



Advancing Care and Treatment of Vascular Dementia (ACT-VaD)

Call for clinical or preclinical proposals

Funding partners: The Stroke Association, British Heart Foundation, Alzheimer's Society

Background to the call

The Stroke Association, British Heart Foundation and Alzheimer's Society have a shared interest in further understanding dementia of predominantly vascular origin (Vascular dementia, VaD). VaD is common post stroke, has strong cardiovascular risk factors and accounts for approximately one in five of all dementia cases. Patients with VaD have limited treatment options and there is an absence of evidence to inform clinical practice. Drugs developed for Alzheimer's disease do not work for people with VaD and there is a lack of clinical trials in the area, pointing to the lack of understanding of disease mechanisms and drug targets.¹

There are multiple recognised sub classifications of vascular dementia including multi-infarct dementia (Cortical VaD); small vessel dementia (Subcortical VaD); strategic infarct dementia; hypoperfusion dementia; haemorrhagic dementia; and hereditary vascular dementia (CADASIL).

All these forms of dementia are in scope for this call and it is not a requirement that a proposal is targeted towards any particular subtype of VaD. Research towards asymptomatic (prodromal) stages of these diseases, referred to as vascular cognitive impairment, is also in scope.

Out of scope for this particular call is research that furthers understanding the contribution of vascular changes to neurodegeneration and ageing, for instance vascular contributions to Alzheimer's. Applicants interested in this topic are guided towards the funding programmes

¹ For background, see Vascular Dementia, O'Brien & Thomas *Lancet* 2015; 386: 1698–706

of the individual charities or the highlight notice on neurovascular ageing that has been issued by the Medical Research Council.²

Priorities for vascular dementia research

In 2015, the Stroke Association convened two workshops that brought together leading clinicians, researchers and people affected by VaD to review current understanding of VaD, with the purpose of developing future priorities for research.³ The key research challenges for vascular dementia (VaD) outlined in the report are: lack of treatments; inadequate screening and diagnostic tests; lack of standardised classification and identification; lack of brain tissue to study the disease; few representative experimental models; and finally, trials in this population are difficult due to a range of issues including poor diagnosis, difficulties with patient consent and multiple co-morbidities.

The six key research priorities identified cover preclinical and clinical research:

- 1) Mechanistic studies are needed to identify new pathways to target. There is a need for pre-clinical or experimental medicine approaches to understand the relevant pathways and mechanisms behind disease development.
- 2) Development and refinement of pre-clinical models of vascular cognitive impairment.
- 3) Identification and validation of informative biomarkers, including MRI. Existing datasets should be maximised and biomarkers to detect changes in the brain over time should be identified and validated.
- 4) Further refinement and larger scale validation of VaD clinical diagnostic criteria.
- 5) Development of ways to stratify VaD patients to identify those at most risk and to improve methods for clinical trials.
- 6) Rigorous observational studies and trials of best strategies are required to inform optimal management.

The priority setting exercise identified that understanding disease mechanisms and defining which patients to target was a higher current priority than large randomised trials of candidate drugs, which are therefore out of scope for this current call.

² <http://www.mrc.ac.uk/funding/how-we-fund-research/highlight-notice/neurovascular-ageing-research-highlight-notice/>

³ <https://www.stroke.org.uk/news/vascular-dementia-workshop-priority-setting>

The full 'Vascular Dementia State of Play' review developed by the Stroke Association and research experts in the field of VaD during the Spring and Summer of 2015 is available [here](#). A lay summary of this review document was also prepared which is available [here](#). Both documents contain research priorities that were identified from the State of Play review and our first workshop. The final six key research priorities stated above were agreed at the second workshop held by the Stroke Association in September 2015.

Call for proposals

Recognising the unmet need, the Stroke Association, British Heart Foundation and Alzheimer's Society have combined resources to fund high quality, ambitious and relevant studies that will advance the field of vascular dementia.

We invite applications for between £500k - £1m over 3-5 years that address one or more of the VaD priorities listed above. Applicants may request more than £1m at outline stage, but should contact the Stroke Association in the first instance to seek prior approval to do so. It is accepted that some techniques are expensive, and we wish to fund well-powered, definitive studies in this call.

The funders have allocated up to £2.2m to this call and hope to fund two or more programmes.

The process will be managed in two stages with an outline application and estimate budget required, before selected proposals are invited to full application. A funding board with representation of the interests of the three partner funders, expertise of vascular dementia and people affected by vascular dementia will be convened to guide funding decisions.

Considerations for developing a project

- Collaborative research of a multi-disciplinary nature is strongly encouraged.
- We hope that this initiative will attract expertise from other fields into VaD research to enhance innovation.
- Applications that consist of a series of separate projects, rather than an integrated research programme, will not be fundable.
- The programme must define clear objectives, deliverables and pathways to patient impact. The proposal does not have to demonstrate direct impact for patients but should clearly articulate the subsequent steps that would be required.
- Applications for clinical studies or for preclinical and mechanistic studies (which could include use of human post-mortem material) are encouraged.

- Following assessment of outline applications, the funders may request that researchers who are not already working together do so to submit a full application. We do not wish to see proposals for a 'Centre' type model – the funded programmes should reach completion of their objectives within the requested timeframe.

How to apply:

Please send your outline research application in no more than 4 sides of A4 to research@stroke.org.uk by no later than 5pm on 4th July 2016.

The following information is required in the 4 page outline application:

- 1) Title of the study and names of the Lead Investigator and Co-applicants
- 2) Background to the proposal and aims of the research
- 3) Outline of the research proposal, including research objectives, an outline of the methods to be used and the predicted outcomes of the research
- 4) The potential benefit of the research to people affected by VaD
- 5) An explanation why the proposed research requires the specified time period
- 6) Summary of expected costs
- 7) Long term research objectives

In addition to the 4 page outline

- 8) Brief CV of the Lead Investigator (2 sides of A4 max)
- 9) Relevant current awards held by Principle Investigator and Co-applicants

Please keep points 1-7 within 4 sides of A4, Arial 10 point. An additional page is permitted for references.

This call is open to UK applicants based at higher education or NHS sites only. Research costs for applicants based outside the UK can be included where specific expertise is required, but the bulk of the work must be completed in the UK and the Principal Investigator must be in the UK.

Key Dates:

9 May 2016 – Call opens
4 July 2016 – Outline application deadline
5 August 2016 – Invitation for full applications
21 October 2016 – Full application deadline
March 2017 – Applicants notified of outcome

Details of the full application procedure will be supplied to successful applicants following the outline application stage.

Funding decisions will be made in March 2017 and awards will be expected to begin within 6 months.

Contact:

For further information regarding the application procedure, or if you would like to discuss your ideas for this call, please contact Kate Holmes in the Stroke Association Research Department at research@stroke.org.uk or on 020 7566 0341.