NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Specialist Adviser questionnaire

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

Please respond in the boxes provided.

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

Procedure Name:	**Therapeutic hypothermia following ischaemic stroke**
Name of Specialist Advisor:	**Professor Nikola Sprigg**
Specialist Society:	**British Association of Stroke Physicians (BASP)**

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.

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

☐

Comments:

Yes as this potentially requires input from ITU depending on the depth of cooling. Currently no clinical evidence to support use of hypothermia outside a RCT in stroke..

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 done this only as part of a randomised controlled trial

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:

Not applicable – as above I have done surface cooling on the acute stroke unit as part of an RCT.

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

☐

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

☐

☐ Other (please comment)

Comments:

I was the UK coordinator for EuroHyp-1 a RCT of hypothermia. I was also PI at Nottingham.

3 Status of the procedure

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

☐

☐ Definitely novel and of uncertain safety and efficacy.

☐

Comments:

As above this should only be performed as part of a clincial trial. Type of cooling (surface or endo vascular) or depth and duration of cooling are uncertain.

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

Standard care on a stroke unit with no cooling.

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.

☐ Cannot give an estimate.

Comments:

We had 6 centres in the EuroHyp clincial study – only approx. 6 doctors in the Uk have done 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)

Infection particularly pneumonia

2. Anecdotal adverse events (known from experience)

   Infection particularly pneumonia

3. Theoretical adverse events

Bradycardia and hypotension seen in cardiac studies does not seem to be a problem so date in stroke patients.

4.2 What are the key efficacy outcomes for this procedure?

Disability and death (mRS at day 90)

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

Yes – depth, duration of cooling
Cooling method – surface or endovascukar

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

This is to be determined and depends on depth and duration of cooling. Certainly at the very least for surface cooling continual ecg and oxygen sat monitoring.
If deeper cooling to 33 degrees will need ITU admission for sedation. If endovascular cooling will need training and facilities for insertion (ultrasound guidance, sterile etc).

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

EuroHyp-1

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).

EuroHyp-1 results due to be presented at WSO Montreal Oct 2018

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

As above there is no clincial evidence to support efficacy of this at present. Device, duration, depth (temp atarget) are all uncertain, as is efficacy and safety.

I agree with this statement - *The ideal target temperature for neuroprotection is unknown. Re Cooling may be continued for at least 12 to 24 hours, maintaining a temperature of 33 to 35°C. EuroHyp1 aimed for 35 degrees – which is possible for awake patients. 33 degrees requires sedation and ITU admission*

5 Audit Criteria

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

Not in clinical practise so should not be appropriate to be audited at present. Could provide criteria after

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:

mRS day 90, EQ5D day 90

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:

In my experience and that of the pilot studies no increase in bleeding. Shivering and lack of tolerance of shivering was the main problem – which leads to inability to reach target temperature…

6 Trajectory of the procedure

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

Not at all unless there is very clear evidence and then will need very significant training and support to be performed outside major hyperacute stroke units. But surface cooling is possible on the acute stroke units so should be possible with adequate support and training.

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

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

Comments:

As above training needed but surface cooling is possible on acute stroke units. Concern re sedation secondary to pethidine (anti-shivering) so need constant monitoring.

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:

☐ Moderate.

Comments:

Impossible to predict until know efficacy – study had restricted inclusion criteria – likely only patients suitable for reperfusion will be suitable (as needs to be given hyperacutely) so 5-8% of stroke patients. However experimental studies suggest can reduce infarct size by 30% which would be very significant.

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?

Need to wait for the results of EuroHyp1 and planned IPDMA of the other hypothermia studies (ICTUS)-due in Oct 2018 – at present no evidence to support 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. **YES**

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 ☐ **NO**

Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice** ☐ **YES**

Shareholdings – any shareholding, or other beneficial interest, in shares of the healthcare industry ☐ **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 ☐ **NO**

Investments – any funds that include investments in the healthcare 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? ☐ **YES**

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 ☐ **YES**

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

Comments:
I was the UK coordinator for this study EuroHyp1 which bought grant income into the university of Nottingham to employ a number of staff. These confilicts end when the study finishes.

Thank you very much for your help.

Dr Tom Clutton-Brock, Interventional Procedures Advisory Committee Chair

Mark Campbell
Acting Programme Director
Devices and Diagnostics

Jan 2016

[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).

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.