology	Data source: Retrospective data from adult patients at a tertiary referral centre Recruitment: Consecutive adult patients at a tertiary referral centre, from January 1st 1998 to December 31st 2007.
Number of patients	n = 241
Patient characteristics	Age, mean (SD): 50.3 (14.2) Gender (male to female ratio): 105/136 Setting: a tertiary referral centre Country: Switzerland Inclusion criteria: Patients who underwent both technically adequate catheter angiography and CTA for a suspicion of a ruptured aneurysm Exclusion criteria: not specified

Reference	**Kelliny 2011[105]**
Target condition(s)	aSAH
Index test(s) and reference standard	Index test - CTA A timed test injection was used to determine the optimal timing of the CTA data acquisition. It consisted of a single 5 to 10 mm-thick slice (80 kVp/100 mA) positioned at the top of the frontal sinuses, acquired in a cine mode at a rate of one image every 2 s during intravenous administration of 20 mL of iodinated contrast material (2.36 mol/L [300 mg/mL] iodine) followed by 40 mL of water. The injection rate was 4-5 mL/s into an antecubital vein by means of a power injector, with a 10 s delay between the injection and the onset of data acquisition. The CTA data acquisition was performed in a spiral mode according to the typical parameters. Reference standard – DSA Every patient underwent four-vessel DSA via a transfemoral intra-arterial approach with multiple projections. Time between measurement of index test and reference standard: not specified
2×2 table Per patient	

	Reference standard +	Reference standard −	Total
Index test +	160	3	163
Index test −	6	72	78
Total	166	75	241

Statistical measures	Index text Per aneurysm: Sensitivity 96.4% Specificity 96% PPV 98.2% NPV 92.3%
Source of funding	Not specified
Limitations	Risk of bias: Serious Indirectness: No indirectness
Comments	

Reference	**Kouskouras 2004[113]**
Study type	Cross-sectional study

Reference	Kouskouras 2004[113]
Study methodology	Data source: Aristotle's University of Thessaloniki, Greece Recruitment: Patients between October 1999 and March 2002, 35 patients were enrolled in the study for preoperative investigation of a possible aneurysm
Number of patients	n = 32
Patient characteristics	Age, mean (range): 53.5 (28 – 78) Gender (male to female ratio): 20/15 Setting: Department of Neurosurgery, AHEPA University Hospital, Aristotle's University of Thessaloniki Country: Greece Inclusion criteria: Patients who presented with SAH or neurological symptoms (cranial nerve palsy) who underwent helical CTA and DSA Exclusion criteria: Not specified
Target condition(s)	Intracranial aneurysms
Index test(s) and reference standard	<u>Index test – CTA/MRA</u> CT angiography was performed on a spiral CT scanner (Tomoscan SR 7000, Philips Medical Systems). The gantry was un-angled, starting at the level of sphenoid sinus. The area of interest was determined by taking unenhanced 5 mm-thick slices up to the level of genu/body of corpus callosum. These images were taken in order to determine the presence of any haemorrhagic material in the area of interest. Using an 18-gauge needle into a peripheral arm vein, injection of 100–140 ml of non-ionic contrast material (Ultravist 370) was performed using a power injector at a rate of 3–4 ml/s. The area of interest was scanned with 40–50 one-second rotations of 1.5 mm thickness and 1 mm table speed. Other parameters were 512·512 matrix, 120–140 kV, 100 mA, 17 cm FOV and reconstruction index of 1 mm. The source images were post-processed using maximum intensity projection (MIP), multi-planar reconstruction (MPR) and surface shaded display (SSD) methods. <u>Reference standard - DSA</u> Underwent the standard, selective four-vessel DSA with anteroposterior, lateral and oblique views. Selective catheterisations were performed in both internal carotids and vertebral arteries using 12 ml of a non-ionic contrast media at a flow rate of 3 ml/s and a film rate of 6 frames/s for a total of 40 to 50 frames. Calibration and digital measurement of the aneurismal sac and, when possible, of the aneurismal neck was performed. The angiographer (CG) performed the DSA examinations blindly from the CTA/MRA results.

Reference	Kouskouras 2004[113]
	All three imaging methods were correlated with the intraoperative findings. Initially the axial source images (both CTA and MRA) were viewed in cine mode, and the presence of aneurysm was determined by using a three-point scale of confidence. To determine the value of CTA/MRA as a preoperative tool, a neurosurgeon analysed the CTA and MRA data preoperatively and determined whether he had enough information and could operate based only on these data without DSA. Time between measurement of index test and reference standard: DSA within 24 hours of CTA
2×2 table	(see below)

	Reference standard +	Reference standard −	Total
Index test +	28	3	31
Index test −	1	3	4
Total	29	6	35

Statistical measures	<u>Index text</u> Sensitivity 97% Specificity 50% PPV 92% (reported PPV differs from 2x2 table above) NPV 75%
Source of funding	Not specified
Limitations	Risk of bias: Serious Indirectness: No indirectness
Comments	

Reference	Lenhart 1997[120]
Study type	Cross-sectional study
Study methodology	Data source: Department of Radiology, University of Regensburg, Regensburg, Germany Recruitment: Between June 1994 and May 1996, patients suffering with acute non traumatic SAH
Number of patients	n = 53
Patient characteristics	Age, mean (range): 53 (21 – 72 years)

Reference	Lenhart 1997[120]
	Gender (male to female ratio): 32/21 Setting: Department of Radiology, University of Regensburg Country: Germany Inclusion criteria: patients suffering with acute non traumatic SAH who underwent CTA after non enhanced CT and DSA examination Exclusion criteria: not specified
Target condition(s)	aSAH
Index test(s) and reference standard	Index test - CTA Was performed with a Somatom Plus-s CT scanner. The spiral acquisition consisted of contiguous 360degrees tube rotations (210mA). Collimation was set at 1mm and the table speed at 2mm/s. Gantry tilt was parallel to the frontal skull base and CT imaging started just caudal to the sella turcica. In addition to the circle of willis, the insular vessels with their peripheral branches could be identified within a range of 60mm. Reference standard – DSA Not specified CTA and DSA were interpreted independently by 2 experienced radiologists who were unaware of the interpretation of the corresponding imaging study. Time between measurement of index test and reference standard: within 14 hours of CTA DSA was completed
2×2 table Per aneurysm	see table below
Statistical measures	Index text Per aneurysm: Sensitivity 98% Specificity 100% PPV 100% NPV 93%

	Reference standard +	Reference standard −	Total
Index test +	50	0	50
Index test −	1	14	15
Total	51	14	65

Reference	Lenhart 1997[120]
	PLR NLR AUC
Source of funding	Not specified
Limitations	Risk of bias: Serious Indirectness: No indirectness
Comments	

Reference	Li 2014[123]
Study type	Cross-sectional study
Study methodology	Data source: Department of Neurology, The First Affiliated Hospital of Chongqing Medical University, Chongqing, China Recruitment: Patients presenting with suspected non traumatic SAH scheduled to undergo CTA as their first diagnostic study
Number of patients	n = 88
Patient characteristics	Age, mean (range): 49 years (21 – 79) Gender (male to female ratio): 46/42 Setting: The First Affiliated Hospital of Chongqing Medical University Country: China Inclusion criteria: Patients were enrolled into the study if they had signs and symptoms suggestive of SAH or presented with SAH on non enhanced CT scan and completed both CTA and DSA Exclusion criteria: History of head trauma before onset of symptoms.

<table>
<tr><td>Reference</td><td colspan="5">Li 2014[123]</td></tr>
<tr><td>Target condition(s)</td><td colspan="5">aSAH</td></tr>
<tr><td>Index test(s) and reference standard</td><td colspan="5">Index test - CTA
All patients underwent CTA which was done using a 64 – row multi-detector CT scanner. For subtraction CTA an additional non enhanced scan was performed to identify bone structures that were subtracted from the enhanced scan. A total of 80ml of non-ionic contrast medicum were injected through an 18 gauge needle via antecubital vein with an automated injector set at 4ml/s. Enhanced scan was obtained with the following parameter: 120kV, 300mA, pitch of 0.531, section thickness of 5mm, 5mm increment, 180mm field of view, 512x512 matrix with a soft reconstruction kernel.

Reference standard -DSA
Three or four vessel DSA was performed in all patients with femoral catheterization by the Seldinger technique with biplane DSA unit. Standard anteroposterior, lateral, and oblique DSA views were obtained.

All CTA images were prepared by a trained technician. DSA results were judged by the same neuroradiologist who performed the examination. Two reviewers who were blinded to the results of the DSA and the other reader’s assessments retrospectively analysed the CTA results.

Time between measurement of index test and reference standard: Not specified</td></tr>
<tr><td rowspan="4">2×2 table
Per patient</td><td></td><td>Reference standard +</td><td>Reference standard −</td><td>Total</td><td rowspan="4">Insufficient detail reported to calculate 2x2 tables</td></tr>
<tr><td>Index test +</td><td>72</td><td></td><td></td></tr>
<tr><td>Index test −</td><td>0</td><td></td><td></td></tr>
<tr><td>Total</td><td>72</td><td></td><td></td></tr>
<tr><td rowspan="4">2×2 table
Per aneurysm</td><td></td><td>Reference standard +</td><td>Reference standard −</td><td>Total</td><td rowspan="4"></td></tr>
<tr><td>Index test +</td><td>79</td><td></td><td></td></tr>
<tr><td>Index test −</td><td>0</td><td></td><td></td></tr>
<tr><td>Total</td><td>79</td><td></td><td></td></tr>
<tr><td>Statistical measures</td><td colspan="5">Index text
Per patient:
Sensitivity 100%
Specificity 100%
PPV 100%
NPV 100%
PLR
NLR
AUC</td></tr>
</table>

Reference	**Li 2014[123]**
	Per aneurysm: Sensitivity 100% Specificity 100% PPV 100% NPV 100% PLR NLR AUC
Source of funding	Not reported
Limitations	Risk of bias: Serious Indirectness: No indirectness
Comments	

1

Reference	**Li 2017[124]**
Study type	Cross-sectional study
Study methodology	Data source: Department of Radiology, Shanghai Jiao Tong, University-Sixth Affiliated People's hospital, Shanghai, China Recruitment: February 2009 to August 2015, with patients who had non-traumatic subarachnoid haemorrhage that was confirmed with non-enhanced CT scan
Number of patients	n = 277
Patient characteristics	Age, mean (SD): 53.87 (11.87) Gender (male to female ratio): 117/160 Setting: University-Sixth Affiliated People's hospital Country: China Inclusion criteria: patients who had non-traumatic subarachnoid haemorrhage that was confirmed with non-enhanced CT scan and underwent MRA and DSA

Reference	Li 2017[124]			
	Exclusion criteria: Pacemaker or steel implants, allergy to contrast material, renal dysfunction that precluded the use of contrast material and symptom deterioration.			
Target condition(s)	aSAH			
Index test(s) and reference standard	<u>Index test - MRA</u> A 3.0T system with a sense-head 8 receiver head coil was used. The 3D TOF MR angiograms were obtained by using 3D TI-weighted fast field echo sequences (repetition time msec/echo time msec, 35/7; flip angle, 20; field of view 250x190x108; four slabs (180 sections); section thickness 0.8mm and matrix 732 x 1024. MRA began 50.87 minutes ± 21.48 (range 20 – 124 minutes) after the completion of the non-enhanced CT examination <u>Reference standard –</u> DSA Four vessels – the ICAs and the vertebral arteries on both side were catheterized for DSA. Posteroanterior and lateral projections were acquired with a biplanar unit with a 1024x1024 matrix and a 17-20cm field of view in all patients. Three observers with 8 – 20 years of experience in interventional radiology who were blinded to clinical findings and DSA results independently analysed the 3D TOF MR angiography with volume rendering image data sets. Time between measurement of index test and reference standard: DSA was performed 5.53 hours ± 4.98 (range 1 – 36 hours) after MR angiography			
2×2 table Per patient		Reference standard +	Reference standard −	Total
	Index test +	219	5	224
	Index test −	4	49	53
	Total	223	54	277
2×2 table Per aneurysm		Reference standard +	Reference standard −	Total
	Index test +	260	6	266
	Index test −	5	49	54
	Total	265	55	320
Statistical measures	<u>Index text</u> Per patient: Sensitivity 98.2% Specificity 91% PPV 97.8% NPV 92% Per aneurysm:			

Reference	Li 2017[124]
	Sensitivity 98.1% Specificity 89% PPV 97.7% NPV 91%
Source of funding	Not specified
Limitations	Risk of bias: Serious Indirectness: No indirectness
Comments	

Reference	Lv 2011[132]
Study type	Cross-sectional study
Study methodology	Data source: The Department of Radiology, The First Affiliated Hospital, Chongqing medical university Chongqing, China Recruitment: Retrospective review of patients who underwent dual energy subtraction CTA for suspected intracranial aneurysms
Number of patients	n = 97
Patient characteristics	Age, mean (range): 49 years (19 – 78) Gender (male to female ratio): 56 / 41 Setting: The First Affiliated Hospital, Chongqing medical university Chongqing Country: China Inclusion criteria: Patients were eligible if they had undergone both dual energy subtraction CTA and DSA for suspected intracranial aneurysms. Exclusion criteria: refusal of DSA

Reference	**Lv 2011[132]**			
Target condition(s)	aSAH			
Index test(s) and reference standard	Index test - CTA All patients underwent subtraction CTA with a 64 row multidetector CT scanner. A total of 80ml non-ionic contrast medium was injected through a 18 gauge needle via antecubital vein with an automated injected at a flow rate of 4ml/s/. Enhanced scan was obtained with the following parameters: 120kV, 300mA, pitch of 0.531, section thickness of 0.5, 0.5mm increment, 180mm field of view, 512x512 matrix with soft construction kernel. Reference standard - DSA DSA was performed in all patients with a femoral catheterization by the Seldinger technique with a biplane DSA unit. DSA was performed with selective bilateral internal carotid artery and vertebral artery injections. All subtraction CTA and DSA images were randomized before interpretation. Two skilled reviewers of 10 years of experience and 3 years of experience were blinded to the results of the DSA and the other readers judgements. Time between measurement of index test and reference standard: not specified			
2×2 table Per patient		Reference standard +	Reference standard −	Total
	Index test +	95	0	95
	Index test −	1	0	1
	Total	96	0	96
2×2 table Per aneurysm		Reference standard +	Reference standard −	Total
	Index test +			
	Index test −			
	Total			
Statistical measures	Index text Per patient: Sensitivity 98.9% Specificity 100% PPV 100% NPV 94.1% Per aneurysm: Sensitivity 97.9% Specificity 100% PPV 100% NPV 94.1%			

Reference	**Lv 2011[132]**
Source of funding	Not specified
Limitations	Risk of bias: Serious Indirectness: No indirectness
Comments	

Reference	**Lu 2012[129]**
Study type	Cross-sectional study
Study methodology	Data source: Department of Medical Imaging, Jinling Hospital, Clinical School of Medical College, Nanjing University, Nanjing, Jiangsu, China Recruitment: Between January 2007 and October 2010,clinically suspected of having or with known intracranial aneurysms and other cerebral vascular diseases
Number of patients	n = 525
Patient characteristics	Age, mean (range): 50 (6 – 82) Gender (male to female ratio): 228/297 Setting: Jinling Hospital, Nanjing University Country: China Inclusion criteria: Inclusion criteria were patients who first underwent dual-source CT angiography and then 3D DSA, with a time interval of 1 day. Exclusion criteria: The exclusion criteria for CT were poor image quality and previous coiling or clipping surgery.
Target condition(s)	aSAH
Index test(s) and reference standard	<u>Index test - CT</u> Digital subtraction CT angiography was performed by using a dual-source CT system (Somatom Definition; Siemens Healthcare, Forcheim, Germany). Unenhanced volume CT was routinely performed at 130 mA and 120 kVp. The collimation was 32 3 0.6 mm, with a 0.33-second rotation time and pitch of 1.0. Images were reconstructed with a 0.75-mm section thickness and a 0.5-mm increment

Reference	Lu 2012[129]			
	with an H45f kernel. A 70 mL dose of iodinated contrast medium (iopromide, 300 mg of iodine per millilitre, Ultravist 300 ; Bayer Schering, Berlin, Germany) was injected at a rate of 4.0 mL/sec into the antecubital vein. <u>Reference standard – DSA</u> Three-dimensional DSA was performed with femoral catheterization by using the Seldinger technique with a bi-plane DSA unit with rotational capabilities (Axiom Artis dTA; Siemens Healthcare). Typically, 6–9 mL of non-ionic contrast medium (iopromide, 300 mg of iodine per millilitre, Ultravist 300; Bayer Schering) was used per acquisition, usually consisting of one anteroposterior, one lateral, and one or two oblique views. The acquisitions consisted of a 38-cm 2 field of view for the anteroposterior images, 30-cm 2 field of view for the lateral and oblique images, and a 1024 3 1024 matrix. The spatial resolution was 0.32 3 0.32 mm. For the quantification of inter- and intrareader variability in detecting aneurysms using digital subtraction CT angiography, 100 patients in this group were randomly selected and analysed separately by the two neuroradiologists (10 and 4 years of reading experience). All other digital subtraction CT angiographic images were analysed in consensus by the two neuroradiologists. A staff neuroradiologist reviewer blinded to the results of digital subtraction CT angiography evaluated conventional DSA and digital subtraction CT angiographic images and made the diagnosis. If an aneurysm was present, the neuroradiologists measured the diameter and recorded the location of each aneurysm on the 3D DSA images in the appropriate projection. Time between measurement of index test and reference standard: median interval of 1 day			
2×2 table **Per patient**		Reference standard +	Reference standard −	Total
	Index test +	398	12	410
	Index test −	9	94	103
	Total	407	106	513
2×2 table **Per aneurysm**		Reference standard +	Reference standard −	Total
	Index test +	443	13	456
	Index test −	16	94	110
	Total	459	107	566
Statistical measures	<u>Index text</u> Per patient: Sensitivity 97.8% Specificity 88.6% PPV 97% NPV 91.2% Per aneurysm: Sensitivity 96.5% Specificity 87.9%			

Reference	Lu 2012[129]
	PPV 97.1% NPV 90.1%
Source of funding	Not stated
Limitations	Risk of bias: Serious risk of bias Indirectness: No indirectness
Comments	

1

Reference	Luo 2012[131]
Study type	Cross-sectional
Study methodology	Data source: Patients admitted to participating hospital between Sep 2009 and January 2010. Recruitment: Unclear
Number of patients	n = 56
Patient characteristics	Age, mean (SD): Gender (male to female ratio): Setting: The fourth affiliated hospital Country: China Inclusion criteria: Patients with spontaneous SAH and suspected intracranial aneurysms. Exclusion criteria: Not reported
Target condition(s)	aSAH

Reference	**Luo 2012[131]**			
Index test(s) and reference standard	Index test CTA All underwent 320-detector row volume CT-CTA examinations. Non-contrast CT of each patient's head with the same scan range was performed before the routine CTA scan as the mask image for subtraction. The subtraction CTA volume data was obtained by subtracting the mask image volume data from the conventional non-subtracted CTA volume data. Subtraction and conventional CTA volume data were transmitted to a VOXAR workstation and two physicians with experience in diagnostic imaging of the nervous system independently carried out image post-processing and judged the results. CT angiograms were interpreted by two senior neuroradiologists blinded to the DSA results. Reference standard DSA All patients underwent DSA through femoral catheterisation by the Seldinger technique with a biplane DSA unit. Time between measurement of index test and reference standard: Not reported			
2×2 table Per patient		Reference standard +	Reference standard −	Total
	Index test +	42	0	42
	Index test −	0	14	14
	Total	42	14	56
2×2 table Per aneurysm		Reference standard +	Reference standard −	Total
	Index test +	50.72		
	Index test −	0.28		
	Total	51		
Statistical measures	Index text Per patient: Sensitivity 100% Specificity 100% PPV 100% NPV 100% Per aneurysm: Sensitivity 99.45%* *mean of two readers			
Source of funding	Funded by graduate innovation and creativity funds of Harbin Medical University.			
Limitations	Risk of bias: Very serious			

Reference	**Luo 2012[131]**
	Indirectness: No indirectness
Comments	Non-subtracted and subtracted CTA results reported by study. Subtracted results extracted for analysis

Reference	**MacKinnon 2013[134]**
Study type	Prospective Cross-sectional
Study methodology	Data source: 200 consecutive patients who underwent CTA for SAH Recruitment: Consecutive patients recruited
Number of patients	n = 176
Patient characteristics	Age, mean (range): 52 (20-81) Gender (male to female ratio): 80/96 Setting: Atkinson Morley Regional Neuroscience Centre, St. George's Healthcare NHS Trust Country: UK Inclusion criteria: SAH was diagnosed on CT of the brain, cerebrospinal fluid (CSF) analysis, or overwhelming clinical suspicion in the context of equivocal CSF analysis. Exclusion criteria: 24 patients were excluded from the study (five traumatic SAH; one SAH secondary to an arteriovenous malformation (AVM) flow-related aneurysm; one with severe iliac artery stenoses that precluded passage of the guidewire for DSA; the remaining 17 had not undergone prior CTA.
Target condition(s)	aSAH
Index test(s) and reference standard	<u>Index test</u> CTA All CTA assessments were performed using a 16-channel MDCT system. <u>Reference standard</u> DSA DSA was performed using standard techniques via femoral catheterization and 5 or 6 F catheters on a biplanar digital subtraction angiography unit.

Reference	**MacKinnon 2013[134]**				
	Time between measurement of index test and reference standard: Not reported				
2×2 table Per patient		Reference standard +	Reference standard −	Total	
	Index test +	69	5	74	
	Index test −	2	100	102	
	Total	71	105	176	
Statistical measures	Index text Per patient (recently ruptured aneurysm): Sensitivity 95.2% Specificity 97.2% PPV 98.1% NPV 93.2%				
Source of funding	Not reported				
Limitations	Risk of bias: Very serious Indirectness: No indirectness				
Comments					

1

Reference	**McKinney 2008[139]**
Study type	Retrospective Cross-sectional study
Study methodology	Data source: Department of Radiology, Hennepin County and University of Minnesota Medical Centres, Minneapolis, Minn Recruitment: patients who had clinical histories requesting urgent evaluation for intracranial aneurysm via 64MSCTA were identified via CT logs
Number of patients	n = 66
Patient characteristics	Age, mean (range): 54.5 years; age range, 14–93 years) Gender (male to female ratio): 35/93 Setting: Hennepin County and University of Minnesota Medical Centres, Minneapolis,

Reference	McKinney 2008[139]
	Country: USA Inclusion criteria: patients who had clinical histories requesting urgent evaluation for intracranial aneurysm via64MSCTA Exclusion criteria: undergone clipped/coiled aneurysms (due to the presence of streak artefact), significant trauma (due to the unlikelihood of an aneurysm being present), or SAH with delayed presentation to CT angiography (CTA) (>24 hours, to exclude cases of vasospasm).
Target condition(s)	aSAH
Index test(s) and reference standard	<u>Index test - CTA</u> CTAs were obtained by a 64-channel multi-detector CT scanner (Brilliance CT; Philips Medical Systems, Best, the Netherlands), located in the emergency department. An 18- or 20-gauge needle was placed in the antecubital vein. The CTAs were initiated via “triggering” off of the aortic arch at an HU threshold of 140 HU after the intravenous contrast bolus was initiated; this delay varied, but typically ranged from 10–25 seconds. Contrast material (Iohexol 350 [Omnipaque]; GE Healthcare Ireland, Cork, Ireland) was injected at a rate of 4 mL/s via power injection for a total volume of 80 mL in each study. <u>Reference standard – DSA</u> DSA was performed with femoral catheterization by the Seldinger technique with a biplane DSA unit that has rotational capabilities (Integris Allura; Philips Medical Systems). Typically, 6–9mL of non-ionic contrast (Iodixanol 320 [Visipaque]; Amersham Health AS, Oslo, Norway) was used per run, usually consisting of one anteroposterior (AP), 1 lateral, and 1–2 oblique views. The runs consisted of a 38-cm FOV (AP), 30 cm FOV (lateral and oblique), and a 1024x1024 matrix. The spatial resolution was 0.32x0.32 mm. While the catheter was within each of the 3 major arteries (bilateral internal carotid and >1 vertebral artery), standard AP, lateral, and oblique DSA runs were obtained; a single rotational 3DRA acquisition was typically obtained before removing the catheter from each vessel; if the contralateral vertebral artery was not visualized on 3DRA, then a single contralateral vertebral artery DSA run was performed to clear the posterior inferior cerebellar artery. 3DRA was performed in each patient who underwent DSA unless there was clinical necessity based on patient instability and emergent need to treat. For the purposes of this study, 2 staff neuro-radiologists with experience in catheter and CTA (A.M.M. and C.S.P.), retrospectively, and independently reviewed the examinations in the remaining 63 patients via non-contrast CT and CTA. When reviewing the CTA examinations, the reviewers were blinded to each other and to the DSA/3DRA images and results, but when evaluating the DSA/3DRA results, the neuro-radiologists were not blinded to the initial non-contrast CT/CTA findings. The source, 3D-VR, MIP, and MPR images, were initially reviewed emergently by an experienced neuroradiologist and later by the 2 reviewers independently, who did not read the initial, emergent report. After the 2 reviewers reached consensus as to the presence of an aneurysm in each positive MSCTA and after the3DRA sequences (if available) were reviewed, a single staff neuroradiologist reviewer (A.M.M.) measured the aneurysm’s maximum size on each positive CTA in a similar projection as that of the 3DRA to obtain a correlation

Reference	McKinney 2008[139]				
	of the maximum size between modalities. After determining consensus in each case as to the presence of an aneurysm with DSA, a single staff neuroradiologist reviewer (A.M.M.) measured each aneurysm's maximum size on3DRA(if available) in a similar projection as that measured on the CTA to obtain a correlation of the maximum size between modalities. Time between measurement of index test and reference standard: not specified				
2×2 table Per aneurysm		Reference standard +	Reference standard −	Total	Aneurysm numbers reported in narrative do not correlate with sensitivity and specificity per aneurysm below
	Index test +	37	1	38	
	Index test −	1	2	3	
	Total	38	3	41	
Statistical measures	<u>Index text</u> Per patient: Sensitivity 96% Specificity 90% PPV 96% NPV 90% Per aneurysm: Sensitivity 97.4% Specificity 90% PPV 97.4% NPV 90%				
Source of funding	Not specified				
Limitations	Risk of bias: Very serious Indirectness: Serious				
Comments	Not all patients had DSA and some may have had surgery (as a reference test) due to their clinical condition				

Reference	Milosevic 1999[145]
Study type	Prospective Cross-sectional
Study methodology	Data source: Patients meeting the inclusion criteria admitted to the participating hospital. Recruitment: Not reported

Reference	**Milosevic 1999[145]**				
Number of patients	n = 52				
Patient characteristics	Age, mean (SD): 51.7 (32-81) Gender (male to female ratio): 22/30 Setting: Institute of radiology in Ljubljana. Country: Slovenia Inclusion criteria: Patients with acute SAH. Confirmation of the haemorrhage by a conventional CT scan was immediately followed by intracranial CTA. Exclusion criteria: Not reported				
Target condition(s)	aSAH				
Index test(s) and reference standard	Index test CTA CTA examinations were performed with a Siemens Somatom Plus 4 scanner. The intracranial arteries were analysed in axial CT images and in 3D reconstructions. Reference standard DSA (and surgery) 4 vessel DSA study of intracranial arteries was performed. DSA was performed after the CTA examination and so did not influence the interpretation of CTA images. In 7 patients who underwent surgery on the basis of CTA findings, results were compared with neurological findings. Time between measurement of index test and reference standard: Unclear				
2×2 table Per patient		Reference standard +	Reference standard −	Total	*results with DSA as reference. Surgery confirmed CTA results in 7 patients with aneurysm.
	Index test +	32 (39)	1		
	Index test −	3	9		
	Total	35	10		
2×2 table Per aneurysm		Reference standard +	Reference standard −	Total	
	Index test +	35 (42)	1		

Reference	Milosevic 1999[145]				
	Index test −	<u>3</u>	<u>9</u>		
	Total	<u>38</u>	<u>10</u>		
Statistical measures	<u>Index text</u> Per patient: Sensitivity 93% Specificity 90% PPV 97.5% NPV 75% Per aneurysm: Sensitivity 93% Specificity 90% PPV 98% NPV 75%				
Source of funding	<u>Not stated</u>				
Limitations	Risk of bias: Very serious Indirectness: No indirectness				
Comments					

Reference	Milosevic Medenica 2010[144]
Study type	Cross-sectional
Study methodology	Data source: Clinical symptomatology was SAH in 28 patients, SAH and ICH in 12 patients, IVH in two patients, headache in two patients, seizures in one patient, hemiparesis in one patient, while the aneurysm was incidentally found in one patient. Recruitment: Not reported
Number of patients	n = 47
Patient characteristics	Age, mean (range): 54.26 (13-76) Gender (male to female ratio): 7/40 Setting: Not reported

<table>
<tr><td>Reference</td><td>Milosevic Medenica 2010[144]</td></tr>
<tr><td></td><td>Country: Serbia

Inclusion criteria: Not reported
Exclusion criteria: Not reported</td></tr>
<tr><td>Target condition(s)</td><td>aSAH</td></tr>
<tr><td>Index test(s) and reference standard</td><td><u>Index test</u>
CTA
MSCTA was performed on 64-slice CT equipment, GE VCT Light Speed.

<u>Reference standard</u>
DSA
DSA was performed on an Axiom Artis unit, Siemens.

Time between measurement of index test and reference standard: Not reported</td></tr>
<tr><td>2×2 table</td><td>
<table>
<tr><td></td><td>Reference standard +</td><td>Reference standard −</td><td>Total</td></tr>
<tr><td>Index test +</td><td>35</td><td>1</td><td>36</td></tr>
<tr><td>Index test −</td><td>5</td><td></td><td></td></tr>
<tr><td>Total</td><td>40</td><td></td><td></td></tr>
</table>
</td></tr>
<tr><td>Statistical measures</td><td><u>Index text</u>
Sensitivity: 87.5%*
Specificity: n/a
PPV: 97.2%
NPV: n/a

*paper reports sensitivity of 97.22%, appears to have calculated PPV in error.</td></tr>
<tr><td>Source of funding</td><td><u>Not reported</u></td></tr>
<tr><td>Limitations</td><td>Risk of bias: Very serious
Indirectness: Potential indirectness.</td></tr>
<tr><td>Comments</td><td>Subset with DSA comparison included for analysis (n=21)</td></tr>
</table>

Reference	**Ni 2016**[157]
Study type	Cross-sectional
Study methodology	Data source: Patients who underwent true non-enhanced CT (TNCT), contrast-enhanced DE-CTA and digital subtraction angiography (DSA) for evaluating aSAH. Recruitment: Consecutive patients recruited
Number of patients	n = 105
Patient characteristics	Age, mean (SD): 50 ± 13 Gender (male to female ratio): 46/59 Setting: ICU Country: China Inclusion criteria: Patients were enrolled in this study if they were clinically suspected subarachnoid haemorrhage or aneurysms, i.e., patients presented with severe headache, vomiting, or a lowered level of consciousness, or suspicion of intracranial aneurysm after medical examinations. Exclusion criteria: history of prior reaction to iodinated contrast media, hemodynamic instability, renal insufficiency (i.e., creatinine level > 120 mol/L), and under the age of 18.
Target condition(s)	aSAH
Index test(s) and reference standard	<u>Index test</u> DE-CTA All CT examinations were performed in a second-generation dual-source CT scanner CT angiography was performed in the dual-energy mode using 140 kVp tube voltage and 112 effective milliampere second for measurement system A and 80 kVp tube voltage and 224 effective milliampere second for measurement system B, respectively; 0.33-second rotation time; 32 × 2 × 0.6 mm collimation; and a pitch of 0.7. <u>Reference standard</u> DSA

Reference	**Ni 2016[157]**				
	DSA was performed in all 105 patients involved using a biplane DSA unit with rotational capabilities by femoral catheterization Time between measurement of index test and reference standard: Unclear				
2×2 table Per patient		Reference standard +	Reference standard −	Total	
	Index test +	57	1		
	Index test −	1	46		
	Total				
2×2 table Per aneurysm		Reference standard +	Reference standard −	Total	
	Index test +	67	2	69	
	Index test −	2	46	48	
	Total	69	48		
Statistical measures	Index text Per patient: Sensitivity 98.3 (90.9-99.7) Specificity 97.9 (88.9-99.6) PPV 98.3 (90.9-99.7) NPV 97.9 (88.9-99.6) Per aneurysm: Sensitivity 97.1 (90-99.2) Specificity 95.8 (86-98.9) PPV 97.1 (90-99.2) NPV 95.8 (86-98.9)				
Source of funding	Not reported				
Limitations	Risk of bias: Very serious Indirectness: No indirectness				
Comments					

1

Reference	**Papke 2007[163]**
Study type	Prospective Cross-sectional
Study methodology	Data source: Patient admitted to participating hospital between January 2003 and August 2005 suspected of having SAH undergoing CTA. Recruitment: Prospective study of patients, selection unclear

Reference	Papke 2007[163]
Number of patients	n = 87
Patient characteristics	Age, mean (range): 54 (20-84) Gender (male to female ratio): 36-51 Setting: Specialised tertiary care centre Country: Germany Inclusion criteria: Patients with clinical symptoms of SAH and be able to undergo both CTA and DSA. Exclusion criteria: Patients who did not undergo both DSA and CTA.
Target condition(s)	aSAH
Index test(s) and reference standard	<u>Index test</u> CTA Multidetector 16-detector CTA with 130 mAs and 120 kV. A 50ml dose of iodine was injected. Actual diagnostic spiral CT angiography was started manually with a 2 second delay as soon as the contrast material bolus arrived in the carotid arteries at the C4 level. <u>Reference standard</u> DSA DSA was performed on either a biplanar digital angiography unit or a monoplanar system. All analyses were performed in consensus by two of four neuroradiologists with 2-6 years of experience. Time between measurement of index test and reference standard: DSA performed as soon as feasibly possible after CTA (median time 9 hours)

2×2 table Per patient		Reference standard +	Reference standard −	Total
	Index test +	62	0	62
	Index test −	1	24	25
	Total	63	24	
2×2 table Per aneurysm		Reference standard +	Reference standard −	Total
	Index test +	<u>80</u>	<u>2</u>	<u>82</u>
	Index test −	<u>1</u>		

Reference	Papke 2007[163]
	Total 81
Statistical measures	Index text Per patient: Sensitivity 98.4% Specificity 100% PPV 100% NPV 96%
Source of funding	Not reported
Limitations	Risk of bias: Serious Indirectness: No indirectness
Comments	Study uses a reference standard of combined interpretation of CTA, DSA and clinical findings. DSA results used as reference standard for this analysis.

Reference	Pedersen 2001[170]
Study type	Retrospective Cross-sectional
Study methodology	Data source: During 1997 and 1998 all patients admitted to the participating hospital with acute SAH were scheduled for immediate CTA and IA-DSA. Recruitment: Not reported
Number of patients	n = 162
Patient characteristics	Age, mean (range): 51 (18-78) Gender (male to female ratio): 70/92 Setting: The National Hospital, University of Oslo Country: Norway Inclusion criteria: SAH was confirmed by the patient history and subarachnoid blood demonstrated at plain CT or by lumbar puncture.

Reference	Pedersen 2001[170]			
	Exclusion criteria: Patients with known adverse reaction to contrast media, diabetes mellitus, pregnancy, renal failure or severe heart failure were excluded.			
Target condition(s)	aSAH			
Index test(s) and reference standard	Index test CTA All patients were examined with CT. All images were handled at the work station where 7 standard views were reconstructed using multi-projection volume reconstruction (MPVR) with maximum intensity projection (MIP) algorithm. Reconstructed multi-slices were done through the carotid siphons and in some cases 3D surface reconstructions were done. Hard copies were taken of every third source image. When an aneurysm was detected, its size was measured and its largest diameter was used to classify the aneurysm size. Whenever an aneurysm initially was only seen at IA-DSA, we performed supplementary CTA reconstructions in order to visualise it also at CTA. Reference standard DSA All angiographies were performed with a monoplane DSA unit. In local anaesthesia the right femoral artery was catheterised. Usually the same neuroradiologist performed the CTA as well as the IA-DSA and the diagnoses were discussed with one or more of the other neuroradiologists in the department, obtaining a consensus. Time between measurement of index test and reference standard: All DSA performed within 24 h after CTA			
2×2 table Per patient		Reference standard +	Reference standard −	Total
	Index test +	112	2	
	Index test −	9	41	
	Total	119	43	162
2×2 table Per aneurysm		Reference standard +	Reference standard −	Total
	Index test +	131	2	
	Index test −	13	41	
	Total	144	43	
Statistical measures	Index text Per patient: Sensitivity 92.4%* Specificity 95.3% PPV 98.2% NPV82%			

Reference	Pedersen 2001[170]
	*Value reported in study, calculation from 2x2 differs. Per aneurysm: Sensitivity 91% Specificity 95% PPV 98% NPV 76%
Source of funding	Not reported
Limitations	Risk of bias: Very Serious Indirectness: No indirectness
Comments	

Reference	Philipp 2017[172]
Study type	Retrospective Cross-sectional
Study methodology	Data source: The medical records of each of the eligible patients were reviewed, and data were collected regarding patient demographics and key aspects of their clinical presentation. Data were collected from radiology documentation regarding aneurysm size observed on each CTA and DSA. Recruitment: Retrospective analysis of consecutive patient records
Number of patients	n = 401
Patient characteristics	Age, mean (SD): 53.8±13.7 Gender (male to female ratio): 127/274 Setting: Emory University School of Medicine, ICU Country: Georgia Inclusion criteria: patients who were consecutively admitted to the participating institution between December 2009 and December 2013 with a diagnosis of acute, nontraumatic SAH

Reference	**Philipp 2017[172]**			
	Exclusion criteria: Some patients were too unstable either neurologically or hemodynamically to ever undergo either CTA or DSA, and were thus excluded from the study population. Additionally, any patient who was found to harbour >5 aneurysms, detected by CTA or DSA, was excluded from the study.			
Target condition(s)	aSAH			
Index test(s) and reference standard	Index test CTA CTA and DSA were performed according to the hospital's standard protocols Reference standard DSA Data were collected from radiology documentation regarding aneurysm size observed on each CTA and DSA. Time between measurement of index test and reference standard: Unclear. CTA usually served as triage before DSA			
2×2 table Per patient		Reference standard +	Reference standard −	Total
	Index test +			
	Index test −			
	Total	271	160	431
2×2 table Per aneurysm		Reference standard +	Reference standard −	Total
	Index test +	306	24	
	Index test −	125	125	
	Total	431		
Statistical measures	Per aneurysm: Sensitivity 71 (66.5-75.3) Specificity 83.9 (78-89.8) PPV 92.7 (89.4-95.3) NPV 50 (43.8-56.2) ROC 0.77			
Source of funding	Not reported			
Limitations	Risk of bias: Very serious Indirectness: No indirectness			

Reference	**Philipp 2017[172]**
Comments	

1

Reference	**Pierot 2013[174]**
Study type	Cross-sectional study
Study methodology	Data source: Department of Radiology, Maison Blanche Hospital, Universite Reims-Champagne-Ardenne, Reims, France Recruitment: From March 2006 to December 2007, patients with acute non-traumatic SAH (≤10 days)
Number of patients	n = 84
Patient characteristics	Age, mean (SD): 59.4 (12.4) Gender (male to female ratio): 39/45 Setting: Maison Blanche Hospital Country: France Inclusion criteria: all consecutive adult patients admitted with acute non traumatic SAH, confirmed by non enhanced CT or lumbar puncture. Exclusion criteria: Previously treated intracranial aneurysms and or arteriovenous malformations or DSA performed before inclusion.
Target condition(s)	aSAH
Index test(s) and reference standard	<u>Index test - MRA</u> All MRA examinations were performed with an Achieva 3.0T system in the anterior commissure-posterior commissure plane and included both 3D-TOF and CE-MRA. 3D-TOF imaging parameters were echo time 3.45ms; repetition time 18ms; flip angle 20; slice thickness 0.55mm; FOV 210mm; reduced FOV 90%; acquisition matrix 464; reconstruction matrix 512; scan percentage 60% and SENSE factor 2. CE-MRA used a randomly sampled central k-space during venous injection of the gadolinium based contrast agent gadoterate meglumin. A 20ml bolus was delivered at a flow rate of 2mL/s, followed by 30mL of saline and scope based detection of the bolus. CE-MRA imaging parameters were echo time 1.96 ms; repetition time 5.4ms; flip angle 30; slice thickness 0.50mm; FOV 210mm; reduced FOV 85%; acquisition matrix 480; reconstruction matrix 512; scan percentage 60% and SENSE factor 2.5. <u>Reference standard –</u> DSA

Reference	**Pierot 2013[174]**
	Conventional 2D DSA performed on a biplane angiography system with a 1024x1024 matrix and a 20x20cm field of view. DSA was performed with bilateral selective internal carotid artery injections and either unilateral or bilateral vertebral artery injections using a transfemoral approach with the Seldinger technique. Each injection contained 10mL of the Iodinated contrast agent Iodixanol delivered by a power injector. Two expert neuroradiologists with 20 years and 12 years of experience independently evaluated the DSA and MRA images. Both readers were blinded to patient's identity, assessment by other techniques, clinical findings and site of SAH. Time between measurement of index test and reference standard: Not specified

2×2 table

	Reference standard +	Reference standard −	Total	
Index test +				Insufficient data reported to calculate full 2x2 table.
Index test −				
Total	37			

Statistical measures	<u>Index text</u> 3D-TOF: Sensitivity 86 % (0.75-0.98) Specificity 80% (0.64-0.96) PPV 86% (0.75-0.98) NPV 80% (0.64-0.96) CE-MRA: Sensitivity 95% (0.97-1) Specificity 80% (0.64-0.96) PPV 88% (0.77-0.98) NPV 91% (0.79-1)
Source of funding	Not specified
Limitations	Risk of bias: Serious Indirectness: No indirectness
Comments	

Reference	**Poon 2006[176]**
Study type	Retrospective Cross-sectional
Study methodology	Data source: Results obtained during the 19-month period from April 2003 to October 2004.

Reference	Poon 2006[176]
	Recruitment: Not reported
Number of patients	n = 11
Patient characteristics	Age, mean (range): 58 (38-85) Gender (male to female ratio): 4/7 Setting: Pamela Youde Nethersole Eastern Hospital Country: Hong Kong Inclusion criteria: Patients with ruptured cerebral aneurysms had undergone surgical interventions who had both CTA and DSA performed as preoperative diagnostic imaging. Subarachnoid haemorrhage (SAH) was confirmed in all the CT scans of the brain. Exclusion criteria: Not reported
Target condition(s)	aSAH
Index test(s) and reference standard	Index test CTA All the CTA were performed with a helical 16-row multi-slice scanner. Raw image data acquisition used the following protocol: 0.5 mm × 16 thickness, level from C2 to midbrain, 90 mL Iopamiro 370 IVI at 4 mL/s. 3-D reconstruction of the raw data was performed using the computer workstation. All the 3-D images were ready before the start of any surgical intervention. Reference standard DSA (no further detail) Time between measurement of index test and reference standard: Patients had both CTA and DSA performed as preoperative imaging for detection of cerebral aneurysms within 48 h of symptom onset.

2×2 table Per patient		Reference standard +	Reference standard −	Total
	Index test +	11	0	
	Index test −	0	0	
	Total	11	0	0
2×2 table Per aneurysm		Reference standard +	Reference standard −	Total
	Index test +	12	0	

Reference	**Poon 2006**[176]			
	Index test −	0	0	
	Total	12	0	0
Statistical measures	Index text Per patient: Sensitivity 100% Specificity n/a PPV100% NPV n/a Per aneurysm: Sensitivity 100% Specificity n/a PPV100% NPV n/a			
Source of funding	Not reported			
Limitations	Risk of bias: Very serious Indirectness: No indirectness			
Comments				

Reference	**Pozzi-Mucelli 2007**[177]
Study type	Cross-sectional
Study methodology	Data source: Patients admitted to participating hospital between January 2006 and January 2007. Recruitment: Recruitment process unclear
Number of patients	n = 29
Patient characteristics	Age, mean (range): 61.9 (40-84) Gender (male to female ratio): 10-19 Setting: Hospital care Country: Italy

Reference	Pozzi-Mucelli 2007[177]			
	Inclusion criteria: Patients with clinical and imaging findings strongly suggesting the presence of SAH. All patients underwent CT. Those without CT confirmation of SAH but with strong clinical suspicion were still included. Exclusion criteria: Not reported			
Target condition(s)	aSAH			
Index test(s) and reference standard	Index test CTA CT parameters were: 64 mm x 0.5 mm collimation, pitch-0.828 and helical pitch-53. Reference standard DSA DSA were performed with standard technique (four vessel catheterization) and multiple projections. Axial CT scans as well as maximum intensity projection, volume rendering and multiplanar reformations and angiographic views were independently reviewed by four readers (two for 64MDCT-angiography and two for DSA). Consensus was reached for discordant cases. Time between measurement of index test and reference standard: Short interval between the two examinations (less than 12 h-5 days)			
2×2 table Per patient		Reference standard +	Reference standard −	Total
	Index test +	20	0	20
	Index test −	0	9	9
	Total	20	9	29
2×2 table Per aneurysm		Reference standard +	Reference standard −	Total
	Index test +	26	0	26
	Index test −	2	9	11
	Total	28	9	37
Statistical measures	Index text Per patient: Sensitivity 100% Specificity 100% PPV 100% NPV 100% Per aneurysm:* Sensitivity 92.8%			

Reference	**Pozzi-Mucelli 2007**[177]
	Specificity 100% PPV 100% NPV 99.4% *negatives reflect possible aneurysm sites.
Source of funding	Not reported
Limitations	Risk of bias: Serious Indirectness: No indirectness
Comments	

1

Reference	**Preda 1998**[179]
Study type	Retrospective Cross-sectional
Study methodology	Data source: Patients admitted to participating hospital. Recruitment: Patients retrospectively included for data analysis, unclear how selected.
Number of patients	n = 26
Patient characteristics	Age, mean (SD): 53.1 (1.8) Gender (male to female ratio): 9/17 Setting: Participating hospital Country: Italy Inclusion criteria: Patients examined with CTA for suspected intracranial malformations. The diagnosis on admission was SAH in 19 cases, third cranial nerve palsy in 2 cases, and persistent headache in 5 cases. Exclusion criteria: Not reported
Target condition(s)	aSAH

Reference	**Preda 1998[179]**
Index test(s) and reference standard	Index test CTA Computed tomography angiography was performed in all cases, before cerebral angiography, with spiral technique. CTA source images were reviewed independently by four radiologists blinded to the DSA findings. Reference standard DSA Cerebral DSA was performed in all patients to assess the presence/absence of an intracranial malformation. Time between measurement of index test and reference standard: Unclear
2×2 table Per patient	<table><tr><td></td><td>Reference standard +</td><td>Reference standard −</td><td>Total</td></tr><tr><td>Index test +</td><td></td><td>2</td><td></td></tr><tr><td>Index test −</td><td>0</td><td></td><td></td></tr><tr><td>Total</td><td></td><td></td><td>26</td></tr></table>
2×2 table Per aneurysm	<table><tr><td></td><td>Reference standard +</td><td>Reference standard −</td><td>Total</td></tr><tr><td>Index test +</td><td>22</td><td>2</td><td>24</td></tr><tr><td>Index test −</td><td>0</td><td>7</td><td>7</td></tr><tr><td>Total</td><td>22</td><td>9</td><td>31</td></tr></table>
Statistical measures	Index text Per aneurysm: Sensitivity 100% Specificity 77.8% PPV 91.7% NPV 100%
Source of funding	Not reported
Limitations	Risk of bias: Very serious Indirectness: No indirectness
Comments	

Reference	**Ramasundara 2010[182]**
Study type	Retrospective Cross-sectional

Reference	Ramasundara 2010[182]
Study methodology	Data source: Patients with suspected subarachnoid haemorrhage who had CTA scans that had matching DSA studies between November 2005 and December 2006 were reviewed. Recruitment: Patient selection unclear
Number of patients	n = 36
Patient characteristics	Age, mean (SD): Not reported Gender (male to female ratio): Not reported Setting: Royal Melbourne Hospital Country: Australia Inclusion criteria: Patients with suspected subarachnoid haemorrhage who had CTA scans that had matching DSA studies. Exclusion criteria: Not reported
Target condition(s)	aSAH
Index test(s) and reference standard	<u>Index test</u> CTA (CTA 3D VR/MPR combined) Scans were performed on 16 and 64 slice spiral CT scanners. The initial non-contrast scan from CCA to vertex was followed by a contrast enhanced scan from the vertex to the aortic arch with 40 mL of non-ionic contrast material. Contrast was injected through an antecubital vein whenever possible. A 10-mL timing bolus followed by 50-mL saline flush at the level of the mid pituitary was given, with the aim of achieving optimal timing to minimise venous penetration, while preserving arterial opacification. <u>Reference standard</u> DSA Results were then compared to the gold standard DSA results. Time between measurement of index test and reference standard: Not reported
2×2 table Per patient	

	Reference standard +	Reference standard −	Total
Index test +			
Index test −			

Reference	Ramasundara 2010[182]			
	Total	27	9	36
2×2 table Per aneurysm		Reference standard +	Reference standard −	Total
	Index test +	34	1	
	Index test −	0	9	
	Total	34	10	
Statistical measures	Index text Per aneurysm: Sensitivity 100% Specificity 90% PPV 97% NPV 100%			
Source of funding	Not reported			
Limitations	Risk of bias: Very serious Indirectness: No indirectness			
Comments				

Reference	Ramgren 2015[184]
Study type	Retrospective Cross-sectional
Study methodology	Data source: Patient data from a single institution between 2005 and 2011 were prospectively gathered, and imaging results retrospectively analysed. Recruitment: Consecutive patient data included
Number of patients	n=326
Patient characteristics	Age, mean (range): 56 (15-86) Gender (male to female ratio): 137/189 Setting: Skan university hospital Country: Sweden

<table>
<tr><td>Reference</td><td>Ramgren 2015[184]</td></tr>
<tr><td></td><td>Inclusion criteria: Patients in whom non-traumatic SAH was suspected and later confirmed by either non-enhanced CT (NECT) or lumbar puncture.
Exclusion criteria: Patients who did not have a non-traumatic SAH</td></tr>
<tr><td>Target condition(s)</td><td>aSAH</td></tr>
<tr><td>Index test(s) and reference standard</td><td><u>Index test</u>
CTA
Acute NECT and CTA was performed on one of the four available clinical scanners: MX 8000 IDT, 16-slice (71 patients); Brilliance, 40-slice (87 patients); Brilliance, 64-slice (164 patients), and iCT, 128-slice (7 patients). All image evaluation was done by neuroradiologists (14 specialists in neuroradiology and 5 radiologists in training to become neuroradiologists with experience in neuroradiology of minimum 1 year) with access to reconstructed thin-slab maximum intensity projection (MIP) images.

<u>Reference standard</u>
DSA
DSA was performed on a biplane angiography unit or a monoplane unit Images were acquired in at least four standard projections for each vessel. Three dimensional acquisition was performed in approximately 60% of the patients. All 326 DSA examinations were evaluated by either three interventional neuroradiologists (312 examinations) or two senior neuroradiologists (14 examinations).

Time between measurement of index test and reference standard: Unclear</td></tr>
<tr><td>2×2 table
Per patient</td><td><table>
<tr><td></td><td>Reference standard +</td><td>Reference standard −</td><td>Total</td></tr>
<tr><td>Index test +</td><td>209</td><td>12</td><td></td></tr>
<tr><td>Index test −</td><td>19</td><td>87</td><td></td></tr>
<tr><td>Total</td><td></td><td></td><td></td></tr>
</table></td></tr>
<tr><td>2×2 table
Per aneurysm</td><td><table>
<tr><td></td><td>Reference standard +</td><td>Reference standard −</td><td>Total</td></tr>
<tr><td>Index test +</td><td><u>266</u></td><td><u>12</u></td><td></td></tr>
<tr><td>Index test −</td><td><u>19</u></td><td><u>88</u></td><td></td></tr>
<tr><td>Total</td><td></td><td></td><td></td></tr>
</table></td></tr>
<tr><td>Statistical measures</td><td><u>Index text</u>
Per patient:
Sensitivity 91.6 (87.3-94.9)
Specificity 87.9 (79.8-93.6)
PPV 94.6 (90.7-97.2)
NPV 82.1 (73.4-88.8)</td></tr>
</table>

Reference	Ramgren 2015[184]
	Per aneurysm: Sensitivity 93.3 (89.7-95.9) Specificity 88 (79.9-93.6) PPV 95.7 (92.9-97.7) NPV 82.2 (73.7-89)
Source of funding	This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.
Limitations	Risk of bias: Serious Indirectness: No indirectness
Comments	

Reference	Romijn 2008[185]
Study type	Cross-sectional study
Study methodology	Data source: Departments of Radiology and Medical Physics, Academic Medical Centre, University of Amsterdam, Amsterdam, the Netherlands; and the Department of Radiology, St. Elisabeth Ziekenhuis, Tilburg, the Netherlands Recruitment: January 2004 and February 2006, 108 patients who presented with clinically suspected subarachnoid haemorrhage
Number of patients	n = 108
Patient characteristics	Age, mean (range): 56 years (range 19–92 years) Gender (male to female ratio): 27/81 Setting: Academic Medical Centre, University of Amsterdam Country: Netherlands Inclusion criteria: patients who presented with clinically suspected SAH underwent both CTA-MMBE and DSA for diagnosis of an intracranial aneurysm Exclusion criteria: Not specified

<table>
<tr><td>Reference</td><td>Romijn 2008[185]</td></tr>
<tr><td>Target condition(s)</td><td>aSAH</td></tr>
<tr><td>Index test(s) and reference standard</td><td><u>Index test - CTA</u>
In MMBE, an additional non-enhanced low-dose spiral CT scan (65 mAs) was used to identify bony structures that were subsequently masked on CTA images (Fig 1A–C). These scans were made on a 4-section spiral CT scanner (MX8000; Philips Medical Systems, Best, the Netherlands or Sensation 4; Siemens Medical Solutions, Erlangen, Germany).We used the following parameters: 120 kV, 250 mAs, 4x1mm detector collimation; pitch of 0.875, section thickness of 1.3 mm, increment of 0.5 mm, 150-mm FOV, 512[redacted]512 matrix, and reconstruction kernels B (Philips Medical Systems) and H30f (Siemens Medical Solutions). Eighty to 100 mL of non-ionic contrast material was injected in a cubital vein at a rate of4mL/s. Scanning delay was automatically adjusted by a bolus-tracking technique.

<u>Reference standard- DSA</u>
DSA and 3DRA were performed by an experienced neuroradiologist on a single-plane angiographic unit (Integris Allura Neuro; Philips Medical Systems). Most angiograms were obtained with the patient under general anaesthesia before coiling. Through a 6F catheter positioned in an internal carotid artery (ICA) or vertebral artery, 6- to 8-mL non-ionic contrast was injected, and filming was performed in 2–3 projections at a frame rate of 2 per second. For 3DRA, 100 images were acquired during a 240° rotational run in 8 seconds with 15- to 21-mL contrast medium at 3 mL/s. On a dedicated workstation, 3D images were constructed and evaluated. Screen shots in multiple projections of volume-rendered 3D images were stored.

For the purpose of this study, CTA source images and MIP images were anonymized and evaluated independently by 2 neuro-radiologists blinded to clinical data and diagnostic CT and DSA results.

Time between measurement of index test and reference standard: Not specified</td></tr>
<tr><td>2×2 table
Per patient</td><td><table>
<tr><td></td><td>Reference standard +</td><td>Reference standard −</td><td>Total</td></tr>
<tr><td>Index test +</td><td>87</td><td>2</td><td>89</td></tr>
<tr><td>Index test −</td><td>1</td><td>18</td><td>19</td></tr>
<tr><td>Total</td><td>88</td><td>20</td><td>108</td></tr>
</table></td></tr>
<tr><td>Statistical measures</td><td><u>Index text</u>
Per patient:
Sensitivity 99%
Specificity 90%
PPV 98%
NPV 95%</td></tr>
<tr><td>Source of funding</td><td>Not specified</td></tr>
</table>

Reference	**Romijn 2008[185]**
Limitations	Risk of bias: Serious Indirectness: No indirectness
Comments	

Reference	**Rotim 2007[188]**
Study type	Cross-sectional study
Study methodology	Data source: Department of Neurosurgery, Dubrava University Hospital, Zagreb, Croatia Recruitment: November 2005 to September 2006, consecutive patients with SAH confirmed by CT scan.
Number of patients	n = 29
Patient characteristics	Age, mean (range): not specified Gender (male to female ratio): not specified Setting: Dubrava University Hospital Country: Croatia Inclusion criteria : Patients with suspected SAH, confirmed by CT scan who underwent CTA and DSA examinations Exclusion criteria: not specified
Target condition(s)	aSAH
Index test(s) and reference standard	Index test - CTA CTA was performed with SomatoM 16 sections. Image data acquisition was done with: patient in t he supine position; 18G cannula in non dominant antecubital fossa, 340 strength iodinated contrast medium; 60 – 80ml at 4ml.s contrast; followed by 40ml saline. Slice thickness 3-5mm, reconstruction interval 1mm. Scanning was performed in an area extending from the patients C2 vertebral body to 2cm from the vertex to include low PICA origins and distal pericallosal arteries. Reference standard - DSA DSA was performed with via transfemoral approach with intra-arterial catheter injection of 340 strength iodinated contrast medium, 9ml at 6mlL/s contrast for ateria carotis communis. Diagnostic DSA was performed with the patients under intravenous sedation. Standard anteroposterior and lateral projection images and magnified oblique projections were obtained. CTA and DSA findings were separately assessed by radiologist and neurosurgeon.

Reference	Rotim 2007[188]				
	Time between measurement of index test and reference standard: Not specified				
2×2 table		Reference standard +	Reference standard −	Total	Insufficient data reported to calculate full 2x2 tables
	Index test +				
	Index test −				
	Total				
Statistical measures	Index text Per aneurysm: Sensitivity 96.6% Specificity 100% PPV 100% NPV 0%				
Source of funding	Not reported				
Limitations	Risk of bias: Serious Indirectness: No indirectness				
Comments					

1

Reference	Saboori 2011[189]
Study type	Descriptive analytic study
Study methodology	Data source: Department of neurosurgery, Alzahra Hospital, Isfahan University of Medical Sciences, Iran Recruitment: emergency or neurosurgical wards between 2008 and 2009
Number of patients	n = 19
Patient characteristics	Age, mean (SD): 49.5 ± 9.13 Gender (male to female ratio): 8/11 Setting: Alzahra Hospital, Isfahan University of Medical Sciences Country: Iran

Reference	**Saboori 2011[189]**
	Inclusion criteria: Patients with a confirmatory CT scan of SAH and underwent CTA and DSA Exclusion criteria: Patients who were post-operative
Target condition(s)	aSAH
Index test(s) and reference standard	Index test - CTA Not specified Reference standard – DSA Not specified Time between measurement of index test and reference standard: Not specified
2×2 table Per patient	(see table below)
Statistical measures	Index text Per patient: Sensitivity 89% Specificity 100% PPV 100% NPV 85%
Source of funding	Not specified
Limitations	Risk of bias: Very serious Indirectness: No indirectness
Comments	

2×2 table Per patient

	Reference standard +	Reference standard −	Total
Index test +	17	0	17
Index test −	2	11	13
Total	19	11	30

Reference	**Seruga 2011[199]**
Study type	Cross-sectional study

Reference	**Seruga 2011[199]**
Study methodology	Data source: Department of Radiology and Neurosurgery, Maribor teaching Hospital, Maribor, Slovenia; and the Karl-Franzens Medical School University Hospital, Graz, Austria Recruitment: Patients undergoing further imaging for SAH confirmed on CT
Number of patients	n = 30
Patient characteristics	Age, mean (range): 49.9 (range 9 – 80) Gender (male to female ratio): 11/19 Setting: Maribor teaching Hospital Country: Slovenia Inclusion criteria: Patients with confirmed SAH on CT scan or lumbar puncture, including further CTA Exclusion criteria: No evidence of SAH on CTA
Target condition(s)	aSAH
Index test(s) and reference standard	Index test - CTA Standard 3 dimensional CT angiography scanning parameters were used. The slice thickness was 1.5mm, the pitch was 1, the reconstruction index 0.5 slice collimation was 1mm, the slab thickness was 9 to 12cm, the linear Interpolation was 180 degrees and linear interval reconstruction was used. Through a needle inserted in an antecubital vein, 80ml of iodinated contrast medium was injected at a rate of 2.5ml/s Reference standard – DSA Additional conventional selective 4 vessel angiographic studies were performed on a 1 plane C-arm with a 512x512 matrix and a 1024x1024 matrix and 0.3mm and 0.7mm focal spots. Both internal carotid arteries and both vertebral arteries were selectively catheterized by the Seldinger technique via a trans-femoral approach. We injected 6 to 8 ml of 300mg iodine with an injector at a flow rate of 7ml/s. Anteroposterior, lateral, and oblique projections were obtained. Time between measurement of index test and reference standard: within 12 hours

2×2 table Per aneurysm

	Reference standard +	Reference standard −	Total
Index test +	31		
Index test −	2		

Reference	**Seruga 2011**[199]				
	Total	33			
Statistical measures	Index text Per aneurysm: Sensitivity 94%				
Source of funding	Not specified				
Limitations	Risk of bias: Very serious Indirectness: No indirectness				
Comments					

1

Reference	**Schmieder 1999**[196]
Study type	Cross-sectional
Study methodology	Data source: Not reported Recruitment: Not reported
Number of patients	n = 54
Patient characteristics	Age, mean (range): 50.6 (17-76) Gender (male to female ratio): 18-36 Setting: Hospital care Country: Germany Inclusion criteria: Patients with acute SAH or with CT scans showing anomalies being suspicious of aneurysms. Exclusion criteria: Accompanying ICH which required urgent evacuation or patients graded Hunt and Hess IV or V when no operative consequences were planned.

<table>
<tr><td>Reference</td><td>Schmieder 1999[196]</td></tr>
<tr><td>Target condition(s)</td><td>aSAH</td></tr>
<tr><td>Index test(s) and reference standard</td><td><u>Index test</u>
MRA
Transverse angiography was performed with 64 partitions over a 64 mm slab. The 3D-TOF MRA was done flow compensated in read and selection-select directions with a steady state free precession sequence. No contrast agents were used.

<u>Reference standard</u>
DSA
MRA was followed by transfemoral four-vessel DSA.

Time between measurement of index test and reference standard: Not reported</td></tr>
<tr><td>2×2 table
Per patient</td><td><table>
<tr><td></td><td>Reference standard +</td><td>Reference standard −</td><td>Total</td></tr>
<tr><td>Index test +</td><td></td><td></td><td></td></tr>
<tr><td>Index test −</td><td></td><td></td><td></td></tr>
<tr><td>Total</td><td>47</td><td>7</td><td></td></tr>
</table></td></tr>
<tr><td>2×2 table
Per aneurysm</td><td><table>
<tr><td></td><td>Reference standard +</td><td>Reference standard −</td><td>Total</td></tr>
<tr><td>Index test +</td><td><u>61</u></td><td><u>3</u></td><td><u>64</u></td></tr>
<tr><td>Index test −</td><td><u>3</u></td><td><u>7</u></td><td><u>10</u></td></tr>
<tr><td>Total</td><td><u>64</u></td><td><u>10</u></td><td><u>74</u></td></tr>
</table></td></tr>
<tr><td>Statistical measures</td><td><u>Index text</u>
Per aneurysm:
Sensitivity 95.3%
Specificity 70%
PPV 95.3%
NPV 70%</td></tr>
<tr><td>Source of funding</td><td><u>Not reported</u></td></tr>
<tr><td>Limitations</td><td>Risk of bias: Serious
Indirectness: No indirectness</td></tr>
<tr><td>Comments</td><td></td></tr>
</table>

1

Reference	**Shahzad 2011[200]**
Study type	Cross-sectional study
Study methodology	Data source: Patients admitted to the Department of Diagnostic Imaging, Lahore General Hospital and Postgraduate Medical Institute, Lahore, from January to June 2007. Recruitment: Not reported
Number of patients	n = 30
Patient characteristics	Age, mean (SD): 41±14.1 years Gender (male to female ratio): 14/16 Setting: Department of Diagnostic Imaging, Lahore General Hospital and Postgraduate Medical Institute, Lahore Country: Pakistan Inclusion criteria: Patients of either gender and all ages presented with non-traumatic SAH, were included. The diagnosis of SAH was made by either CT scan or lumber puncture. Exclusion criteria: Patients with traumatic SAH or those having contraindications to MRA were excluded.
Target condition(s)	aSAH
Index test(s) and reference standard	Index test MRA All MR angiographic studies were performed using 1.5 T superconducting MR system. A three dimensional time of flight magnetic resonance angiography (3D-TOF MRA) technique was used with imaging parameters of 30/6.4 and ramped pulse from 15 to 25 with a centre flip angle of 20. The whole volume was divided into 4 slabs with 38% overlap. Each slab consist of 48 partitions, resulting in total of 150 sections of 0.7 mm. The overall vessel coverage with this technique was 210 mm. It was placed to include the structures from foramen of magnum to A3 branch of ACA. Scan time was reduced to 8 minutes using SENSE factor II. Reference standard DSA

Reference	Shahzad 2011[200]
	Intra-arterial digital subtraction angiographic examinations were performed using digital subtraction system with standard transfemoral technique using 6F sheath and catheter systems. 8-10 ml of non-ionic contrast medium (Ultravist 300 mg I/mL) was injected at a rate of 3-4 ml per second. Interpretation of 3D-TOF MRA and IA-DSA was performed independently by two radiologists. Time between measurement of index test and reference standard: Intra-arterial digital subtraction angiography (IA-DSA) was performed within 24 hours (n=25) to one week (n=5) of 3D-TOF MRA.
2×2 table Per aneurysm	<table><tr><td></td><td>Reference standard +</td><td>Reference standard −</td><td>Total</td></tr><tr><td>Index test +</td><td><u>29</u></td><td><u>0</u></td><td></td></tr><tr><td>Index test −</td><td><u>1</u></td><td><u>0</u></td><td></td></tr><tr><td>Total</td><td><u>30</u></td><td><u>0</u></td><td></td></tr></table>
Statistical measures	<u>Index text</u> Per aneurysm: Sensitivity 96.7% Specificity n/a PPV 100% NPV n/a
Source of funding	Not reported
Limitations	Risk of bias: Serious Indirectness: No indirectness
Comments	Twenty two (73.3%) patients presented with subarachnoid haemorrhage, 5 (16.7%) patients with subarachnoid haemorrhage and focal neurological signs and 3 (10%) patients were having ICH along with SAH.

1

Reference	Strayle-Batra 1998[202]
Study type	Cross-sectional study
Study methodology	Data source: Department of neuroradiology, University of Tubingen, Tubingen, Germany Recruitment: Patients examined by CT angiography and DSA for the detection of aneurysms
Number of patients	n = 17

Reference	**Strayle-Batra 1998[202]**
Patient characteristics	Age, mean (SD): 51.1 (25 -77) Gender (male to female ratio): 5/12 Setting: Department of neuroradiology, University of Tubingen Country: Germany Inclusion criteria: Patients examined by CT angiography and DSA for the detection of aneurysms or for planning interventional procedures Exclusion criteria: Not specified
Target condition(s)	aSAH
Index test(s) and reference standard	Index test - CTA The region to be imaged was selected from the lateral topogram; the bony structures of the sella were usually placed in the centre. Raw data were registered with a 1mm slice thickness and a table feed of 1.5mm rotation. Examination parameters: 120kV; 170 mA; rotation time 1.5s; maximum spiral length 57mm; slice thickness 1mm; table speed 1.5mm/s; reconstruction increment 0.5mm; pitch 1.5; contrast medium 100 – 130ml total volume Reference standard – DSA DSA were carried out on a DSA unit. Via a femoral artery, the cerebral vessels were selectively catheterized and imaged in a.p and lateral views. Oblique projections wand series with compression of one carotid were added if the standard projections were not sufficient. The CT angiographies and the conventional angiographies were evaluated separately according to identical previously defined criteria by two other independent and experience investigators with no knowledge of the diagnosis or examinations results. Time between measurement of index test and reference standard: within 1 – 4 weeks (mean 2 days)

2×2 table Per aneurysm		Reference standard +	Reference standard −	Total
	Index test +	17		
	Index test −	3		
	Total	20		

Reference	**Strayle-Batra 1998**[202]
Statistical measures	Index text Per aneurysm: Sensitivity 85%
Source of funding	Not specified
Limitations	Risk of bias: Serious Indirectness: No indirectness
Comments	

Reference	**Teksam 2005**[211]
Study type	Retrospective Cross-sectional study
Study methodology	Data source: Department of Radiology, University of Minnesota Medical School, Minneapolis Recruitment: August 1999 through September 2003 consecutive patients who underwent MSCTA and DSA and or surgery were included within this study
Number of patients	n = 103
Patient characteristics	Age, median (range) : 52 years (23 – 76 years) Gender (male to female ratio): 46/57 Setting: University of Minnesota Medical School Country: USA Inclusion criteria: Not specified Exclusion criteria: Not specified
Target condition(s)	aSAH

Reference	**Teksam 2005[211]**
Index test(s) and reference standard	Index test - CTA MSCTA scans were performed with a four channel multi-slice row detector CT scanner. Ct angiography was initiated 15-20s after the start of an intravenous infusion of non-ionic iodinated contrast material. The scanning parameters were 120kV, 225mA, slick thickness of 1.25mm, reconstruction interval of 1mm and table speed of 2 – 3mm/s Reference standard - DSA DSA was performed with femoral catherization by the Seldinger technique with a biplane DSA unit. Three of four vessel angiograms were obtained in anteroposterior, lateral, bilateral, oblique and additional projections depending on the location of the aneurysm as needed for each patient. DSA was performed with a 22cm field of view and a 1024x1024 matrix. The images were reviewed by a neuroradiologist blinded to the results of the other modality. Time between measurement of index test and reference standard: within 2 weeks of MSCTA

2×2 table Per aneurysm

	Reference standard +	Reference standard −	Total
Index test +	41	8	49
Index test −	7	15	22
Total	48	23	71

Statistical measures	Index text Per aneurysm: Sensitivity 85% (0.75-0.95) Specificity 65% (0.46-0.84) PPV 83% (0.73-0.94) NPV 68% (0.49-0.87)
Source of funding	Not specified
Limitations	Risk of bias: Indirectness: Serious indirectness (large proportion of patients had other medical conditions aside from SAH)
Comments	

Reference	**Tipper 2005[215]**
Study type	Cross-sectional study

Reference	Tipper 2005[215]
Study methodology	Data source: University Department of Radiology and the Academic Neurosurgery Unit, Addenbrooke's Hospital, Cambridge, UK Recruitment: Between March and October 2003, consecutive adults who were scheduled for conventional DSA for suspected intracranial aneurysm actively recruited to have a CTA.
Number of patients	n = 57
Patient characteristics	Age, mean (range) 53 years (range 22 – 81) Gender (male to female ratio): 31/26 Setting: Addenbrooke's Hospital Country: UK Inclusion criteria: Patients with positive findings for SAH on initial examination indicated for DSA and further imaging Exclusion criteria: not specified
Target condition(s)	aSAH
Index test(s) and reference standard	Index test - CTA The CTA examinations were performed on a 16 multidetector row spiral CT machine based on a standardized protocol. Using an intravenous cannula in the antecubital fossa, 100ml of contrast agent were injected with a powered injector at the rate of 5ml/s. An automatic fluoroscopic bolus trigger system with the aortic arch as a reference point and a delay of 6s determined the optimal timing of the data acquisition according to the following protocol: spiral mode, 0.5 rotations/s, 16 detector rows at 0.75mm intervals, table speed 10/mm rotation, reconstruction interval 0.40mm at kernel H20 and acquisition parameters 120KVp/130mA. Reference standard - DSA Conventional four vessel DSA was performed by one of three attending neuroradiologists, on a digital angiographic unit via the femoral artery using the Seldinger technique. Standard anteroposterior and lateral projections were routinely acquired, with additional selected oblique projections at the discretion of the radiologist. Images were acquired with a 33cm field of view, 1024x1024 matrix resolution of 0.32 x 0.32mm. The DSA studies were reviewed on hard copy films by one of three attending neuroradiologists. The CTA examinations were reviewed in a randomized order by two independent neuroradiologists. The CTA examinations were masked for patient identifiers and review was performed blinded to the DSA results.

Reference	Tipper 2005[215]				
	Time between measurement of index test and reference standard: within 3 days				
2×2 table Per patient		Reference standard +	Reference standard −	Total	Insufficient data to calculate full 2x2 tables
	Index test +				
	Index test −				
	Total	42			
2×2 table Per aneurysm		Reference standard +	Reference standard −	Total	
	Index test +				
	Index test −				
	Total	51			
Statistical measures	Index text Per patient: Sensitivity 97.7% (88.2-99.6) Specificity 100% (77.2 – 100) PPV 100% (91.8 – 100) NPV 92.9% (68.5 – 98.7) Per aneurysm: Sensitivity 96.2% (87.5-99.0) Specificity 100% (77.2 – 100) PPV 100% (93.0 – 100) NPV 86.7% (62.7 – 93.3)				
Source of funding	Not reported				
Limitations	Risk of bias: Serious Indirectness: No indirectness				
Comments					

1

Reference	Uysal 2005[219]
Study type	Cross-sectional study
Study methodology	Data source: Departments of Radiology and Neurosurgery, Şişli Etfal Training and Research Hospital, İstanbul, Turkey Recruitment: retrospective review of patients with aneurysms between September 2002 to May 2004

Reference	**Uysal 2005**[219]
Number of patients	n = 32
Patient characteristics	Age, mean (range):45.5 (32 – 75) Gender (male to female ratio):15/17 Setting: Şişli Etfal Training and Research Hospital Country: Turkey Inclusion criteria: Patients who had CTAs and DSAs with suspicion of aneurysm due to SAH detected by non-enhanced cranial CT Exclusion criteria: Not specified
Target condition(s)	Subarachnoid Haemorrhage
Index test(s) and reference standard	<u>Index test - CTA</u> All CTA examinations were performed with spiral technique by a single row detector CT machine (General Electric Hi-Speed, Milwaukee, WI, USA). After detection of the location from lateral scanogram, slices parallel to orbito-meatal line were obtained in caudo-cranial direction starting from 1 cm below the base of sella turcica up to the level of lateral ventricles. Spiral CTA was obtained with 1 mm collimation, 1.5:1 pitch, 120 kV, 150 mAs and 25 cm field-of-view. Slice reconstruction thickness was 0.5 mm. One hundred and twenty ml non-ionic iodinated contrast (Iomeron 400, Bracco Diagnostic, Milan, Italy) was administered through a 20 G needle from the antecubital vein with a rate of 3 ml/second. Acquisition of images started after 15 seconds and examination lasted for about 40-60 seconds. Spiral CTA images were processed from the obtained source images using the maximum intensity projection (MIP) technique. Presence of an aneurysm, location, number, size and orientation were detected in MIP images. Aneurysm size is determined by measuring the widest dimension. <u>Reference standard – DSA</u> Cerebral DSA (Philips V 3000, Best, The Netherlands) examination was performed in another centre outside our hospital with Seldinger method and percutaneous femoral catheterization. Diagnostic and Interventional Radiology total of 33 DSA examinations were performed with one case having a second DSA for follow-up. Magnified images were obtained besides conventional images in cases with aneurysms. No complications occurred during DSA procedures. DSA images were evaluated by a radiologist uninformed of spiral CTA findings. Student paired t test was used to compare the sizes of aneurysms demonstrated by DSA and CTA. Obtained images were transferred to a workstation where they were evaluated by two radiologists blinded to the DSA findings. They evaluated images in “cine” mode using different density levels and formed a common decision at the end. Evaluation of images took 10-20 minutes.

Reference	**Uysal 2005**[219]			
	Time between measurement of index test and reference standard: Not specified			
2×2 table		Reference standard +	Reference standard −	Total
	Index test +	32	0	32
	Index test −	1	0	1
	Total	33	0	33
Statistical measures	Index text: CTA Sensitivity: 96% (3-5mm: 94% and >5mm: 100% as reported within paper) Specificity: 100% PPV: 100% NPV: 100%			
Source of funding	Not specified			
Limitations	Risk of bias: Serious Indirectness: None			
Comments	2x2 table completed from narrative within paper and results reported differ			

1

Reference	**Van Zwam 2012**[225]
Study type	
Study methodology	Data source: Patients admitted to participating hospital with a diagnosis of non-traumatic SAH between 2004 and 2006 Recruitment: Consecutive patients included for analysis.
Number of patients	n = 75
Patient characteristics	Age, mean (SD): Gender (male to female ratio): Setting: not reported Country: not reported

Reference	Van Zwam 2012[225]
	Inclusion criteria: Patients admitted with a diagnosis of non-traumatic SAH established by CT or lumbar puncture. Exclusion criteria: Patients in whom there was a contraindication for MRI or in whom no further treatment was considered. A poor clinical condition was not considered a contraindication for inclusion, but if no reasonable chance of survival was expected by the treating physician, then no further diagnostic or treatment procedures would be undertaken and the patient was not included in the study.
Target condition(s)	aSAH
Index test(s) and reference standard	<u>Index test</u> CTA CTA was performed on a 2-slice (Elscint Dual, Elscint, Haifa, Israel) or on a 4-slice multidetector-row spiral CT scanner. In most cases a semi-automatic bone subtraction method, matched mask bone elimination (MMBE), was used. In this method a low dose-mask is acquired of the bony skull, after which the bone-containing voxels are extracted from the post-contrast images using a computer algorithm that compensates for movements between the scans. In cases where the patient was too restless to undergo a mask CT scan before the contrast scan or in cases where the contrast scan could not be matched with the mask due to excessive movement between the scans, the contrast scan was evaluated using manual segmentation to remove the bony structures. <u>MRA</u> MRA was performed on a 1.5 Tesla Philips scanner using a dedicated head coil. The scan protocol included an ultra-short first-pass CEMRA with concentric k-space filling. <u>Reference standard</u> DSA All patients underwent conventional catheter DSA technique. All four feeding arteries to the brain were catheterised and imaged with the exception of a few patients whom, due to patient unrest, only the vessel which contained the suspected aneurysm was catheterised. A 4 or 5F catheter system was used for diagnostic DSA and a 6F system in cases of immediate treatment. Automatic contrast injections were performed by a power injector, of 9 ml iobitridol 350 mg/ml at 5 ml/s for the carotid arteries and 8 ml at 4 ml/s for the vertebral arteries. Internal carotid arteries were imaged in antero-posterior, lateral and oblique projections and the vertebral arteries in antero-posterior and lateral projections. Additional angiographic projections were obtained, if necessary, of the vessels that harboured an aneurysm, for better visualisation of the aneurysm, its neck and its surrounding arteries. Time between measurement of index test and reference standard: Unclear.

2×2 table Per patient CTA

	Reference standard +	Reference standard −	Total
Index test +			
Index test −			

Reference	Van Zwam 2012[225]				
	Total	57	18	75	
2×2 table Per aneurysm CTA		Reference standard +	Reference standard −	Total	
	Index test +	59.5	1		
	Index test −	5.5	17		
	Total	65	18		
2×2 table Per patient MRA		Reference standard +	Reference standard −	Total	
	Index test +				
	Index test −				
	Total	57	18	75	
2×2 table Per aneurysm MRA		Reference standard +	Reference standard −	Total	
	Index test +	62	3		
	Index test −	3	15		
	Total	65	18		
Statistical measures	Index text CTA Per aneurysm: Sensitivity 91.5% Specificity 94.4% PPV 98.3% NPV 75.6% MRA Per aneurysm: Sensitivity 95.4% Specificity 83.3% PPV 95.4% NPV 83.3%				
Source of funding	Not reported				
Limitations	Risk of bias: Serious Indirectness: No indirectness				
Comments					

Reference	Vieco 1995[227]
Study type	Cross-sectional study

Reference	Vieco 1995[227]
Study methodology	Data source: Department of radiology, University of Vermont Medical Centre Hospital, USA Recruitment: Consecutive patients with recent subarachnoid haemorrhage
Number of patients	n = 30
Patient characteristics	Age, mean (range): 49 years (19 – 76) Gender (male to female ratio): 13/17 Setting: University of Vermont Medical Centre Hospital Country: USA Inclusion criteria: Unenhanced CT scan showing SAH blood or spinal tap showing recent intrathecal bleeding Exclusion criteria: Not specified
Target condition(s)	aSAH
Index test(s) and reference standard	Index test - CTA Helical CT angiography was obtained with a GE Hi speed scanner. For contrast enhancement, 100ml of Omnipaque 300 was injected at 2ml/sec in an antecubital vein. The number of helical slices increased during the study from 30 to 60 slices. CT technique used 1mm slice thickness with a table speed of 1mm, 120 kV, 280mA and a 12.5cm field of view in all patients. Total CT acquisition was 30 or 60 seconds depending on the number of images obtained. Reference standard – DSA Conventional DSA was obtained via femoral catherization using a 0.3mm focal spot and a 1024.1024 matrix. Selective bilateral carotid and vertebral injections were obtained to get images in the anteroposterior and lateral projections; an additional oblique lateral projection was obtained to better image the anterior communicating artery in each case. Oblique views of aneurysms detected were also obtained at the discretion of the angiographer. CT angiography source images and 3D displays were reviewed by two of the authors, both experienced neuroradiologists, working independently. Each reviewer was blinded to patient identification and DSA findings. Time between measurement of index test and reference standard: within 4 hours of each other

Reference	**Vieco 1995[227]**			
2×2 table Per aneurysm		Reference standard +	Reference standard −	Total
	Index test +	29	0	29
	Index test −	1	0	1
	Total	30	0	30
Statistical measures	<u>Index text</u> Per aneurysm: Sensitivity 97% Specificity 100% PPV 100% NPV			
Source of funding	NIH grant GCRC M01RR109			
Limitations	Risk of bias: Serious Indirectness: No indirectness			
Comments				

Reference	**Wang 2010[234]**
Study type	Cross-sectional
Study methodology	Data source: Patients who presented with spontaneous SAH with or without intracerebral or intraventricular haemorrhage. Recruitment: Unclear
Number of patients	n = 121
Patient characteristics	Age, median (range): 55 (17-86) Gender (male to female ratio): 48/86 Setting: Chang Gung University & Chang Gung Memorial Hospital Country: China

Reference	Wang 2010[234]
	Inclusion criteria: Patients with clinical symptoms of SAH and the ability to undergo multidetector. Exclusion criteria: Eight of the patients were excluded because they died shortly after CTA without DSA study.
Target condition(s)	aSAH
Index test(s) and reference standard	<u>Index test</u> CTA CTA performed with a multi-section spiral CT scanner <u>Reference standard</u> DSA DSA was performed with femoral catheterization by the Seldinger technique with a biplane digital subtraction angiography unit Time between measurement of index test and reference standard: DSA was scheduled 1 or 2 days later if no aneurysm was found in the reconstructed CTA images; once surgical clipping of the aneurysm was performed, DSA was scheduled within the following week; or if transarterial embolization of the aneurysm was attempted, complete four-vessel DSA was completed before the embolization procedure.

2×2 table Per patient		Reference standard +	Reference standard −	Total
	Index test +	93	0	93
	Index test −	1	19	20
	Total	94	19	113

2×2 table Per aneurysm		Reference standard +	Reference standard −	Total
	Index test +	103	3	106
	Index test −	2	19	21
	Total	105	22	127

Reference	Wang 2010[234]
Statistical measures	Index text Per patient: Sensitivity 98.9% Specificity 100% PPV 95% NPV 100% Per aneurysm: Sensitivity 98.1% Specificity 86.4% PPV 90.5% NPV 97.2%
Source of funding	Not stated
Limitations	Risk of bias: Serious Indirectness: No indirectness
Comments	

1

Reference	Wang 2013[232]
Study type	Cross-sectional study
Study methodology	Data source: The department of Neurosurgery, the Third Affiliated hospital, Sun Yat-sen University, Guangzhou, China Recruitment: Between January 2009 to October 2011 patients with spontaneous SAH who were suspected to have intracranial aneurysms
Number of patients	n = 52
Patient characteristics	Age, mean (range): 39.5 years (5 – 68 years) Gender (male to female ratio): 23/29 Setting: the Third Affiliated hospital Country: China

<table>
<tr><th>Reference</th><th>Wang 2013[232]</th></tr>
<tr><td></td><td>Inclusion criteria: Patients with diagnosis of spontaneous SAH established by either unenhanced CT examination or xanthochromia at lumbar puncture who underwent CTA and DSA
Exclusion criteria: not specified</td></tr>
<tr><td>Target condition(s)</td><td>aSAH</td></tr>
<tr><td>Index test(s) and reference standard</td><td><u>Index test - CTA</u>
All 3D CTA examinations were performed using a 320 detector row volume CT system with a detector width of 160mm. Contrast enhancement was provided by the intravenous antecubital administration of 50ml bolus of non-iondinated contrast material. CT parameters were as follows 0.75s/r gantry rotation speed; 320x0.5mm detector width; 0.25mm reconstruction; 512x512 matrix 180 – 240mm field of view; 80kVtube voltage; 350mA; 150mA tube current.

<u>Reference standard - </u>DSA
A standard single plane DSA unit with matrix resolution of 1024x1024 was used. Selected carotid angiograms usually consisted of one anteroposterior; one lateral; and one to two oblique views. Non-ionic contrast medium was injected at a flow rate of 5ml/s.

All CTA and DSA were independently interpreted by two neuroradiologists who had more than 7 years of experience and were blinded to the assessment of the other technique or of the other investigator and only knew that the patients were suspected of having a intracranial aneurysm.

Time between measurement of index test and reference standard: within 48 hours after CTA examinations</td></tr>
<tr><td>2×2 table
Per aneurysm</td><td><table>
<tr><th></th><th>Reference standard +</th><th>Reference standard −</th><th>Total</th></tr>
<tr><td>Index test +</td><td>52</td><td>0</td><td>52</td></tr>
<tr><td>Index test −</td><td>2</td><td>0</td><td>2</td></tr>
<tr><td>Total</td><td>54</td><td>0</td><td>54</td></tr>
</table></td></tr>
<tr><td>Statistical measures</td><td><u>Index text</u>
Per aneurysm:
Sensitivity 96.3%
Specificity 100%
PPV 100%
NPV</td></tr>
<tr><td>Source of funding</td><td><u>Not specified</u></td></tr>
</table>

Reference	**Wang 2013[232]**
Limitations	Risk of bias: Serious Indirectness: No indirectness
Comments	

Reference	**Wintermark 2003[248]**
Study type	Cross-sectional
Study methodology	Data source: Adult patients admitted to participating hospital department between July 1999 and September 2001. Recruitment: Consecutive patients included.
Number of patients	n = 50
Patient characteristics	Age, median (range): 51 (20-77) Gender (male to female ratio): 22/28 Setting: Department of Diagnostic and Interventional Radiology and Neurosurgery, University Hospital, Lausanne Country: Switzerland Inclusion criteria: Successive performance of MSCT angiography and IADS angiography within a 0-5 day interval. Exclusion criteria: Patients with low suspicion of SAH and did not undergo IADS angiography.
Target condition(s)	aSAH
Index test(s) and reference standard	<u>Index test</u> CTA CTA performed with a 4-detector row CT unit based on a standardised protocol. Two neuroradiologists independently reviewed the CTA results. <u>Reference standard</u> DSA Four vessel IADS angiography was performed via a tranfemoral approach after induction of general anaesthesia in cases of acute SAH workup. Three experienced interventional neuroradiologists who were not involved in the interpretation of MSCT angiograms performed the IADS and evaluated the results.

Reference	**Wintermark 2003[248]**			
	Time between measurement of index test and reference standard: within a 0-5 day interval			
2×2 table Per patient		Reference standard +	Reference standard −	Total
	Index test +	39		
	Index test −	1		
	Total	40	10	
2×2 table Per aneurysm		Reference standard +	Reference standard −	Total
	Index test +	46		
	Index test −	3		
	Total	49		
Statistical measures	Index text Per patient: Sensitivity 99% Specificity 95.2% PPV 99% NPV 95.2% Per aneurysm: Sensitivity 94.8% Specificity 95.2% PPV 98.9% NPV 80%			
Source of funding	Not reported			
Limitations	Risk of bias: Serious Indirectness: No indirectness			
Comments				

Reference	**Yan 2018[253]**
Study type	Retrospective Cross-sectional
Study methodology	Data source: From January 2010 to December 2015, 183 consecutive patients with SAH (GCS=15′) and 228 consecutive patients with non-SAH, confirmed by a non-contrast head computed tomographic scan. Recruitment: Consecutive patients included in analysis

Reference	Yan 2018[253]
Number of patients	n = 183
Patient characteristics	Age, mean (SD): 52.49 ± 12.90 Gender (male to female ratio): 85/98 Setting: The First Affiliated Hospital Country: China Inclusion criteria: Patients with SAH (GCS=15′) and 228 consecutive patients with non-SAH, confirmed by a non-contrast head computed tomographic scan. Exclusion criteria: Not reported
Target condition(s)	aSAH
Index test(s) and reference standard	<u>Index test</u> MRA All MRA examinations were performed on a 3.0 T system with a Sense-Head-8 receiver head coil. Briefly, the 3D-TOF-MRA was obtained using 3D-T1-weighted fast field (T1-FFE) sequences with TR/TE, 35/7; flip angle, 20°; field of view (FOV) 250×190×108; four slabs (180 slices), slice thickness, 0.8 mm; matrix, 732×1024; and an acquisition time of 8 min and 56 s. The acquired image data sets were then transferred to a workstation for 3D-volume inspection. <u>Reference standard</u> DSA All patients with possible intracranial aneurysms underwent 2D-DSA and VR-DSA of the affected and contralateral arteries, obtained in 2–4 projections. 2D-DSA was performed for the remaining arteries. A complete DSA was consisted of at least a 3-vessel 2D-DSA and a 2-vessel VR-DSA for each patient. Time between measurement of index test and reference standard: DSA was performed by an interventional neuroradiologist within 14 days after the MRA.
2×2 table Per patient	

	Reference standard +	Reference standard −	Total
Index test +	147	1	
Index test −	4	31	
Total			183

Reference	Yan 2018[253]			
2×2 table Per aneurysm		Reference standard +	Reference standard −	Total
	Index test +	181	2	
	Index test −	4	31	
	Total			218
Statistical measures	<u>Index text</u> Per patient: Sensitivity 97.4 (94.8-99.9) Specificity 96.9 (96.5-103.2) PPV 99.3 (98-100.7) NPV 88.6 (77.5-99.7) Per aneurysm: Sensitivity 97.8 (95.7-100) Specificity 93.9 (85.3-102.5) PPV 98.9 (97.4-100.4) NPV 88.6 (77.5-99.7)			
Source of funding	<u>Study was supported by the National Health and Family Planning Commission of the People's Republic of China</u>			
Limitations	Risk of bias: None Indirectness: No indirectness			
Comments	Only SAH subset included			

Reference	Yoon 2007[258]
Study type	Prospective Cross-sectional
Study methodology	Data source: Between December 2003 and June 2005, 121 consecutive patients with suspected intracranial aneurysms were referred to the participating hospital's institution. Recruitment: Consecutive patients recruited to study.
Number of patients	n = 85
Patient characteristics	Age, mean (SD): 49.6 (14.2) Gender (male to female ratio): 38/47 Setting:

Reference	**Yoon 2007[258]**			
	Country: Inclusion criteria: Patients were selected by the referring physicians for DSA on the basis of clinical or radiologic findings, including presentation with acute subarachnoid haemorrhage confirmed by nonenhanced CT or lumbar puncture (n=75); symptoms and signs suggestive of aneurysm, such as headache or cranial neuropathy (n=6); or a previous routine CT scan or MR angiogram suggesting the presence of an intracranial aneurysm (n=4). Exclusion criteria: Patients who had undergone prior surgical clipping or endovascular coiling for their intracranial aneurysm were excluded from the study because of author's belief that postoperative follow-up with MDCTA is a different issue. Patients who did not undergo DSA because of rapid clinical deterioration were also excluded from our study.			
Target condition(s)	aSAH			
Index test(s) and reference standard	Index test CTA All MDCTA examinations were performed with a 16-channel MDCT scanner. Parameters for the CT angiographic acquisition were 1-mm section thickness, 6-mm table feed per rotation, 0.5-second gantry rotation time, pitch of 6, 120 kV, and 200–280mA,512x512 matrix, and 20-cm FOV. MDCTA was performed in all patients without any technical failures or complications during scanning. Reference standard DSA All DSA was performed transfemorally with 5F catheters by using a DSA unit with an image intensifier matrix of 1024 x 1024 pixels. DSA was performed with bilateral selective internal carotid artery injections and either unilateral or bilateral vertebral artery injections, as necessary. Time between measurement of index test and reference standard: All patients in the series underwent MDCTA before DSA, with the longest interval between the 2 examinations being 3 days (mean interval between examinations, 13.7 hours ± 6.9).			
2×2 table Per patient		Reference standard +	Reference standard −	Total
	Index test +		0	
	Index test −		14	
	Total	71	14	85
2×2 table Per aneurysm		Reference standard +	Reference standard −	Total
	Index test +	86	1	87
	Index test −	7	14	21

Reference	Yoon 2007[258]			
	Total	93	15	108
Statistical measures	Index text Per aneurysm: Sensitivity 92.5% Specificity 93.3% PPV 98.9% NPV 66.7%			
Source of funding	Not reported			
Limitations	Risk of bias: None Indirectness: No indirectness			
Comments				

Reference	Zhang 2010[263]
Study type	Cross-sectional study
Study methodology	Data source: Department of Medical Imaging, Jinling Hospital, Clinical School of Medical College, Nanjing University Recruitment: Between June and November 2008, with spontaneous subarachnoid haemorrhage were enrolled in this prospective study
Number of patients	n = 46
Patient characteristics	Age, mean (SD): 52 ± 8 Gender (male to female ratio): 21/25 Setting: Jinling Hospital, Nanjing University Country: China Inclusion criteria: The inclusion criteria were that the patient have clinical evidence of intracranial aneurysm and be able to undergo both CTA and DSA. The indication for CTA and DSA was established on the basis of the clinical findings. Exclusion criteria: The exclusion criteria for CT were history of allergy to iodine-containing contrast medium, renal insufficiency (creatinine level, ≥ 120 μmol/L), pregnancy, hemodynamic instability, and previous coiling or clipping surgery

Reference	Zhang 2010[263]
Target condition(s)	aSAH
Index test(s) and reference standard	<u>Index test - CTA</u> Dual-energy CTA and digital subtraction CTA were performed with a dual-source CT system (Somatom Definition, Siemens Healthcare). Dual-energy CTA is performed with only one acquisition. The CT parameters in the dual-energy mode were 140- and 80-kV tube voltage at 51 and 360 effective mAs, 0.5-second rotation time, collimation of 64 × 0.6 mm with z-flying focal spot, and pitch of 0.6. The 140- and 80-kV images (dual-energy images) were reconstructed separately in sections that were 0.75 mm wide at 0.5-mm increments with a D30 kernel, for a field of view of 180 mm2. The contrast-enhanced CT scan in the dual-energy mode was obtained with a 4.0-mL/s injection of 80 mL of iopromide (Ultravist 300 mg I/ mL, Bayer Schering Pharma) followed by 30 mL of saline solution into the antecubital vein through an 18-gauge catheter. <u>Reference standard - DSA</u> DSA was performed with femoral catheterization by the Seldinger technique with a biplane DSA unit with rotational capabilities (Axiom Artis dTA, Siemens Healthcare). Typically, 6–9 mL of non-ionic contrast medium (iopromide, Ultravist 300 mg I/mL) was used per acquisition, usually consisting of one anteroposterior, one lateral, and one or two oblique views. The acquisitions consisted of a 38-cm2 field of view for the anteroposterior images, 30-cm2 field of view for the lateral and oblique images), and a 1,024 × 1,024 matrix. The spatial resolution was 0.32 × 0.32 mm. With the catheter in each of the three major arteries (both ICAs, one or more vertebral arteries), standard anteroposterior, lateral, and oblique DSA images were obtained. All analyses of dual-energy CTA and digital subtraction CTA images were performed in consensus by the two neuroradiologists. After consensus was reached in each case as to the presence of an aneurysm, a staff neuroradiologist reviewer blinded to the dual-energy CTA results measured the maximum size of each aneurysm on 3D DSA images in the optimal projection for obtaining correlation of the maximum size between techniques. Time between measurement of index test and reference standard: Not specified

2×2 table Per patient		Reference standard +	Reference standard −	Total
	Index test +	34	0	34
	Index test −	1	11	12
	Total	35	11	46

2×2 table Per aneurysm		Reference standard +	Reference standard −	Total
	Index test +	38	0	38
	Index test −	2	696	698
	Total	40	696	736

Reference	**Zhang 2010[263]**
Statistical measures	<u>Index text</u> Per patient Sensitivity: 97.1% Specificity: 100% PPV: 100% NPV: 91.7% Per aneurysm: Sensitivity: 95.0% Specificity: 100% PPV: 100% NPV: 99.7%
Source of funding	Not specified
Limitations	Risk of bias: Serious Indirectness: No indirectness
Comments	

Appendix E: Coupled sensitivity and specificity forest plots and sROC curves

E.1 Coupled sensitivity and specificity forest plots

Figure 2: Diagnostic test accuracy for CTA (per patient) (Reference standard: DSA)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Aulbach 2016	70	0	1	45	0.99 [0.92, 1.00]	1.00 [0.92, 1.00]
Chen 2013	197	0	1	84	0.99 [0.97, 1.00]	1.00 [0.96, 1.00]
Fluss 2020	29	1	0	7	1.00 [0.88, 1.00]	0.88 [0.47, 1.00]
Gamal 2015	19	2	1	0	0.95 [0.75, 1.00]	0.00 [0.00, 0.84]
Haghighatkhah 2008	35	5	0	45	1.00 [0.90, 1.00]	0.90 [0.78, 0.97]
Hashemi 2011	81	1	0	17	1.00 [0.96, 1.00]	0.94 [0.73, 1.00]
Jayaraman 2004	19	1	2	13	0.90 [0.70, 0.99]	0.93 [0.66, 1.00]
Kelliny 2011	160	6	3	72	0.98 [0.95, 1.00]	0.92 [0.84, 0.97]
Lu 2012	398	12	9	94	0.98 [0.96, 0.99]	0.89 [0.81, 0.94]
Luo 2012	42	0	0	14	1.00 [0.92, 1.00]	1.00 [0.77, 1.00]
Lv 2011	95	0	1	0	0.99 [0.94, 1.00]	Not estimable
MacKinnon 2013	69	5	2	100	0.97 [0.90, 1.00]	0.95 [0.89, 0.98]
Milosevic 1999	39	1	3	9	0.93 [0.81, 0.99]	0.90 [0.55, 1.00]
Ni 2016	57	1	1	46	0.98 [0.91, 1.00]	0.98 [0.89, 1.00]
Papke 2007	62	0	1	24	0.98 [0.91, 1.00]	1.00 [0.86, 1.00]
Pedersen 2001	112	2	9	41	0.93 [0.86, 0.97]	0.95 [0.84, 0.99]
Poon 2006	11	0	0	0	1.00 [0.72, 1.00]	Not estimable
Pozzi-Mucelli 2007	20	0	0	9	1.00 [0.83, 1.00]	1.00 [0.66, 1.00]
Ramgren 2015	209	12	19	87	0.92 [0.87, 0.95]	0.88 [0.80, 0.94]
Romijn 2008	87	2	1	18	0.99 [0.94, 1.00]	0.90 [0.68, 0.99]
Saboori 2011	17	0	2	11	0.89 [0.67, 0.99]	1.00 [0.72, 1.00]
Taschner 2007	21	1	0	5	1.00 [0.84, 1.00]	0.83 [0.36, 1.00]
Wang 2010	93	0	1	19	0.99 [0.94, 1.00]	1.00 [0.82, 1.00]
Zhang 2010	34	0	1	11	0.97 [0.85, 1.00]	1.00 [0.72, 1.00]

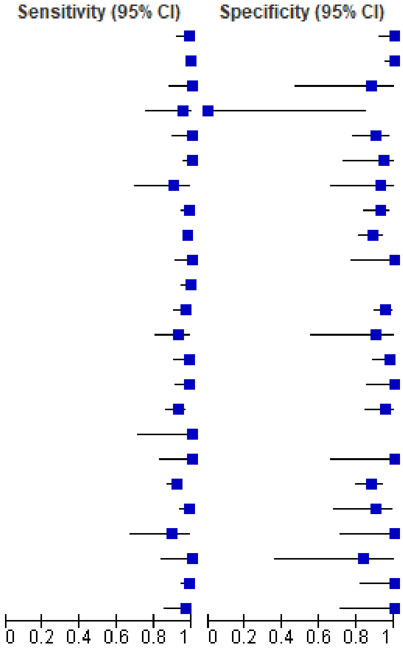


Figure 3: Diagnostic test accuracy for CTA (per aneurysm) (Reference standard: DSA)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Anderson 1997	37	1	6	9	0.86 [0.72, 0.95]	0.90 [0.55, 1.00]
Aulbach 2016	73	1	1	45	0.99 [0.93, 1.00]	0.98 [0.88, 1.00]
Chen 2009	90	0	2	198	0.98 [0.92, 1.00]	1.00 [0.98, 1.00]
Chen 2010	282	4	5	128	0.98 [0.96, 0.99]	0.97 [0.92, 0.99]
Chen 2013	237	0	2	84	0.99 [0.97, 1.00]	1.00 [0.96, 1.00]
Dammert 2004	46	1	5	8	0.90 [0.79, 0.97]	0.89 [0.52, 1.00]
Gamal 2015	18	2	2	0	0.90 [0.68, 0.99]	0.00 [0.00, 0.84]
Gerardin 2009	37	0	1	8	0.97 [0.86, 1.00]	1.00 [0.63, 1.00]
Kangasniemi 2004	170	8	8	260	0.96 [0.91, 0.98]	0.97 [0.94, 0.99]
Kouskouras 2004	28	3	1	3	0.97 [0.82, 1.00]	0.50 [0.12, 0.88]
Lenhart 1997	50	0	1	14	0.98 [0.90, 1.00]	1.00 [0.77, 1.00]
Lu 2012	443	13	16	94	0.97 [0.94, 0.98]	0.88 [0.80, 0.93]
McKinney 2008	37	1	1	2	0.97 [0.86, 1.00]	0.67 [0.09, 0.99]
Milosevic 1999	42	1	3	9	0.93 [0.82, 0.99]	0.90 [0.55, 1.00]
Ni 2016	67	2	2	46	0.97 [0.90, 1.00]	0.96 [0.86, 0.99]
Pedersen 2001	131	2	13	41	0.91 [0.85, 0.95]	0.95 [0.84, 0.99]
Philipp 2017	306	24	125	125	0.71 [0.66, 0.75]	0.84 [0.77, 0.89]
Poon 2006	12	0	0	0	1.00 [0.74, 1.00]	Not estimable
Pozzi-Mucelli 2007	26	0	2	9	0.93 [0.76, 0.99]	1.00 [0.66, 1.00]
Preda 1998	22	2	0	7	1.00 [0.85, 1.00]	0.78 [0.40, 0.97]
Ramasundara 2010	34	1	0	9	1.00 [0.90, 1.00]	0.90 [0.55, 1.00]
Ramgren 2015	266	12	19	88	0.93 [0.90, 0.96]	0.88 [0.80, 0.94]
Taschner 2007	24	1	0	5	1.00 [0.86, 1.00]	0.83 [0.36, 1.00]
Teksam 2005	41	8	7	15	0.85 [0.72, 0.94]	0.65 [0.43, 0.84]
Uysal 2005	32	0	1	0	0.97 [0.84, 1.00]	Not estimable
Van Zwam 2012	60	1	6	17	0.91 [0.81, 0.97]	0.94 [0.73, 1.00]
Vieco 1995	29	0	1	0	0.97 [0.83, 1.00]	Not estimable
Wang 2010	103	3	2	19	0.98 [0.93, 1.00]	0.86 [0.65, 0.97]
Wang 2013	52	0	2	0	0.96 [0.87, 1.00]	Not estimable
Yoon 2007	86	1	7	14	0.92 [0.85, 0.97]	0.93 [0.68, 1.00]
Zhang 2010	38	0	2	696	0.95 [0.83, 0.99]	1.00 [0.99, 1.00]

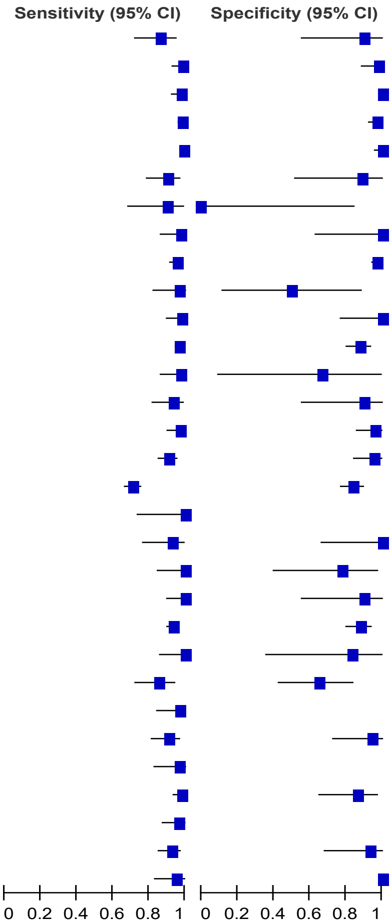


Figure 4: Diagnostic test accuracy for MRA (per patient) (Reference standard: DSA)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Chen 2012	132	1	4	28	0.97 [0.93, 0.99]	0.97 [0.82, 1.00]
Chung 1999	38	0	1	0	0.97 [0.87, 1.00]	Not estimable
Farahmand 2013	42	1	9	8	0.82 [0.69, 0.92]	0.89 [0.52, 1.00]
Ida 1997	25	0	1	2	0.96 [0.80, 1.00]	1.00 [0.16, 1.00]
Li 2017	219	5	4	49	0.98 [0.95, 1.00]	0.91 [0.80, 0.97]
Yan 2018	147	1	4	31	0.97 [0.93, 0.99]	0.97 [0.84, 1.00]

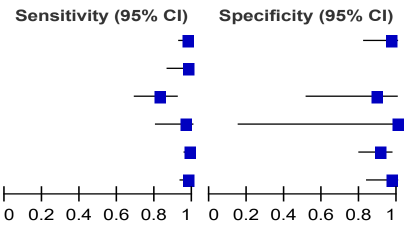
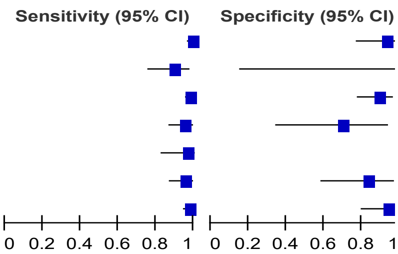


Figure 5: Diagnostic test accuracy for MRA (per aneurysm) (Reference standard: DSA)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Chen 2012	162	2	1	27	0.99 [0.97, 1.00]	0.93 [0.77, 0.99]
Ida 1997	35	0	4	2	0.90 [0.76, 0.97]	1.00 [0.16, 1.00]
Li 2017	260	6	5	49	0.98 [0.96, 0.99]	0.89 [0.78, 0.96]
Schmieder 1999	61	3	3	7	0.95 [0.87, 0.99]	0.70 [0.35, 0.93]
Shahzad 2011	29	0	1	0	0.97 [0.83, 1.00]	Not estimable
Van Zwam 2012	62	3	3	15	0.95 [0.87, 0.99]	0.83 [0.59, 0.96]
Yan 2018	181	2	4	31	0.98 [0.95, 0.99]	0.94 [0.80, 0.99]



E.2 SROC curves

Key:

- Solid line represents the ROC summary curve
- Dotted line represents the 95% confidence region of the ROC
- Solid circle represents pooled ROC
- Clear circles represent ROC of individual studies

Figure 6: Diagnostic test accuracy for CTA (per patient) (pooled) (Reference standard: DSA)

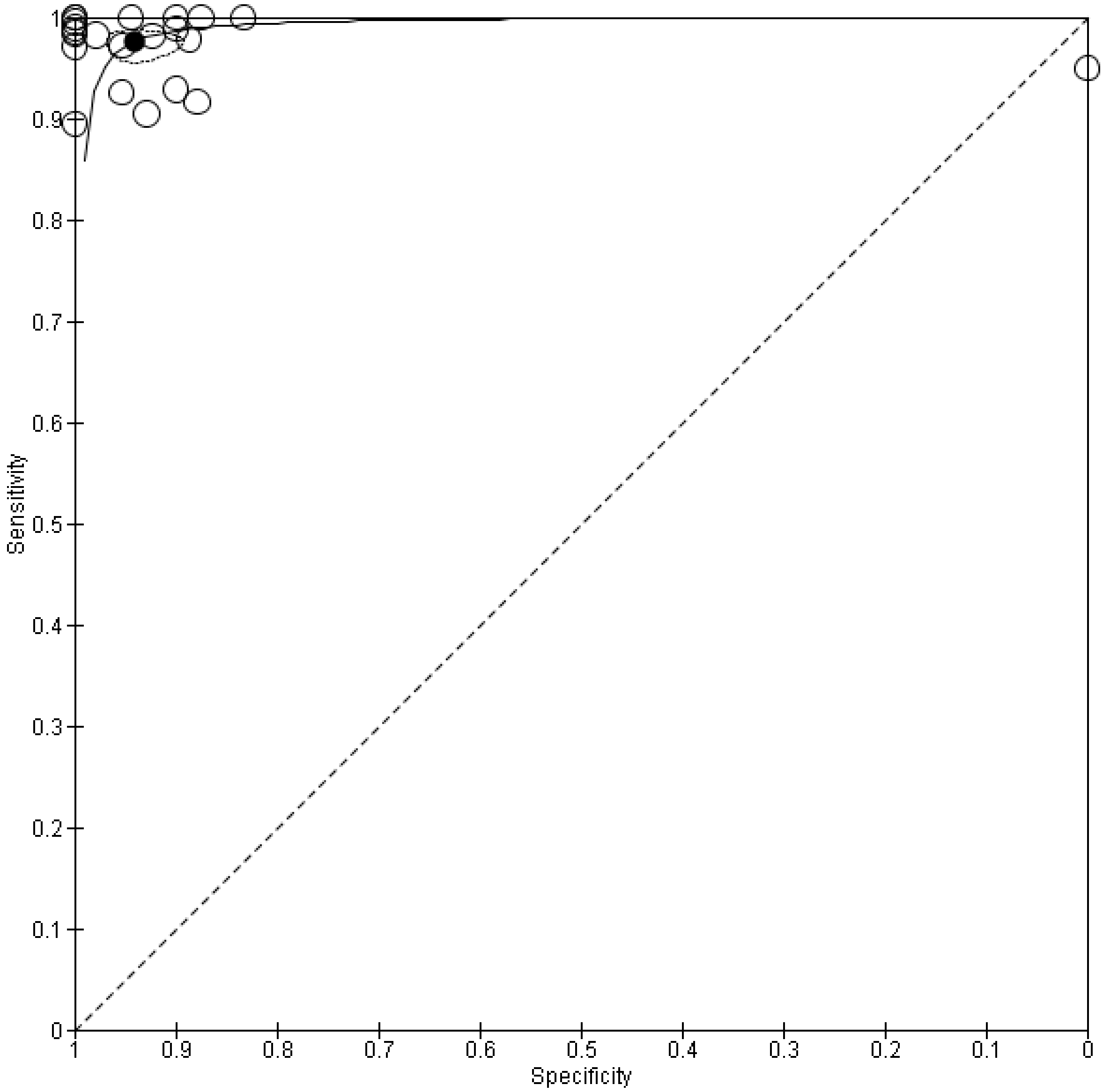


Figure 7: Diagnostic test accuracy for CTA (per aneurysm) (pooled) (Reference standard: DSA)

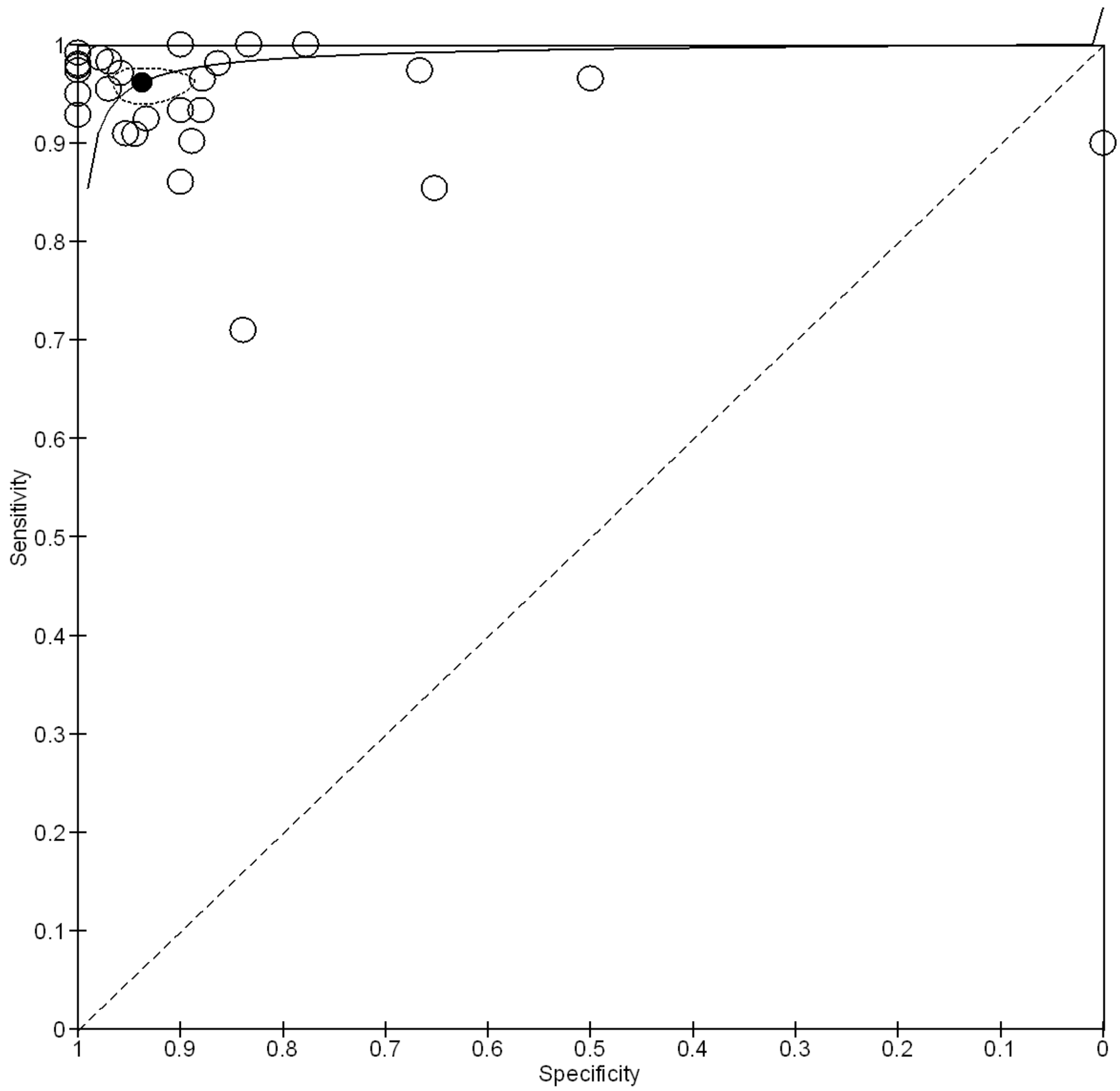
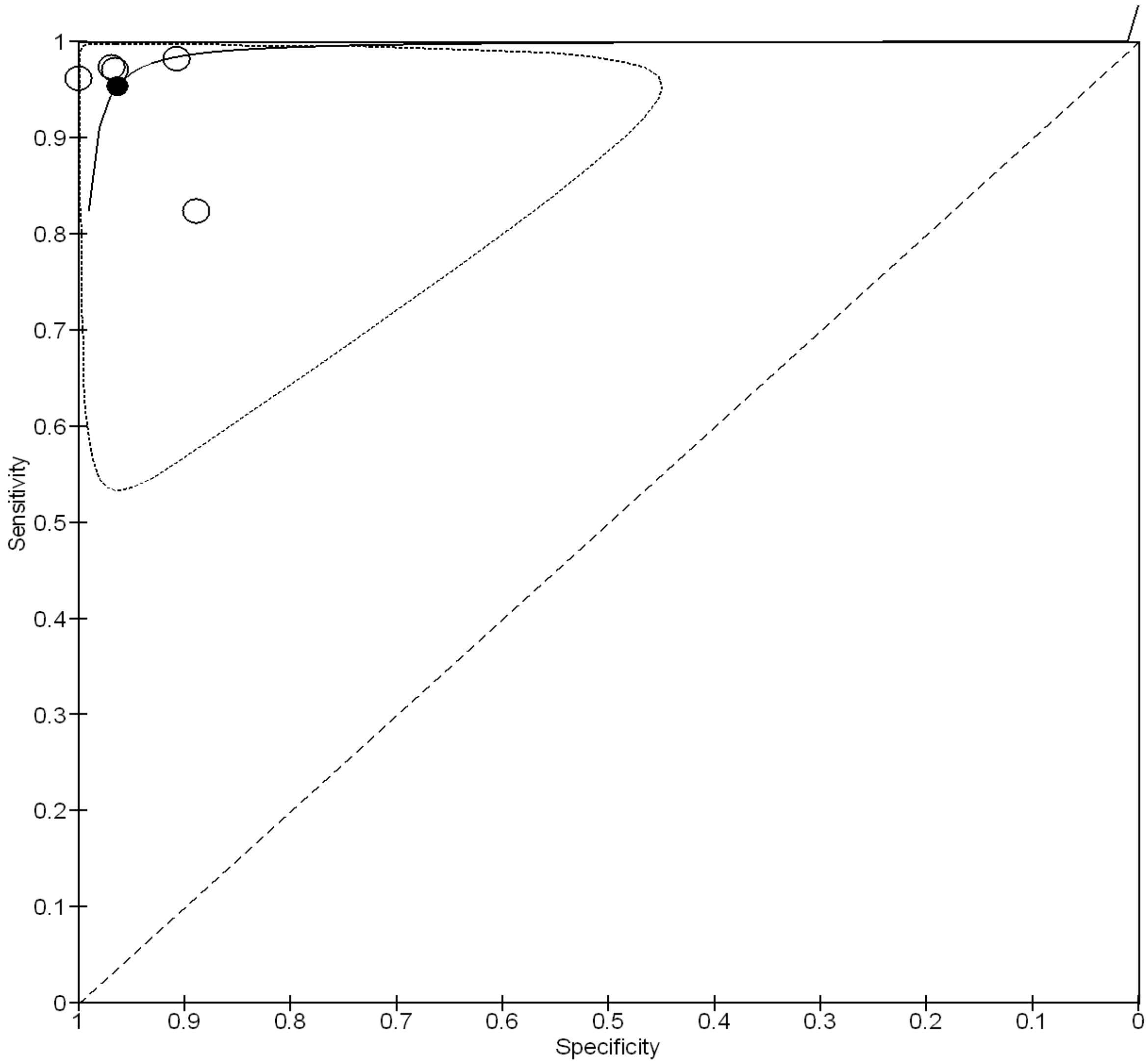
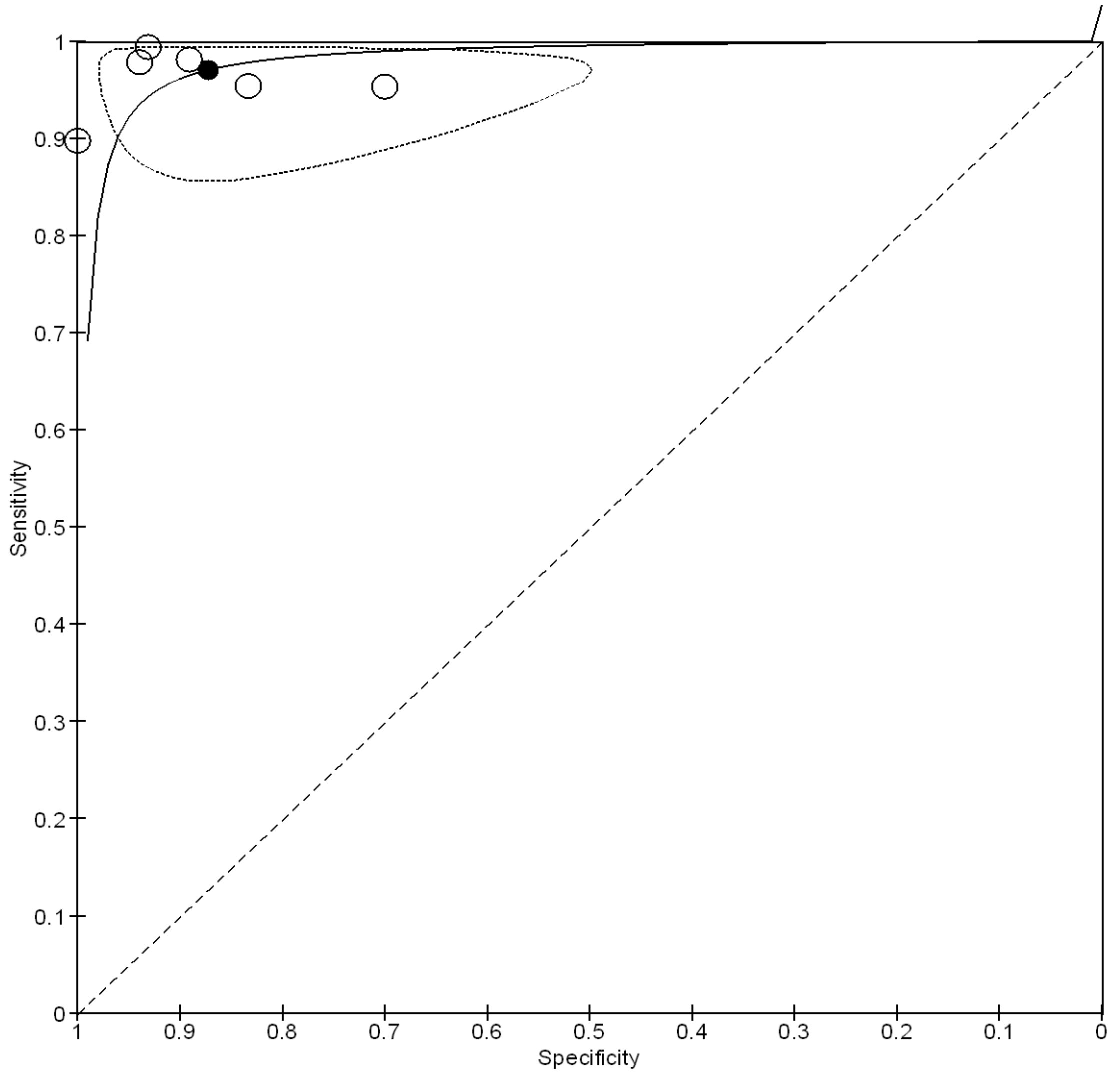


Figure 8: Diagnostic test accuracy for MRA (per patient) (pooled) (Reference standard: DSA)



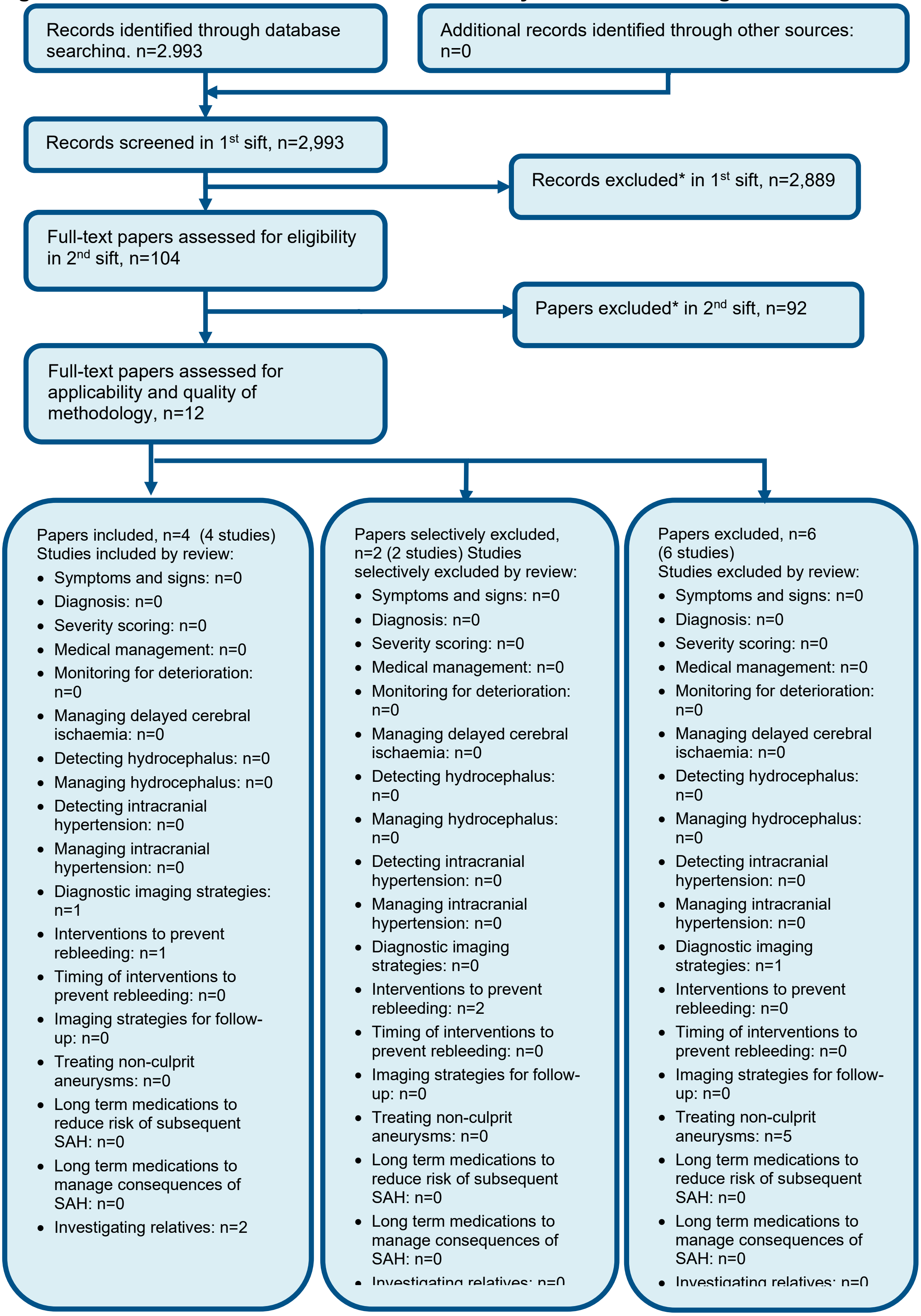
1 **Figure 9: Diagnostic test accuracy for MRA (per aneurysm) (pooled) (Reference**
2 **standard: DSA)**



3

Appendix F: Health economic evidence selection

Figure 10: Flow chart of health economic study selection for the guideline



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

1

Appendix G: Health economic evidence tables

<table>
<tr><td>Study</td><td colspan="4">Sailer 2013[191]</td></tr>
<tr><td>Study details</td><td>Population & interventions</td><td>Costs</td><td>Health outcomes</td><td>Cost effectiveness</td></tr>
<tr>
<td>Economic analysis: CUA (health outcome: QALYs)

Study design: Probabilistic decision analytic model
Approach to analysis: Decision tree of diagnostic pathway and subsequent treatment including three outcomes for patients: well, disabled, dead.
Patients presenting with acute SAH without presence of a ruptured aneurysm were assumed to have no other intracranial vascular pathology to be treated.
Perspective: Dutch hospital
Time horizon: 1 year
Treatment effect duration: n/a
Discounting: Costs: 4%; Outcomes: 1.5%</td>
<td>Population:
Patients with acute non-traumatic subarachnoid haemorrhage

Cohort settings:
Start age: NR
Male: NR

Intervention 1:
Digital subtraction angiography (DSA)
Intervention 2:
Computed tomographic angiography (CTA) - if no aneurysm was detected, DSA was also performed.
Intervention 3:
Magnetic resonance angiography (MRA) - if no aneurysm was detected, DSA was also performed.</td>
<td>Total costs (mean per patient):
Intervention 1: £32,732
Intervention 2: £33,505
Intervention 3: £34,382

For incremental analysis see cost effectiveness column

Currency & cost year:
2010 Dutch Euros (presented here as 2010 UK pounds[(a)])

Cost components incorporated:
Diagnostic tests, personnel, equipment, materials, maintenance, housing, cleaning, administration and overheads. One year costs of surgical clipping or endovascular coiling.</td>
<td>QALYs (mean per patient):
Intervention 1: 0.6039
Intervention 2: 0.5983
Intervention 3: 0.5947

For incremental analysis see cost effectiveness column</td>
<td>Full incremental analysis (pa):[(c) (d)]
<table>
<tr><td>Int</td><td>Cost</td><td>QALY</td><td>Inc cost</td><td>Inc QALY</td><td>ICER</td></tr>
<tr><td>3</td><td>£34,382</td><td>0.5947</td><td colspan="3">Baseline</td></tr>
<tr><td>2</td><td>£33,505</td><td>0.5983</td><td>Saves £773</td><td>0.006</td><td>Extendedly dominated by 1</td></tr>
<tr><td>1</td><td>£32,732</td><td>0.6039</td><td>Saves £1,650</td><td>0.009</td><td>Dominant</td></tr>
</table>
ICER:
Intervention 1 dominates (lowest cost and highest QALYs)

Analysis of uncertainty:
Probability intervention cost effective £20/£30K threshold: NR
Probability intervention 1 (DSA) cost effective ~£65K (€80K): 98-100%. However, this is not applicable for the NICE reference case.

Higher sensitivity and specificity for detection of aneurysms and determination of feasibility of coiling for CTA and MRA up to 96% or a reduction of sensitivity and specificity for DSA to 90% yielded stable results.
Results remained stable for the assumption of higher costs for DSA up to factor 2.8.
Assuming the same treatment cost for coiling and clipping does not change the conclusion.</td>
</tr>
</table>

				These sensitivity analyses were undertaken using a willingness to pay threshold of ~£65K and therefore it is difficult to interpret these results. **Scenario analysis:** Included two additional strategies to assess the cost effectiveness of CTA followed by DSA if aneurysm deemed not suitable for coiling on CTA, and MRA followed by DSA if aneurysm deemed not suitable for coiling on MRA. In this scenario CTA followed by DSA is the most cost effective strategy (lowest cost and highest QALYs).
Data sources				
Health outcomes: Diagnostic accuracy data from van Zwam 2012[225]. Diagnostic accuracy for detecting aneurysm - CTA: sensitivity = 91.5% (85.0%-95.5%), specificity = 94.4% (79.0% -99.0%); MRA: sensitivity = 95.4% (89.8% - 98.1%), specificity = 83.3% (66.5% - 93.0%). Diagnostic accuracy for determining the feasibility of coiling – CTA: sensitivity = 71.9% (59.0% – 82.1%), specificity = 75.4% (62.0%-85.5%); MRA: sensitivity = 60.6% (48.2% - 71.7%), specificity = 81.4% (68.7% - 89.9%). DSA as reference standard had sensitivity and specificity of 100% for aneurysm detecting and suitability of coiling. Health outcome after 1 year of treatment was derived from ISAT. **Quality-of-life weights:** Utility values identified from Post et al. 2001 which uses Assessment of Quality of Life questionnaire, Australia. **Cost sources:** Cost of diagnostic imaging taken from Manual for costing research, Dutch Health Care Insurance Board. One year costs of surgical clipping or endovascular coiling were taken from Wolstenholme 2010[250].				
Comments				
Source of funding: NR. **Limitations:** Dutch 2010 unit costs may not reflect current NHS context – current UK NHS cost of DSA much higher than that used in the economic evaluation. The calculation of QALYs is not in line with the NICE reference case, as utility values were not derived from EQ-5D. Discounting of costs and outcomes not in line with NICE reference case. However, as the analysis only assess a one year time horizon this is likely to have a minimal effect. Diagnostic accuracy data taken from one study and therefore may not reflect the full body of available evidence. One year time horizon may not capture full costs and health benefits. **Other:** None.				
Overall applicability:[(d)] Partially applicable **Overall quality:**[(e)] Potentially serious limitations				

Abbreviations: CUA= cost–utility analysis; ICER= incremental cost-effectiveness ratio; NR= not reported; QALYs= quality-adjusted life years
(a) Converted using 2010 purchasing power parities[162]
(b) Intervention number in order of least to most effective (in terms of QALYs)
(c) Full incremental analysis of available strategies: first strategies are ruled out that are dominated (another strategy is more effective and has lower costs) or subject to extended dominance (the strategy is more effective and more costly but the incremental cost effectiveness ratio is higher than the next most effective option and so it would never be the most cost effective option); incremental costs, incremental effects and incremental cost effectiveness ratios are calculated for the remaining strategies by comparing each to the next most effective option

(d) Directly applicable / Partially applicable / Not applicable
(e) Minor limitations / Potentially serious limitations / Very serious limitations

Appendix H: Excluded studies

H.1 Excluded clinical studies

Table 11: Studies excluded from the clinical review

Reference	Reason for exclusion
Ahmed 2019[2]	Inappropriate population – cerebral aneurysm follow up
Anderson 1999[4]	Inappropriate study design – not all patients had reference test
Atlas 1997[6]	Incorrect population – cerebral aneurysm
Azhari 2018[8]	Inappropriate population – cerebral aneurysm follow up
Basiratnia 2004[9]	Inappropriate population – people with headache, convulsion or cranial nerve compression
Bechan 2015[10]	Inappropriate comparison – CTA compared to 3D rotational angiography
Bekelis 2012[11]	Inappropriate population – non SAH patients
Bell 2020[12]	Inappropriate study design - literature review
Bharatha 2010[13]	Inappropriate population – CTA compared to DSA
Brinjikji 2009[14]	Inappropriate comparison – comparison of different DSA techniques
Brouwers 2013[15]	Inappropriate study design – no relevant outcomes
Buhk 2009[16]	Inappropriate population – cerebral aneurysm follow up
Burkhardt 2017[17]	Inappropriate study design – no relevant outcomes
Carstairs 2006[18]	Inappropriate comparison – CT compared to CT/LP
Carvi y Nievas 2010[19]	Inappropriate study design – narrative review
Catapano 2019[20]	Inappropriate study design - No relevant outcomes
Chang 2008[22]	Inappropriate comparison – surgery as reference standard
Chalouhi 2020[21]	Inappropriate intervention – combined MRI/MRA
Chappell 2003[23]	Systematic review - references screened
Chen 2001[24]	Inappropriate comparison – no reference test
Chen 2008[28]	Inappropriate comparison – not all patients had reference standard
Chen 2014[26]	Inappropriate study design – no relevant outcomes
Chen 2018[34]	Systematic review - references screened
Chen 1999[27]	Inappropriate comparison – unclear reference standard
Chen 2017[30]	Inappropriate population – intracranial aneurysm
Chen 2016[32]	Inappropriate population – cerebral aneurysm follow up
Chen 2017[25]	Inappropriate population – posterior inferior cerebellar artery aneurysm
Cho 2014[36]	Inappropriate population – cerebral aneurysm follow up
Cortnum 2010[39]	Inappropriate comparison – no reference test
Cruz 2011[40]	Inappropriate comparison – negative CTA and DSA
D'Sa 2020[41]	Inappropriate population - patients with vertebral artery fenestration, No DSA
Dai 2020[42]	Inappropriate study design - Tool development study for automatic detection of aneurysms from medical images. CTA images were studied
Daniele 2002[44]	Inappropriate study design – narrative review

Reference	Reason for exclusion
Dehdashti 2006[45]	Inappropriate population – imaging post intervention
Delgado Almandoz 2009[47]	Inappropriate population – intraparenchymal cerebral haemorrhage
Delgado Almandoz 2013[46]	Inappropriate study design – no relevant outcomes
Denby 2020[48]	Systematic review: references checked
Deutschmann 2007[49]	Inappropriate population – cerebral aneurysm follow up
Dundar, 2019[51]	Inappropriate study design – no relevant outcomes
El Khaldi 2007[52]	Incorrect intervention – not all patients had pre-intervention DSA
Elsamman 2010[53]	Inappropriate population – not all patients had reference test
Feng 2016[57]	Systematic review - references screened
Feng 2002[56]	Inappropriate population – unclear if all patients had reference test
Ferre 2009[59]	Inappropriate population – imaging post intervention
Flores, 2020[60]	Inappropriate population – patients without aneurysmal SAH
Fontanella 2011[62]	Inappropriate study design – no relevant outcomes
Franklin 2010[63]	Inappropriate population – mixed population (IVH, SAH, headache)
Gandhi 2004[65]	Inappropriate study design – literature review
Garrett 2018[66]	Inappropriate comparison – CTA compared to CT for brain death
Gerardin 2010[68]	Inappropriate population – postoperative clipped aneurysms
Gill 2019[69]	Inappropriate study design - non-comparative study/case series
Golitz 2014[70]	Inappropriate comparison – postoperative imaging
Gouliamos 1992[71]	Inappropriate population – mixed population (pre/post intervention)
Grandin 1998[72]	Inappropriate population – mixed population & unclear outcome data
Granja 2020[73]	Systematic review: references checked
Griffiths 2006[74]	Inappropriate study design – no relevant outcomes
Gross 2012[75]	Inappropriate comparison – no reference test
Guo 2014[76]	Systematic review - references screened
HaiFeng 2017[78]	Systematic review - references screened
Han 2007[79]	Inappropriate comparison – postoperative follow up
Hanihara 2019[80]	Inappropriate study design - non comparative study/ case series
Hanley 2008[81]	Inappropriate study design – no relevant outcomes (test correlation data)
Hauser 2019[83]	No relevant outcome - vasospasm
Heit 2016[84]	Incorrect intervention – DSA in CTA negative patients
Hirai 2003[85]	Inappropriate comparison – different DSA techniques
Hochmuth 2002[86]	Inappropriate comparison – 3D rotational angiography vs DSA
Hope 1996[87]	Inappropriate comparison – unclear if reference test is DSA
Horikoshi 1994[88]	Inappropriate population – majority non SAH
Huttner 2006[89]	Inappropriate population – perimesecephalic SAH/ repeated DSA
Iosif 2018[91]	Inappropriate study design – no relevant outcomes
Ishida 2001[92]	Inappropriate outcome data – DSA and CTA comparison
Jabbarli 2014[93]	Inappropriate comparison – unclear reference standard
Jager 2000[94]	Inappropriate population – pre and post intervention
Jiang 2015[96]	Inappropriate comparison – dual energy angiography compared to non-contrast CT
Jung 2006[97]	Inappropriate analysis – DSA negative patients only
Kahara 1999[98]	Inappropriate population – cerebral aneurysm follow up

Reference	Reason for exclusion
Karamessini 2004[100]	Inappropriate comparison – CTA/DSA compared to surgical findings
Kato 2001[101]	Inappropriate population – cerebral aneurysm follow up
Kau 2009[102]	Inappropriate population – cerebral aneurysm follow up
Kaufmann 2010[103]	Inappropriate population – cerebral aneurysm follow up
Kawashima 2005[104]	Inappropriate comparison - 3D digital subtraction angiography vs DSA
Killeen 2014[106]	Inappropriate study design – detecting DCI / vasospasm
Kim 2020[107]	Inappropriate study design – no relevant outcome
Kim 2020[108]	Inappropriate comparison - detection of junctional dilatation
Kitkhuandee 2012[109]	Inappropriate study design – no relevant outcomes
Kokkinis 2008[110]	Inappropriate population – pre and post intervention
Korogi 1999[111]	Inappropriate comparison – no reference test
Korogi 1996[112]	Inappropriate population - various intracranial vascular lesions
Kowalewski 2008[114]	Inappropriate comparison – CTA compared to CT
Ku 2010[115]	Inappropriate intervention – investigation of false negative DSA
Kwee 2007[116]	Inappropriate population – cerebral aneurysm follow up
Lane 2015[117]	Inappropriate population – post intervention imaging
Lee 2005[118]	Inappropriate population – post intervention imaging
Leemans 2019[119]	Inappropriate comparison – all patients with unruptured intracranial aneurysm
Leung 2012[121]	Inappropriate study design – no relevant outcomes
Levent 2014[122]	Inappropriate population – cerebral aneurysm follow up
Li 2011[125]	Inappropriate population - mixed population (less than 50% SAH)
Li 2009[127]	Inappropriate population – intracranial aneurysms
Li 2009[126]	Inappropriate population – intracranial aneurysms
Lim 2014[128]	Inappropriate population – CT scan negative patients
Lubicz 2008[130]	Inappropriate population – cerebral aneurysm follow up
Ma 2012[133]	Systematic review – references checked
Mallouhi 2003[135]	Inappropriate population - mixed population (less than 50% SAH)
Marshall 2010[136]	Inappropriate study design – literature review
Maslehaty 2012[137]	Inappropriate study design – no relevant outcomes
Matsumoto 2001[138]	Inappropriate study design – non comparative study with 3D CTA
Menendez 2016[140]	Inappropriate study design – no relevant outcomes
Menke 2011[141]	Systematic review - references screened
Metens 2000[142]	Inappropriate population – unclear if aneurysms SAH
Michelozzi 2018[143]	Inappropriate study design - non-comparative study/case series
Mine 2015[146]	Inappropriate population – unruptured aneurysms
Mizutani 2019[147]	Inappropriate population - patients with arteriovenous shunt disease, intracranial tumour and 1 patient with intracranial haemorrhage
Mohan 2009[150]	Inappropriate population – SAH, arteriovenous malformation and sinus thrombosis
Mohan 2019[148]	Systematic review - references screened
Mohan 2019[149]	Systematic review - references screened
Moran 2010[151]	Inappropriate study design - narrative review
Moscovici 2013[152]	Inappropriate study design – no relevant outcomes
Murai 1999[153]	Inappropriate comparison – no reference test

Reference	Reason for exclusion
Nakatsuka 2000[154]	Incorrect intervention – not all patients had reference test
Ni 2013[158]	Inappropriate population –cerebral aneurysm follow up
Nijjar 2007[159]	Inappropriate comparison – no reference test
Ogawa 1996[160]	Inappropriate population – cerebral aneurysm follow up
Okahara 2002[161]	Inappropriate population – SAH and ischaemic stroke
Pavcec 2006[164]	Inappropriate population – Circle of Willis aneurysms
Payner 1998[165]	Inappropriate intervention – intraoperative imagine with mixed population
Pechlivanis 2009[166]	Incorrect population - DSA in CTA negative patients
Pechlivanis 2005[168]	Incorrect population - DSA in CTA negative patients
Pechlivanis 2008[167]	Inappropriate population – MRA post intervention
Pechlivanis 2011[169]	Inappropriate population - DSA in CTA negative patients
Peker 2014[171]	Inappropriate study design – no relevant outcomes
Pierot 2012[173]	Inappropriate population – cerebral aneurysm follow up
Piotin 2003[175]	Inappropriate study design – no relevant outcomes
Pradilla 2013[178]	Inappropriate population – unruptured aneurysms
Prestigiacomo 2010[180]	Incorrect intervention - DSA in CTA negative patients
Raaymakers 1999[181]	Inappropriate population – relatives of people with SAH
Ramgren 2008[183]	Inappropriate population – cerebral aneurysm follow up
Rosch 2018[186]	Inappropriate study design - non-comparative study/case series
Ross 1990[187]	Inappropriate population – cerebral aneurysm follow up
Sagara 2005[190]	Inappropriate intervention – post intervention imaging
Sailer 2014[192]	Systematic review- references screened
Sakuma 2006[193]	Inappropriate intervention – post intervention imaging
Sankhla 1996[194]	Inappropriate population – mixed population (pre and post intervention imaging)
Schaafsma 2010[195]	Inappropriate intervention – post intervention imaging
Schuierer 1992[197]	Inappropriate study design – no relevant outcomes
Sen 2008[198]	Inappropriate study design – literature review
Song 2020[201]	Inappropriate population - follow up of remnant aneurysms
Sun 2013[204]	Inappropriate population - cerebral aneurysm surgery follow-up
Sun 2012[203]	Inappropriate population – intracranial aneurysms
Suzuki 2020[205]	Inappropriate comparison - dual phase CTA was performed on all patients, the frequency of contrast extravasation was compared between phases/ no DSA
Takao 2010[206]	Inappropriate study design – no relevant outcomes
Tan 2011[207]	Inappropriate population – arteriovenous malformation
Tang 2007[208]	Inappropriate population – unruptured aneurysms
Teksam 2004[210]	Inappropriate population – cerebral aneurysm follow up
Thaker 2012[212]	Inappropriate intervention - post intervention imaging
Thines 2010[213]	Inappropriate intervention – post intervention imaging
Timsit 2016[214]	Inappropriate population – cerebral aneurysm follow up
Topcuoglu 2003[216]	Inappropriate comparison - repeated angiography in negative DSA patients
Uysal 2008[218]	Inappropriate population – intracranial aneurysms
Uysal 2009[217]	Inappropriate population – cerebral aneurysm follow up
Vakharia 2019[220]	Inappropriate study design - non diagnostic accuracy study

Reference	Reason for exclusion
van Amerongen 2014[221]	Systematic review - references screened
van der Jagt 2008[222]	Inappropriate study design – feasibility study
van Gelder 2003[223]	Systematic review - references screened
van Loon 1997[224]	Inappropriate intervention – post intervention imaging
Velthuis 1998[226]	Inappropriate population – mixed population (pre and post intervention)
Villablanca 2002[228]	Inappropriate population – small aneurysms only
Vujotich 2003[229]	Inappropriate comparison – unclear reference standard
Walkoff 2016[230]	Inappropriate population – mycotic and oncotic aneurysms
Wang 2020[233]	Inappropriate study design – postoperative evaluation of patients with intracranial aneurysms
Wang 2018[231]	Inappropriate comparison – risk factors for unstable aneurysms / no reference test
Wei 2019[235]	Inappropriate study design – not a diagnostic accuracy study
Weng 2008[236]	Inappropriate population – cerebral aneurysm follow up
Westerlaan 2004[239]	Inappropriate population – DSA in CTA negative patients
Westerlaan 2011[240]	Systematic review- references screened
Westerlaan 2007[237]	Inappropriate comparison – not all patients had reference test
Westerlaan 2005[238]	Inappropriate population – cerebral aneurysm follow up
White 2000[244]	Systematic review - references screened
White 2001[243]	Inappropriate population – mixed population (less than 50% SAH)
White 2009[241]	Inappropriate intervention – not all patients had reference test
White 2001[242]	Inappropriate population – mixed population (less than 50% SAH)
White 2003[245]	Inappropriate population – mixed population (less than 50% SAH)
Wikstrom 2008[246]	Inappropriate comparison – post intervention imaging
Wilcock 1996[247]	Inappropriate comparison – no reference test
Wisniewski 2019[249]	Inappropriate study design – no relevant outcomes
Wu 2012[251]	Inappropriate population – mixed population (less than 50% SAH)
Xing 2011[252]	Inappropriate population – mixed population (less than 50% SAH)
Yang 2007[254]	Inappropriate comparison – no reference test
Yap 2015[255]	Inappropriate analysis – CTA negative patients only
Yeung 2009[256]	Inappropriate population – SAH excluded
Yi 2019[257]	Inappropriate comparison – index test CTA, reference standard CT
Young 2001[259]	Inappropriate population – mixed population (less than 50% SAH)
Yu 2012[260]	Inappropriate analysis – DSA negative patients only
Zeng 2020[261]	Inappropriate study design - literature review
Zhang 2014[262]	Inappropriate population – mixed population (less than 50% SAH)
Zhu 2004[264]	Inappropriate population – large intracranial aneurysms (not specified SAH)
Zouaoui 1997[265]	Inappropriate population – pre and post intervention imaging

H.2 Excluded health economic studies

Published health economic studies that met the inclusion criteria (relevant population, comparators, economic study design, published 2003 or later and not from non-OECD country or USA) but that were excluded following appraisal of applicability and methodological quality are listed below. See the health economic protocol for more details.

Table 12: Studies excluded from the health economic review

Reference	Reason for exclusion
Jabbarli 2014[93]	Excluded due to a combination of applicability and methodological limitations. Retrospective before and after analysis of people tested at a German university hospital. Unclear what resource use and unit costs were included in the analysis, potentially only diagnostic test costs which were determined from in-hospital price regulations and therefore this may not reflect current UK NHS costs or practice. No discounting applied. Unclear whether QALYs were estimated in line with NICE reference case.