Author’s response to reviews

Title: The effect of long-term homocysteine-lowering on vascular structure and function in stroke: a randomized controlled trial and meta-analysis

Authors:

Kathleen Potter (pottek04@cyllene.uwa.edu.au)  
Graeme J Hankey (gihankey@cyllene.uwa.edu.au)  
Daniel J Green (d.j.green@ljmu.ac.uk)  
John Eikelboom (eikelbj@mcmaster.ca)  
Konrad Jamrozik (konrad.jamrozik@adelaide.edu.au)  
Leonard F Arnolda (Leonard.Arnolda@health.wa.gov.au)

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Dear Sir/Madam

I hope that you will consider the proposed manuscript for publication in BMC Cardiovascular Disorders.

We conducted a large, randomised, double-blinded, placebo-controlled trial to test the effects of long-term homocysteine-lowering on carotid intima-medial thickness (CIMT) and flow-mediated dilation (FMD) in subjects with a history of stroke (n=173). We found that the treatment did not improve these either of the vascular outcomes. Although similar studies have been published previously, ours is larger than all but one[1] and is the only study thus far to test the effects of long-term B-vitamin treatment on CIMT or FMD in stroke patients. A recently published meta-analysis of clinical trial data has suggested that homocysteine-lowering treatment, while failing to reduce cardiovascular events or mortality, may prevent recurrent stroke.[2] Our data tend to argue against this hypothesis, showing that B-vitamin treatment does not significantly improve markers of vascular risk in stroke patients.

Although the results are negative, our study is large and well-designed, with a long treatment period (>2 years) and sufficient power to exclude clinically significant improvements in the vascular endpoints. We believe our data provide important balance in an area of considerable current interest, especially as many small, short-term intervention studies have previously reported that homocysteine-lowering improves vascular structure and function. We have also included a systematic review and meta-analysis of published randomised data in our paper, to place our results in context and to provide a pooled estimate of the effect of homocysteine-lowering treatment on CIMT and FMD.
Many thanks for considering our data for publication and I look forward to hearing from you in due course.

Yours faithfully,
Dr Kathleen Potter