Top ten research priorities for brain and spine cavernous malformations ('cavernomas')

Cavernous malformations – also known as cavernomas – affect people at any age and occur throughout the central nervous system including the brain (where they may cause haemorrhagic stroke[1] and epileptic seizures[2]) and the spinal cord (where they may bleed and cause myelopathy[3]).

Despite the availability of microsurgical excision and stereotactic radiosurgery for cavernoma treatment, and known genetic causes of most familial forms of cavernoma,[4] uncertainties about cause, diagnosis, prognosis, treatment and care remain.

Therefore, in order to prioritise these uncertainties about brain and spine cavernomas for researchers and funding agencies,[5] we undertook a James Lind Alliance (JLA) priority setting partnership (PSP) (www.jla.nihr.ac.uk/priority-setting-partnerships/cavernoma). This PSP was conducted by a multidisciplinary steering group of patients, carers, healthcare professionals, representatives of patient support organisations, an information specialist, a JLA adviser, and an administrator according to a protocol developed in August 2014 and approved in January 2015. The methods are described in full online (https://www.cavernoma.org.uk/our-projects-and-campaigns/priority-setting-partnership-psp-project/).

In January-March 2015, we gathered uncertainties using a web-based survey that was distributed by professional and support organisations in the UK via email, post and social media to patients, carers, and healthcare professionals. We received 2,268 uncertainties from 299 respondents (63% patients, 18% healthcare professionals, and 19% others), and identified a further 34 uncertainties from literature searches. An information specialist subsequently: de-duplicated these submissions; rejected submissions that were out of the scope of the PSP; rejected uncertainties if there was

evidence in published systematic reviews that they had been answered; and added uncertainties identified by these systematic reviews, resulting in a long list of 79 unique uncertainties. The Steering Group worked in pairs to further shorten the long list to 54 uncertainties, which we circulated to 246 survey respondents who had volunteered to prioritise the long list of uncertainties. 136 (55%) respondents participated in the web-based prioritisation exercise, in which we used the rank order technique to generate a short list of 31 uncertainties. At a final in-person workshop involving 29 participants (41% patients, 31% healthcare professionals, and 28% others), facilitated by three JLA advisers, we achieved consensus on a final prioritised list of 27 uncertainties (listed in the UK Database of Uncertainties about the Effects of Treatments [DUETs], www.library.nhs.uk/duets/SearchResults.aspx?tabID=294&catID=15622), of which the 'top ten' are immediate priorities for future research (panel).

The top ten uncertainties reflect the concerns of patients, carers and healthcare professionals in the UK: five concerned prognosis, three concerned treatment/care, and two concerned cause. The JLA process assures the internal validity and reliability of these priorities, but their generalisability to other populations is unknown. The 27 uncertainties identified by this JLA PSP, and in particular the top ten, can now inform the projects that the research community pursue and that funding bodies support in the UK and perhaps other parts of the world.

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Panel: Top ten research priorities for cavernous malformations (‘cavernomas’)

1. Does treatment (with neurosurgery or stereotactic radiosurgery) or no treatment improve outcome for people diagnosed with brain or spine cavernoma?

2. How do brain or spine cavernomas start and develop?

3. What is the risk of brain or spine cavernomas bleeding for the first and subsequent times?

4. Could drugs targeted at cavernomas improve outcome for people with brain or spine cavernomas compared to no drug treatment?

5. What mechanisms trigger bleeding or epileptic seizures in people with brain or spine cavernomas?

6. Are any features of brain or spine cavernoma on imaging associated with a higher or lower risk of bleeding?

7. Does the use of anticoagulant drugs increase the risk of bleeding from brain or spine cavernoma?

8. Does regular monitoring of brain or spine cavernoma improve outcome compared to no monitoring?

9. What features of brain cavernoma lead to the development of epilepsy, or influence the severity of existing epilepsy?

10. Do any specific activities undertaken by people with brain or spine cavernomas provoke bleeds or other symptoms?