

REPLY: Rejuvenating Pheidippides and the Evergreen Benefits of Endurance Training

We thank Dr. Pingitore and colleagues for their interest in our recent data demonstrating that central aortic blood pressure and aortic stiffness are lowered after training and completion of a first-time marathon and appreciate the comments that they raise (1).

The correspondence highlights an area of opportunity for more investigation. Our a priori hypothesis was to investigate the effect on individuals training and completing a first marathon. Individuals with injuries or who failed to complete the marathon were therefore excluded from the primary analysis, although there were no differences in baseline vascular measures between marathon completers and noncompleters. Noncompleters may have demonstrated vascular responsiveness over exercise training before injury, but variable duration and intensity of training before follow-up would make post hoc analysis difficult to interpret. This limitation was highlighted in the paper and similarly we recognized that participants may have incorporated additional lifestyle interventions into their training regimens with impact on the vasculature, although measured changes in body fat and mass were not associated with the change in aortic stiffness parameters.

Finally, we acknowledge that age-related arterial stiffening is broadly a nonlinear process with added complexity because of structural variation across the vascular tree (2). Distensibility and (pressure- independent) beta-stiffness were therefore measured at different anatomic levels of the aorta; however, we found a strong relationship between age and aortic stiffness at all levels that could be modeled linearly (distensibility) or log-linearly (beta-stiffness). Established methods, such as multilevel statistical modeling (rather than machine learning–based resampling), could be applied to larger studies that have described a more complex relationship. These methods were not required for this dataset, but would likely describe more pronounced changes with exercise training in older individuals than the modeling techniques used.

Our study clearly raises important questions requiring further investigation but provides a valuable platform for multidisciplinary research (3), and hence we would welcome collaboration with other groups. We recognize the value of blood sampling pre and post training to understand further the underlying biological mechanisms, and work is currently underway using a multi-omics approach to clarify molecular pathways. We are happy to provide access to data (imaging and blood samples) if it can deepen our understanding of the effects of real-world exercise on specific aging biomarkers.

Anish N. Bhuvu, MBBS

Andrew D'Silva, MBBS

Alun D. Hughes, PhD

James C. Moon, MD

*Charlotte H. Manisty, MD

*Department of Cardiac Imaging

Barts Heart Centre, King George V Building West Smithfield

London EC1A 7BE United Kingdom

E-mail: c.manisty@ucl.ac.uk

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