Stroke in Childhood

Clinical guideline for diagnosis, management and rehabilitation

May 2017

Appendix 5

Contains:

- Delphi consensus method

Royal College of Paediatrics and Child Health
5-11 Theobalds Road, London, WC1X 8SH

The Royal College of Paediatrics and Child Health (RCPCH) is a registered charity in England and Wales (1057744) and in Scotland (SC038299).
Appendix 5: Delphi consensus method

Delphi Plan

Aim

The Delphi consensus method is a research method that can be used to gather the consensus opinion/agreement of experts and stakeholders when published evidence is lacking or inconclusive. It is an anonymous and iterative process where statements on the topic of interest are scored or ranked and then amended following comments until consensus of expert opinion is reached.

Delphi consensus method rules

The Delphi consensus method follows four simple rules:

- Anonymity of participants
- Structured information flow and feedback to the participants
- Statistical analysis of responses
- Iterations (allowing the participants to change their views in subsequent rounds)

Beyond these rules, individual Delphi consensus methods can vary. The specifics of the process should be laid down before the start of the first round. For this Delphi consensus method the specific rules were as follows:

<table>
<thead>
<tr>
<th>Rules</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definition of consensus</td>
<td>A 10-point Likert scale will be used for panellists to provide their responses to statements. Consensus agreement will be defined as 75% of panellists selecting 7, 8, 9 or 10 on the Likert scale.</td>
</tr>
<tr>
<td>Information for participants</td>
<td>Participants will be informed of the purpose of the Delphi. Following each round, participants will be given a summary of the comments on each statement not achieving consensus and the revised statement.</td>
</tr>
</tbody>
</table>
| Panel knowledge base            | Experts from the following five specialities will be invited to participate:  
                                      - General Paediatrics  
                                      - Paediatric neurology  
                                      - Radiology  
                                      - Haematology  
                                      - Neurosurgery |
| Panel size                      | A minimum of 40                                                           |

Select the panel

Potential participants will be given two weeks to respond to an invitation to participate circulated by their professional body. A minimum of eight experts from each of the five specialities is required.

To allow for non-response and drop-out recruitment will not be stopped if the target number is reached before the end of the two week recruitment period and instead extra clinicians will be recruited. If insufficient numbers of experts are recruited within this period, recruitment will be extended until target numbers are achieved and any specialities with low numbers will be targeted.
**Design of the questionnaire**

The statements used in the Delphi survey will be developed by the expert members of the guideline development group (GDG).

The survey will include:

- Detailed instructions to the participants including the purpose of the study
- Five statements covering various aspects of the management of stroke in children
- A 10-point Likert scale for participants to rate agreement
- A ‘Not my area of expertise’ opt out response option
- Space for participants to comment

The statements will be agreed during a meeting of the GDG when all members present will have an opportunity to shape them. Following each round of the survey, a summary of the results will be circulated to the GDG with a request that the statements requiring amendment are re-drafted by the members with expertise in the relevant areas. The re-drafted statements will then be circulated for sign-off by the GDG.

Delphi participants will be required to rate each statement on a scale of 1 to 10 according to their level of agreement (with 1 being strongly disagree and 10 being strongly agree) or use the ‘Not my area of expertise’ option. A space for comments or alternative wording will also be provided.

The Delphi survey will be designed in and administered using Survey Monkey. A link to the online survey will be sent out to participants via email.

**Round 1**

An email containing a link to the survey and some brief instructions will be sent to the respondents explaining that they are to complete the survey before the closing date which will be two weeks from the date the email is sent. A reminder email will be sent at the end of the first week.

It will be emphasised to participants that they are required to respond to a minimum of two and a maximum of three rounds of survey.

**Rounds 2 and 3**

Statements that have reached consensus (see below) will not be included in subsequent rounds. After each round the comments and ratings for statements not achieving consensus will be analysed as described below and used to revise the statement for inclusion in the next round of the survey by the relevant GDG member up to a maximum of three rounds. Revised statements will be circulated to the GDG for comments and sign-off.

A new Survey Monkey survey will be created including anonymous, summarised feedback informing the participants of the results of the previous round.

If consensus is not achieved for any statement after three rounds of survey the GDG will review the ratings and comments and a recommendation with a detailed explanation of the process that was gone through for inclusion in the guideline.

**Summarise and analyse results**

A systematic reviewer will compile the responses to the Delphi survey to present to the GDG. The following information will be compiled:

- Number of experts from each speciality responding to the round
- Percentage agreement rating for each statement (excluding those who opted out and non-responders)
- Frequency of selection of each response option for each statement
• If any statement has less than 25 useable responses (excluding those who opted out and non-responders) further efforts to gather more responses will be undertaken.

Reaching a consensus
• If at least 75% of the ratings fall within 7 to 10, a consensus has been reached and the statement will be formed into a recommendation for inclusion in the guideline.
• A minimum of 25 responses (not including those who opted out or non-responders) is required for a consensus to be reached.

Delphi results

Delphi Rules
In this Delphi analysis, results have been combined as follows:

• Agree: 7, 8, 9, 10
• Neither agree nor disagree: 4, 5, 6
• Disagree: 1, 2, 3

Consensus is considered to be achieved if at least 75% of the panellists agree with the statement.

Panel Response

<table>
<thead>
<tr>
<th></th>
<th>Round 1</th>
<th>Round 2</th>
<th>Round 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response rate (out of 70)</td>
<td>99%</td>
<td>80%</td>
<td>77%</td>
</tr>
<tr>
<td>General paediatrics</td>
<td>15</td>
<td>9</td>
<td>8</td>
</tr>
<tr>
<td>Paediatric neurology</td>
<td>14</td>
<td>13</td>
<td>9</td>
</tr>
<tr>
<td>Radiology</td>
<td>18</td>
<td>17</td>
<td>16</td>
</tr>
<tr>
<td>Haematology</td>
<td>12</td>
<td>10</td>
<td>14</td>
</tr>
<tr>
<td>Neurosurgery</td>
<td>8</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>69</td>
<td>56</td>
<td>54</td>
</tr>
</tbody>
</table>

Each statement and the panel responses are presented graphically below along with a summary of the comments from the panel.

Round One - statements and results

Statement 1
Testing for genetically inherited thrombophilia mutations (protein C, protein S, antithrombin deficiency, prothrombin gene mutation, Factor V Leiden and MTHFR) does not influence the management of paediatric arterial ischaemic stroke and therefore should not be performed routinely.
Forty-one clinicians gave an answer to this question, not including those who answered ‘not my area of expertise’. There were three non-responders. Forty-six percent of the respondents agreed with this statement and consensus was not reached. Text responses included that these tests are sometimes useful for treatment planning and prognosis and that they should be carried out where the stroke is idiopathic or the family history suggests testing might be useful.

**Statement 2**

If the delayed post-treatment angiogram shows no residual AVM no further catheter angiography is required.

Thirty-six clinicians gave an answer to this question, not including those who answered ‘not my area of expertise’. There were five non-responders. Seventy-five percent of the respondents agreed with this statement and consensus was reached. Text responses included suggestions that the method used to treat the angiogram be specified, as well as how long (post-treatment) the delayed angiogram would take place, and perhaps one final catheter angiogram be added at age 18.
Statement 3
If the patient has single or multiple untreated cavernous malformation(s) then surveillance imaging should be undertaken until radiological stability is demonstrated.

Forty-two clinicians gave an answer to this question, not including those who answered 'not my area of expertise'. There were six non-responders. Fifty percent of the respondents agreed with this statement and consensus was not reached. Text responses included requests for clarification on what is meant by radiological stability (size or resolution of haemorrhage), and that clinical surveillance is also important.

Statement 4a
Intravenous thrombolysis in children with arterial ischaemic stroke could be considered for children who would have met the following criteria: arterial ischaemic stroke defined as acute onset neurological deficit with a pattern consistent with arterial ischaemia And Paediatric National Institute of Health Stroke Scale (PedNIHSS) ≥4 and ≤24 And Treatment can be administered within 4.5 hours of stroke onset And Radiological confirmation of an arterial ischaemic by: a) magnetic resonance (MR) showing acute stroke on diffusion imaging plus magnetic resonance angiogram (MRA) showing arterial or partial complete arterial occlusion of the corresponding intracranial artery Or b) computerised tomography (CT) and computerised tomography angiography (CTA) confirmation showing a normal brain parenchyma or minimal early ischaemic change plus partial or complete arterial occlusion of the corresponding intracranial artery And No evidence of any intracranial haemorrhage PROVIDING no contraindications are present².
Thirty-eight clinicians gave an answer to this question, not including those who answered ‘not my area of expertise’. There were seven non-responders. Seventy-four percent of the respondents agreed with this statement and consensus was reached (the GDG decided that the percentage agreeing to the statement was close enough to be called consensus). Text responses included concerns about the time frame in that the time taken to transfer children or get the imaging needed will often prevent this treatment from happening and that the treatment should only be done in centres with the expertise to do it.

**Statement 4b**

**Question 4b:** The above criteria should apply to:

- No children
- All children > two years
- > eight years
- > 12 years of age

Thirty-two clinicians answered this question, not including those who answered ‘not my area of expertise’. There were seven non-responders. Fifty-nine percent of respondents ‘all children > two years of age’. Text comments include that there is less safety data in younger children and extreme caution should be used. There were again comments that only specialist clinicians in expert centres should be carrying out this treatment.
Statement 5
In children with diagnosed unruptured AVM, the threshold for active management is lower than in adults.

![Question 5](image)

Forty-two clinicians answered this question, not including those who answered ‘not my area of expertise’. There were eight non-responders. Forty-five percent of respondents agreed with this statement, consensus was not reached. Text comments include that it depends on the type and location of arteriovenous malformation (AVM) and that the higher lifetime risk of rupture makes treatment more worthwhile.

Round Two - statements and results

Statement 1
Testing for genetically inherited thrombophilia mutations (protein C, protein S, antithrombin deficiency, prothrombin gene mutation, Factor V Leiden and MTHFR) in children with arterial ischaemic stroke should only be considered if there is a strong family or personal history of thrombosis.

![Question 1](image)

Thirty-seven clinicians gave an answer to this question, not including those who answered ‘not my area of expertise’. There were five non-responders. Forty-six percent of the respondents agreed with this statement and consensus was not reached, there was no change in the level of consensus from the previous round. Comments tended to be polarised for this statement. Those disagreeing
commented that genetic testing should not be considered only in the presence of personal or family history but should be considered on an individual basis, and that these tests helped to identify causes when a stroke was unexplained. Strikingly, both those agreeing and disagreeing with the statement commented that these tests had no effect on the management of the child, but for those agreeing with it this meant that the tests should not be done.

Statement 2
All children with a previously treated brain arteriovenous malformation and angiographic confirmation of obliteration should have a final catheter angiogram at 18 years of age, prior to transition to adult services, to exclude arteriovenous malformation recurrence or a de novo lesion.

This statement achieved consensus at the first round of Delphi.

Statement 3
If a child has single or multiple untreated cavernous malformation(s) then surveillance imaging should only be undertaken if there are attributable clinical symptoms.

<table>
<thead>
<tr>
<th>Question 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image.png" alt="Diagram" /></td>
</tr>
</tbody>
</table>

Thirty-nine clinicians gave an answer to this question, not including those who answered ‘not my area of expertise’. There were five non-responders. Fifty-nine percent of the respondents agreed with this statement and consensus was not reached, this was an increase of 9% from the previous round. Comments included that ‘attributable clinical symptoms’ should be removed as important new or changing symptoms are not always attributed to the cavernous malformation at first, and that there may be a case for more frequent imaging if the child was very young or child or parent anxiety was particularly high.

Statement 4a
Intravenous thrombolysis in children with arterial ischaemic stroke could be considered for children who would have met the following criteria: arterial ischaemic stroke defined as acute onset neurological deficit with a pattern consistent with arterial ischaemia And PedNIHSS ≥4 and ≤24 And Treatment can be administered within 4.5 hours of stroke onset And Radiological confirmation of an arterial ischaemic by: a) MR showing acute stroke on diffusion imaging plus MRA showing arterial or partial complete arterial occlusion of the corresponding intracranial artery Or b) CT and CTA confirmation showing a normal brain parenchyma or minimal early ischaemic change plus partial or complete arterial occlusion of the corresponding intracranial artery And No evidence of any intracranial haemorrhage PROVIDING no contraindications are present.

This question achieved consensus in the first round.
Statement 4b
Please select the age bracket that the above statement should be applied to:

- Intravenous thrombolysis could be offered to all children > eight years of age and may be considered for children aged between two and eight years of age on a case by case basis.
- Intravenous thrombolysis could be offered to all children > eight years of age
- Not my area of expertise

Twenty-eight clinicians answered this question, not including those who answered ‘not my area of expertise’. There were six non-responders. Ninety percent of respondents answered ‘Intravenous thrombolysis could be offered to all children > eight years of age and may be considered for children aged between two and eight years of age on a case by case basis’ and consensus was achieved. Comments included references to trials and instances of successful treatment of children from age two years. There were also suggestions of that a paediatric stroke database be established to collect data on the effectiveness and safety of this treatment and that the caveat that treatment is only carried out in specialist centres be included.

Statement 5
In children with diagnosed unruptured arteriovenous malformations, active management should be more readily considered than in adults due to the higher cumulative risk of rupture attributable to the projected longer life span.
Thirty-four clinicians answered this question, not including those who answered ‘not my area of expertise’. There were six non-responders. Seventy-six percent of respondents agreed with this statement and consensus was achieved. Comments on this statement included that each case should be considered based on its own unique clinical scenario and that the size and nature of the AVM should be considered.

**Round Three - statements and results**

**Statement 1**

It was decided that for this round statement 1 would be changed so that the recommendation to not carry out testing for genetically inherited thrombophilia mutations was removed as this was the cause of the majority of the disagreement. In this round is was simply a statement that the results of these tests do not influence acute management and read as follows: A positive finding from testing for genetically inherited thrombophilia mutations (protein C, protein S, antithrombin deficiency, prothrombin gene mutation, Factor V Leiden and MTHFR) in children with arterial ischaemic stroke does not alter the acute management.

![Question 1](image)

Twenty-nine clinicians gave an answer to this question, not including those who answered ‘not my area of expertise’. There were four non-responders. Eighty-three percent of the respondents agreed with this statement and consensus was reached. Many comments agreed that acute treatment would not be affected by these genetic tests and that the results may even be misleading in the acute phase but that they might be useful for long term management.

**Statement 2**

All children with a previously treated brain arteriovenous malformation and angiographic confirmation of obliteration should have a final catheter angiogram at 18 years of age, prior to transition to adult services, to exclude arteriovenous malformation recurrence or a de novo lesion.

This question achieved consensus at the first round of Delphi.

**Statement 3**

Consider surveillance imaging in children with a single or multiple untreated cavernous malformation(s) for the first two years following diagnosis, with further follow-up imaging offered if there are new or changing clinical symptoms which could be attributable to the cavernous malformation(s).
Thirty-seven clinicians gave an answer to this question, not including those who answered ‘not my area of expertise’. There were four non-responders. Ninety-five percent of the respondents agreed with this statement and consensus was reached. Comments included that surveillance is particularly important in younger children where there is a risk that changes in, for example, sensory symptoms are not recognised, and that surveillance may need to be extended if cavernous malformations were to change or form de novo on imaging.

**Statement 4a**

Intravenous thrombolysis in children with arterial ischaemic stroke could be considered for children who would have met the following criteria: arterial ischaemic stroke defined as acute onset neurological deficit with a pattern consistent with arterial ischaemia AND PedNIHSS ≥4 and ≤24 AND Treatment can be administered within 4.5 hours of stroke onset AND Radiological confirmation of an arterial ischaemic by: a) MR showing acute stroke on diffusion imaging plus MRA showing arterial or partial complete arterial occlusion of the corresponding intracranial artery OR b) CT and CTA confirmation showing a normal brain parenchyma or minimal early ischaemic change plus partial or complete arterial occlusion of the corresponding intracranial artery AND No evidence of any intracranial haemorrhage PROVIDING no contraindications are present\(^6\).

This question achieved consensus in the first round.

**Statement 4b**

Please select the age bracket that the above statement should be applied to:

- Intravenous thrombolysis could be offered to all children >eight years of age and may be considered for children aged between two and eight years of age on a case by case basis.

Consensus was achieved in round 2.

**Statement 5**

In children with diagnosed unruptured arteriovenous malformations, active management should be more readily considered than in adults due to the higher cumulative risk of rupture attributable to the projected longer life span.

Consensus was achieved in round 2.
Final Delphi recommendations

The statements which reached consensus during the three rounds of the Delphi consensus method are summarised below. They were used to help form the recommendations which make up the final guideline.

- A positive finding from testing for genetically inherited thrombophilia mutations (protein C, protein S, antithrombin deficiency, prothrombin gene mutation, Factor V Leiden and MTHFR) in children with arterial ischaemic stroke does not alter the acute management.
- Offer all children with a previously treated brain arteriovenous malformation and angiographic confirmation of obliteration a final catheter angiogram at 18 years of age, prior to transition to adult services, to exclude arteriovenous malformation recurrence or a de novo lesion.
- Consider surveillance imaging in children with a single or multiple untreated cavernous malformations for the first two years following diagnosis, with further follow-up imaging offered if there are new or changing clinical symptoms which could be attributable to the cavernous malformation(s).
- Intravenous thrombolysis could be considered in children with arterial ischaemic stroke who are > eight years of age and may be considered for children aged between two and eight years of age on a case by case basis when the following criteria have been met: arterial ischaemic stroke defined as acute onset neurological deficit with a pattern consistent with arterial ischaemia And PedNIHSS ≥4 and ≤24 And Treatment can be administered within 4.5 hours of stroke onset And Radiological confirmation of an arterial ischaemic by: a) MR showing acute stroke on diffusion imaging plus MRA showing arterial or partial complete arterial occlusion of the corresponding intracranial artery Or b) CT and CTA confirmation showing a normal brain parenchyma or minimal early ischaemic change plus partial or complete arterial occlusion of the corresponding intracranial artery And No evidence of any intracranial haemorrhage PROVIDING no contraindications are present³.
- Consider active management more readily in children with diagnosed unruptured arteriovenous malformations than in adults due to the higher cumulative risk of rupture attributable to the projected longer life span.