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: tristan.mckenna@nice.org.uk

Procedure Name:	IP685/3 Transcatheter aortic valve implantation for aortic stenosis
Name of Specialist Advisor:	Dr Blackman
Specialist Society:	**British Cardiovascular Intervention Society (BCIS)**

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:

I do currently about 150 of these procedures annually

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?

Surgical aortic valve replacement

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:

About 10% of interventional cardiologists, perhaps 5-10%

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)

Death 2-3%

Major stroke 2-3%

Minor stroke 2-3%

Major bleeding 5-10%

Major vascular complications 5-10%

Permanent pacemaker implantation 15%

Coronary obstruction 0.5%

Aortic Annular rupture 0.5%

Acute renal failure 1-2%

Thoracic aortic dissection or rupture 0.5%

Device embolisation 1%

Clinically significant valve thrombosis 0.5%

Subclinical valve thrombosis 10%

Extensive literature

Most relevant and contemporary data are:-

PARTNER 2 intermediate risk randomised controlled trial

PARTNER 2 Sapien 3 study

Corevalve High-risk IDE randomised trial

2. Anecdotal adverse events (known from experience)

Included above

3. Theoretical adverse events

Included above

4.2 What are the key efficacy outcomes for this procedure?

Procedural success with resolution of aortic stenosis - 99%
30-day survival 97%
12-month survival 85%
Improved quality of life
Improved exercise capacity
Resolution of symptoms of breathlessness, chest pain, and presynsope/syncope

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

Long-term valve durability is uncertain (beyond 5 years)
Long-term clinical outcomes including survival are uncertain (beyond 5 years)

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

High-quality cardiac catheterisation laboratory
On-site cardiac surgery
Expert trans-thoracic and trans-oesophageal echocardiography
Cardiac CT
On-site renal replacement therapy
On-site or rapidly available vascular surgery and vascular radiology expertise
Cardiac anaesthetic back-up

Prior training in interventional cardiology
Dedicated training in TAVI including a formal didactic training programme, training on simulators, and a period of supervised or proctored TAVI cases

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

Yes:-
SURTAVI trial - RCT of TAVI vs surgical AVR in intermediate risk patients
UK TAVI trial - RCT of TAVI vs surgical AVR in high and intermediate risk patients
Safety & Efficacy of the SAPIEN 3 heart valve in low-risk patients with aortic stenosis - RCT of TAVI vs SAVR in low-risk patients
NOTION 2 - RCT of TAVI vs SAVR in low-risk patients
Medtronic TAVI in Low-risk patients - RCT of TAVI vs SAVR in low-risk patients

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).

Dvir et al. Presentation at EuroPCR Conference. Small study evaluating long-term durability of TAVI valves

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

The TAVI procedure is evolving at variable rates in different centres. There is some variability, if not perhaps controversy, in procedural technique. Most centres do almost all procedures trans-femoral and percutaneous. Some centres still do a

significant proportion of cases via trans-apical and direct aortic access. Most centres do not send patients routinely to ICU, while some still do.
There is controversy over which patients should have TAVI versus surgical AVR. There is very strong clinical evidence in favour of TAVI in high-risk surgical patients, and emerging good evidence in intermediate-risk patients.
There is some controversy over where TAVI should be undertaken. There is unanimity amongst clinicians that all cardiac surgical centres should do TAVI, but this is not happening in some centres due to rationing by commissioners.

5 Audit Criteria

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

There is a comprehensive national TAVI dataset under the auspices of NICOR which is appropriate and effective.

5.1 Outcome measures of benefit (including commonly used clinical outcomes, both short and long - term; and quality-of-life measures):

Survival
Symptom status measured by NYHA Heart Failure Class
Quality of life parameters e.g. Minnesota Living with Heart Failure, Kansas City Health Questionnaire, SF-scores, EQ5D scores

5.2 Adverse outcomes (including potential early and late complications):

Death 2-3%

Major stroke 2-3%

Minor stroke 2-3%

Major bleeding 5-10%

Major vascular complications 5-10%

Permanent pacemaker implantation 15%

Coronary obstruction 0.5%

Aortic Annular rupture 0.5%

Acute renal failure 1-2%

Thoracic aortic dissection or rupture 0.5%

Device embolisation 1%

Clinically significant valve thrombosis 0.5%

Subclinical valve thrombosis 10%

6 Trajectory of the procedure

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

This procedure is spreading very rapidly and will continue to do so. Across the UK there has been an annual 20-30% increase in numbers, which is undoubtedly an

underestimate of the true demand because of restricted commissioning and capacity in the NHS. TAVI has grown much faster in other health care systems in Western Europe, where TAVI procedure rates per million are between 2- and 4-fold those in the UK.
This expansion is appropriate because TAVI is a highly effective procedure which has evolved rapidly with dramatic reductions in procedural mortality and morbidity. In parallel with these improvements the evidence base shows that TAVI is as good if not better than surgical AVR in high- and intermediate risk patients with further randomised trials in intermediate and low-risk patients ongoing. The main outstanding question is long-term valve durability and clinical outcomes.

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:

All cardiac surgical centres in the UK, which is a total of 37. Some large district hospitals may carry out TAVI in the future. There is an urgent need to increase capacity in the 37 cardiac surgical centres to meet mushrooming demand.

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:
This procedure is expensive, and is rapidly expanding. However, it is safe, effective, and probably cost-effective. It is also much preferred by patients compared to surgical aortic valve replacement. There is scope to reduce cost, but nonetheless the impact on the NHS is large.

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?

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**

[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).

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**
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:

1. I have contracts with 2 manufacturers of TAVI valves, Boston Scientific, and Medtronic, for paid teaching and training of the TAVI procedure
2. I have received research grant support from Boston Scientific for research in the field of TAVI
3. I am Honorary Secretary of the British Cardiovascular Intervention Society, which has written to NHS England regarding commissioning of the TAVI procedure.

Thank you very much for your help.

Dr Tom Clutton-Brock, Interventional Procedures Advisory Committee Chair

Professor Carole Longson, Director, Centre for Health Technology Evaluation.

Jan 2016

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: tristan.mckenna@nice.org.uk

Procedure Name:	IP685/3 Transcatheter aortic valve implantation for aortic stenosis
Name of Specialist Advisor:	Mr Moat
Specialist Society:	**Society for Cardiothoracic Surgery In Great Britain and Ireland (SCTS)**

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

X Yes.

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

1.1 Does the title used above describe the procedure adequately?

X 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?

X Yes.

X 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:

International guidelines state that the whole conduct of TAVI should be by a multi-disciplinary heart team – there is a degree of controversy that in some Units this does not work in an effective way and the whole programme is dictated and directed by interventional cardiology.

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.

X 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.

X 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):

X I have done bibliographic research on this procedure.

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

X 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):

X 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?

Surgical aortic valve replacement

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.

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

☐ Cannot give an estimate.

Comments:

The proportion of cardiac specialists involved in this procedure is steadily growing

4 Safety and efficacy

4.1 What is the potential harm of the procedure?

The potential complications are well documented in the literature. From randomised trials and real world registry such as the UK TAVI Registry (UK TR). The main adverse events are death (4%), stroke (2%), vascular complications (5% - 7%), moderate or greater paravalvular regurgitation (3% - 7%), pacemaker implantation (6% – 30% dependent upon device used), coronary occlusion (0.5%), annular rupture (0.5%)

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?

Early and late mortality, stroke, length of hospital stay, symptom relief and quality of life.

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

The principle uncertainty relates to the long term durability of these devices, i.e. how long will it be before one would see structural valve degeneration. Another cause for concern is the finding of leaflet thickening or thrombosis, the incidence of which is not clear at the present time.

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

The procedure needs to be carried out in a cardiac catheter lab or hybrid operating theatre – to do the procedure safely it needs to be done in a cardiac surgical centre.

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

The Partner and US CoreValve randomised trials are published. There is good real world data from the UK and US TAVI registries. There are ongoing randomised trials

in patients at less high risk, namely US Sapien 3 trial, US CoreValve low risk trial, NOTION 2 and the UK TAVI trial.

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).

The only recent publication that you may not have picked up in your literature search is the meta-analysis of the current randomised trials published in the European Heart Journal this year.

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

Perhaps the controversy relates to the dissemination of TAVI into patients who are at less high risk from surgical AVR. The current randomised trials relate to patients who are in the highest decile of risk (i.e. top 10%) of patients undergoing surgical aortic valve replacement. In these trials there is good evidence that TAVI is non-inferior to AVR and in the meta-analysis that TAVI was superior to AVR in terms of early and mid term mortality. TAVI is also associated with a lower instance of most complications such as atrial fibrillation, a shorter hospital stay, although more vascular complications.

5 Audit Criteria

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

An appropriate dataset would be that used for the UK TAVI registry which can be found on the BCIS website.

5.1 Outcome measures of benefit (including commonly used clinical outcomes, both short and long - term; and quality-of-life measures):

See previous answers

5.2 Adverse outcomes (including potential early and late complications):

See previous answers

6 Trajectory of the procedure

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

The current use of this procedure is controlled / limited by commissioning policies and practices. If there were no financial constraints then I think this procedure would grow rapidly.

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

☐ Most or all district general hospitals.

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

☐ Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

There is a move for this procedure to be carried out in hospitals which do not have cardiac surgical programmes. This would be against both European and North American guidelines and should not be supported.

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:

X 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?

The UK TAVI trial will provide real world, relevant UK data as to this procedure in a somewhat lower risk cohort than in the currently publicised trials. In an ideal world this trial should be supported and completed as quickly as possible.

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	X	**YES**
	☐	**NO**
Fee-paid work – any work commissioned by the healthcare industry – **this includes income earned in the course of private practice**	X	**YES**
	☐	**NO**
Shareholdings – any shareholding, or other beneficial interest, in shares of the healthcare industry	☐	**YES**
	X	**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**
	X	**NO**
Investments – any funds that include investments in the healthcare industry	☐	**YES**
	X	**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
	X	NO
Do you have a **non-personal** interest? The main examples are as follows:		
Fellowships endowed by the healthcare industry	☐	YES
	X	NO
Support by the healthcare industry or NICE that benefits his/her position or department, eg grants, sponsorship of posts	☐	YES
	X	NO

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

Comments:

I have received Speaker's fees, sponsorship to attend International meetings and Consulting fees from most of the major heart valve companies (both for surgical and catheter based valve interventions – these include Edwards, Medtronic, Abbott and Direct Flow).

Thank you very much for your help.

Dr Tom Clutton-Brock, Interventional Procedures Advisory Committee Chair

Professor Carole Longson, Director, Centre for Health Technology Evaluation.

Jan 2016

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: tristan.mckenna@nice.org.uk

Procedure Name:	IP685/3 Transcatheter aortic valve implantation for aortic stenosis
Name of Specialist Advisor:	Dr Douglas Muir
Specialist Society:	**British Cardiovascular Intervention Society (BCIS)**

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:

The procedure is usually abbreviated to TAVI in UK and Europe but TAVR in North America. (Transcatheter Aortic Valve Implantation or Replacement, respectively). The terms are synonymous.

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:

Severe Aortic stenosis may be treated by conventional open heart surgery (longstanding standard of care) or by TAVI. Therefore there is the possibility of "competition" between cardiac surgeons and interventional cardiologists over the benefits of one mode of therapy over another. However, cardiac surgeons are often involved in TAVI implants from non femoral access routes and are also involved in assessing patients through the MDT or heart team meeting. These factors may mitigate the possibility of "turf wars" between specialities.

TAVI is most commonly performed via percutaneous transfermoral (TF) access. Around 85-90% of patients are suitable for this form of access which is the route of choice due to superior outcomes and as the least invasive option. In general, these cases are led by interventional cardiologists. Non TF cases (direct aortic, trans-apical, subclavian, jugular) tend to be led by cardiothoracic surgeons with assistance from interventional cardiologists. Thus, there is much closer interplay between these subspecialties than with other cardiac treatments and a team approach is fostered. This applies to decision-making and to the procedure itself.

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:

My own unit has performed around 400 procedures since 2009. I have personal implant experience of over 250 cases. I have proctored other units and lectured on training courses to assist in the learning curve of new TAVI teams.

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:

In addition to section 2.2.1., I take part in patient selection and MDT referral from my own clinical practice. I also lead our MDT, which is the method of decision making for all potential TAVI patients.

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:

I am conversant with relevant clinical trial and registry published data from literature searches, online resources and presentations at national / international conferences.

I have been involved with a small amount of pre-clinical work on valve / system design by means of bench testing and in an animal lab.

I have recruited patients to multi-centre trials and registries (e.g. SOURCE registries, ROUTE registry, UK TAVI trial).

I am involved with ongoing in house research projects on TAVI.

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 has been performed for over a decade now and all major health economies are showing a year on year increase in numbers. This is in part because of the inherent attraction of a less invasive procedure, but also because new RCT data has sequentially shown excellent outcomes compared to standard of care for:

- inoperable patients (PARTNER B trail, Corevalve extreme risk US trial). Demonstrated clear mortality benefits compared to medical therapy for surgically ineligible patients
- very high risk but surgically eligible patients (PARTNER A trial, Corevalve high risk US pivotal trial). Demonstrated results for TAVI at least as good or better than surgical Aortic Valve Replacement (sAVR)
- Intermediate surgical risk patients (PARTNER 2, SAPIEN 3 trials). Demonstrated TAVI non inferior to sAVR overall, superior to surgery in TF implants.
- SAPIEN 3 trial used the latest iteration Edwards Sapien 3 valve and showed a 1 year death rate of 7.4% vs 13.0% with sAVR, stroke rate 4.6% vs 8.2% and much lower rates of mod / severe paravalvar leak (PVL) than previously described 1.5% vs 0.6%
- A smaller RCT in low surgical risk patients (NOTION) has demonstrated comparable outcomes between Corevalve TAVI and surgical AVR. These data are not large enough to be other than exploratory at this point. A larger follow up RCT in younger, low surgical risk patients is recruiting (NOTION-2).

In addition to the above RCT data, large registries (France, GARY, BCIS) have demonstrated excellent real world clinical results.

Almost 10,000 procedures were recorded in the BCIS database between 2007 and end of 2015. Numbers are increasing year on year.

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

Surgical Aortic Valve Replacement (sAVR); with our without concomitant coronary artery bypass grafting

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 and in most of the world, TAVI is limited to surgical centres. Implants are performed mainly by interventional cardiologists with specialist training in structural valve interventions. Thus TAVI implanters are a small subset of a larger subset of interventional cardiologists, which are in turn a subset of cardiologists in general.

Likewise, cardiac surgeons performing TAVI also form a subset of cardiac surgeons in general.

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)

Death 3.9% vs 4.1% in PARTNER 2 TAVI vs sAVR

1.1% at 30d with SAPIEN 3 TF

Stroke / TIA. 6.4% vs 6.5% in PARTNER 2 TAVI vs sAVR

Permanent pacemaker (PPM) this varies widely depending on TAVI valve. Rates of PPM between 5% and 34% have been reported. This compares with a pacemaker rate of ~3-7% with sAVR. Self-expandable devices appear to have a higher pacemaker rate than balloon expandable, but may offer other advantages such as different PVL solutions and ability to reposition the prosthesis.

Major vascular complications. 7.9% vs 5% in PARTNER 2 TAVI vs sAVR. This relates to the large bore sheaths for device delivery

Life threatening or disabling bleeding 10.4% vs 43.4% in PARTNER 2 TAVI vs sAVR

Paravalvar leak (PVL). This has been the source of much discussion. PVL may occur after sAVR but is uncommon, as the surgeon resects the native valve tissue before implanting the new valve and can achieve a perfect seal. With TAVI, the native valve is compressed by the TAVI prosthesis, so an imperfect seal may occur, causing some regurgitation around the outside of the valve and back into the left ventricle, known as a paravalvar leak.

Early data suggested that any PVL was associated with a poorer long term prognosis, but newer studies repeatedly show only moderate or severe PVLs have an impact on long term outcomes. Mild PVLs appear to be clinically irrelevant.

However, recognition of the importance of PVLS has caused a change in practice to reduce the risk of leaving significant PVLs behind after TAVI. CT scanning leads to more accurate sizing of the aortic valve and new device iterations have included unique design characteristics to reduce PVL rates. These include outer sealing skirts and valve repositionability during the procedure. The rate of moderate / severe PVL in the SAPIEN 3 study was only 1.5%, demonstrating the efficacy of newer generation devices.

Coronary obstruction. Less than 1%

Re-intervention (such as acute valve in valve or conversion to open surgery). Less than 1%

Cardiac perforation / tamponade: 1-2%

Renal Replacement Therapy. Less than 1%

Sequential RCT data and registry data show stepwise reduction in all major adverse events associated with TAVI. The reasons for this are likely to include:

a. Increasing clinical experience and higher operator volumes, both of which make complication avoidance or successful management more likely.

b. Large improvements in device technology – especially requirement for smaller access systems. For example, the initial Edwards Sapien valve used in PARTNER A&B required a 22F or 24F femoral sheath. Some current devices may be implanted with 14F systems. This increases eligibility for TF access (associated with better outcomes than non TF access), reduces the incidence of major vascular complications and may reduce the stroke risk with a smaller device traversing the aortic arch.

c. Better valve sizing algorithms with use of CT scanning

d. Improved case selection, especially identification of patients in whom treatment may be futile because of comorbid medical conditions

Overall, trial data suggests that compared to surgery, TF TAVI with the newest generation devices is associated with lower mortality, lower stroke rate, lower life threatening bleeding, less atrial fibrillation, less acute kidney injury, shorter LOS and quicker recovery. This is offset against a higher rate of PPM, PVL and major vascular complications than sAVR.

No RCT data exist comparing outcomes between TF and non TF access. It is difficult to compare the routes directly without this, as the population groups are different. However, there are increasing data suggesting better outcomes with TF than non TF TAVI. Hence this is the access route of choice for most centres, where anatomically feasible.

2. Anecdotal adverse events (known from experience)

We have seen 2 cases with consequences presumably of valve / annular trauma during TAVI implants leading to late “fistulous” connections to adjacent cardiac structures. Neither have produced symptoms. The incidence of this is not known from the literature but is likely to be a very infrequent though possible late feature.

3. Theoretical adverse events

- Longer term problems with device durability requiring re-intervention by either sAVR or “valve in valve” TAVI.

  There has been some recent literature and comment on late TAVI device problems. A phenomenon of reduced leaflet movement seen on detailed 4D CT follow up of TAVI valves was noted. Further work has shown that this phenomenon is not unique to a specific TAVI valve, but occurs on all tissue valves including surgical valves. In the huge majority, this seems to be clinically silent but further surveillance work is needed to determine any clinical significance or required changes in management strategy.

  A recent paper has commented on structural valve failure in the years following TAVI. Structural valve failure may occur after TAVI or sAVR and may be manifest by either re-stenosis or valve regurgitation. This early work is significantly limited by a much more stringent definition of valve failure than that quoted in the surgical literature (using echo rather than more traditionally used clinical measures). Undoubtedly, more long term study on durability of TAVI vs sAVR is required.

It is theoretically possible that valve durability will be greater with TAVI than sAVR as the effective orifice from a TAVI valve is greater than with the equivalent sized surgical valve. In general, larger valves retain more effective orifice are than smaller over time. However, there may be factors related to valve crimping which may negate this theoretical advantage.

If repeat intervention is required, valve in valve TAVI will yield better immediate haemodynamic results with TAVI than sAVR as the true inner diameter (ID) is higher with a TAVI valve. For example, the true ID of a 23mm Hancock surgical valve is 18.5mm, whereas the true ID of a 23mm Edwards Sapien XT TAVI valve is around 22mm. Thus the lumen available for another valve in valve prosthesis is greater with TAVI and will yield a larger orifice and lower post procedural gradient

- Later complications such as infective endocarditis (the rate of endocarditis currently appears comparable to sAVR)

4.2 What are the key efficacy outcomes for this procedure?

1. Mortality – 30day and 1 year +/- longer term. Either compared against medical management for inoperable patients or against sAVR
2. Shorter length of stay compared with sAVR (may include ITU reduction)
3. Improved symptoms. NYHA class or QOL measures
4. Improvements in left ventricular function (if abnormal pre intervention)
5. Reduced re-hospitalisation for cardiac causes, especially heart failure
6. Minimisation of moderate / severe paravalvar leak with newer devices / sizing algorithms
7. Minimisation of need for permanent pacemaker
8. Reduced incidence of Acute Kidney Injury / Renal Replacement Therapy with TAVI vs sAVR

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

No, for the vast majority of patients represented in the clinical trials.

There are some uncertainties about which of the very highest risk patients may be too sick to benefit. There are also some uncertainties about efficacy comparted with sAVR for very low risk and younger patients. This latter group are the subject of ongoing trials, mentioned above.

Finally, there are some uncertainties about efficacy in small subsets of patients with severe AS, such as those with bicuspid valves, pure aortic regurgitation and those with very severe coronary artery disease. These patient groups have largely been excluded from RCTs, but are represented in registries and still appear to benefit.

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

1. **A full heart team including TAVI-trained interventional cardiologists, cardiac surgeons and imaging cardiologists.**
   Certified training for all valve systems is available. This begins with didactic lectures, followed by simulator training. Implants are then performed on site

with an experienced proctor, who then “signs off “ the fully trained team once competent. This mitigates any learning curve issues.

2. **Anaesthetic support on site.**
   Many TF cases are performed under local anaesthetic but immediate on site anaesthetic availability is required to deal with any emergencies. Non TF cases almost always need general anaesthesia.
3. **Trained AHP team**
   Including radiographers, valve crimp & catheter lab nurses, physiologists, standby theatre team & perfusion services for emergencies.
4. **A suitable catheter lab or theatre environment.**
   Most TAVI procedures are performed in catheter labs under aseptic conditions. Most cardiac theatres do not have sufficient radiology / fluoroscopy facilities to enable safe implants. Hybrid catheter lab / theatres are probably the optimal environment but are not widely available.
5. **Back up to deal with complications** – vascular surgery / interventional radiology, renal services
6. **Bail out equipment for emergencies**
   e.g. pericardiocentesis kit, iliac balloons, aortic occlusion balloons
7. **High quality echo imaging** onsite and in catheter lab / theatre
8. **High quality cardiac CT** scanning during work-up
9. **Regular MDT meetings** with opportunity to review all pre-procedural images and investigations from referring sites (angiogram, echo, CT)
10. **Audit support** for data collection and submission to CCAD/ BCIS
11. **Regular case review of mortality / complications**

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

UK TAVI trial – TAVI vs sAVR in intermediate risk patients. Not device specific. Recruitment ongoing. Participation encourage by previous NICE guidance and UK commissioning.
NOTION-2. Nordic trial of TAVI vs sAVR in low risk, young patients. Not device specific.

Several other trials of specific devices will be found on clinical trails register.

Ongoing national registries with regular publications. Larger datasets include FRANCE registry, GARY (German) registry and the UK / BCIS registry. UK data are collected and published on the BCIS website.

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).

Available via PUBMED.

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

- **Uptake / funding – affecting dissemination**
  There is a large difference in uptake of TAVI in different countries. For example, TAVI is now commoner than sAVR in Germany with implant rates around 140 / per million population (pmp). The UK is somewhere under the middle of the range for implants in Europe (around 40 pmp in 2015). Differences in implantation rates are largely influenced by funding constraints in most healthcare systems.
  In the UK, there has been lack of uniformity about funding leading to large discrepancies in implant rates. For example, implants pmp range from 11.6 to 70.7 by LAT in 2015.
- **Implant route.**
  TF implants increasingly appear to offer better outcomes than non TF but with important caveats about data mentioned previously
- **Device type.**
  No large, high quality, RCT exists comparing different valve types, though registries and one small RCT do demonstrate consistent differences in some characteristics
- **Adjunctive therapy.**
  For example dual vs single antiplatelet therapy, cerebral protection devices to potentially reduce strike risk. Further research is needed in both of these areas
- **Management of concomitant coronary artery disease.**
  Ideal strategy not known but subject to research

5 Audit Criteria

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

The current BCIS / CCAD dataset captures a full spread of pre procedural clinical factors and well defined outcome measures. All implanting units should be using this method, which would allow for rigorous data collection and case tracking.

5.1 Outcome measures of benefit (including commonly used clinical outcomes, both short and long - term; and quality-of-life measures):

1. Survival to discharge / 30 days
2. Patient reported symptom response at follow up (initial appointment and 1 year)
3. Rehospitalisation for heart failure or other cardiac diagnosis
4. A limited sample of patients could undergo more formal testing pre and post by means of formal QOL questionnaires or functional testing (e.g. 6 minute walk test). However, these measures are now being included in clinical trials which will probably be a more robust measure. These measures are not practicable for routine use in all patients.

5.2 Adverse outcomes (including potential early and late complications):

As above. BCIS / CCAD dataset + case tracking for mortality / readmission for cardiac causes

6 Trajectory of the procedure

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

It is certain that there will be a yearly rise in use of this procedure, in keeping with the increasing trial data. It could be argued that this increase should be closer to exponential rather than linear over the next 3-5 years.

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:

Should be available to all surgical centres as part of portfolio of options for patients with aortic stenosis. Major guidelines suggest on-site cardiac surgical back-up is required to deal with emergencies.

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:
Aortic stenosis is the commonest cardiac valve lesion and is usually due to age related valve degeneration. As the population ages, more patients with severe AS eligible for treatment will present. Data on TAVI in this population are already clear and show signs of better outcomes and quicker recoveries than sAVR.
Ongoing trial and registry reports suggest efficacy will continue to be demonstrated in younger and lower risk patients, thus expanding eligibility across a different patient range. It seems likely that over a few years that TAVI would numerically be greater than sAVR. Patients, family members and healthcare professionals inherently prefer a less invasive option for intervention if outcomes are similar or better.
Device costs are significantly higher than for sAVR but LOS and hospital resource utilisation is far less with TAVI. Successful intervention reduces readmissions, hospital costs and societal burden.

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 procedure in many centres is becoming less and less invasive, with a minimalist approach being adopted as safety and efficacy improves with new devices. This reduces hospital resources.

For example, in 2009 in my unit a full day would include a full day list of 2 TAVI implants. Cases were all performed under general anaesthesia, involving femoral vascular cut down and repair. A full theatre team, catheter lab team, perfusionist, bypass machine, surgeon, anaesthetist, imaging cardiologist to perform trans-oesophageal echo (TOE) and 2 interventionists were present for each case.

Now a typical list will be 3 cases under local anaesthetic with percutaneous access and device closure. 2 interventionists to perform implant. No GA, TOE required. No imaging cardiologist, surgeon, theatre team, bypass pump required – all simply on standby but immediately available. With this approach, safety has not been compromised, recovery is much quicker and around 50% of cases are discharged the following day. Thus hospital resources and costs are much lower than before.

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**
See point 1 below	☐	**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**
See point 2, below	☒	**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**
See point 3, below	☐	**NO**

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

Fellowships endowed by the healthcare industry	☒	**YES**
See point 4, below	☐	**NO**
Support by the healthcare industry or NICE that benefits his/her position or department, eg grants, sponsorship of posts	☒	**YES**
See point 5, below	☐	**NO**

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

Comments:

1. I have received speakers fees, proctor fees and advisory board fees from Edwards Lifesciences. Proctor fees only in past 12 months.
   I have received proctor fees from Boston Scientific, although unrelated to TAVI. None within last 12 months.
   I have received speaker fees from Medtronic >8 years ago, although unrelated to TAVI.

[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).

2. I have received sponsorship to attend national and international educational meetings by the following companies who offer TAVI products:
   Edwards Lifesciences – within past 12 months
   Boston Scientific
   St Jude Medical – within past 12 months
   Medtronic
   All of these have provided standard accommodation, meals and travel, but declared for transparency.
3. Member of BCIS council
4. I undertook an overseas PCI training Fellowship in 2003, sponsored by Medtronic. Unrelated to TAVI and historic but declared for transparency
5. My department has received grant support for research from Edwards Lifesciences within last 12 months
   My department has received funding for a TAVI training Fellowship from Edwards Lifesciences within last 12 months

Thank you very much for your help.

Dr Tom Clutton-Brock, Interventional Procedures Advisory Committee Chair

Professor Carole Longson, Director, Centre for Health Technology Evaluation.

Jan 2016

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.