

Reviewer #1:

1. The English need improvement since there are some grammatical and syntax errors in the manuscript. For example, the words "with increased" may be as "with an increased"; "of heart" as "for heart"; "heightened risk" as "a heightened risk"; "and on" as "and"; "showed a significant" as "showed significant"; "if higher" as "if the higher"; "as having" as "having"; "chi-square" as "a chi-square"; "minimal" as "a minimal"; "Hardy-Weinberg" as "the Hardy-Weinberg"; "available as" as "available"; "associated high" as "associated with high"; "that it such" as "that such"; "method were" as "method was"; "limitation in" as "limitation of"; "are greatest" as "are the greatest". The grammar mistakes which are not mentioned here are also to be checked and corrected properly.

We thank the reviewer for noticing the grammatical mistakes, specifically neglecting to include the article "a/an." Many changes have been made throughout the document to correct for usage of verbs instead of adjectives and nouns. The "method were" suggestion was not made as the verb refers to the "six beta coefficients" and not the "MR Egger method."

2. There are some typing mistakes as well, and authors are advised to carefully proof-read the text. For example, the words "Also like" may be as "Also, like"; "filesets" as "file sets"; "results we" as "results, we"; "cynicism associated" as "cynicism-associated"; "CD associated" as "CD-associated"; "all candidate" as "all candidates"; "Two sample" as "Two samples"; "work in" as "work on"; "outcomes we" as "outcomes, we"; "larger scale" as "larger-scale"; "regards to" as "regard to"; "sample size" as "sample sizes". The typos not mentioned here are also to be checked and corrected properly.

We appreciate the reviewer's attention to detail when identifying these typographical errors. We have made several modifications including correcting hyphenation and spacing. "Two sample" was not corrected to "two samples", rather it was corrected to include appropriate hyphenation, as the name of the method is "two-sample Mendelian randomization." (Hartwig FP, Davies NM, Hemani G, Davey Smith G. Two-sample Mendelian randomization: avoiding the downsides of a powerful, widely applicable but potentially fallible technique. *Int J Epidemiol*. 2016 Dec 1;45(6):1717-1726. doi: 10.1093/ije/dyx028. PMID: 28338968; PMCID: PMC5722032.)

3. Check the abbreviations throughout the manuscript and introduce the abbreviation when the full word appears the first time in the text and then use only the abbreviation (For example, John Henryism (JH), SNP, Coronary Artery Risk Development in Young Adults (CARDIA), cynical distrust (CD), etc.,). And it should be in both abstract as well as in the remaining part of the manuscript. Make a word abbreviated in the article that is repeated at least three times in the text, not all words need to be abbreviated.

We thank the reviewer for noticing this issue. We replaced the abbreviations throughout the document, except for within figure captions and tables.

4. In materials and methods, the author should give a separate heading for statistical analysis at the end of the same.

We thank the reviewer for requesting this addition. We added a section summarizing the statistical approaches briefly described within the other methods sections. The new statistical analysis section reads: "Statistical analyses for assessing variant associations were performed in R. To confirm the association of the variants identified for the high cynicism and high CD variables, we created a matrix containing the allele counts for each candidate variant. We then performed a chi-square analysis using the `chisq.test` function within base R using the allele count matrix as the input argument. The statistical analyses of the PRS estimators were performed in the scikit-learn package. As the class allocation displayed only slight imbalance (control/case group sample size ratios of 1:2.1, 1:2.5, and 1:2.7 for JH, cynicism, and CD, respectively), we used the ROC AUC for evaluating performance of the PRS classification models."

5. The authors may improve the discussion of their results by focusing on the present findings and introducing data from other authors who also worked with the same or other studies with recent references.

We thank the reviewer for the suggestion of adding insights from other authors with relevant studies. However, to our knowledge, this is the first study investigating genetic associations with John Henryism, cynicism, or cynical distrust. We have been unable to find publications reporting the results of candidate gene, GWAS, or heritability studies. Absent other genetic work in these fields, we incorporated evidence from non-genetic studies that report genetic associations with secondary outcomes of our traits of interest.

6. The last part of the discussion should be shifted to the heading "CONCLUSION" since the authors have given "INSERT TEXT" and it should be rectified. And also the authors have given the limitation of the present investigation and the same maybe given in separate heading.

We thank the reviewer for noticing this mistake and have corrected both concerns. We moved the concluding paragraph to the "CONCLUSION" heading. We also made a new section titled "LIMITATIONS" and moved that portion of the discussion.

Language polishing requirements:

As the revision process results in changes to the content of the manuscript, language problems may exist in the revised manuscript. Thus, it is necessary to perform further language polishing that will ensure all grammatical, syntactical, formatting and other related errors be resolved, so that the revised manuscript will meet the publication requirement (Grade A). Authors are requested to send their revised manuscript to a professional English language editing company or a native English-speaking expert to polish the manuscript further. When the authors submit the subsequent polished manuscript to us, they must provide a new language certificate along with the manuscript. Once this step is completed, the manuscript will be quickly accepted and published online. Please visit the following website for the professional English language editing companies we recommend:

<https://www.wjgnet.com/bpg/gerinfo/240>.

The author is a native English speaker from the United States.

Editorial Office comments:**(1) Science editor:**

The manuscript has been peer-reviewed, and it's ready for the first decision.

Thank you very kindly for the review.

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Medical Genetics, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.

Thank you very much for the opportunity to revise the manuscript. We appreciate the time and effort you, your staff, and your reviewers have put into this manuscript.

Before final acceptance, uniform presentation should be used for figures showing the same or similar contents; for example, "Figure 1 Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...". Please provide the original figure documents. Please prepare and

arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor.

All figures show unique contents. All figures are provided in a PowerPoint file. Figure 1 was created natively in PowerPoint and all arrows and textboxes can be reprocessed by the editor. Figure 2 is provided in PowerPoint with each individual graph and textbox now capable of repositioning by the editor; all graphs were created in R. Figure 3 is provided in PowerPoint with each individual graph and textbox now capable of repositioning by the editor; all graphs were created in scikit-learn, a Python package. Figure 4 is provided in PowerPoint; figure 4A was created natively in R and figures 4B and 4C were created natively in PowerPoint and arrows and textboxes can be reprocessed by the editor.

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Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

Thank you