

**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:** Deonee.Stanislaus@nice.org.uk

**Procedure Name:** Percutaneous fetal balloon valvuloplasty for aortic stenosis  
**Name of Specialist Advisor:** Mr David Howe  
**Specialist Society:** British Maternal and Fetal Medicine 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 procedure would normally be carried out by fetal medicine consultants working with paediatric cardiologists with expertise in fetal diagnosis

**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:**

I regularly see and manage fetuses with aortic stenosis, but have not referred patients for attempts at this treatment due to lack of evidence of improved outcome.

**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:**

Although this procedure has been carried out for a number of years, with first descriptions in the late 1990s the total reported cases is less than 300, with over a third carried out at a single US institution. There have been no randomised trials..

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

No antenatal intervention, with postnatal Norwood's procedure to manage hypoplastic left heart syndrome.

**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:**

Very few centres are attempting this treatment in the UK

**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)

Fetal death directly related to the procedure. An increase in preterm delivery has also been reported..

2. Anecdotal adverse events (known from experience)

Placental abruption causing preterm delivery

3. Theoretical adverse events

#### **4.2 What are the key efficacy outcomes for this procedure?**

The key outcome would be an increase in the number of postnatal two-ventricle repairs, as opposed to single ventricle circulation.

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

There is very limited data about how often this procedure successfully achieves its primary aim of allowing a two ventricle rather than single ventricle repair

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

Training in complex in utero interventional procedures

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

There are no current trials of this procedure but there is an anonymised European registry

#### **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).**

- [Fetal hemodynamic response to aortic valvuloplasty and postnatal outcome: a European multicenter study](#) DOI: 10.1002/uog.18913

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

There are important uncertainties about which patients may benefit (selection criteria for the procedure) and whether there is a genuine improvement in outcomes

**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:**

**Achievement of biventricular repair after delivery. Improvement in size of left ventricle. Resolution of fetal hydrops, if present prior to procedure.**

**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:**

**Fetal death. Premature delivery. Fetal growth restriction.**

**6 Trajectory of the procedure**

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

This procedure will be confined to a small number of centres for the foreseeable future

**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:**

Only a very small number of fetuses are likely to benefit from this procedure even if efficacy was demonstrated by properly conducted clinical trials.

**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.

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.

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**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<sup>1</sup> 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

**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:**

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**

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<sup>1</sup> ‘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).

## Conflicts of Interest for Specialist Advisers

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### 2 Personal pecuniary interests

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  - 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 Advisor 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.

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Interventional Procedures Programme

**Specialist Adviser questionnaire**

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**Please respond in the boxes provided.**

**Please complete and return to:** Deonee.Stanislaus@nice.org.uk

**Procedure Name:** Percutaneous fetal balloon valvuloplasty for aortic stenosis

**Name of Specialist Advisor:** Dr John Thomson

**Specialist Society:** British Congenital Cardiac Association

**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:**

This is a rare procedure and although we work in a very large (by UK standards) fetal cardiac programme, the specialists in this area have never come to me as lead for interventional cardiology asking for this to be done. This may in part reflect the lack of clarity in the very limited literature and therefore limited "buy in" from our local clinicians

**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:**

Whilst working at Guys hospital in the early 2000's this is a procedure that was discussed at MDT's

**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:**

There are a handful of centres worldwide that have an enthusiasm for this procedure (in particular Boston Childrens hospital) and a gradual accumulation of data. The procedure is still associate with high rates of fetal loss and the criteria for intervention remain unclear. There have, however been successes and fetal cardiac intervention forms part of the discussion in may peer group international meetings

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

None-if not treated there is fairly good evidence that the problem progresses to Hypoplastic left heart syndrome where the treatment option is high risk (relatively) surgical palliation i.e. the Norwood operation which leave the child with a single ventricle future.

#### **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)  
Fetal death-nearly all of the problems associated with this procedure result in fetal loss
2. Anecdotal adverse events (known from experience)
3. Theoretical adverse events

### **4.2 What are the key efficacy outcomes for this procedure?**

Prevention of irreverable involution of the left heart structures i.e. preservation of a “2 pump” circulation

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

Uncertainty about which variants of left heart disease respond to the treatment. Some concerns around whether the left heart will work well in the long term after ballooning

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

Tertiary congenital cardiac intervention  
Tertiary fetal cardiology  
Tertiary feto-maternal medicine unit

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

There is a literature and Boston Childrens continue to collect by far the largest volume of information

### **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-everything should be on 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?**

Only that it concerns a tiny number of patients and should not be rolled out to too many centres to concentrate expertise

**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:**

Fetal survival

Left heart growth

Ventricle function

Eventual desintation-2 ventricle or 1 ventricle

**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:**

Fetal death

**6 Trajectory of the procedure**

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

Slowly

**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:**

Tiny numbers-will never be more than 50 procedures in the UK PA even if it develope

**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?**

No

**8 Data protection and conflicts of interest**

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

**8.1 Data Protection**

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**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 (I proctor for percutaneous treatments)**  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

**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:**

Thank you very much for your help.

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<sup>1</sup> ‘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).

**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

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- 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 Advisor 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:** Deonee.Stanislaus@nice.org.uk

**Procedure Name:** Percutaneous fetal balloon valvuloplasty for aortic stenosis

**Name of Specialist Advisor:** Professor John Simpson

**Specialist Society:** British Congenital Cardiac Association

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

Yes.

**1.1 Does the title used above describe the procedure adequately?**

Yes.

**Comments:**

**2 Your involvement in the procedure**

**2.1 Is this procedure relevant to your specialty?**

Yes.

**Comments:**

This procedure is highly relevant to interventional paediatric cardiologists and fetal cardiologists. Performance of the procedure involves fetal medicine specialists who are essential to perform the procedure in the pregnant mother, achieving access to the fetal heart using needles, as well as positioning of the fetus to make this achievable. Thus, three subspecialty groups are necessary: interventionists (to inflate / position balloons etc), fetal cardiologists (imaging of the fetal heart during the procedure) and fetal medicine specialists (gaining position for the procedure, accessing the fetal heart).

**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 done this procedure at least once.

**Comments:**

I have been involved in 3 fetal balloon aortic valvuloplasty procedures.

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

**Comments:**

I will take part in discussions about patient selection for these procedures, probably around 3 times per year. Critical aortic valve stenosis in the fetus is a rare condition and only a proportion of cases might be suitable.

**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.

Other (please comment)

**Comments:**

I was senior author on a recent paper from our unit where we reviewed over 30 cases of fetal critical aortic valve stenosis to gauge whether the published selection criteria for intervention matched the outcomes we had observed in a cohort who had not undergone intervention. I was lead author on one of the first papers on the natural history of critical aortic stenosis diagnosed during fetal life.

**3 Status of the procedure**

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

- Established practice and no longer new.
- Definitely novel and of uncertain safety and efficacy.

**Comments:**

Fetal balloon aortic valvuloplasty has been undertaken since the early 1990s but since 2000 has been undertaken in larger numbers in large centres, particularly Boston Children's Hospital in the USA. Other centres in Linz, Austria and Paris have also published series. There is an International Fetal Cardiac Intervention Registry (IFCIR) to which many centres contribute data. This publishes multicentre data under the auspices of the registry. Multicentre European studies have also reported recently under the auspices of the AEPC. The debate is not so much about technical feasibility (this procedure can usually be achieved) but about whether the procedural risks are worth it in terms of improvement of the outcome of the fetuses undergoing the procedure. This explains my answer above that the procedure is no longer new, but its safety and efficacy is still the subject of ongoing research.

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

The comparator would be to intervene only after the baby is born. i.e. no intervention during fetal life.

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

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

**Comments:**

This procedure is limited to a very few specialist centres : to my knowledge only 2 cardiac centres in the UK will consider this procedure

**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)

The most representative data comes from the International Fetal Cardiac Intervention Registry (IFCIR). The results were published in the Journal of the American College



of Cardiology in 2015 (Moon-Grady et al). The summary table is copied below for reference .

**TABLE 3** Pregnancy Outcomes Among FCI Patients by Procedure Type

Parameter	Total	Aortic Valvuloplasty
Maternal-fetal patients	145	86
GA at intervention (weeks)	26.4 (19.3-36.4)	25.0 (19.3-34.4)
Complications		
Fetal death	16 (11)	10
Bradycardia requiring treatment	47 (32)	29
Hemopericardium requiring drainage	42 (29)	16
Balloon rupture	6 (4)	4
Maternal complication	0	
Pregnancy outcome post-intervention		
Termination	6 (4)	6
Periprocedural demise (<48 h)	9 (6)	5
Late intrauterine demise	2 (1)	1
Term birth	77 (53)	49
Preterm birth (<37 weeks) birth	29 (20)	15
Not stated/in utero	6	0
Survival to first hospital discharge	71 (49)	46

Values are n, median (interquartile range), or n (%).  
Abbreviations as in Table 2.

Thus, fetal death occurred during 10 of 86 procedures. Bradycardia (29/86), haemopericardium (16 / 86) and balloon rupture in 4 / 86 procedures. Beyond the procedure there were a further 6 deaths and preterm delivery occurred in 15 / 86 cases.

A recent European multi-centre study (Gardiner et al 2016) challenged selection criteria for fetal cardiac intervention, and reported that a substantial number of fetuses who met published criteria for intervention, survived with a normal biventricular circulation in the absence of an intervention.

The data from my own centre, previously published criteria for intervention appeared reliable but only a minority of cases of critical aortic stenosis will be judged suitable candidates (Hunter et al 2015)

## 2. Anecdotal adverse events (known from experience)

I have been involved in procedures complicated by bradycardia requiring drug resuscitation and cases with haemopericardium sufficient to require drainage and transfusion. In the past some units used a “mini-laparotomy” on the mother to gain direct access to the uterus, but this is now seldom used.

## 3. Theoretical adverse events

There is a potential risk to the mother by, for example, introducing infection at the time of the procedure. Some units have used maternal anaesthesia for the fetal balloon aortic valvuloplasty with the risk of maternal (and fetal) anaesthetic complications. A recent report (Kovacevic 2017) described placental abruption at 25 weeks in relation to the procedure.

#### **4.2 What are the key efficacy outcomes for this procedure?**

The key efficacy outcomes are:

- Survival of the fetus through the procedure to term
- Absence of maternal complications
- Evidence of growth of left heart structures e.g. aorta, mitral valve, left ventricle and improvement of left ventricular function following the procedure. (Echocardiographic improvement)
- Management towards a biventricular circulation (rather than a Fontan (single ventricle) circulation after birth.
- Number of procedures patients have to undergo to achieve a biventricular versus single ventricle circulation
- Absence of pulmonary hypertension during medium to longer term follow up reflecting absence of severe diastolic dysfunction of the left ventricle.
- Good functional status of longer term survivors

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

There are uncertainties about the efficacy of the procedure.

Advocates of the intrauterine balloon aortic valvuloplasty have produced data demonstrating improved growth of left heart structures in those who have undergone balloon aortic valvuloplasty, but whether this leads to better long term survival, quality of life and functional status compared to non-intervention during fetal life remains controversial. A recent study (Kovacevic 2017) showed no difference in fetuses undergoing intervention versus those who did not with respect to single ventricle versus biventricular repair. However, the postnatal survival of the intervention group was better. Set against this, is the procedural risk of demise of around 10%.

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

This procedure requires a very high level of training, and appropriate facilities. The key aspects are:

1. Excellent quality ultrasound imaging during the procedure to establish needle, catheter and balloon position during the procedure and to recognise complications such as haemipericardium and bradycardia. This imaging is provided both by fetal cardiologist and fetal medicine specialist.
2. Highly trained and experienced fetal medicine specialist (obstetrician) with high level of technical skill in needle placement to gain access to the fetal heart to deliver the balloon catheters etc. The fetal medicine specialists will have such expertise due to invasive procedures such as other fetal shunts, fetal blood sampling, intra-uterine transfusion etc.
3. Experienced interventional paediatric cardiologist. This is critical to select the optimal balloons, obtaining optimal wire and catheter position during the procedure and slick removal of such equipment once the procedure has been performed.

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

1. There is an international fetal cardiac intervention registry (IFCIR). Our unit has obtained ethical approval to submit to this registry.
2. There is an aortic stenosis registry under the auspices of the Association for European Paediatric and Congenital Cardiology.

**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).**

Gardiner H, Kovacevic A, Mellander A et al. Does fetal aortic valvuloplasty alter outcomes in aortic valve stenosis? Results of a retrospective European multinational multicentre study. *Ultrasound Obstet Gynecol* 2014;44(Suppl. 1):1–61.

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

There is uncertainty about the efficacy of the procedure as outlined above. Preparation of the mother for the procedure has also varied. For example, a mini-laparotomy was performed in some units, but not in ours as we felt this was too invasive to be justified. In most units, the procedure is performed with the mother awake and the fetus receiving sedation (fentanyl) and a paralysing agent so that the fetus does not move during the procedure. In some instances, maternal general anaesthesia has been used. In my experience, maternal general anaesthesia was used over five years ago for fetal balloon aortic valvuloplasty.

**5 Audit Criteria**

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

- Survival of the fetus through the procedure.
- Technical success of the procedure i.e. was balloon dilation of the aortic valve achieved.
- Procedural complications e.g. pericardial effusion, bradycardia, resuscitation drugs, balloon rupture.
- Absence of maternal complications during procedure
- Evidence of growth of left heart structures e.g. aorta, mitral valve, left ventricle and improvement of left ventricular function following the procedure through to term (Echocardiographic improvement)
- Type of circulation achieved after birth – single ventricle versus biventricular circulation.
- Number of procedures patients have to undergo to achieve a biventricular versus single ventricle circulation

- Absence of pulmonary hypertension during medium to longer term follow up reflecting absence of severe diastolic dysfunction of the left ventricle.
- Good functional status of longer term survivors judged by e.g. exercise test, six minute walk or CPET in longer term survivors.

**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:**

1. Technical success of the procedure
2. Requirement for resuscitation drugs / pericardiocentesis/ transfusion during the procedure
3. Survival through 48 hours after the procedure
4. Survival to delivery (including gestational age at delivery)
5. Echocardiographic evidence of improvement in cardiac function / hemodynamics.
6. Survival through neonatal period (up to 28 days)
7. Survival through infancy
8. Type of final repair (single ventricle versus biventricular)
9. Presence / absence of pulmonary hypertension or increased pulmonary vascular resistance.
10. Number of operations or catheter procedure to achieve final repair.
11. Quality of life  
This is difficult to gauge in small infants and children. Some possible metrics would include- hospitalisation, requirement for tube feeding/ gastrostomy, ventilation, supplementary oxygen, weight and height centiles, exercise capacity in older children.  
In older children, formal exercise testing, use of mobility aids, developmental assessment / questionnaires

**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:**

1. Early (within one week of procedure)
  - a. Procedural death
  - b. Technically unsuccessful procedure
  - c. Procedural complications e.g. pericardial effusion, bradycardia, requirement for resuscitation drugs or intra-uterine transfusion, balloon rupture
  - d. Death within 48 hours of procedure
  - e. Evidence of infection e.g. amnionitis
2. Medium term (through to delivery and neonatal period)
  - a. Preterm delivery
  - b. Sonographic evidence of neurological insult
  - c. Stillbirth > 1 week after procedure
  - d. Aortic valve regurgitation requiring valve repair / Ross operation
  - e. Neonatal death
3. Long term
  - a. Unsatisfactory haemodynamics precluding single ventricle repair e.g. high PVR
  - b. Pulmonary hypertension / pulmonary vascular disease.
  - c. Requirement for heart transplantation

- d. Requirement for aortic valve repair / replacement
- e. Requirement for MV repair / replacement
- f. Requirement for surgery to resect endocardial fibroelastosis

## **6 Trajectory of the procedure**

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

I believe this procedure will be limited to a very few (1-2) specialist centres in the UK.

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

.

Fewer than 10 specialist centres in the UK.

#### **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:**

Minor.

#### **Comments:**

Critical aortic stenosis represents <2% of fetal cardiac lesions and only a minority will be judged potential candidates for intervention.

## **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.

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## 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<sup>1</sup> have a **personal pecuniary** interest? The main examples are as follows:

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

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<sup>1</sup> ‘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).

industry  **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?  **NO**

Do you have a **non-personal** interest? The main examples are as follows:  
**Fellowships** endowed by the healthcare industry  **NO**

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

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

**Comments:**

I have no conflicts of interest related to this topic.  
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 Advisor 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:** Deonee.Stanislaus@nice.org.uk

**Procedure Name:** Percutaneous fetal balloon valvuloplasty for aortic stenosis  
**Name of Specialist Advisor:** Professor Shakeel Qureshi  
**Specialist Society:** British Congenital Cardiac Association

**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:**

This procedure is rare in its frequency. We perform it about 1 or 2 times a year.

**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 procedure is rare in its frequency. We perform it about 1 or 2 times a year.

**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:**

This procedure was developed (world's first) in our unit and has since been modified. In the USA and Austria, large experience has been gained because of patient referral.

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

None

#### **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)

Fetal demise, cardiac tamponade, premature delivery, arrhythmias needing intracardiac drugs and resuscitation, pleural effusions, failure of technique

2. Anecdotal adverse events (known from experience)

As above

3. Theoretical adverse events

As above

#### **4.2 What are the key efficacy outcomes for this procedure?**

1. Successful performance of the procedure
2. During pregnancy, improvement in size and function of the left ventricle
3. Avoidance of 1-ventricle circulation

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

Yes – about ½ of the patients still manage to go down the route of 1-ventricle circulation pathway rather than 2-ventricle circulation, after birth.

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

Very complex. Need a team approach which consists of fetal medicine obstetrician with skills in obtaining access into the fetal heart, ability to resuscitate with intracardiac drugs; fetal cardiologist to provide optimum fetal echocardiogram images; paediatric cardiology interventionists with assistants competent in performing a variety of interventions in CHD, familiarity with equipment to be used, eg needles, guidewires and balloons.

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

IFCIR registry has collected data on fetal cardiac interventions

#### **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).**

Moon-Grady et al, JACC 2015

Kevin et al, Am J Cardiol 2007  
Tulzer et al, Semin Fetal Neonatol Med 2013  
McElhinney et al, Circulation 2009  
Marshall et al, Circulation 2004  
Pedra et al, Pediatr Cardiol 2014

**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. No universal agreement of its role and value as a significant ratio of fetuses still have 1-ventricle circulation.

**5 Audit Criteria**

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

Overall numbers, complications, gestational data, LV size, aortic root size, evidence of EFE, failure of development of LV, subsequent growth after fetal cardiac intervention, need for procedures (intervention or surgery) after birth, achievement of 2-ventricle circulation, complications of fetal cardiac intervention

**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:**

Overall numbers, complications, gestational data, LV size, aortic root size, evidence of EFE, failure of development of LV, subsequent growth after fetal cardiac intervention, need for procedures (intervention or surgery) after birth, achievement of 2-ventricle circulation, complications of fetal cardiac intervention

**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:**

**As above**

Overall numbers, complications, gestational data, LV size, aortic root size, evidence of EFE, failure of development of LV, subsequent growth after fetal cardiac intervention, need for procedures (intervention or surgery) after birth, achievement of 2-ventricle circulation, complications of fetal cardiac intervention

**6 Trajectory of the procedure**

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

There will only need to be 1 and certainly no more than 2 centres in the UK performing this procedure as there will only be <6 fetuses a year needing this intervention.

**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:**

Only 1 or 2 centres

**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?**

No

**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.



XI 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.

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## 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<sup>1</sup> 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:

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<sup>1</sup> ‘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).

**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 have worked with a company (NuMED Inc to develop a fetal aortic valvoplasty balloon, which is still being developed.

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 Advisor 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.