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27 January 2017

Dear Editor and Reviewers,

We'd like to thank the reviewers for their insightful comments and address the changes made to the manuscript in response to their thoughtful critique. The important content changes are highlighted in red font in the revised manuscript.

Many thanks to Reviewer 00742086 for their suggestion to include a number of recent papers published after the final date of this study's completion. These interesting articles have been included in the Discussion section and have provided contemporary context to the paper.

The same reviewer wished for more evidence of the 'direct relationship between each factor and both diseases as an entirety.' This was, indeed, our primary objective in starting this review. Unfortunately, however, we have found there to be a lack of studies investigating the direct relationship between certain factors and both diseases as an entirety. In sections where the evidence presented appears disparate (for example between sex steroids and AD/osteoporosis) we would argue that this serves to highlight the lack of conclusive evidence linking the two diseases with the factor in question in the current pathological understanding. We hope where linking factors exist this has been discussed in a clear fashion; for example, regarding ApoE and the two disease processes.

In response to the comments of Reviewer 02699714, we have clarified the exact pathway receptor involved in hepatic ApoE uptake and summarized ApoE further in the Discussion and Comments sections.

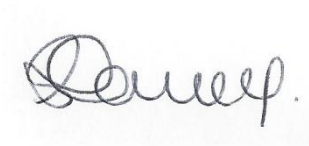
We would like to thank Reviewer 02528832 for their comments about excluding statins and alcohol. We have continued to include these sections, and would like to argue that these are emerging as powerful players in the pathophysiology of aging, and will therefore appeal to a wider audience. We believe it is important to inform a wide range of readers regarding the evidence base around these two very topical subjects. As such, we have also refrained from expanding on bone cell mediators in the interests of brevity and originality.

In response to the Editor's comments, we have rectified the omissions in the contact details of both the First Author and the Corresponding Author. We have also restructured the Abstract and added the Comments section in accordance with your guidance. Please also find the requested Audio Core Tip and Copyright/Conflict of Interest form alongside our revised manuscript.

Finally, we would like to alert the Editor to a classification error. The submitted manuscript is a Review article, and not a Retrospective Study as has been stated in recent correspondence. As such, after reading your Guidelines and Requirements, some of the requested documents have not been prepared; for example, Biostatistics Statement and Informed Consent Statement. Should you have any further queries regarding these documents, we will be more than happy to send clarification. In addition, we welcome any further feedback on our work.

Once again, many thanks for your consideration and thoughtful review of this paper. We hope that our revisions meet with your approval and look forward to a favourable decision.

Yours sincerely,

A handwritten signature in black ink, appearing to read 'Downey', with a large, stylized initial 'D'.

Miss Candice Downey

On behalf of all the authors of this manuscript