NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of endovascular stent insertion for intracranial atherosclerotic disease

Improving blood flow to the brain by widening a narrowed artery inside the head using an expandable tube

Intracranial atherosclerotic disease (ICAD) is the narrowing of the arteries inside the head that supply blood to the brain. ICAD is associated with an increased risk of stroke. In this procedure, a balloon catheter is inserted into an artery in the arm or leg, guided to the affected artery and inflated to open up the narrowing. A small tube made of metal mesh, called a stent, is then positioned at the site of the narrowing to maintain improved blood flow.

Introduction

The National Institute for Health and Clinical Excellence (NICE) has prepared this overview to help members of the Interventional Procedures Advisory Committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in November 2011.

Procedure name

- Endovascular stent insertion for intracranial atherosclerotic disease.

Specialty societies

- British Society of Neuroradiologists.

Description

Indications and current treatment

Intracranial atherosclerotic disease (ICAD) is the narrowing or obstruction of arteries within the skull that supply blood to the brain. It is caused by atheromatous plaques, which can reduce blood flow and which may be

associated with thrombosis or embolism, leading to transient ischaemic attacks (TIA), stroke or death. ICAD is usually diagnosed only after a patient has presented with a TIA or stroke.

Symptomatic ICAD is usually treated with antiplatelet medication to limit platelet aggregation and emboli, together with a statin and attention to risk factors for atherosclerosis such as smoking, hypertension, diabetes and obesity.

Direct intervention to treat the ICAD is not commonly used. It involves balloon angioplasty to dilate diseased arteries, which may then be followed by stent insertion, with the aim of improving patency compared with balloon angioplasty alone.

What the procedure involves

Endovascular intracranial stent insertion is preceded by arterial imaging to identify and select lesions for treatment. The procedure is carried out under general or local anaesthesia, with or without sedation. Antithrombotic medication is administered to the patient before and during the procedure. Under fluoroscopic control, a catheter is inserted into the affected intracranial artery using a percutaneous transfemoral or transbrachial approach. Balloon angioplasty of the target lesion is normally done to dilate it before inserting a stent. It is possible to treat more than one lesion, or to insert more than one stent at one treatment session. Antithrombotic medication is continued after the procedure.

Two main types of stent have been used – balloon expandable and self-expanding. Some studies also use drug-eluting stents. The technology has evolved over the past decade and continues to do so.

Outcome measures

Modified Rankin scale

The modified Rankin scale measures the degree of disability in people who have suffered a stroke and is scored from 0 to 6:

- 0 = No symptoms at all
- 1 = No significant disability despite symptoms; able to carry out all usual duties and activities
- 2 = Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance
- 3 = Moderate disability; requiring some help, but able to walk without assistance
- 4 = Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
- 5 = Severe disability; bedridden, incontinent and requiring constant nursing care and attention
- 6 = Dead.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to endovascular stent insertion for intracranial atherosclerotic disease. Searches were conducted of the following databases, covering the period from their commencement to 19 October 2011: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with intracranial atherosclerotic disease.
Intervention/test	Endovascular stent insertion.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the overview

This overview is based on approximately 2241 patients treated by endovascular stent insertion from 2 systematic reviews, 1 randomised controlled trial (RCT), 1 non-randomised comparative studies and 4 case series[1–8] (patients from the smaller systematic review have not been included in the total as it is likely that they were already included in the larger review).

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Table 2 Summary of key efficacy and safety findings on endovascular stent insertion for intracranial atherosclerotic disease

Abbreviations used: CI, confidence interval; CT, computed tomography; IQR, interquartile range; MR, magnetic resonance; TIA, transient ischaemic attack; WASID, warfarin and aspirin for symptomatic intracranial disease

Study details	Key efficacy findings	Key safety findings	Comments
Chimowitz MI (2011)[1] [SAMMPRIS trial] **RCT** USA Recruitment period: 2008–11 Study population: patients with intracranial arterial stenosis **n = 451 (224 angioplasty and stent insertion vs 227 medical management)** Mean age (years): 61 (stent), 60 (medical) Sex: 60% (272/451) male Patient selection criteria: TIA or non-disabling stroke within 30 days before enrolment, attributed to angiographically verified stenosis of 70 to 99% of the diameter of a major intracranial artery. Technique: procedure was performed under general anaesthesia with the use of the Gateway PTA Balloon Catheter and Wingspan Stent System (Boston Scientific). **Mean follow-up: 12 months** Conflict of interest/source of funding: research was partly supported by AstraZeneca. Stryker Neurovascular provided study devices	Number of patients analysed: **451 (224 vs 227)** Of the 224 patients in the stent group, 15 (6.7%) did not have a stent placed (the procedure was not performed in 4 patients, the procedure was aborted before the lesion was accessed in 7 and angioplasty alone was performed in 4). Of the 227 patients in the medical management group, 9 (4.0%) underwent stent insertion after a TIA during the follow-up period. **Ischaemic stroke in territory of qualifying artery beyond 30 days after enrolment:** • Stent insertion = 5.8% (13/224) • Medical management = 5.7% (13/227) ***Secondary endpoints*** Any stroke or death: • Stent insertion = 23.2% (52/224) • Medical management = 16.3% (37/227), p = 0.06 Death: • Stent insertion = 3.1% (7/224) • Medical management = 3.1% (7/227), p = 0.95 Any stroke: • Stent insertion = 22.3% (50/224) • Medical management = 14.1% (32/227), p = 0.03 Disabling or fatal stroke: • Stent insertion = 8.5% (19/224) • Medical management = 5.7% (13/227), p = 0.21 Myocardial infarction: • Stent insertion = 2.2% (5/224) • Medical management = 3.1% (7/227), p = 0.60	**Stroke or death within 30 days after enrolment or after a revascularisation procedure for the qualifying lesion during the follow-up period:** • Stent insertion = 14.7% (33/224) • Medical management = 5.8% (13/227), p = 0.002 There were 5 (2.2%) stroke-related deaths in the stent group and 1 (0.4%) non-stroke-related death in the medical management group. 30.3% (10/33) of the strokes in the stent group and none of the strokes in the medical management group were symptomatic brain haemorrhages (p = 0.04). Of the 33 strokes in the stent group, 25 occurred within 1 day after the procedure and 8 occurred 2 to 6 days later.	**Study design issues**: • Multicentre (50 sites). • Intention-to-treat analysis. • Medical management was identical in the 2 groups and consisted of aspirin, clopidogrel, management of primary risk factors (elevated systolic blood pressure and elevated low-density lipoprotein cholesterol levels); and management of secondary risk factors (diabetes, elevated non-high-density lipoprotein cholesterol levels, smoking, excess weight, and insufficient exercise) with the help of a lifestyle modification programme. • Any patient with a prolonged TIA or mild ischaemic stroke was assessed by a second neurologist who was unaware of the treatment assignment. • All the end points were adjudicated by independent panels of neurologists and cardiologists who were blinded to treatment allocation. • The primary endpoint was stroke or death within 30 days after enrolment or after a revascularisation procedure for the qualifying lesion during the follow-up period.

Abbreviations used: CI, confidence interval; CT, computed tomography; IQR, interquartile range; MR, magnetic resonance; TIA, transient ischaemic attack; WASID, warfarin and aspirin for symptomatic intracranial disease			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
			Study population issues: • There were no significant differences between the groups with respect to any of the baseline characteristics. **Other issues**: • Enrolment of patients was stopped early because of safety concerns regarding the risk of periprocedural stroke or death in the stent group and because futility analysis indicated that there was virtually no chance that a benefit from stent insertion would be shown by the end of follow-up if enrolment continued. • The authors noted that the rate of stroke in the medical management group was much lower than expected. The rate of periprocedural stroke was higher than expected in the stent insertion group and the authors noted that all patients had stenosis of 70 to 99% and recent symptoms. Rigorous adherence to the protocol for evaluating events could have resulted in the detection of some milder strokes that may not otherwise have been identified.

Abbreviations used: CI, confidence interval; CT, computed tomography; IQR, interquartile range; MR, magnetic resonance; TIA, transient ischaemic attack; WASID, warfarin and aspirin for symptomatic intracranial disease

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Gröschel K (2009)[2]

Systematic review

Search date: April 2008

Study population: patients with atherosclerotic intracranial stenosis (internal carotid, middle cerebral, vertebral or basilar artery) greater than 50%

n = 31 studies; 1134 patients (1177 arteries)

Mean age: 64 years
Sex: 76% males

Study eligibility: English language; > 5 patients with intracranial angioplasty and stent procedures; all patients with atherosclerotic intracranial stenosis (internal carotid, middle cerebral, vertebral or basilar artery) > 50% determined on conventional angiography; peri-interventional complications (stroke or death) were reported.

Technique: 77% (n = 906) of procedures used balloon-mounted stents and 23% (n = 271) of procedures used a self-expanding stent. 6% (66/1047) of procedures used drug-eluting stents (all of them were balloon-mounted).

Mean follow-up: 13.5 months

Conflict of interest/source of funding: one of the authors has received speaker honoraria from a manufacturer.</td>
<td>Number of patients analysed: 1134

Follow-up data of treated vessels to determine a > 50% restenosis ranged from 3 to 21 months with a median follow-up of 6 months.

In the majority of studies, occurrence of restenosis was based on routinely scheduled investigations (conventional angiography, CT angiography, MR angiography, transcranial doppler ultrasound), whereas others were done only if a symptomatic event occurred.

Rate of restenosis (defined as > 50%, symptomatic or asymptomatic; in the majority of studies, only a small number of patients had follow-up imaging [range 2–99]):
0%–50%, median 3.9% (IQR: 0%–19.2%)

A total of 77 (14.4%) restenoses were detected among 535 patients who were investigated in ‘long-term follow-up’. Of these, 32.7% were symptomatic (TIA, stroke or death).

Restenosis (symptomatic and asymptomatic) rates according to stent type:
• Balloon-mounted (n = 443) = 13.8% (mean follow-up = 8.7 months)
• Self-expandable (n = 92) = 17.4% (mean follow-up = 5.4 months)
p < 0.001 for the difference between stent types</td>
<td>Combined periprocedural minor or major stroke and death rates ranged from 0% to 50% with a median of 7.7% (IQR: 4.4%–14.3%).

Periprocedural complications according to the localisation of the treated artery
<table>
<tr><th></th><th>Anterior circulation</th><th>Posterior circulation</th><th>p value</th></tr>
<tr><td>Minor stroke</td><td>1.9% (7/356)</td><td>4.1% (16/387)</td><td>0.088</td></tr>
<tr><td>Major stroke</td><td>2.6% (11/422)</td><td>4.9% (21/421)</td><td>0.07</td></tr>
<tr><td>Death</td><td>2.1% (9/422)</td><td>3.4% (15/437)</td><td>0.248</td></tr>
<tr><td>Any stroke or death</td><td>6.6% (28/422)</td><td>12.1% (55/455)</td><td>0.005</td></tr>
</table>
Periprocedural complications did not differ between the studies in which a balloon-mounted stent was used compared with those in which a self-expandable stent was used (9.5% vs 7.7%, p = 0.47)

There was no significant difference in the rate of periprocedural complications between the studies that used a higher degree of stenosis as inclusion criteria compared with those that used a lower threshold (> 70%: n = 271, 26 complications vs < 70%: n = 748, 52 complications, p = 0.18).</td>
<td>Study design issues:
• The majority of data came from retrospective case series.
• There was wide heterogeneity in study designs, treatment regimens, and patient populations.
• In the majority of studies included in the review, there was no independent neurological evaluation and no systematic clinical follow-up with screening for restenosis.
Other issues:
• The authors noted that this was a newly developed procedure and increasing expertise will likely influence the complication rates.
• Although the authors noted there was wide heterogeneity across the studies, it was not formally assessed and there was no weighting used when estimating the average risk.
• A subsequent editorial from another author suggested that using a different method of statistical analysis produced an overall risk of stroke or death between 8.0% and 13.4%, with no difference between anterior and posterior circulations.</td>
</tr>
</table>

Abbreviations used: CI, confidence interval; CT, computed tomography; IQR, interquartile range; MR, magnetic resonance; TIA, transient ischaemic attack; WASID, warfarin and aspirin for symptomatic intracranial disease

Study details	Key efficacy findings	Key safety findings	Comments
Siddiq F (2009)[3] **Systematic review** Search date: May 2008 Study population: patients with symptomatic intracranial atherosclerotic disease **n = 69 studies (36 angioplasty with stent insertion vs 33 angioplasty alone); 2318 patients (1291 vs 1027)** Mean age: 62 years Sex: 76% males Study selection criteria: endovascular treatment for symptomatic intracranial atherosclerotic disease, defined as 50% or greater stenosis on a preoperative angiogram with symptoms referring to a target vessel; 10 or more patients; reporting clinical outcomes as stroke and death during follow-up periods ranging from 1 month to 1 year. Technique: not reported Follow-up: 1 month–1 year Conflict of interest/source of funding: none.	Number of patients analysed: **2318 (1291 vs 1027)** Mean post-treatment stenosis: • Stent insertion = 10% (range 0–20) • Angioplasty = 30% (range 0–55) Stroke and/or death at 1 year follow-up: • Stent insertion = 11.5% (123/1070) • Angioplasty = 17.1% (125/731), p = 0.0002 Restenosis rates (on follow-up angiography within 1 year, defined as ≥ 50% stenosis of the treated lesion): • Stent insertion = 11.1% (n = 119) • Angioplasty = 14.2% (n = 115), p = 0.043 Technical success rates (defined as ≤ 50% residual stenosis of the target vessel; 25 studies with 850 patients in stent group and 12 studies with 315 patients in angioplasty group): • Stent insertion = 95% (n = 680) • Angioplasty = 79.8% (n = 197), p = 0.0001 (Note: it is unclear what denominators were used to calculate these results) Pooled incidence of stroke and/or death at 1-year using a random-effects model: • Stent insertion = 14.2% • Angioplasty = 19.7%, p = 0.009	Stroke and/or death at 1 month: • Stent insertion = 8.1% (n = 104) • Angioplasty = 8.9% (n = 91), p = 0.49	**Study design issues**: • Studies with longer than 1-year follow-up were truncated at 1 year. • Pooled incidence was calculated using a random-effects model **Other issues**: • There was heterogeneity across studies with regard to patient selection, presence of risk factors and other patient characteristics. • There was no effect of the publication year of the studies on the risk of stroke and/or death.

Abbreviations used: CI, confidence interval; CT, computed tomography; IQR, interquartile range; MR, magnetic resonance; TIA, transient ischaemic attack; WASID, warfarin and aspirin for symptomatic intracranial disease

Study details	Key efficacy findings	Key safety findings	Comments
Samaniego EA (2009)[4] **Non-randomised comparative study** USA Recruitment period: 2004–7 Study population: patients with symptomatic intracranial arterial stenosis **n = 111 (53 angioplasty and stent insertion vs 58 medical management)** Mean age (years): 65 Sex: 37% (41/111) male Patient selection criteria: symptomatic intracranial arterial stenosis, assessed by MR angiography, CT angiography, or intra-arterial digital subtraction angiography. Lesions considered amenable for revascularisation included those with angiographically verified ≥ 50% stenosis of a major intracranial artery and TIA or stroke in the vascular territory of the target lesion. Technique: stents included the Wingspan and Neuroform stent system (Boston Scientific, USA), and various balloon-expandable stent systems. **Mean follow-up: 14 months** Conflict of interest/source of funding: none.	Number of patients analysed: **111 (53 vs 58)** **Rate of events during follow-up (defined as TIA, stroke, vascular death, performance of an extracranial-intracranial bypass in the originally treated vascular territory because of TIA or stroke symptoms, performance of another stent insertion or additional stent placement in a symptomatic in-stent restenosis):** • Stent insertion = 69.8% (37/53) • Medical management = 65.5% (38/58) ***Ischaemic end-points (p values not reported)*** TIAs: • Stent insertion = 20.8% (11/53) • Medical management = 10.3% (6/58) Death: • Stent insertion = 3.8% (2/53) • Medical management = 8.6% (5/58) Any stroke: • Stent insertion = 3.8% (2/53) • Medical management = 5.2% (3/58) There tended to be more favourable outcomes in patients who had a stent placed only in a posterior circulation lesion compared with anterior circulation, but this difference was not statistically different.	Periprocedural complications in stent group (within 24 hours of stent insertion): • Ischaemic stroke = 3.8% (2/53) • Death = 1.9% (1/53) • Stent occlusion = 3.8% (2/53) (both were in balloon-expandable stents). The first occlusion happened 2 days after stent insertion and the patient underwent extracranial-intracranial bypass surgery because of recurrent TIAs. The second occlusion occurred 9 days after stent insertion; while off antiplatelet medication because of a gastrointestinal haemorrhage, the patient had a large middle cerebral artery territory stroke and died.	**Study design issues**: • Retrospective. • Single-centre. • Patient treatment was determined by a multidisciplinary committee comprising a vascular neurologist, a neuroendovascular specialist and, frequently, a vascular neurosurgeon. **Study population issues**: • History of TIA was documented in 55% of the stent group patients and 19% of patients in the medical management group ($p < 0.001$). • Location of atherosclerotic lesions varied significantly between the groups; patients in the medical management group had more diffuse lesions than those in the stent group (67% vs 28%). • Patients in the medical management group were more likely to have presented to the emergency department and typically had higher National Institutes of Health Stroke Scale scores and modified Rankin Scale scores than patients in the stent group.

Abbreviations used: CI, confidence interval; CT, computed tomography; IQR, interquartile range; MR, magnetic resonance; TIA, transient ischaemic attack; WASID, warfarin and aspirin for symptomatic intracranial disease

Study details	Key efficacy findings	Key safety findings	Comments
Vajda Z (2012)[5] **Case series** Germany Recruitment period: 2007–11 Study population: patients who underwent elective endovascular treatment for significant (≥ 50%) intracranial atherosclerotic arterial stenoses **n = 189 patients (209 stenoses)** Median age: 68 years (range 41–88) Sex: 69.8% (132/189) male Patient selection criteria: exclusion criteria included patients with identified or suspected vasculitis or vessel dissection, patients treated for acute ischaemic stroke, and those treated with stent deployment alone without balloon angioplasty. Technique: a self-expanding stent with reduced radial force was used (Enterprise, Codman Neurovascular) in conjunction with balloon angioplasty. Mean follow-up: 7 months Conflict of interest: one of the authors is a proctor and Medical Board member for Codman Neurovascular.	Number of patients analysed: 189 Technical success rate = 100% (189/189) Median stenosis before the procedure = 65.4 ± 1% Median stenosis after the procedure = 25.1 ± 1% Recurrent stenosis (defined as an in-stent stenotic lesion of > 50% on follow-up digital subtraction angiography series) = 24.7% (43/174) of lesions (after mean follow-up of 4 months); 4 of these lesions were symptomatic with TIAs or stroke in the dependent vascular territory. Overall rate of recurrent ischaemia or stroke in the territory of the stented vessel in lesions with at least one follow-up examination = 2.3% (4/174)	**Major procedural complications = 8.5% (16/189):** • Fatal hyperperfusion intracerebral haemorrhage = 0.5% (1/209) • Subarachnoid haemorrhage caused by rupture of middle cerebral artery = 0.5% (1/209) (the patient died of a large hemispherical infarction) • Haemorrhagic transformation of a previously infarcted area with intracerebral haemorrhage 6 days after the procedure = 0.5% (1/209) (complete resolution of symptoms at 30 days) • Subarachnoid haemorrhage on the third post-interventional day = 0.5% (1/209) (symptoms resolved without sequelae) • Subarachnoid haemorrhage caused by microguidewire perforation of artery = 0.5% (1/209) (with subsequent coil occlusion and complete clinical recovery at 30 days) • Symptomatic ischaemic lesions in the territory of the stented artery with resolution of symptoms within 30 days = 4.3% (9/209) • Temporary stent thrombosis = 0.5% (1/209) (successfully treated with lysis therapy and resolution of symptoms within 30 days) • Direct carotid-cavernous sinus fistula, needing further endovascular treatment = 0.5% (1/209) Minor complications = 1.9% (4/209) (2 asymptomatic dissection of the stented segment and 2 access-site adverse events needing surgery) Combined neurological morbidity and mortality rate (stroke, intracerebral haemorrhage, and subarachnoid	**Follow-up issues:** • Angiographic follow-up was only available for 174 stenoses (83%). **Study design issues**: • Consecutive patients. • Single centre. **Study population issues:** • 84% of the lesions were symptomatic. **Other issues:** • The stent used in this study was developed for intracranial aneurysm treatment – its application in the use of atherosclerotic lesions represented off-label use.

Abbreviations used: CI, confidence interval; CT, computed tomography; IQR, interquartile range; MR, magnetic resonance; TIA, transient ischaemic attack; WASID, warfarin and aspirin for symptomatic intracranial disease

Study details	Key efficacy findings	Key safety findings	Comments
		haemorrhage) = 7.7% (16/209) within 30 days and 1.0% (2/209) at 30 days. One additional patient died of pneumonia 10 days after the procedure. Delayed proximal migration of a stent was observed in 1 patient at the 12-week angiographic follow-up, together with a recurrent stenosis at the site of the original lesion.	

Abbreviations used: CI, confidence interval; CT, computed tomography; IQR, interquartile range; MR, magnetic resonance; TIA, transient ischaemic attack; WASID, warfarin and aspirin for symptomatic intracranial disease

Study details	Key efficacy findings	Key safety findings	Comments
Miao ZR (2009)[6] **Case series** China Recruitment period: 2001–6 Study population: patients with symptomatic middle cerebral artery stenosis **n = 113** Mean age (years): 48 (range 25–79) Sex: 77% (87/113) male Patient selection criteria: clinical symptoms attributable to middle cerebral artery stenosis; > 70% stenosis assessed using digital subtraction angiography; antithrombotic therapy had either failed or patients were not expected to benefit from it because of high-grade stenosis. Technique: all patients were started on double-antiplatelet therapy at least 3 days before the procedure and maintained on it for at least 3 months after the procedure. Aspirin was continued indefinitely. General anaesthesia was used for 72% of procedures and conscious sedation for 28%. Balloon-expandable coronary stents were used (AVE s660 and s670 [Medtronic, USA]; Coroflex [B Braun, Germany]; Cypher and BX [Cordis, USA]; Helistent [Hexacath, France]; Firebird [Micropod, China]). There was no pre- or postdilation. **Mean follow-up: 29 months (range 9 months – 5 years)** Conflict of interest/source of funding: none.	Number of patients analysed: **113** **Technical success (complete coverage of the lesion with < 50% residual stenosis) = 96.5% (109/113)** (2 procedures were aborted without complication because the stents could not navigate the tortuous carotid siphon). The degree of stenosis was reduced from 80.8% to 3.7% immediately after stenting. Rate of TIA during follow-up = 4.5% (4/89) Rate of minor stroke during follow-up = 2.3% (2/89) Overall restenosis rate = 18.0% (16/89) Restenosis was associated with diabetes (odds ratio 6.98, 95% CI: 1.44 to 33.81) and hyperlipidaemia (odds ratio 8.77, 95% CI: 1.91 to 40.38). There was no statistical association between restenosis and age, sex, hypertension, stent type, or bare metal stent.	**Complications:** • Vessel rupture during stent navigation = 1.8% (2/113) (1 patient died of massive subarachnoid haemorrhage; the other was treated by emergency craniotomy and surgical clipping of the middle cerebral artery without neurological deterioration). • Stroke and death within 30 days = 4.4% • Perforator occlusion = 2.7% (3/113) (2 patients had minor motor deficits immediately after the procedure and made a good recovery; the other patient presented with symptoms 4 hours after the procedure and died from cerebral haemorrhage after intra-arterial thrombolysis). • Bilateral intracerebral haemorrhage = 0.9% (1/113) (2 weeks after the procedure) (no further information given)	**Follow-up issues**: • Conventional angiography was only performed in 29 patients during follow-up; the majority were followed only with transcranial doppler studies. • 21% (24/113) of patients were lost to follow-up. **Study design issues**: • Consecutive patients. • Single centre. • Restenosis was defined as peak flow velocity of more than 150 cm/s by transcranial doppler or more than 50% luminal stenosis by angiogram. **Study population issues**: • The study population was a relatively young group of patients. **Other issues**: • The paper quotes a restenosis rate of 20.2% but lists the numerator as 16 and the denominator as 89. • The authors note that the low complication rate is likely to be related to technical improvements after the initial learning curve.

Abbreviations used: CI, confidence interval; CT, computed tomography; IQR, interquartile range; MR, magnetic resonance; TIA, transient ischaemic attack; WASID, warfarin and aspirin for symptomatic intracranial disease

Study details	Key efficacy findings	Key safety findings	Comments
Fiorella DJ (2011)[7] [US Wingspan Registry] **Case series** USA Recruitment period: not reported Study population: patients with symptomatic intracranial atherostenosis **n = 158** Mean age (years): 63 (range 33–86) Sex: 60% (95/158) male Patient selection criteria: not reported; 57% of patients presented with a qualifying event of stroke; the average stenosis was 75% and 69% of lesions were in the 70% to 99% stenosis range at presentation. Technique: a dual antiplatelet regimen was used before the procedure and maintained until follow-up angiography was performed. All patients remained on aspirin indefinitely after the procedure. Angioplasty was typically performed with a slow, graded inflation of an angioplasty balloon and then the Wingspan system (Boston Scientific, USA) was used for stent insertion. **Mean follow-up: 14 months** Conflict of interest/source of funding: the registry was supported by a grant from Boston Scientific; however all data collection, analysis, and interpretation were performed by the authors independent of Boston Scientific's input or interpretation.	Number of patients analysed: **158** Cumulative rate of primary endpoint (stroke or death within 30 days of the stenting procedure or ipsilateral stroke after 30 days) = 15.7% Of 13 ipsilateral strokes occurring after 30 days, 3 resulted in death. 77% (10/13) of the ipsilateral strokes that occurred after 30 days occurred within 6 months of the procedure, and no events were recorded after 12 months. An additional 9 patients experienced an ipsilateral TIA after 30 days. Stroke or TIA between 30 days and 12 months = 20% (22 events in 110 patients with 12-month clinical follow-up). Most postprocedural events (86%) were associated with interruption of antiplatelet medication or in-stent restenosis.	Periprocedural stroke = 5.7% (9/158) (in 4 patients, these strokes ultimately resulted in death)	**Follow-up issues**: • 13% of patients were lost to follow-up by 1 year. • The majority of patients underwent scheduled imaging surveillance as part of routine clinical follow-up. **Study design issues**: • Multicentre registry. • Prospective data collection from consecutive patients. **Other issues**: • Repeat angioplasty was typically performed when recurrent stenosis was of a severity greater than or equivalent to the presenting lesion before treatment.

Abbreviations used: CI, confidence interval; CT, computed tomography; IQR, interquartile range; MR, magnetic resonance; TIA, transient ischaemic attack; WASID, warfarin and aspirin for symptomatic intracranial disease

Study details	Key efficacy findings	Key safety findings	Comments
Jiang WJ (2007)[8] **Case series** China Recruitment period: 2001–5 Study population: patients with symptomatic intracranial atherosclerosis **n = 213 (220 lesions)** Mean age (years): 53 (range 20–79) Sex: 83% (176/213) male Patient selection criteria: angiographically verified ≥ 50% stenosis of a major intracranial artery; ischaemic stroke or TIA as a qualifying event; elective stenting; 1 or more atherosclerotic risk factors. Technique: patients were given aspirin and clopidogrel or ticlopidine at least 7 days before the procedure and for ≥ 6 months after the procedure. Balloon-expandable stents were used (intracranial Apollo stent, Microport, China and Biodiv Ysio coronary stent). **Mean follow-up: 27 months** Conflict of interest/source of funding: none.	Number of patients analysed: **213 patients (220 lesions)** **Stent success rate = 92.3% (203/220)** Stent failures occurred in 17 lesions because of failed positioning of the guided catheter or microwire or failed navigation of the stent system through severe or moderate tortuosity. Lesion-related ischaemic stroke after 30 days: • Severe stenosis = 3.3% (4/121) • Moderate stenosis = 3.3% (3/92) Non-lesion-related ischaemic stroke after 30 days: • Severe stenosis = 1.7% (2/121) • Moderate stenosis = 1.1% (1/92) Cumulative probability of primary endpoint for patients with severe stenosis : • 1 year = 7.2% (95% CI: 2.6% to 11.8%) • 2 years = 8.2% (95% CI: 1.9% to 14.5%) Cumulative probability of primary endpoint for patients with moderate stenosis : • 1 year = 5.3% (95% CI: 0.7% to 9.9%) • 2 years = 8.3% (95% CI: 1.3% to 15.3%) Univariate analysis showed that 4 factors were potentially associated with primary endpoints in the severe stenosis group: diabetes, no antithrombic therapy at the time of the qualifying event, lesion in the posterior circulation, stent failure. Multivariable analysis showed that stent failure was an independent risk factor. No risk factors were identified for patients in the moderate stenosis group. Restenosis identified on follow-up angiography (at mean follow-up of 8.5 months): • Severe stenosis = 25.0% (14/56) • Moderate stenosis = 11.6% (5/43) • Overall = 19.2% (19/99)	**Primary events within 30 days** Lesion-related ischaemic stroke: • Severe stenosis = 3.2% (4/126) • Moderate stenosis = 3.2% (3/94) Symptomatic brain haemorrhage: • Severe stenosis = 0% (0/126) • Moderate stenosis = 1.1% (1/94) Symptomatic subarachnoid haemorrhage: • Severe stenosis = 1.6% (2/126) • Moderate stenosis = 0% (0/94) **Secondary events within 30 days** Emergent cerebral revascularisation: • Severe stenosis = 2.4% (3/126) • Moderate stenosis = 4.3% (4/94) Asymptomatic brain haemorrhage: • Severe stenosis = 0% (0/126) • Moderate stenosis = 2.1% (2/94)	**Follow-up issues**: • 5 patients were lost to follow-up after 30 days. • Follow-up angiograms were only performed for 47% (99/213) of patients. **Study design issues**: • Primary endpoints included lesion-related ischaemic stroke, symptomatic brain haemorrhage, and symptomatic subarachnoid haemorrhage. • Severe stenosis was defined as ≥ 70% and moderate was defined as 50–69% stenosis.

Efficacy

Technical success

A systematic review comparing 36 studies on angioplasty and endovascular stent insertion with 33 studies on angioplasty alone reported technical success rates (defined as ≤ 50% residual stenosis of the target vessel) of 95% (n = 680) for stent insertion and 80% (n = 197) for angioplasty alone[3]. Three case series of 113, 189 and 213 patients (220 lesions) reported technical success rates of 97% (109/113), 100% (189/189) and 92% (203/220), respectively[6,5,8].

Stroke rate

An RCT of 451 patients treated by angioplasty and stent insertion or medical management alone reported ischaemic stroke in the area of the brain supplied by the artery with the index lesion more than 30 days after enrolment in 6% of patients in both groups (13/224 and 13/227, respectively, p value not stated) at a mean follow-up of 12-months[1]. A case series of 158 patients reported that 20% (22/110) of patients had a stroke or TIA between 30 days and 12 months after the procedure[7]. A case series of 213 patients reported lesion-related ischemic stroke more than 30 days after the procedure in 3% (7/213) of patients, at a mean follow-up of 27 months[8].

Mortality

The RCT of 451 patients treated by angioplasty and stent insertion or medical management alone reported a death rate of 3% in both groups (7/224 and 7/227, respectively, p = 0.95) at a mean follow-up of 12-months[1]. The systematic review comparing 36 studies on angioplasty and endovascular stent insertion with 33 studies on angioplasty alone reported stroke and/or death in 12% (123/1070) and 17% (125/731) of patients respectively at 1-year follow-up (p = 0.0002)[3].

Restenosis

The case series of 113 patients reported an overall restenosis rate of 18% (16/89; identified by transcranial Doppler ultrasound or angiography) at a mean follow-up of 29 months[6]. The case series of 213 patients reported an overall restenosis rate of 19% (19/99) identified on follow-up angiography at mean follow-up of 9 months[8]. The case series of 189 patients reported recurrent stenosis in 25% (43/174) of lesions identified on angiography at a mean follow-up of 4 months[5].

Safety

Stroke and/or death within 30 days

The RCT of 451 patients treated by angioplasty and stent insertion or medical management alone reported stroke or death within 30 days of enrolment in 15% (33/224) and 6% (13/227) of patients, respectively (p = 0.002). There were 5 stroke-related deaths in the stent group and 1 non-stroke-related death in the medical management group[1].

The systematic review comparing 36 studies on angioplasty and endovascular stent insertion with 33 studies on angioplasty alone reported stroke and/or death in 8% (104/1291) and 9% (91/1027) of patients respectively at 1-month follow-up (p = 0.49)[3].

In a non-randomised comparative study, 4% (2/53) of patients treated by endovascular stent insertion had an ischaemic stroke within 24 hours of stent insertion and 1 patient died[4].

The case series of 113 patients reported stroke and/or death within 30 days in 4% of patients (actual numbers not stated) [6]. The case series of 158 patients reported periprocedural stroke in 6% (9/158) of patients; in 4 patients, these strokes ultimately resulted in death[7].

Vessel rupture

Vessel rupture during stent navigation was reported in 2% (2/113) of patients in the case series of 113 patients; 1 patient died of massive subarachnoid haemorrhage, the other was treated by emergency craniotomy and surgical clipping of the middle cerebral artery[6]. Vessel rupture during the procedure was reported in 1 patient in the case series of 189 patients; the patient died of a large hemispherical infarction[5].

Stent occlusion

In the non-randomised comparative study, stent occlusion occurred in 4% (2/53) of patients treated by endovascular stent insertion. One occlusion occurred 2 days after stent insertion and the patient had extracranial-intracranial bypass surgery because of recurrent TIAs. The second occlusion occurred 9 days after stent insertion in a patient who was not receiving antiplatelet medication because of a gastrointestinal haemorrhage; the patient had a large middle cerebral artery territory stroke and died[4].

Perforator occlusion

The case series of 113 patients reported perforator occlusion in 3% (3/113) of patients; 2 patients had minor motor deficits immediately after the procedure and made a good recovery, the other patient presented with symptoms 4 hours after the procedure and died from cerebral haemorrhage after intra-arterial thrombolysis[6].

Cerebral haemorrhage

The case series of 113 patients reported bilateral intracerebral haemorrhage in 1 patient 2 weeks after the procedure (no further information supplied)[6]. The case series of 213 patients (220 lesions) reported a symptomatic brain haemorrhage in 1 patient and a symptomatic subarachnoid haemorrhage (not otherwise described) in 1% (2/213) of patients[8] within 30 days of the procedure. The case series of 189 patients reported 1 fatal intracerebral haemorrhage (timing not reported). There were haemorrhages in 3 other patients; 1 intracerebral haemorrhage 6 days after the procedure (resolved within 30 days) and 2 subarachnoid haemorrhages (1 resolved without treatment and the other was successfully treated by coil occlusion)[5].

Other

The case series of 189 patients reported 1 patient with direct carotid-cavernous sinus fistula, needing further endovascular treatment[5].

Validity and generalisability of the studies

- Enrolment of patients into the RCT was stopped early because of safety concerns regarding the risk of periprocedural stroke or death in the stent group and because futility analysis indicated that there was virtually no chance that a benefit from stent insertion would be shown by the end of follow-up if enrolment continued[1].
- The RCT only used 1 particular type of self-expanding stent[1].
- All of the studies summarised in table 2 are reported from the USA or China.
- Different stents were used between and within studies. Some studies used balloon-expandable stents, some used self-expanding stents and others used drug-eluting stents. Only a proportion of stents were specifically designed to be used for intracranial stenoses.
- The population included in 1 case series had a relatively low mean age compared with the other studies[6].
- Inclusion criteria differed between studies, some series specifying more severe baseline stenosis than others; all patients in the studies had symptomatic disease.

- The location and size of the lesion differed between studies. Some authors suggest that this is likely to impact on the safety and efficacy of the procedure.

Existing assessments of this procedure

An Australian Horizon Scanning Technology Prioritising Summary on Intracranial angioplasty and stenting (WingSpan™ self-expanding stent) for cerebral atherosclerotic stenosis was published in June 2006[9]. The report concluded: 'Balloon angioplasty and WingSpan stent deployment offers a potentially safe treatment for intracranial atherosclerotic stenosis. However, the evidence available is limited and despite good clinical outcomes there is a need for larger multicentre trials with long-term follow-up to determine long-term patency and stroke rates. Comparative studies with standard balloon angioplasty or stenting would be valuable in determining the value of this procedure as well.'

Reporting standards for angioplasty and stent-assisted angioplasty for intracranial atherosclerosis were published in 2009 under the auspices of the US Joint Writing Group of the Technology Assessment Committee, Society of NeuroInterventional Surgery, Society of Interventional Radiology; Joint Section on Cerebrovascular Neurosurgery of the American Association of Neurological Surgeons and Congress of Neurological Surgeons; and the Section of Stroke and Interventional Neurology of the American Academy of Neurology[10]. The report recommends definitions for constructing useful research data sets.

A Position Statement of the American Society of Interventional and Therapeutic Neuroradiology, Society of Interventional Radiology and the American Society of Neuroradiology was published in 2009[11]. The report concluded: 'sufficient evidence now exists to recommend that intracranial angioplasty with or without stenting should be offered to patients with intracranial stenoses who have failed medical therapy….Similar to revascularization for extracranial carotid artery stenosis, patient benefit from revascularization for symptomatic intracranial arterial stenosis is critically dependent on a low periprocedural stroke and death rate and should thus be performed by experienced neurointerventionists.'

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B gives details of the recommendations made in each piece of guidance listed.

Interventional procedures

- Extracranial to intracranial bypass for intracranial atherosclerosis. NICE interventional procedures guidance 348 (2010). Available from www.nice.org.uk/guidance/IPG348

Specialist Advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and does not represent the view of the society.

Trevor Cleveland, Andrew Clifton (British Society of Interventional Radiology); Naga Kandasamy, Wilhelm Kueker, Maneesh Patel (British Society of Neuroradiologists)

- Four Specialist Advisers had performed the procedure at least once and 1 performs it regularly.
- Three Specialist Advisers considered the procedure to be novel and of uncertain safety and efficacy; 1 described it as established practice. One Adviser noted that the procedure was not novel but the safety and efficacy were uncertain.
- Best medical treatment would be the appropriate comparator.
- Theoretical adverse events include stroke caused by embolic events or vessel occlusion, death, vessel dissection, embolisation, myocardial infarction, recurrent stenosis, groin haematoma, contrast reactions.
- Anecdotal adverse events include basilar artery rupture resulting in patient death, disabling thalamic infarction, reperfusion haemorrhage, stent occlusion.
- Adverse events reported in the literature include stroke, death, injury to vessels, delayed complications (stent occlusion or restenosis).
- One Adviser noted that there is uncertainty about the correct drug regime to give to patients after the procedure.
- There are concerns about the periprocedural complications.
- A recent US trial for intracranial stent insertion using one particular stent was stopped because of safety concerns (SAMMPRIS).
- One Adviser noted that the SAMMPRIS study was limited to one device that is less frequently used in the UK than in the USA.
- Key efficacy outcomes include reduction in TIA or stroke frequency.
- Uncertainty remains about efficacy compared with best medical treatment as well as which device should be used: angioplasty alone, self-expanding stent, balloon-mounted stent, drug-eluting stent.
- The stents that are used are evolving and this may impact on the benefit of the procedure. The initial stents that were used were cardiac stents, but there are now neurospecific stents being produced.
- Specialist neurointervention endovascular training is required.
- One Adviser stated that there should be a multidisciplinary team (MDT) attended by a stroke physician/neurologist and the appropriate interventionalists to allow case selection for this procedure.
- All the Specialist Advisers thought that this procedure would have a minor impact on the NHS, in terms of patient numbers and use of resources.

Patient Commentators' opinions

NICE's Patient and Public Involvement Programme sent 26 questionnaires to 1 trust for distribution to patients who had the procedure (or their carers). NICE received 15 completed questionnaires.

The Patient Commentators' views on the procedure were consistent with the published evidence and the opinions of the Specialist Advisers.

Issues for consideration by IPAC

- Most recent studies on intracranial stent insertion compare their results with the WASID (Warfarin and Aspirin for Symptomatic Intracranial Disease) trial, which was published in 2005[12]. This was a randomised, double-blind multicentre trial comparing aspirin with warfarin for the treatment of symptomatic intracranial disease. A total of 569 patients were randomised and the primary end point (ischaemic stroke, brain haemorrhage, or death from vascular causes other than stroke) occurred in 22% of patients, irrespective of their treatment group. The rate of death was significantly higher among patients assigned to warfarin (4% in the aspirin group compared with 10% in the warfarin group; hazard ratio, 0.46; 95 percent confidence interval, 0.23 to 0.90; p = 0.02).
- There is an ongoing UK RCT comparing vertebral angioplasty and stent insertion with best medical treatment for symptomatic vertebral stenosis (VIST trial). The trial started in 2008 and is expected to end in 2016, with a target number of 1302 participants.

References

1. Chimowitz MI, Lynn MJ, Derdeyn CP et al. (2011) Stenting versus aggressive medical therapy for intracranial arterial stenosis. New England Journal of Medicine 365: 993–1003

2. Gröschel K, Schnaudigel S, Pilgram SM et al. (2009) A systematic review on outcome after stenting for intracranial atherosclerosis. Stroke 40: e340–7

3. Siddiq F, Memon MZ, Vazquez G et al. (2009) Comparison between primary angioplasty and stent placement for symptomatic intracranial atherosclerotic disease: meta-analysis of case series. Neurosurgery 65: 1024–34

4. Samaniego EA, Hetzel S, Thirunarayanan S et al. (2009) Outcome of symptomatic intracranial atherosclerotic disease. Stroke 40: 2983–7

5. Vajda Z, Schmid E, Güthe T et al. (2012) The modified Bose method for the endovascular treatment of intracranial atherosclerotic arterial stenoses using the Enterprise stent. Neurosurgery 70: 91–101

6. Miao ZR, Feng L, Li S et al. (2009) Treatment of symptomatic middle cerebral artery stenosis with balloon-mounted stents: long-term follow-up at a single center. Neurosurgery 64: 79–85

7. Fiorella DJ, Turk AS, Levy EI et al. (2011) US Wingspan registry 12-month follow-up results. Stroke 42: 1976–81

8. Jiang WJ, Xu XT, Du B et al. (2007) Comparison of elective stenting of severe vs moderate intracranial atherosclerotic stenosis. Neurology 68: 420–6

9. Australia and New Zealand Horizon Scanning Network. Intracranial angioplasty and stenting (WingSpan™ self-expanding stent) for cerebral atherosclerotic stenosis. Horizon Scanning Technology Prioritising Summary Update. Commonwealth of Australia, June 2006

10. Schumacher HC, Meyers PM, Higashida RT et al. (2009) Reporting standards for angioplasty and stent-assisted angioplasty for intracranial atherosclerosis. Stroke 40: e348–e365

11. Higashida RT, Meyers PM, Connors III JJ et al. (2009) Intracranial Angioplasty and Stenting for Cerebral Atherosclerosis: A Position Statement of the American Society of Interventional and Therapeutic Neuroradiology, Society of Interventional Radiology, and the American Society of Neuroradiology. Journal of Vascular and Interventional Radiology 20: S312–S316

12. Chimowitz MI, Lynn MJ, Howlett-Smith H et al. (2005) Comparison of Warfarin and Aspirin for Symptomatic Intracranial Arterial Stenosis. New England Journal of Medicine 352:1305–131

Appendix A: Additional papers on endovascular stent insertion for intracranial atherosclerotic disease

The following table outlines the studies that are considered potentially relevant to the overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies. Case reports and series with fewer than 25 patients have been excluded unless they report safety outcomes that have not been reported elsewhere.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Abou-Chebl A, Krieger DW, Bajzer CT et al. (2006) Intracranial angioplasty and stenting in the awake patient. Journal of Neuroimaging 16: 216–223	n = 40	Technical success rate = 94% (45/48) Mortality rate = 3% (1/40) Subarachnoid haemorrhage = 5% (2/40) Branch artery infarction = 5% (2/40)	Larger studies are included. (Included in table 2 of original overview).
Albuquerque FC, Levy EI, Turk AS et al. (2008) Angiographic patterns of Wingspan in-stent restenosis. Neurosurgery 63: 23–27	n = 127 FU = 3–16 months	In-stent restenosis = 28% (36/127) Stent occlusion = 4% (5/127)	Main focus of the study was to present a classification system to characterise in-stent restenosis.
Bang JS, Oh CW, Jung C et al. (2010) Intracranial stent placement for recanalization of acute cerebrovascular occlusion in 32 patients. American Journal of Neuroradiology 31: 1222–1225	n = 32	Technical success = 100% Major symptomatic intracerebral haemorrhage = 13% (4/32) Intracranial vascular dissection = 13% (4/32) Extracranial vascular dissection = 9% (3/32)	Larger studies are included.
Blasel S, Yukzek Z, Kurre W et al. (2010) Recanalization results after intracranial stenting of atherosclerotic stenoses. Cardiovascular and Interventional Radiology 33: 914–920	n = 40	Residual stenosis = 5% (2/40) There were no major vessel complications.	Larger studies are included.
Bose A, Hartmann M, Henkes H et al. (2007) A novel, self-expanding, nitinol stent in medically refractory intracranial atherosclerotic stenoses: the Wingspan study. Stroke 38: 1531–1537	n = 45 FU = 6 months	Technical success rate: 98% (44/45) Restenosis (> 50%): 8% (3/40) Overall stroke rate: 10% (4/43) 30-day mortality: 5% (2/44)	Larger studies are included. (Included in table 2 of original overview).

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Broussalis E, Kunz AB, Luthringshausen G et al. (2011) Treatment of vertebral artery origin stenosis with a Pharos stent device: a single center experience. Interventional Neuroradiology 17: 316–322	n = 22 FU = 12 months	Restenosis rate at 1 year = 55% (11/20) In-stent occlusion rate = 10% All patients were without new neurological deficit or MRI changes at the follow-ups.	Larger studies with longer follow-up are included in table 2.
Brus-Ramer M, Starke RM, Komotar RJ et al. (2010) Radiographic evidence of cerebral hyperperfusion and reversal following angioplasty and stenting of intracranial carotid and middle cerebral artery stenosis: Case report and review of the literature. Journal of Neuroimaging 20: 280–283	n = 1	Continuous transcranial doppler monitoring after stent placement indicated developing cerebral hyperperfusion. The patient had an uneventful postoperative course and was discharged with development of neurological sequelae.	Case report.
Buszman PP, Szymanski R, Debinski M et al. (2012) Long-term results of cephalad arteries percutaneous transluminal angioplasty with stent implantation (The CAPTAS registry). Catheterization and Cardiovascular Interventions 79: 532–540	n = 434 FU = 4 years	At 4 years (1–11 years), the mortality rate was 11.5%, 6% of patients had stroke, and 3% MIs. Restenosis occurred in 3%.	It is difficult to establish how many, if any, patients had intracranial atherosclerosis rather than extracranial. No new safety outcomes are reported.
Canyigit M, Arat A, Cil BE et al. (2007) Distal embolization after stenting of the vertebral artery: diffusion-weighted magnetic resonance imaging findings. Cardiovascular and Interventional Radiology 30: 189–195	n = 35	33% (5/15) of patients had new diffusion-weighted imaging abnormalities; stenting of stenoses of the vertebral artery origin may be associated with a significant risk of asymptomatic distal embolisation.	Larger studies are included.
Chow MM, Masaryk TJ, Woo HH et al. (2005) Stent-assisted angioplasty of intracranial vertebrobasilar atherosclerosis: midterm analysis of clinical and radiologic predictors of neurological morbidity and mortality. American Journal of Neuroradiology 26: 869–874	n = 39 FU = 13 months	Technical success rate: 97% (38/39) Mortality rate: 5% (2/39)	Larger studies are included. (Included in table 2 of original overview).
Costalat V, Maldonado IL, Vendrell JF et al. (2011) Endovascular treatment of symptomatic intracranial stenosis with the Wingspan stent system and Gateway PTA balloon: a multicenter series of 60 patients with acute and midterm results. Journal of Neurosurgery 115: 686–693.	n = 60 FU = 13 months	Technical success = 95% Procedural complications = 21% Permanent postoperative morbidity and death = 5% In-stent restenosis = 17%	Larger studies are included.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Costalat V, Maldonado IL, Zerlauth JB et al. (2010) Endovascular treatment of symptomatic intracranial arterial stenosis: six-year experience in a single-center series of 42 consecutive patients with acute and mid-term results. Neurosurgery 67: 1505–1514	n = 42 (9 with isolated angioplasty) FU = 20 months	Technical success = 98% Procedural complications = 21% Postoperative permanent morbidity/mortality rate = 7% In-stent thrombosis = 7% (3/42) (1 fatal) Asymptomatic restenosis = 12%	Larger studies are included.
Coward LJ, McCabe DJ, Ederle J et al. (2007) Long-term outcome after angioplasty and stenting for symptomatic vertebral artery stenosis compared with medical treatment in the Carotid And Vertebral Artery Transluminal Angioplasty Study (CAVATAS): a randomized trial. Stroke 38: 1526–1530	n = 16 (8 balloon angioplasty or stenting vs 8 best medical treatment) FU = 5 years	No patients experienced a vertebrobasilar territory stroke. 3 patients in each group died of myocardial infarction or carotid artery stroke. The trial failed to show a benefit of endovascular treatment of vertebral artery stenosis.	Larger studies are included.
Coward L, Featherstone R, Brown MM. (2005) Percutaneous transluminal angioplasty and stenting for vertebral artery stenosis. Cochrane Database of Systematic Reviews: Reviews 2005 Issue 2: DOI: 10.1002/14651858	1 RCT included (n = 16)	Insufficient evidence to support the use of endovascular treatment for vertebral artery stenosis in routine clinical practice.	Includes only 1 small RCT.
Cruz FS, Diamond AL. (2006) Angioplasty for intracranial artery stenosis. Cochrane Database of Systematic Reviews: Reviews 2006 Issue 3: DOI: 10.1002/14651858	79 case series included (angioplasty with or without stenting)	Perioperative stroke = 8% (95% CI 6% to 10%) Perioperative death = 3% (95% CI 2% to 5%) Insufficient evidence to support the use of angioplasty for intracranial artery stenosis.	Includes angioplasty with or without stenting.
Fiorella DJ, Levy EI, Turk AS et al. (2009) Target lesion revascularization after wingspan: assessment of safety and durability. Stroke 40: 106–110	n = 36 patients with in-stent restenosis after endovascular stent insertion	Of 29 patients undergoing target lesion revascularisation, 9 required 1 or more interventions for recurrent in-stent restenosis. 1 post-procedural reperfusion haemorrhage.	Larger studies are included.
Fiorella D, Levy EI, Turk AS et al. (2007) US multicenter experience with the wingspan stent system for the treatment of intracranial atheromatous disease: periprocedural results. Stroke 38: 881–888	n = 78 FU = 30 days	Technical success rate = 99% Major periprocedural complications = 6% (5/78) 30-day mortality = 5% (4/78)	A more recent report from the same author is included.
Fiorella D, Chow MM, Anderson M et al. (2007) A 7-year experience with balloon-mounted coronary stents for the treatment of symptomatic vertebrobasilar intracranial atheromatous disease. Neurosurgery 61: 236–242	n = 44 FU = 44 months	Technical success rate = 96% Periprocedural neurological morbidity and mortality = 26% In-stent restenosis/occlusion rate = 13% (4/32)	Larger studies are included.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Fiorella D, Levy EI, Turk AS, Albuquerque FC et al. (2007) US multicenter experience with the Wingspan stent system for the treatment of intracranial atheromatous disease: Periprocedural results. Stroke 38: 881–887	n = 78	Technical success rate: 99% (81/82) 30-day mortality: 5% (4/82)	Larger studies are included. (Included in table 2 of original overview).
Freitas JM, Zenteno M, Aburto-Murrieta Y et al. (2007) Intracranial arterial stenting for symptomatic stenoses: a Latin American experience. Surgical Neurology 68: 378–386	n = 32 FU = 10 months	Mortality = 9% (3/32) Stroke rate = 0% Restenosis = 9%	Larger studies are included.
Gao F, Du B, Xu XT et al. (2009) Safety of low-dose heparin for intracranial stent-assisted angioplasty: a randomized controlled pilot study. Journal of endovascular therapy: an official journal of the International Society of Endovascular Specialists 16: 642–648.	n = 64	Assessment of low-dose versus high-dose heparin during the procedure. The use of low-dose heparin did not increase the incidence of target lesion thrombosis or intracranial haemorrhage.	Larger studies are included.
Guo X-B, Ma N, Hu X-B et al. (2011) Wingspan stent for symptomatic M1 stenosis of middle cerebral artery. European Journal of Radiology 80: e356–e360	n = 53 FU = 6 months	Complications associated with the procedure include subarachnoid haemorrhage (1.9%) and occlusion (3.8%). 'Wingspan stent for symptomatic stenosis of middle cerebral artery is a safe and feasible procedure. It improves clinical outcome in the intermediate follow up, but its long-term effect remains to be further evaluated.'	Larger studies with longer follow-up are included in table 2.
Gralla J, Rennie AT, Squire W et al. (2009) Fatal hemorrhage after attempted treatment of a basilar artery stenosis. Case report. Journal of Neurosurgery 111: 102–104	n = 1	After successful balloon dilation, an attempt to deploy a self-expanding stent failed due to the severe kinking of the stenotic segment; fatal haemorrhage was caused by vascular rupture distant from the site of angioplasty.	Case report of safety outcome already described.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Gupta R, Al Ali F, Thomas AJ et al. (2006) Safety, feasibility, and short-term follow-up of drug-eluting stent placement in the intracranial and extracranial circulation. Stroke 37: 2562–2566	n = 59 (65 lesions: 29 intracranial, 36 extracranial)	Stenosis reduction to < 50%: 61/62 stents (98%) Restenosis rate: 5% (1/20) Periprocedural complication rate: 8% (2/26)	Larger studies are included. (Included in table 2 of original overview).
Jiang WJ, Yu W, Du B et al. (2011) Outcome of patients with ≥ 70% symptomatic intracranial stenosis after wingspan stenting. Stroke 42: 1971–1975	n = 100 FU = 2 years	Technical success = 99% Stroke or death within 30 days and ipsilateral ischaemic stroke after 30 days = 9% (9/100)	Another study from the same centre is included.
Jiang WJ, Yu W, Du B et al. (2010) Wingspan experience at Beijing Tiantan Hospital: New insights into the mechanisms of procedural complication from viewing intraoperative transient ischemic attacks during awake stenting for vertebrobasilar stenosis. Journal of Neurointerventional Surgery 2: 99–103	n = 43 FU = 30 days	Technical success = 98% 7% (3/43) periprocedural strokes	Larger studies are included.
Jiang WJ, Xu XT, Du B et al. (2007) Long-term outcome of elective stenting for symptomatic intracranial vertebrobasilar stenosis. Neurology 68: 856–859	n = 79 FU = 812 days	Annual stroke rate = 5%	Another study from the same centre is included.
Jiang WJ, Xu XT, Jin M et al. (2007) Apollo stent for symptomatic atherosclerotic intracranial stenosis: Study results. American Journal of Neuroradiology 28: 830–834	n = 46 FU = 24 months	Technical success rate = 92% Minor strokes within 30 days = 7% (3/46) Restenosis = 28% (7/25)	Larger studies are included.
Jiang WJ, Du B, Leung TW et al. (2007) Symptomatic intracranial stenosis: cerebrovascular complications from elective stent placement. Radiology 243: 188–197	n = 169	Complication rate = 12% (20/169) Stroke rate = 6% (10/169) Target lesion thrombosis = 4% (6/169)	Another study from the same centre is included.
Jiang W-J, Wang Y, Du B et al. (2004) Stenting of symptomatic M1 stenosis of middle cerebral artery. Stroke 35: 1–6	n = 40 FU = 10 months	Technical success rate: 98% (41/42) No recurrent stroke or TIA during follow-up. Procedure-related mortality: 3% (1/40) (2 hours after procedure, because of subarachnoid haemorrhage)	Larger studies are included. (Included in table 2 of original overview).

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Ito K, Kai Y, Hyodo A et al. (2011) Long-term outcome of angioplasty or stent placement for stenosis of the cavernous or petrous portion of the internal carotid artery. Neurologia Medico-Chirurgica 51: 813–818	n = 54 FU = 30 months	Restenosis and occlusion = 7.4% (4/54) Five patients died (2 of malignancy and 3 of myocardial infarction) during the follow-up period. 'Percutaneous transluminal angioplasty and stent placement are safe and effective in patients with stenosis of the cavernous or petrous portion of the ICA, and result in low long-term rates of restenosis.	Larger studies are included.
Lanfranconi S, Bersano A, Branca V et al. (2010) Stenting for the treatment of high-grade intracranial stenoses. Journal of Neurology 257: 1899–1908	n = 34 FU = 30 days	Technical success rate = 100% 30-day stroke/death rate = 18%	Larger studies are included.
Lawson MF, Fautheree GL, Waters MF et al. (2010) Acute intraprocedural thrombus formation during wingspan intracranial stent placement for intracranial atherosclerotic disease. Neurosurgery 67 (3: Suppl Operative) Suppl-70	n = 41	Acute intraprocedural thrombus formation within 20 minutes of stent placement = 15% (6/41) There was no morbidity.	Larger studies are included.
Levy EI, Turk AS, Albuquerque FC et al. (2007) Wingspan in-stent restenosis and thrombosis: incidence, clinical presentation, and management. Neurosurgery 61: 644–650	n = 78	In-stent restenosis = 30% In-stent restenosis was more frequent within the anterior circulation than the posterior circulation.	Larger studies are included.
Li J, Zhao ZW, Gao GD et al. (2011) Wingspan stenting with modified predilation for symptomatic middle cerebral artery stenosis. Catheterization and Cardiovascular Interventions 78: 286–293	n = 48 FU = 13 months	Technical success = 98% 2% minor stroke and 4% TIA within 30 days. Recurrent stroke/TIA = 5% Balloon predilation can reduce the rate of restenosis.	Larger studies are included.
Lylyk P, Vila JF, Miranda C et al. (2005) Endovascular reconstruction by means of stent placement in symptomatic intracranial atherosclerotic stenosis. Neurological Research 27 Suppl 1: S84–S88	n = 106 FU = 6 months	Technical success rate: 98% (104/106) Procedure-related mortality: 4% (4/104) Restenosis (within 6 months): 12.5% Repeated angioplasty: 2% (2/104)	Larger studies are included. (Included in table 2 of original overview).

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Mazighi M, Yadav JS, Abou-Chebl A. (2008) Durability of endovascular therapy for symptomatic intracranial atherosclerosis. Stroke 39: 1766–1769	n = 53 (69 lesions) FU = 24 months	Technical success rate = 99% (68/69) 30-day stroke/death rate = 10% (7/69) TIA/stroke rate during follow-up = 6% (4/69) Restenosis at 1 year = 8% (4/53)	Larger studies are included. Includes some patients treated by angioplasty alone.
Miao ZLF, Li S, Zhu F et al. (2003) Treatment and short-term follow-up of symptomatic atherosclerotic intracranial artery stenosis by stent-assisted angioplasty. Interventional Neuroradiology 9: 153–162	n = 32 FU = 4 months	Technical success rate: 97% (31/32) Restenosis = 12% (3/26) No stroke / TIA within follow-up = 92% (24/26) 1 patient had vessel rupture during procedure.	Larger studies are included. (Included in table 2 of original overview).
Nahab F, Lynn MJ, Kasner SE et al. (2009) Risk factors associated with major cerebrovascular complications after intracranial stenting. Neurology 72: 2014–2019	n = 160	Major cerebrovascular complications after intracranial stenting may be associated with posterior circulation stenosis, low volume sites, stenting soon after a qualifying event, and stroke as the qualifying event.	Another study reporting data from this registry is included in the meta-analysis (Siddiq F et al. 2009).
Nguyen TN, Zaidat OO, Gupta R et al. (2011) Balloon angioplasty for intracranial atherosclerotic disease: periprocedural risks and short-term outcomes in a multicenter study. Stroke 42: 107–111	n = 74 FU = 3 months	Technical success = 92% 4 major procedure-related strokes, 2 of which resulted in death. 30-day stroke/death rate = 5% 3-month stroke/death rate = 9% Retreatment rate = 3%	Larger studies are included.
Puetz V, Gahn G, Becker U et al. (2008) Endovascular therapy of symptomatic intracranial stenosis in patients with impaired regional cerebral blood flow or failure of medical therapy. American Journal of Neuroradiology 29: 273–280	n = 38 FU = 21 months	Technical success rate = 92% (35/38) Periprocedural major complications = 11% (4/38) Recurrent ischaemic strokes = 8% (3/38)	Larger studies are included.
Steinbauer MG, Pfister K, Greindl M (2008) Alert for increased long-term follow-up after carotid artery stenting: results of a prospective, randomized, single-center trial of carotid artery stenting vs carotid endarterectomy. Journal of Vascular Surgery 48 (1) 93–98	n = 84 (42 carotid artery stenting vs 42 carotid endarter-ectomy) FU = 65 months	Stroke rate: • Carotid artery stenting = 10% (4/42) • Endarterectomy = 0% (0/42) Restenosis: • Carotid artery stenting = 19% (6/32) • Endarterectomy = 0% (0/29)	It is not clear if the indications include intracranial stenosis or just extracranial.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Suh DC, Kim JK, Choi JW et al. (2008) Intracranial stenting of severe symptomatic intracranial stenosis: results of 100 consecutive patients. American Journal of Neuroradiology 29: 781–785.	n = 100 FU = 6 months	Technical success rate = 99% Adverse events within 6 months: • Minor stroke = 4% • Major stroke = 3% • Death = 3% Restenosis = 0%	Larger studies are included.
Teraa M, Moll FL, Van Der Worp B H et al. (2010) Symptomatic vertebral artery stent fracture: A case report. Journal of Vascular and Interventional Radiology 21: 1751–1754	n = 1	Symptoms recurred 4 months after stent placement and arteriogram revealed a fractured stent, which was treated surgically.	Case report.
Terada T, Tsuura M, Matsumoto H et al. (2001) Endovascular treatment for intracranial atherosclerotic stenosis. Pitfalls and problems. Interventional Neuroradiology 7: 1–8	n = 45 FU = 29 months	Technical success rate = 98% (44/45) No strokes were reported during follow-up.	Larger studies are included.
The SSYLVIA Study Investigators. (2004) Stenting of Symptomatic Atherosclerotic Lesions in the Vertebral or Intracranial Arteries (SSYLVIA). Stroke 35: 1388–1392	n = 61 (43 = intracranial; 18 = extracranial)		Most results not reported separately for extracranial vs intracranial stenting.
Turk AS, Levy EI, Albuquerque FC et al. (2008) Influence of patient age and stenosis location on wingspan in-stent restenosis. American Journal of Neuroradiology 29: 23–27	n = 93	In-stent restenosis by age: • Age ≤ 55 years = 45% (14/31) • Age > 55 years = 24% (15/62) There was a higher prevalence of anterior circulation lesions in the younger group.	Larger studies are included.
Weber W, Mayer TE, Henkes H et al. (2005) Stent-angioplasty of intracranial vertebral and basilar artery stenoses in symptomatic patients. European Journal of Radiology 55: 231–236	n = 21 FU = 10 months	Restenosis rate: 33% (2/9) Procedure-related mortality rate: 5% (1/21) Major stroke = 5% (1/21) Minor stroke = 5% (1/21)	Larger studies are included. (Included in table 2 of original overview).
Werner M, Braunlich S, Ulrich M et al. (2010) Drug-eluting stents for the treatment of vertebral artery origin stenosis. Journal of Endovascular Therapy 17: 232–241	n = 28 FU = 16 months	No strokes, worsening of symptoms or deaths occurred during follow-up. Angiographic restenosis = 21% (6/28) 1 stent fracture Stent compression and recoil were the major contributing factors to restenosis.	Larger studies are included.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Wojak JC, Dunlap DC, Hargrave KR et al. (2006) Intracranial angioplasty and stenting: long-term results from a single center. American Journal of Neuroradiology 27: 1882–1892	n = 60 (62 procedures) (22 = stent, 40 = PTA only) FU = 2–12 months		Results not reported separately for stent vs angioplasty only.
Wolfe TJ, Fitzsimmons BF, Hussain SI et al. (2009) Long term clinical and angiographic outcomes with the Wingspan stent for treatment of symptomatic 50–99% intracranial atherosclerosis: single center experience in 51 cases. Journal of Neurointerventional Surgery 1: 40–43	n = 51 FU = 15 months	Technical success = 98% Stroke or death within 24 hours = 2% (1/51) Stroke or death within 30 days or ipsilateral stroke beyond 30 days = 10% (5/51). Restenosis (≥ 50%) on follow-up imaging = 24% (7/29) at 9 months.	Larger studies are included.
Yu J, Wang L, Deng JP et al. (2010) Treatment of symptomatic intracranial atherosclerotic stenosis with a normal-sized Gateway(TM) balloon and Wingspan(TM) stent. Journal of International Medical Research 38: 1968–1974	n = 72	Technical success = 100% Major periprocedural neurological complications = 9% In-stent restenosis was significantly less frequent when a normal sized balloon was used compared with an undersized balloon.	Larger studies are included.
Yu SC, Leung TW, Lee KT et al. (2011) Angioplasty and stenting of atherosclerotic middle cerebral arteries with Wingspan: evaluation of clinical outcome, restenosis, and procedure outcome. American Journal of Neuroradiology 32: 753–758	n = 60	There were no significant differences in procedural safety, patient outcome, and restenosis rates of stent placement between the group with middle cerebral artery stenosis and the group with stenoses located at other sites.	Larger studies are included.
Yue X, Yin Q, Xi G et al. (2011) Comparison of BMSs with SES for symptomatic intracranial disease of the middle cerebral artery stenosis. Cardiovascular and Interventional Radiology 34: 54–60	n = 67	The prevalence of restenosis was higher in the self-expandable stent group than the balloon-mounted stent group, but the perioperative complications and follow-up clinical outcomes had no significant difference.	Larger studies are included.
Zaidat OO, Klucznik R, Alexander MJ et al. (2008) The NIH registry on use of the Wingspan stent for symptomatic 70-99% intracranial arterial stenosis. Neurology 70: 1518–1524	n = 129 FU = 6 months	Technical success rate = 97% Stroke, intracerebral haemorrhage, or death within 30 days or ipsilateral stroke beyond 30 days = 14% at 6 months. Restenosis = 25% (13/52)	Study is included in meta-analysis (Siddiq F et al. 2009).

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Zhang R, Zhou G, Xu G et al. (2009) Posterior circulation hyperperfusion syndrome after bilateral vertebral artery intracranial stenting. Annals of Vascular Surgery 23: 686–5	n = 1	3 hours after stent insertion, the patient had severe headache with vomiting and gradually went into a coma. Brain scan showed haemorrhage in right cerebellum and subarachnoid region.	Case report.
Zhang L, Huang Q, Zhang Y et al. (2012) Wingspan stents for the treatment of symptomatic atherosclerotic stenosis in small intracranial vessels: safety and efficacy evaluation. Ajnr: American Journal of Neuroradiology 33: 343–347	n = 53 FU = 18 months	Technical success = 98% 1 small cerebral haemorrhage Restenosis (identified on imaging) = 33% (13/39) (mean follow-up = 10 months)	Larger studies are included.
Zhao ZW, Deng JP, He SM et al. (2009) Intracranial angioplasty with Gateway-Wingspan system for symptomatic atherosclerotic stenosis: preliminary results of 27 Chinese patients. Surgical Neurology 72: 607–611	n = 27	Technical success rate = 100% Complications = 15% (4/27) No new ischaemic events within 30 days.	Larger studies are included.
Zhou Y, Yang QW, Xiong H Y. (2012) Angioplasty with stenting for intracranial atherosclerosis: a systematic review. Journal of International Medical Research 40:18–27.	Systematic review n = 1 study	The SAMMPRIS trial indicated that percutaneous transluminal angioplasty and stenting is associated with high complication and morbidity rates. Definitive recommendations cannot be made until convincing results from additional robustly designed randomised trials become available.	Only 1 RCT is included, which is already summarised in table 2.
Zhu SG, Zhang RL, Liu WH et al. (2010) Predictive factors for in-stent restenosis after balloon-mounted stent placement for symptomatic intracranial atherosclerosis. European Journal of Vascular and Endovascular Surgery 40: 499–506	n = 61 FU = 7 months	In-stent restenosis = 30% (18/61). Diabetes and lesion length are associated with increased risk of in-stent restenosis.	Larger studies are included.

Appendix B: Related NICE guidance for endovascular stent insertion for intracranial atherosclerotic disease

Guidance	Recommendations
Interventional procedures	**Extracranial to intracranial bypass for intracranial atherosclerosis. NICE interventional procedures guidance 348 (2010).** 1.1 Current evidence on the efficacy and safety of extracranial to intracranial (EC–IC) bypass for intracranial atherosclerosis is inconsistent and remains limited in quantity and quality. Therefore, this procedure should only be used with special arrangements for clinical governance, consent and audit or research. 1.2 Clinicians wishing to undertake EC–IC bypass for intracranial atherosclerosis should take the following actions.• Inform the clinical governance leads in their Trusts. • Ensure that patients and their carers understand the uncertainty about the procedure's safety and efficacy in relation to symptom reduction and stroke prevention, and provide them with clear written information. In addition, the use of NICE's information for patients ('Understanding NICE guidance') is recommended (available from www.nice.org.uk/guidance/IPG348/publicinfo). • Audit and review clinical outcomes of all patients having EC–IC bypass for intracranial atherosclerosis (see section 3.1). 1.3 Patient selection for EC–IC bypass for intracranial atherosclerosis should be carried out by a multidisciplinary team with experience of managing patients with cerebral hypoperfusion syndromes who are undergoing this procedure. The team should include a neuroradiologist, neurologist/stroke physician and vascular neurosurgeon. The procedure should be done only by surgeons with specific training. 1.4 NICE encourages further research into EC–IC bypass for intracranial atherosclerosis. Research studies should clearly define patient selection criteria and report symptomatic and quality of life outcomes. NICE is aware of current clinical trials involving this procedure and may review the procedure on publication of further evidence.

Appendix C: Literature search for endovascular stent insertion for intracranial atherosclerotic disease

Databases	Date searched	Version/files	No. retrieved
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	27/03/12	N/A	8
Database of Abstracts of Reviews of Effects – DARE (CRD website)	27/03/12	N/A	0
HTA database (CRD website)	27/03/12	N/A	0
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	27/03/12	N/A	4
MEDLINE (Ovid)	23/03/12	1946 to March Week 2 2012	30
MEDLINE In-Process (Ovid)	23/03/12	March 21, 2012>	34
EMBASE (Ovid)	23/03/12	1980 to 2012 Week 11	50
CINAHL (NLH Search 2.0 or EBSCOhost)	23/03/12	-	74
Zetoc			

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1 exp Intracranial Arterial Diseases/
2 intracran*.tw.
3 arteri*.tw.
4 2 and 3
5 ICAD.tw.
6 1 or 4 or 5
7 exp Balloon Dilatation/
8 (balloon* adj3 (cathet* or dilat* or tamponad* or valvo* or angioplast*)).tw.
9 (Percutan* adj3 translum* adj3 angioplast*).tw.
10 PTA.tw.
11 stents/
12 stent*.tw.
13 11 or 12
14 Vascular Surgical Procedures/
15 7 or 8 or 9 or 10 or 14
16 13 and 15
17 (intracranial adj3 stenos$).tw.
18 ((brain or ischemic) adj3 attack).tw.
19 (intracranial adj3 arterioscleros$).tw.
20 ((brain or cerebral) adj3 (infarction or ischemia)).tw.

21 (Intracranial adj3 (artherosclerotic or atherosclerotic or arterial) adj3 (disease or stenos$)).tw.
22 Brain Ischemia/
23 Brain infarction/
24 Ischemic attack, transient/
25 Intracranial Arteriosclerosis/
26 Intracranial Arterial Diseases/
27 or/17-26
28 (Wingspan or Pharos).tw.
29 6 or 27
30 16 and 29