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From here onwards, the paper should be written with line spacing of 1.5.

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The abstract should not exceed 250 words and should be structured in: Objective, Methods, Results, Conclusions.

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Provide up to 5 key words using Mesh terms for indexing purposes.

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Text should not exceed 5000 words from the Introduction to the Conflict of Interest Statement, excluding the title page, abstract and references.

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This section should provide enough details to allow full replication of the study by suitably skilled investigators.

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Include a review of the key literature. If there are relevant controversies or disagreements in the field, they should be mentioned so that a non-expert reader can delve into these issues further. The discussion should consider the major conclusions of the work along with some explanation and/or speculation on their significance. How do the conclusions affect the existing assumptions and models in the field? How can future research build on these observations? What are the key experiments that remain? The discussion should be concise with solid arguments.

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**Acknowledgements**

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