NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Specialist Adviser questionnaire

Before completing this questionnaire, please read Conflicts of Interest for Specialist Advisers. Certain conflicts exclude you from offering advice, however, please return the questionnaire to us incomplete for our records.

Please respond in the boxes provided.

Please complete and return to: azad.hussain@nice.org.uk and IPSA@nice.org.uk

Procedure Name: Percutaneous insertion of a cerebral protection device to prevent cerebral embolism during transcatheter aortic valve implantation

Name of Specialist Advisor: Rajesh Kharbanda

Specialist Society: British Cardiovascular Society
(British Cardiac Intervention Society)

1 Do you have adequate knowledge of this procedure to provide advice?

☒ **Yes.**

☐ No – please return the form/answer no more questions.

1.1 Does the title used above describe the procedure adequately?

☒ **Yes.**

☐ No. If no, please enter any other titles below.

Comments:

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

☒ **Yes.**

☐ Is there any kind of inter-specialty controversy over the procedure?

☐ No. If no, then answer no more questions, but please give any information you can about who is likely to be doing the procedure.

Comments:

The next 2 questions are about whether you carry out the procedure, or refer patients for it. If you are in a specialty that normally carries out the procedure please answer question 2.2.1. If you are in a specialty that normally selects or refers patients for the procedure, please answer question 2.2.2.

2.2.1 If you are in a specialty that does this procedure, please indicate your experience with it:

☐ I have never done this procedure.

☒ **I have done this procedure at least once.**

☐ I do this procedure regularly.

Comments:

2.2.2 If your specialty is involved in patient selection or referral to another specialty for this procedure, please indicate your experience with it.

☐ I have never taken part in the selection or referral of a patient for this procedure.

☐ I have taken part in patient selection or referred a patient for this procedure at least once.

☒ **I take part in patient selection or refer patients for this procedure regularly.**

Comments:
This would be undertaken within my speciality as part of the TAVI procedure by any of the clinicians performing TAVI.

2.3 Please indicate your research experience relating to this procedure (please choose one or more if relevant):

☒ **I have done bibliographic research on this procedure.**

☐ I have done research on this procedure in laboratory settings (e.g. device-related research).

☐ I have done clinical research on this procedure involving patients or healthy volunteers.

☐ I have had no involvement in research on this procedure.

☐ Other (please comment)

Comments:

3 Status of the procedure

3.1 Which of the following best describes the procedure (choose one):

☐ Established practice and no longer new.

☐ A minor variation on an existing procedure, which is unlikely to alter the procedure's safety and efficacy.

☒ **Definitely novel and of uncertain safety and efficacy.**

☐ The first in a new class of procedure.

Comments:
TAVI is an established procedure involving the implantation of an aortic biological valve prosthesis for the treatment of aortic stenosis. Stroke is a recognised, but unpredictable, complication of the TAVI procedure. A proportion of strokes occur because debris is dislodged from the aorta, valve or hear during TAVI procedure, and if this enters the circulation to the brain, the debris can cause a stroke.

A number of devices are being developed to protect the brain from this embolic debris (Percutaneous insertion of a cerebral protection device). There are 3 devices that currently have a CE Mark for human use (Sentinel, Triguard, Embrella). The Sentinel device is the most widely studied. This cerebral protection device is based on delivering filters into the arteries that supply the brain through the right radial artery (the artery at the wrist) through a small calibre tube. This approach of delivering filters into the artery to catch debris is already well established for other procedures on the brain such as carotid artery stenting and is also used in stenting of the heart arteries, particularly bypass grafts. The use of filters therefore is not novel, and the clinicians undertaking TAVI will be familiar with this technique. The device used to deliver these filters to the blood vessels supplying the brain, however, is novel. These other filter devices used in the carotid stenting or heart artery stenting procedures are delivered using different devices.

EFFICACY data:

The Sentinel device is the most widely tested device. There are ongoing clinical trials for the TriGuard device. To date, the primary endpoints for the randomised clinical trials have been MRI **imaging** assessment (either the number of new lesions ***and/or*** the volume of new brain lesions). These studies have ***not*** been powered for clinical endpoints of minor or major disabling stroke and death.

The available randomised clinical trial efficacy data therefore suggests a reduction in the surrogate measure of brain lesions imaged by MRI in patients treated with cerebral embolic protection devices. There was a reduction in clinical stroke in this trial, but this did not reach statistical significance and the trial was not powered for this endpoint. Therefore the relevance of the imaging endpoints is uncertain. There has been a suggestion that these lesions identified on MRI after TAVI may influence longer-term brain function and cognition. (JACC 2017 69 367)

Clinical efficacy data using the endpoint of clinically apparent stroke is available from three single-centre, non-randomised registry reports. One of these has been published and two have been presented as abstracts. (Ulm - Seeger 2017. JACC Card Int. 10: 2297, Erasmus - van Mieghem and Cedars Sinai - Chakravarty TVT 2018 presentations). These show a consistent reduction in clinical stroke from about 5% of cases to about 1.4% using cerebral protection, with an absolute 3-4% reduction and a relative risk reduction of 70-80%. If this were an accurate assessment of the clinical efficacy it would translate into a number needed to treat of 26 to prevent 1 stroke.

SAFETY data

The delivery of the device requires an additional artery to be cannulated. There is a small additional risk with this procedure. There is no sham control data available on whether instrumentation of the carotid vessels itself increases stroke risk, but given the registry data, this is not likely to be of major concern. In the Sentinal study there was a vascular injury rate of 0.4% associated with use of the device. This is low in comparison to the risk from the TAVI procedure itself.

3.2 What would be the comparator (standard practice) to this procedure?

Currently we have no specific devices or other interventions to reduce the risk of cerebral embolic complications. The comparator is therefore, standard clinical practice without device deployment.

3.3 Please estimate the proportion of doctors in your specialty who are doing this procedure (choose one):

☐ More than 50% of specialists engaged in this area of work.

☐ 10% to 50% of specialists engaged in this area of work.

☒ **Fewer than 10% of specialists engaged in this area of work.**

☐ Cannot give an estimate.

Comments:

In the UK there are now just over 30 TAVI centres, which is about one-third of all the cardiac interventional centres. This activity and technology is therefore limited to a few highly specialized centres undertaking TAVI.

4 Safety and efficacy

4.1 What is the potential harm of the procedure?

Please list adverse events and major risks (even if uncommon) and, if possible, estimate their incidence, as follows:

1. Adverse events reported in the literature (if possible please cite literature)

As described above the potential major risks associated with the deployment of additional devices are related to the vascular access needed to introduce the device (defined as a major vascular access site complication) or the potential to increase debris and cause stroke by introduction of the device itself.

The safety aspects are most well reported in the Sentinel trial. 1 event (0.4%) vascular complication was reported in the device arm. This is a low-risk in comparison to the major risk associated with the TAVI procedure itself, where the risk of major vascular complication is 2-3%. Sham device control is not likely to be a necessary control.

2. Anecdotal adverse events (known from experience)

None

3. Theoretical adverse events

Stroke induced as a result of introducing the cerebral protection device.

Vascular injury from access site used for introducing the cerebral protection device.

4.2 What are the key efficacy outcomes for this procedure?

EFFICACY data:

The primary clinical outcome should be stroke and death. The secondary outcomes should include length of stay, discharge location (ie did the patient get back home), quality of life metrics, and neurocognitive function.

The Sentinel device is the most widely tested device. There are ongoing clinical trials for the TriGuard device. To date, the primary endpoints for the randomised clinical trials have been MRI **imaging** assessment (either the number of new lesions ***and/or*** the volume of new brain lesions). These studies have ***not*** been powered for clinical endpoints of minor or major disabling stroke and death.

The available randomised trial efficacy data therefore suggests a reduction in the surrogate measure of brain lesions imaged by MRI in patients treated with cerebral embolic protection devices. There was a reduction in clinical stroke in this trial, but this did not reach statistical significance and the trial was not powered for this endpoint. Therefore the relevance of the imaging endpoints is uncertain. There has been a suggestion that these lesions identified on MRI after TAVI may influence longer-term brain function and cognition. (JACC 2017 69 367)

Clinical efficacy data using the endpoint of clinically apparent stroke is available from three single-centre, non-randomised registry reports. One of these has been published and two have been presented as abstracts. (Ulm - Seeger 2017. JACC Card Int. 10: 2297, Erasmus - van Mieghem and Cedars Sinai - Chakravarty TVT 2018 presentations). These show a consistent reduction in clinical stroke from about 5% of cases to about 1.4% using cerebral protection, with an absolute 3-4% reduction and a relative risk reduction of 70-80%. If this were an accurate assessment of the clinical efficacy it would translate into a number needed to treat of 26 to prevent 1 stroke.

4.3 Are there uncertainties or concerns about the *efficacy* of this procedure? If so, what are they?

There are no large adequately powered clinical studies testing the efficacy of cerebral embolic protection devices on major stroke or death during TAVI. There is a however a good level of registry data from Europe and the USA to suggest that the device(s) would be clinically effective.

Stroke cannot be predicted and so it is unclear who might benefit from the device. There is uncertainty about whether this should be used in all patients undergoing TAVI or those at high-risk – although we cannot identify these patients currently.

4.4 What training and facilities are needed to do this procedure safely?

The devices are easy to use and clinicians undertaking TAVI will be very familiar with the access routes and the nature of these devices. Training is therefore straightforward. No additional facilities are needed.

4.5 Are there any major trials or registries of this procedure currently in progress? If so, please list.

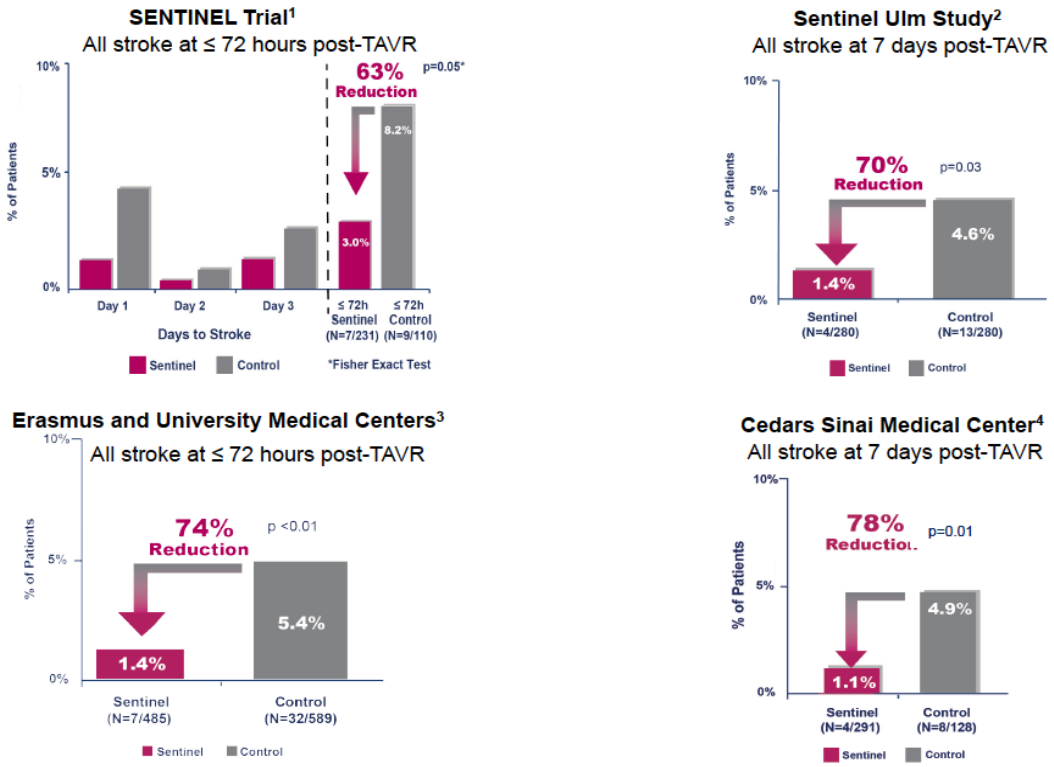
The largest published evidence is for the Sentinel device. JACC 2017 69 367

4.6 Are you aware of any abstracts that have been *recently* presented/ published on this procedure that may not be listed in a standard literature search, for example PUBMED? (This can include your own work). If yes, please list.
Please note that NICE will do a literature search: we are only asking you for any very recent or potentially obscure abstracts and papers. Please do not feel the need to supply a comprehensive reference list (but you may list any that you think are particularly important if you wish).

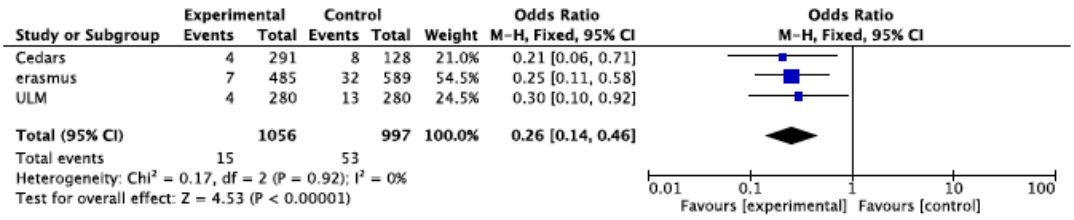
2017 Ulm Registry - Seeger. JACC Card Int. 10: 2297.

2018 Erasmus Registry - van Mieghem. Transcatheter Valve Therapeutics Presentation

2018 Cedars Sinai Registry - Chakravarty Transcatheter Valve Therapeutics Presentation



The figure above is from a recent presentation at London valve 2018. This compares the outcomes of the 3 registry reports against the randomised Sentinel trial. There is consistent clinical efficacy in the non-randomised registry reports. The important considerations are that the comparison is against historical control practice, stroke adjudication is self-reported, and the statistical power of these individual study data is likely to be small. I have conducted a brief meta-analysis of the 3 registry studies, which suggests a powerful clinical effect of cerebral protection on stroke (unpublished data). The summary outcome is presented below for the committee.



(Footnote: This is a crude and preliminary analysis of event rates from these registry data. The heterogeneity analysis is not appropriate as the data is not sufficient for that analysis. Therefore a full metanalysis would be appropriate if indicated)

4.7 Is there controversy, or important uncertainty, about any aspect of the way in which this procedure is currently being done or disseminated?

No. The device is being used in Europe and USA. UK experience is currently very small with a small number of centres using the device in selected cases. The device was used in 70 out of 3787 TAVI cases in the UK 2017 (1.8%).

The TAVI community is keen for guidelines to be developed, and in the UK this will help to inform commissioning and funding.

5 Audit Criteria

Please suggest a minimum dataset of criteria by which this procedure could be audited.

Safety – access site complication from the device introduction site

Efficacy – disabling stroke and /or death in the first 7 and 30 days after procedure. Modified Rankin scale for stroke severity.

The primary clinical outcome should be stroke and death.
The secondary outcomes should include length of stay, discharge location (ie did the patient get back home), quality of life metrics, and neurocognitive function.

5.1 Outcome measures of benefit (including commonly used clinical outcomes, both short and long - term; and quality-of-life measures). Please suggest the most appropriate method of measurement for each:

One major controversy has been the recording of stroke and the disparity between a routine neurologist review or standard self-reporting to define stroke. In the most recent UK dataset the incidence of self-reported stroke was 2.6%. The Sentinel trial reported a stroke rate of 9% after routine neurologist review, and this was much higher than the average 4% stroke rate reported in most series of self-reported stroke It is possible therefore that stroke is under-reported when relying upon self-reporting. This is particularly relevant as ‘small stroke’ in this elderly group may have significant impact on the ability to return to full function and this maybe unrecognised in present reporting methods.

The impact on stroke and related disability, length of stay, discharge destination, cognitive function and quality of life measures would be important metrics to assess device efficacy.

There is debate about the exact methodology that is best used in this context both to assess the incidence of stroke and its effects. More specialist input from stroke specialists maybe helpful in this aspect.

5.2 Adverse outcomes (including potential early and late complications). Please state timescales for measurement e.g. bleeding complications up to 1 month post-procedure:

Major vascular complications, which are recorded according to International criteria in these procedures already. In the UK thsese are reported to the national TAVI database.

6 Trajectory of the procedure

6.1 In your opinion, how quickly do you think use of this procedure will spread?

There will be increasing need to consider using this device. Stroke is a devastating complication of TAVI with direct effects on patient outcomes including morbidity and mortality.

In the UK 70 devices were used in 2017, but with the accumulating data, albeit of moderate quality, there will be increasing clinician uptake and patient requests. UK practice is relatively conservative and NICE or other guideline would have major influence on the trajectory. There remains debate about whether all suitable patients should have this device used or whether it should be used selectively. There is no robust data on which to decide the best approach, or to identify those at higher risk for whom the benefit would be greatest.

In the UK the current limited use is probably in line with the evidence base. However, with increased uptake in other health care systems it is likely we will see the growth of this technology in the UK, which will need to be managed within the context of evolving evidence.

6.2 This procedure, if safe and efficacious, is likely to be carried out in (choose one):

☐ Most or all district general hospitals.

☒ **A minority of hospitals, but at least 10 in the UK.**

☐ Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

TAVI is a very specialist procedure carried out only in about 30 UK hospitals.

6.3 The potential impact of this procedure on the NHS, in terms of numbers of patients eligible for treatment and use of resources, is:

☒ Major.

☐ Moderate.

☐ Minor.

Comments:
TAVI is an expensive and resource intensive treatment. The number of patients is relatively small (3800 TAVI in the UK in 2017) in comparison to other procedures. The impact of stroke reduction is significant and its reduction will have important positive resource implications. If major stroke could be reduced by 1% there would be important clinical, social impacts and cost-savings in terms of care for longterm disability. A full economical modelling would inform this debate.

7 Other information

7.1 Is there any other information about this procedure that might assist NICE in assessing the possible need to investigate its use?

The device has been approved by the FDA for use in the USA, and there is partial reimbursement in place. This is ahead of any clinical guideline recommendations. The trend to increased use of the device has been seen in Europe already.

Currently, there is no clinical guideline recommendation. The evidence is strongly suggestive of efficacy, but the quality of evidence is moderate. The UK practice remains very limited.

There is a need to evaluate and develop the evidence base, and consider a recommendation for the unique UK healthcare system so that clinicians can cite a National body when patients rightly ask questions about access to cerebral protection devices.

8 Data protection and conflicts of interest

8. Data protection, freedom of information and conflicts of interest

8.1 Data Protection

The information you submit on this form will be retained and used by the NICE and its advisers for the purpose of developing its guidance and may be passed to other approved third parties. Your name and specialist society will be published in NICE publications and on the NICE website. The specialist advice questionnaire will be published in accordance with our guidance development processes and a copy will be sent to the nominating Specialist Society. Please avoid identifying any individual in your comments.

X I have read and understood this statement and accept that personal information sent to us will be retained and used for the purposes and in the manner specified above and in accordance with the Data Protection Act 1998.

8.2 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

Nothing in your submission shall restrict any disclosure of information by NICE that is required by law (including in particular, but without limitation, the Freedom of Information Act 2000).

Please submit a conflicts of interest declaration form listing any potential conflicts of interest including any involvement you may have in disputes or complaints relating to this procedure.

Please use the "Conflicts of Interest for Specialist Advisers" policy as a guide when declaring any conflicts of interest. Specialist Advisers should seek advice if needed from the Associate Director – Interventional Procedures.

Do you or a member of your family[1] have a **personal pecuniary** interest? The main examples are as follows:

Consultancies or directorships attracting regular or occasional payments in cash or kind	☐	**YES**
	☒	**NO**
Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice**	☒	**YES**
	☐	**NO**
Shareholdings – any shareholding, or other beneficial interest, in shares of the healthcare industry	☒	**YES**
	☐	**NO**
Expenses and hospitality – any expenses provided by a healthcare industry company beyond those reasonably required for accommodation, meals and travel to attend meetings and conferences	☐	**YES**
	☒	**NO**
Investments – any funds that include investments in the healthcare industry	☐	**YES**
	☒	**NO**
Do you have a **personal non-pecuniary** interest – for example have you made a public statement about the topic or do you hold an office in a professional organisation or advocacy group with a direct interest in the topic?	☐	**YES**
	☒	**NO**

Do you have a **non-personal** interest? The main examples are as follows:

Fellowships endowed by the healthcare industry	☐	**YES**
	☒	**NO**

[1] 'Family members' refers to a spouse or partner living in the same residence as the member or employee, children for whom the member or employee is legally responsible, and adults for whom the member or employee is legally responsible (for example, an adult whose full power of attorney is held by the individual).

Support by the healthcare industry or NICE that benefits his/her position or department, eg grants, sponsorship of posts

☐ **YES**

☒ **NO**

If you have answered YES to any of the above statements, please describe the nature of the conflict(s) below.

Comments:

I am a Proctor for Boston Scientific. This means that I train other TAVI doctors to implant the TAVI valves. I receive a per session fee, as well as reimbursement of travel and accommodation as necessary.

Thank you very much for your help.

Dr Tom Clutton-Brock, Interventional Procedures Advisory Committee Chair

Mark Campbell
Acting Programme Director
Devices and Diagnostics

June 2018

Conflicts of Interest for Specialist Advisers

1 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

1.1 Any conflicts of interest set out below should be declared on the questionnaire the Specialist Adviser completes for the procedure.

1.2 Specialist Advisers should seek advice if required from the Associate Director – Interventional Procedures.

2 Personal pecuniary interests

2.1 A personal pecuniary interest involves a current personal payment to a Specialist Adviser, which may either relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as **'specific'** or to the industry or sector from which the product or service comes, in which case it is regarded as **'non-specific'**. The main examples are as follows.

2.1.1 **Consultancies** – any consultancy, directorship, position in or work for the healthcare industry that attracts regular or occasional payments in cash or kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.2 **Fee-paid work** – any work commissioned by the healthcare industry for which the member is paid in cash or in kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.3 **Shareholdings** – any shareholding, or other beneficial interest, in shares of the healthcare industry that are either held by the individual or for which the individual has legal responsibility (for example, children, or relatives whose full Power of Attorney is held by the individual). This does not include shareholdings through unit trusts, pensions funds, or other similar arrangements where the member has no influence on financial management.

2.1.4 **Expenses and hospitality** – any expenses provided by a healthcare industry company beyond that reasonably required for accommodation, meals and travel to attend meetings and conferences (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place.

2.1.5 **Investments** – any funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

2.2 No personal interest exists in the case of:

2.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

2.2.2 accrued pension rights from earlier employment in the healthcare industry.

3 **Personal family interest**

3.1 This relates to the personal interests of a family member and involves a **current payment** to the family member of the Specialist Adviser. The interest may relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as '**specific**', or to the industry or sector from which the product or service comes, in which case it is regarded as '**non-specific**'. The main examples include the following.

3.1.1 Any consultancy, directorship, position in or work for a healthcare industry that attracts regular or occasional payments in cash or in kind.

3.1.2 Any fee-paid work commissioned by a healthcare industry for which the member is paid in cash or in kind.

3.1.3 Any shareholdings, or other beneficial interests, in a healthcare industry which are either held by the family member or for which an individual covered by this Code has legal responsibility (for example, children, or adults whose full Power of Attorney is held by the individual).

3.1.4 Expenses and hospitality provided by a healthcare industry company (except where they are provided to a general class of people such as attendees at an open conference)

3.1.5 Funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

3.2 No personal family interest exists in the case of:

3.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

3.2.2 accrued pension rights from earlier employment in the healthcare industry.

4 **Personal non-pecuniary interests**

These might include, but are not limited to:

4.1 a clear opinion, reached as the conclusion of a research project, about the clinical and/or cost effectiveness of an intervention under review

4.2 a public statement in which an individual covered by this Code has expressed a clear opinion about the matter under consideration, which could reasonably be interpreted as prejudicial to an objective interpretation of the evidence

4.3 holding office in a professional organisation or advocacy group with a direct interest in the matter under consideration

4.4 other reputational risks in relation to an intervention under review.

5 Non-personal interests

5.1 A non-personal interest involves payment that benefits a department or organisation for which a Specialist Advisor is responsible, but that is not received by the Specialist Advisor personally. This may either relate to the product or service being evaluated, in which case it is regarded as **'specific,'** or to the manufacturer or owner of the product or service, but is unrelated to the matter under consideration, in which case it is regarded as **'non-specific'**. The main examples are as follows.

5.1.1 **Fellowships** – the holding of a fellowship endowed by the healthcare industry.

5.1.2 **Support by the healthcare industry or NICE** – any payment, or other support by the healthcare industry or by NICE that does not convey any pecuniary or material benefit to a member personally but that does benefit his/her position or department. For example:

- a grant from a company for the running of a unit or department for which a Specialist Advisor is responsible
- a grant, fellowship or other payment to sponsor a post or member of staff in the unit for which a Specialist Adviser is responsible. This does not include financial assistance for students
- the commissioning of research or other work by, or advice from, staff who work in a unit for which the specialist advisor is responsible
- one or more contracts with, or grants from, NICE.

5.2 Specialist Advisers are under no obligation to seek out knowledge of work done for, or on behalf of, the healthcare industry within departments for which they are responsible if they would not normally expect to be informed.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Specialist Adviser questionnaire

Before completing this questionnaire, please read Conflicts of Interest for Specialist Advisers. Certain conflicts exclude you from offering advice, however, please return the questionnaire to us incomplete for our records.

Please respond in the boxes provided.

Please complete and return to: azad.hussain@nice.org.uk and IPSA@nice.org.uk

Procedure Name:	**Percutaneous insertion of a cerebral protection device to prevent cerebral embolism during transcatheter aortic valve implantation**
Name of Specialist Advisor:	Dr Dan Blackman
Specialist Society:	British Cardiovascular Intervention Society

1 Do you have adequate knowledge of this procedure to provide advice?

☒ Yes.

☐ No – please return the form/answer no more questions.

1.1 Does the title used above describe the procedure adequately?

☒ Yes.

☐ No. If no, please enter any other titles below.

Comments:

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

☒ Yes.

☐ Is there any kind of inter-specialty controversy over the procedure?

☐ No. If no, then answer no more questions, but please give any information you can about who is likely to be doing the procedure.

Comments:

The next 2 questions are about whether you carry out the procedure, or refer patients for it. If you are in a specialty that normally carries out the procedure please answer question 2.2.1. If you are in a specialty that normally selects or refers patients for the procedure, please answer question 2.2.2.

2.2.1 If you are in a specialty that does this procedure, please indicate your experience with it:

☐ I have never done this procedure.

☐ I have done this procedure at least once.

☒ I do this procedure regularly.

Comments:

2.2.2 If your specialty is involved in patient selection or referral to another specialty for this procedure, please indicate your experience with it.

☐ I have never taken part in the selection or referral of a patient for this procedure.

☐ I have taken part in patient selection or referred a patient for this procedure at least once.

☒ I take part in patient selection or refer patients for this procedure regularly.

Comments:

2.3 Please indicate your research experience relating to this procedure (please choose one or more if relevant):

☐ I have done bibliographic research on this procedure.

☐ I have done research on this procedure in laboratory settings (e.g. device-related research).

☒ I have done clinical research on this procedure involving patients or healthy volunteers.

☐ I have had no involvement in research on this procedure.

☐ Other (please comment)

Comments:

3 Status of the procedure

3.1 Which of the following best describes the procedure (choose one):

☐ Established practice and no longer new.

☐ A minor variation on an existing procedure, which is unlikely to alter the procedure's safety and efficacy.

☒ Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

3.2 What would be the comparator (standard practice) to this procedure?

There is no active comparator. Therefore the comparator is Transcatheter aortic valve implantation performed without the use of a cerebral protection device.

3.3 Please estimate the proportion of doctors in your specialty who are doing this procedure (choose one):

☐ More than 50% of specialists engaged in this area of work.

☐ 10% to 50% of specialists engaged in this area of work.

☒ Fewer than 10% of specialists engaged in this area of work.

☐ Cannot give an estimate.

Comments:

4 Safety and efficacy

4.1 What is the potential harm of the procedure?

Please list adverse events and major risks (even if uncommon) and, if possible, estimate their incidence, as follows:

1. Adverse events reported in the literature (if possible please cite literature)

Radial artery vascular access complication e.g. false aneurysm. Reported incidence 0.4% (SENTINEL trial)

2. Anecdotal adverse events (known from experience)

None in our experience

3. Theoretical adverse events

Device fracture

Cerebral embolization

Systemic embolization

Vascular access site complication

4.2 What are the key efficacy outcomes for this procedure?

New lesions on brain MRI
Clinical Stroke

4.3 Are there uncertainties or concerns about the *efficacy* of this procedure? If so, what are they?

Yes. The largest RCT (SENTINEL) did not show a statistically significant reduction in its primary end-point of new MRI brain lesions, or in clinical stroke. However, it did show a strong trend to benefit. Other smaller RCTs, and large registries, and meta-analyses, have shown clear benefit. Ideally a much larger randomised controlled trial would be performed to reach a more definitive verdict on efficacy.

4.4 What training and facilities are needed to do this procedure safely?

All TAVI centres would have the necessary facilities to perform the procedure. It is a straightforward procedure technically.
Some training is needed which should include didactic training, bench practice with the device, and supervision by a representative of the company supplying the device for the first 5-10 cases.

4.5 Are there any major trials or registries of this procedure currently in progress? If so, please list.

YES. See clinicaltrials.gov for details.
REFLECT trial. RCT of Triguard device

4.6 Are you aware of any abstracts that have been *recently* presented/ published on this procedure that may not be listed in a standard literature search, for example PUBMED? (This can include your own work). If yes, please list.
Please note that NICE will do a literature search: we are only asking you for any very recent or potentially obscure abstracts and papers. Please do not feel the need to supply a comprehensive reference list (but you may list any that you think are particularly important if you wish).

NO

4.7 Is there controversy, or important uncertainty, about any aspect of the way in which this procedure is currently being done or disseminated?

YES. There is controversy about the clinical trial results to date, and whether the device should be used in all patients or in selected groups.

5 Audit Criteria

Please suggest a minimum dataset of criteria by which this procedure could be audited.

Procedure time
Radiographic dose
Contrast volume
Clinical stroke rate
Vascular access major and minor rate.

5.1 Outcome measures of benefit (including commonly used clinical outcomes, both short and long - term; and quality-of-life measures). Please suggest the most appropriate method of measurement for each:

Stroke
TIA

5.2 Adverse outcomes (including potential early and late complications). Please state timescales for measurement e.g. bleeding complications up to 1 month post-procedure:

Major and minor vascular access site complications
Major and minor bleeding

6 Trajectory of the procedure

6.1 In your opinion, how quickly do you think use of this procedure will spread?

I believe there will be gradual uptake of the technique, not rapid

6.2 This procedure, if safe and efficacious, is likely to be carried out in (choose one):

☐ Most or all district general hospitals.

☒ A minority of hospitals, but at least 10 in the UK.

☐ Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

Most TAVI centres, which is about 35 hospitals in the UK

6.3 The potential impact of this procedure on the NHS, in terms of numbers of patients eligible for treatment and use of resources, is:

☐ Major.

☒ Moderate.

☐ Minor.

Comments:
Likely to be used selectively, estimated 10-20% of all TAVIs maximum, which is equivalent to 400-800 patients annually in the UK..

7 Other information

7.1 Is there any other information about this procedure that might assist NICE in assessing the possible need to investigate its use?

Literature review.
Patient input

8 Data protection and conflicts of interest

8. Data protection, freedom of information and conflicts of interest

8.1 Data Protection

The information you submit on this form will be retained and used by the NICE and its advisers for the purpose of developing its guidance and may be passed to other approved third parties. Your name and specialist society will be published in NICE publications and on the NICE website. The specialist advice questionnaire will be published in accordance with our guidance development processes and a copy will

be sent to the nominating Specialist Society. Please avoid identifying any individual in your comments.

☑ I have read and understood this statement and accept that personal information sent to us will be retained and used for the purposes and in the manner specified above and in accordance with the Data Protection Act 1998.

8.2 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

Nothing in your submission shall restrict any disclosure of information by NICE that is required by law (including in particular, but without limitation, the Freedom of Information Act 2000).

Please submit a conflicts of interest declaration form listing any potential conflicts of interest including any involvement you may have in disputes or complaints relating to this procedure.

Please use the "Conflicts of Interest for Specialist Advisers" policy as a guide when declaring any conflicts of interest. Specialist Advisers should seek advice if needed from the Associate Director – Interventional Procedures.

Do you or a member of your family[1] have a **personal pecuniary** interest? The main examples are as follows:

Consultancies or directorships attracting regular or occasional payments in cash or kind	☒ **YES** ☐ **NO**
Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice**	☐ **YES** ☐ **NO**
Shareholdings – any shareholding, or other beneficial interest, in shares of the healthcare industry	☐ **YES** ☐ **NO**
Expenses and hospitality – any expenses provided by a healthcare industry company beyond those reasonably required for accommodation, meals and travel to attend meetings and conferences	☐ **YES** ☐ **NO**
Investments – any funds that include investments in the healthcare industry	☐ **YES** ☐ **NO**

[1] 'Family members' refers to a spouse or partner living in the same residence as the member or employee, children for whom the member or employee is legally responsible, and adults for whom the member or employee is legally responsible (for example, an adult whose full power of attorney is held by the individual).

Do you have a **personal non-pecuniary** interest – for example have you made a public statement about the topic or do you hold an office in a professional organisation or advocacy group with a direct interest in the topic?

☐ **YES**

☐ **NO**

Do you have a **non-personal** interest? The main examples are as follows:

Fellowships endowed by the healthcare industry

☐ **YES**

☐ **NO**

Support by the healthcare industry or NICE that benefits his/her position or department, eg grants, sponsorship of posts

☐ **YES**

☐ **NO**

If you have answered YES to any of the above statements, please describe the nature of the conflict(s) below.

Comments:

I work occasionally as a Proctor and Consultant for Boston Scientific, who are the Suppliers of the Sentinel cerebral embolic protection device. I am paid for the work I do for Boston.

Thank you very much for your help.

Dr Tom Clutton-Brock, Interventional Procedures Advisory Committee Chair

Mark Campbell
Acting Programme Director
Devices and Diagnostics

June 2018

Conflicts of Interest for Specialist Advisers

1 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

1.1 Any conflicts of interest set out below should be declared on the questionnaire the Specialist Adviser completes for the procedure.

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2 Personal pecuniary interests

2.1 A personal pecuniary interest involves a current personal payment to a Specialist Adviser, which may either relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as **'specific'** or to the industry or sector from which the product or service comes, in which case it is regarded as **'non-specific'**. The main examples are as follows.

2.1.1 **Consultancies** – any consultancy, directorship, position in or work for the healthcare industry that attracts regular or occasional payments in cash or kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

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2.1.3 **Shareholdings** – any shareholding, or other beneficial interest, in shares of the healthcare industry that are either held by the individual or for which the individual has legal responsibility (for example, children, or relatives whose full Power of Attorney is held by the individual). This does not include shareholdings through unit trusts, pensions funds, or other similar arrangements where the member has no influence on financial management.

2.1.4 **Expenses and hospitality** – any expenses provided by a healthcare industry company beyond that reasonably required for accommodation, meals and travel to attend meetings and conferences (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place.

2.1.5 **Investments** – any funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

2.2 No personal interest exists in the case of:

2.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

2.2.2 accrued pension rights from earlier employment in the healthcare industry.

3 Personal family interest

3.1 This relates to the personal interests of a family member and involves a **current payment** to the family member of the Specialist Adviser. The interest may relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as '**specific**', or to the industry or sector from which the product or service comes, in which case it is regarded as '**non-specific**'. The main examples include the following.

3.1.1 Any consultancy, directorship, position in or work for a healthcare industry that attracts regular or occasional payments in cash or in kind.

3.1.2 Any fee-paid work commissioned by a healthcare industry for which the member is paid in cash or in kind.

3.1.3 Any shareholdings, or other beneficial interests, in a healthcare industry which are either held by the family member or for which an individual covered by this Code has legal responsibility (for example, children, or adults whose full Power of Attorney is held by the individual).

3.1.4 Expenses and hospitality provided by a healthcare industry company (except where they are provided to a general class of people such as attendees at an open conference)

3.1.5 Funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

3.2 No personal family interest exists in the case of:

3.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

3.2.2 accrued pension rights from earlier employment in the healthcare industry.

4 Personal non-pecuniary interests

These might include, but are not limited to:

4.1 a clear opinion, reached as the conclusion of a research project, about the clinical and/or cost effectiveness of an intervention under review

4.2 a public statement in which an individual covered by this Code has expressed a clear opinion about the matter under consideration, which could reasonably be interpreted as prejudicial to an objective interpretation of the evidence

4.3 holding office in a professional organisation or advocacy group with a direct interest in the matter under consideration

4.4 other reputational risks in relation to an intervention under review.

5 Non-personal interests

5.1 A non-personal interest involves payment that benefits a department or organisation for which a Specialist Advisor is responsible, but that is not received by the Specialist Advisor personally. This may either relate to the product or service being evaluated, in which case it is regarded as **'specific,'** or to the manufacturer or owner of the product or service, but is unrelated to the matter under consideration, in which case it is regarded as **'non-specific'**. The main examples are as follows.

5.1.1 **Fellowships** – the holding of a fellowship endowed by the healthcare industry.

5.1.2 **Support by the healthcare industry or NICE** – any payment, or other support by the healthcare industry or by NICE that does not convey any pecuniary or material benefit to a member personally but that does benefit his/her position or department. For example:

- a grant from a company for the running of a unit or department for which a Specialist Advisor is responsible
- a grant, fellowship or other payment to sponsor a post or member of staff in the unit for which a Specialist Adviser is responsible. This does not include financial assistance for students
- the commissioning of research or other work by, or advice from, staff who work in a unit for which the specialist advisor is responsible
- one or more contracts with, or grants from, NICE.

5.2 Specialist Advisers are under no obligation to seek out knowledge of work done for, or on behalf of, the healthcare industry within departments for which they are responsible if they would not normally expect to be informed.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Specialist Adviser questionnaire

Before completing this questionnaire, please read Conflicts of Interest for Specialist Advisers. Certain conflicts exclude you from offering advice, however, please return the questionnaire to us incomplete for our records.

Please respond in the boxes provided.

Please complete and return to: azad.hussain@nice.org.uk and IPSA@nice.org.uk

Procedure Name:	**Percutaneous insertion of a cerebral protection device to prevent cerebral embolism during transcatheter aortic valve implantation**
Name of Specialist Advisor:	Helen Rodgers
Specialist Society:	Royal College of Physicians of London

1 Do you have adequate knowledge of this procedure to provide advice?

☒ Yes.

☐ No – please return the form/answer no more questions.

1.1 Does the title used above describe the procedure adequately?

☐ Yes.

☒ No. If no, please enter any other titles below.

Comments:

1. **The title is seeking to look at cerebral embolism during TAVI - does this include symptomatic and asymptomatic cerebral emboli?**
2. **Should the question be about reducing all stroke/TIA/cognitive impairment post TAVI? It can be tricky to be sure if stroke is definitely due to embolism and from a patient's perspective it is the neurological deficit which is important rather than the pathological process.**

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

☐ Yes.

☐ Is there any kind of inter-specialty controversy over the procedure?

☒ No. If no, then answer no more questions, but please give any information you can about who is likely to be doing the procedure.

Comments:

Stroke physicians do not undertake TAVI but do see patients with stroke, TIA and cognitive problems post TAVI.

My understanding is that I have been proposed by RCP (London) as a non specialist.advisor.

My mother has participated in the UK TAVI trial and was randomised to receive a TAVI.

The next 2 questions are about whether you carry out the procedure, or refer patients for it. If you are in a specialty that normally carries out the procedure please answer question 2.2.1. If you are in a specialty that normally selects or refers patients for the procedure, please answer question 2.2.2.

2.2.1 If you are in a specialty that does this procedure, please indicate your experience with it:

☐ I have never done this procedure.

☐ I have done this procedure at least once.

☐ I do this procedure regularly.

Comments:

2.2.2 If your specialty is involved in patient selection or referral to another specialty for this procedure, please indicate your experience with it.

☐ I have never taken part in the selection or referral of a patient for this procedure.

☐ I have taken part in patient selection or referred a patient for this procedure at least once.

☐ I take part in patient selection or refer patients for this procedure regularly.

Comments:

2.3 Please indicate your research experience relating to this procedure (please choose one or more if relevant):

☐ I have done bibliographic research on this procedure.

☐ I have done research on this procedure in laboratory settings (e.g. device-related research).

☐ I have done clinical research on this procedure involving patients or healthy volunteers.

☐ I have had no involvement in research on this procedure.

☐ Other (please comment)

Comments:

3 Status of the procedure

3.1 Which of the following best describes the procedure (choose one):

☐ Established practice and no longer new.

☐ A minor variation on an existing procedure, which is unlikely to alter the procedure's safety and efficacy.

☐ Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

3.2 What would be the comparator (standard practice) to this procedure?

3.3 Please estimate the proportion of doctors in your specialty who are doing this procedure (choose one):

☐ More than 50% of specialists engaged in this area of work.

☐ 10% to 50% of specialists engaged in this area of work.

☐ Fewer than 10% of specialists engaged in this area of work.

☐ Cannot give an estimate.

Comments:

4 Safety and efficacy

4.1 What is the potential harm of the procedure?

Please list adverse events and major risks (even if uncommon) and, if possible, estimate their incidence, as follows:

1. Adverse events reported in the literature (if possible please cite literature)

2. Anecdotal adverse events (known from experience)

3. Theoretical adverse events

4.2 What are the key efficacy outcomes for this procedure?

4.3 Are there uncertainties or concerns about the *efficacy* of this procedure? If so, what are they?

4.4 What training and facilities are needed to do this procedure safely?

4.5 Are there any major trials or registries of this procedure currently in progress? If so, please list.

4.6 Are you aware of any abstracts that have been *recently* presented/ published on this procedure that may not be listed in a standard literature search, for example PUBMED? (This can include your own work). If yes, please list.
Please note that NICE will do a literature search: we are only asking you for any very recent or potentially obscure abstracts and papers. Please do not feel the need to supply a comprehensive reference list (but you may list any that you think are particularly important if you wish).

4.7 Is there controversy, or important uncertainty, about any aspect of the way in which this procedure is currently being done or disseminated?

5 Audit Criteria

Please suggest a minimum dataset of criteria by which this procedure could be audited.

5.1 Outcome measures of benefit (including commonly used clinical outcomes, both short and long - term; and quality-of-life measures). Please suggest the most appropriate method of measurement for each:

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6 Trajectory of the procedure

6.1 In your opinion, how quickly do you think use of this procedure will spread?

6.2 This procedure, if safe and efficacious, is likely to be carried out in (choose one):

☐ Most or all district general hospitals.

☐ A minority of hospitals, but at least 10 in the UK.

☐ Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

6.3 The potential impact of this procedure on the NHS, in terms of numbers of patients eligible for treatment and use of resources, is:

☐ Major.

☐ Moderate.

☐ Minor.

Comments:

7 Other information

7.1 Is there any other information about this procedure that might assist NICE in assessing the possible need to investigate its use?

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8. Data protection, freedom of information and conflicts of interest

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	☐	**NO**
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	☒	**NO**
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	☒	**NO**
Investments – any funds that include investments in the healthcare industry	☐	**YES**
	☒	**NO**
Do you have a **personal non-pecuniary** interest – for example have you made a public statement about the topic or do you hold an office in a professional organisation or advocacy group with a direct interest in the topic?	☐	**YES**
	☒	**NO**

Do you have a **non-personal** interest? The main examples are as follows:

Fellowships endowed by the healthcare industry	☐	**YES**
	☒	**NO**
Support by the healthcare industry or NICE that benefits his/her position or department, eg grants, sponsorship of posts	☐	**YES**
	☒	**NO**

If you have answered YES to any of the above statements, please describe the nature of the conflict(s) below.

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I chair an annual meeting for BAYER about stroke and cardiovascular disease for which I receive personal renumeration.

Comments:

Thank you very much for your help.

Dr Tom Clutton-Brock, Interventional Procedures Advisory Committee Chair

Mark Campbell
Acting Programme Director
Devices and Diagnostics

June 2018

Conflicts of Interest for Specialist Advisers

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- the commissioning of research or other work by, or advice from, staff who work in a unit for which the specialist advisor is responsible
- one or more contracts with, or grants from, NICE.

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