National Institute for Health and Clinical Excellence

008/2 – Carotid artery stent placement for symptomatic extracranial carotid stenosis

Consultation Comments table

IPAC date: Friday 11 February 2011

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
1	Consultee 1 Specialist Adviser BSIR representative	**1**	These are sensible and workable recommendations.	Thank you for your comment.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
2	Consultee 2 Three Private NHS Professionals	**1.3**	Section 1.3 addresses the medical team that should select patients for CAS placement and Section 1.4 addresses the clinician who should perform CAS placement. The NICE recommendations are not based on “outcomes” data. Â The quality of CAS is related to both hospital volume and operator experience. Â This statement does not address the hospital volume (1-4). Â This statement fails to address minimum case numbers for operator experience. Â Furthermore the NICE document states “patient selection should be carried out by a multi-disciplinary team which should include an interventional radiologist or a neuroradiologist, a vascular surgeon and a physician with a special interest in stroke.” Â Lead in data from the CREST carotid stent trial demonstrated that physicians with cardiologists and radiologists had half the number of complications than vascular surgeons (2). Â This population included both interventional cardiologists and radiologists. Â Furthermore after the lead in phase the complication rate for vascular surgeons decreased underscoring the importance of operator experience. Â Finally the last sentence of section 1.3 states that cardiac surgeons and cardiologists should “liaise” with the multi-disciplinary team when treating patients with asymptomatic carotid stenosis who are being evaluated for CABG. Â Cardiologists must be part of the multi-disciplinary team. References 1. Fiehler J, Jansen O, Berger J, Eckstein HH, Ringleb PA, Stingele R. Differences in complication rates among the centres in the SPACE study. Neuroradiology 200850:1049-53. 2. Hopkins LN, Roubin GS, Chakhtoura EY, et al. The Carotid Revascularization Endarterectomy versus Stenting Trial: credentialing of interventionalists and final results of lead-in phase. J Stroke Cerebrovasc Dis 201019:153-62. 3. Lin PH, Bush RL, Peden EK, et al. Carotid artery stenting with neuroprotection: assessing the learning curve and treatment outcome. Am J Surg 200519:850-7. 4. Roffi M, Mukherjee D, Clair DG. Carotid artery stenting vs. endarterectomy. Eur Heart J 200930:2693-704.	Thank you for your comment. The Committee considered this comment and decided not to change the guidance. The Committee was advised that there is variation in carotid artery stenting practice. The committee considered the matter of MDT profile and decided that local circumstances might preclude direct cardiologist involvement. References used by the consultee: 1) Subgroup analysis of patients from SPACE trial included in table 2 Eckstein H-H (2008) 2) CREST trial included in table 2 Brott TG (2010) 3) This study was identified in the updated literature search 4) Larger, and more recent meta analysis is included in table 2 of the overview [Meier P (2010)]

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
3	Consultee 3 Vascular Society of Great Britain and Ireland	**1**	Patient choice should also be taken into account	Thank you for your comment. This is explicit in section 1.2 of the guidance.
4	Consultee 4 Association of British Neurologists	**1**	We support these provisional recommendations With regard to the introduction headed: “Treating symptomatic narrowed or blocked carotid artery using stents” Â we note that the first paragraph of the consultation states misleadingly that: “Fragments of these fatty deposits become detached from the walls of the carotid artery and become lodged in thinner arteries that supply blood to the brain, causing a transient ischaemic attack or a stroke”. Â It is rare for TIA or stroke to be caused by embolism of fragments of the fatty deposits. Â Instead, these symptoms are caused by thrombus forming on the area of narrowing. Â Therefore, the first phrase of this sentence should be rephrased to read: “Blood clots can form on these fatty deposits and become detached.....”	Thank you for your comment. The lay description in the overview will be changed.
5	Consultee 5 Vascular Society of Great Britain and Ireland Specialist Society	**2.1**	There needs to be greater emphasis on the need to intervene as soon as possible after the index event. The recomendations should reinfoce the need to offer CEA or CAS within 14 days. The document should mention that treatment by stenting in the first 14 days after onset of symptoms may be associated with a higher risk of stroke and that this needs to be considered when planning whether the patient should undergo stenting or surgery. In an individual patient meta-analysis of 3433 patients randomised within EVA-3S, ICSS or SPACE, patients undergoing stenting within 14 days of their most recent symptom were almost three times more likely to suffer a stroke or death within 30 days than patients undergoing surgery (OR 2.7 95%CI 1.4-5.5) Lancet 20103761062-1073	Thank you for your comment. The positioning and timing of this procedure within the care pathway is outside the scope of this guidance.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
6	Consultee 1 Specialist Adviser BSIR representative	**2.1**	Carotid endarterectomy (CEA) is not the standard of care in those units already experienced in Carotid Artery Stenting (CAS). For example, in our own unit we take note that our published outcomes are at least as good as CEA. In addition we take note of the results of the ICSS trial, in particular (a) the outcome important to the patient of major stroke and death is equivalent, (b) all adverse neurological Â outcome of death, stroke and cranial nerve palsy (rather than cherry picking stroke and death) is equivalent, and if MI is included then outcomes favour CAS. Some patient subgroups were demonstrated to be equivalent or actually do better with CAS women, contralateral ICA occlusion, aged 64 yrs, presenting with TIA or ocular symptoms. Finally, units experienced in CAS had equivalent to CEA. The therapies are therefore complementary, some patients are better with CEA, others with CAS, and some patients should offered both.	Thank you for your comment. Section 1.4 of the guidance states that 'This procedure should only be carried out by clinicians with specific training and expertise in the technique who regularly perform complex endovascular interventions.' The outcome of perioperative MI from Brott (2010) will be added to the guidance document at section 2.4.3.
7	Consultee 2 Three Private NHS Professionals	**2.1.2**	Section 2.1.2 states the importance of medical secondary prevention. Given the results of recent HMG-CoA-reductase inhibitor (statin) trials, the use of statins should be emphasized for primary prevention of stroke in the asymptomatic carotid stenosis population. No recommendation or data are provided regarding the need for anti-platelet regimens after CAS placement in the NICE document.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.
8	Consultee 3 Vascular Society of Great Britain and Ireland	**2.1.2**	We disagree with the wording of paragraph 2.1.2. which Â should read: Â Current evidence suggests that carotid endarterectomy is safer than carotid stenting and is the standard treatment for both symptomatic and asymptomatic patients. This procedure can be performed under both local and general anaesthetic	Thank you for your comment. This guidance relates only to patients with symptomatic stenosis. NICE is also developing IP guidance on use of this procedure in asymptomatic patients. The guidance will not be changed.
9	Consultee 4 Association of British Neurologists	**2.1**	We agree.	Thank you for your comment.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
10	Consultee 1 Specialist Adviser BSIR representative	**2.2**	There is also risk of stroke caused by embolisaton during carotid endarterectomy. In addition (a) CEA has complications not encountered with CAS, e.g. cranial nerve palsy, which may be just as debilitating as a minor stroke, and (b) CREST demonstrated that CEA has a higher risk of MI than CAS - why not also mention those facts?	Thank you for your comment. Complication rates for comparator procedures are not usually described in Interventional procedures guidance. Further details of the CREST trial, Brott TG (2010) can be found in Table 2 of the overview and the outcome of perioperative MI will be added to section 2.4.3 of the guidance..
11	Consultee 6 Specialist Adviser	**2.2.1**	“A guideword is passed into the carotid artery, often followed by a small balloon catheter to pre-dilate the narrowed artery” is factually incorrect in that it is implied that this step is performed prior to establishment of an embolic protection (or “cerebral protection”) device. Very few experienced carotid stenters would countenance the pre-dilatation of a tight, friable lesion that has recently given rise to cortical or ocular symptoms prior to establishment of embolic protection. Pre-dilatation (if it is necessary) is mostly performed after protection is in place.	Thank you for your comment. Section 2.2.1 of the guidance will be changed.
12	Consultee 2 Three Private NHS Professionals	**2.2.2**	Section 2.2.2 states that CAS placement is less invasive than CEA. Â However the statement mentions Â “there has been concern about the risk of stroke caused by embolic material becoming dislodged during the procedure.” Â In the United States the standard of care involves the use of embolic protection devices when treating symptomatic carotid artery stenosis. Â The quoted statement should be tempered with data from the EMPIRE trial and NASCET study for CAS placement and CEA respectively. Finally no information is provided regarding the difference in recovery time from CAS verses CEA.	Thank you for your comment. The committee weighed up the potential advantages of stenting with the potential risks. The EMPiRE trial became available after the cut-off date of the literature search carried out by NICE for this guidance. However, other larger case series are included in Table 2 and Appendix A of the overview. The NASCET study involves CEA and is not therefore relevant to the guidance.
13	Consultee 3 Vascular Society of Great Britain and Ireland	**2.2**	Agreed	Thank you for your comment.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
14	Consultee 4 Association of British Neurologists	**2.2.2**	The statement: “Carotid stenting is a less invasive percutaneous procedure than endarterectomy” is misleading. Stent deployment causes more direct arterial damage than carotid endarterectomy (CEA). However, the groin incision during carotid stenting (CAS) causes less soft tissue trauma. In the past, CAS was considered less invasive than CEA, because CAS was done under local anaesthesia (LA). However, CEA is now often done under LA. All the RCTs, including CREST, have shown that CAS carries a higher risk of stroke and death than CEA. Thus, it is wrong to refer to CAS as “less invasive”. We therefore recommend that this paragraph should be rephrased to read as follows: “Carotid stenting is a percutaneous procedure that avoids some of the access complications associated with endarterectomy, but there has been concern about the risk of stroke caused by embolic material becoming dislodged during the procedure”.	Thank you for your comment. Section 2.2.2 of the guidance will be changed.
15	Consultee 2 Three Private NHS Professionals	**2.3.1**	Section 2.3.1 describes efficacy data from carotid stent studies. Â It is factual.Section 2.3.2 describes the mortality rate, incidence of disabling stroke or mortality and stroke rate among 953 patients in a British registry treated with CAS placement. These statistics should be tempered from data generated in larger post-market registries (1, 2). References 1. Gray WA, Chaturvedi S, Verta P. Thirty-day outcomes for carotid artery stenting in 6320 patients from 2 prospective, multicenter, high-surgical-risk registries. Circ Cardiovasc Interv 20092:159-66. 2. Massop D, Dave R, Metzger C, et al. Stenting and angioplasty with protection in patients at high-risk for endarterectomy: SAPPHIRE Worldwide Registry first 2,001 patients. Catheter Cardiovasc Interv 200973:129-36.	Thank you for your comment. The overview represents a rapid review of the literature and is not a full systematic review. 1) Gray WA (2009) is included in Appendix A of the overview. 2) Massop D (2009) is included in Appendix A of the overview

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
16	Consultee 3 Vascular Society of Great Britain and Ireland	**2.3**	We disagree with the NICE on their conclusions of the meta analysis published in September 2010's Lancet. This showed that overall there is a significantly higher risk of stroke and death from stenting when compared to surgery. When sub-analysis was performed then there was equivalence for these procedures in patients less then 70 years of age, but clear superiority of surgery in those over 70. The wording in the reccomendations needs to be stronger to reflect these results.	Thank you for your comment. The committee recognised the importance of the outcomes from the Bonati LH (2010) meta analaysis which is speficic to symptomatic patients, but weighed up the potential advantages of stenting with the potential risks.
17	Consultee 4 Association of British Neurologists	**2.3**	No comments	Thank you for your comment
18	Consultee 1 Specialist Adviser BSIR representative	**2.4**	These 30 day data are included in the efficacy outcomes since they essentially look at the same outcomes - death and stroke. The principal message should therefore be that the long term prevention of stroke and death is equivalent for the 2 procedures. Why have you ignored the CREST data which shows higher MI following CEA in symptomatic patients?	Thank you for your comment, further details of the CREST trial, Brott TG (2010) can be found in Table 2 of the overview and details will be added to the guidance.
19	Consultee 5 Vascular Society of Great Britain and Ireland Specialist Society	**2.4**	In the meta-analsysi of SPACE, EVA-3S and SPACE stenting was associated with a significantly higher 30-day risk of death/disabling stroke using a per-protocol analysis (OR 1.8 95%CI 1.2-2.7). Lancet 20103761062-1073 In addition, this safety summary makes no reference to the fact that ICSS observed a five fold increase in new and persisting brain lesion on MRI following stenting as compared with surgery (OR 5.2 95%CI 2.8-9.8)(Lancet Neurol 20109:353-62). No-one knows the significance of this but the patient should be warned that there is a potential for cognitive impairment long term.	Thank you for your comment. The Committee considered this comment but in the absence of good clinical data, decided not to change the guidance.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
20	Consultee 6 Specialist Adviser	**2.4**	1. The meta-analysis of 3433 symptomatic patients demonstrated that in patients under 70 years, the 120-day risk of stroke & death was 50 of 869 (5.8%) in the carotid stenting (CAS) group and 48 of 843 (5.7%) in the endarterectomy (CEA) group. RR 1.00 [0.68-1.47] The confidence intervals are narrow and the results are very comparable to outcome data from CREST (US randomised trial) for patients under 70 years, so the influence of age on outcome for CAS is a consistent finding. It is as important for referring physicians & patients alike to understand that the risk of stenting may increase in the over 70s but that the results of CAS & CEA are equivalent for the under 70s. 2. NICE assumes that the rates of MI for CAS & CEA are equivalent based on one trial. They are not. The absolute results depend on definition & independent adjudication. The CREST trial showed a significant difference in MI in favour of CAS (& the definition was NOT based on enzyme rise only). A procedural Q- or non-Q wave MI confers an increased risk of death by a factor of 6 and an increased six month risk of further MI by a factor of 27 (Kim LJ, et al. Circulation 2002 106:2366-2371).	Thank you for your comment. Bonati LH (2010) is included in table 2 of the overview. Kim LJ (2002) is not related to carotid stenting. The guidance will not be changed.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
21	Consultee 4 Association of British Neurologists	**2.4.1**	Paragraph 2.4.1 and also the overview of carotid artery stent placement for symptomatic extracranial carotid stenosis published on 21st December 2010 (IP008_2) fail to give the interim results from the largest trial of carotid artery stenting versus carotid endarterectomy for symptomatic carotid stenosis, namely the International Carotid Stenting Study (ICSS Investigators, Lancet 2010,375,985-997). Â This trial recruited more patients with symptomatic carotid stenosis than the other relevant trials and has provided the most robust information to date on the safety of carotid endarterectomy for symptomatic carotid stenosis. The trial enrolled 1713 patients and the individual data numbers and hazard ratios are given in the publication. Between randomisation and 120 days, the incidence of stroke, death or procedural myocardial infarction was 8.5% in the stenting group compared with 5.2% in the endarterectomy group. Â The results should be quoted in paragraph 2.4.1 and also added to the Tables in the full overview.	Thank you for your comment. This study was identified in the updated literate search and will be added to table 2 of the overview.
22	Consultee 2 Three Private NHS Professionals	**2.4.1**	Section 2.4 attempts to address the safety of CAS placement. Section 2.4.1 lists the rate of myocardial infarction from one randomized trial comparing patients who underwent CEA and CAS placement. Â Data from CREST, the largest randomized trial of CAS vs CEA, with systematic collection of cardiac enzymes demonstrates a lower rate of myocardial infarction among patients undergoing CAS placement(1).	Thank you for your comment. Complication rates for comparator procedures are not usually described in Interventional procedures guidance.
23	Consultee 2 Three Private NHS Professionals	**2.4.4**	Â Furthermore section 2.4.4 lists potential complications from CAD placement. Â This should be balanced by listing potential complications from CEA, particularly cranial nerve palsy and infection. References 1. Brott TG, Hobson RW, 2nd, Howard G, et al. Stenting versus endarterectomy for treatment of carotid-artery stenosis. N Engl J Med 2010363:11-23.	Thank you for your comment. Brott TG (2010) is included in table 2 of the overview. Outcomes for perioperative MI will be added to the guidance.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
24	Consultee 3 Vascular Society of Great Britain and Ireland	**2.4.4**	Adverse events as listed should also include cardiac adverse events.	Section 2.4.4 is the opinion of the Specialist Advisers sought from the societies as listed in the overview document.
25	Consultee 4 Association of British Neurologists	**General**	I am providing these comments on behalf of the Association of British Neurologists. I am also the Chief Investigator of the International Carotid Stenting Study, funded by the MRC, which is the largest clinical randomised trial to examine this technology	Thank you for your comment.