June 3, 2025

Dear Editor in Chief,

We would like to thank the reviewers and the editorial team for their insightful comments and suggestions. We have set out point-by-point RESPONSE to the questions and comments raised below and have made relevant and substantial changes to the manuscript.

We have addressed the comments as follows: 1. ‘Reviewers/editorial’ comment (black color font & bold), and 2. ‘Authors’ RESPONSE (black color font). Please refer to the ‘Revised Manuscript with Track Changes document for the revised manuscript with the changes made in a marked-up copy (red color font). We have also submitted a clean version manuscript.

We look forward to your review and feedback.

Sincerely,

On behalf of co-authors,

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**REVIEWER #1:**

**This is potentially important paper from a respected group. It needs some revision to make it more accessible for readers.**  
  
**- Abstract aims: please state the research question or hypothesis to be addressed**

RESPONSE: The study aims are provided in Abstract, page 3.

“This study aims to assess aspects of health knowledge: i) awareness of health of effect of tobacco smoking and ii) awareness of preventive actions for heart disease and stroke, and their relationships with adoption of heart healthy behaviours (smoking cessation and utilisation of antihypertensive treatment).” **Page 3.**

**- Abstract aims: "awareness of health of effect of tobacco smoking " does not make sense.  Do you mean "awareness of health effects of tobacco smoking"?  Please clarify here and throughout**

RESPONSE: Thanks for pointing out the typo. This has been corrected.

“i) awareness of health effect of tobacco smoking”. **Page 3.**

**- Abstract methods I think another sentence on what you are adjusting for and your interest in income and education would be helpful. You mention education and wealth in the conclusion but no where in the abstract**

RESPONSE: We have revised the methods texts in abstract to incorporate more information on variable information. See revised texts below.

“A logistic regression analyses were used to examine the relationship with the outcomes of smoking cessation and use of antihypertensive treatment adjusting for adjusting for possible confounders.” **Page 3.**

**- Abstract: Explain what aOR means**

RESPONSE: We have spelled out for the first use of aOR in the texts. See the revised texts below:

“Among current and former smokers, knowledge of health effect of tobacco smoking on heart disease Adjusted Odds Ratio (aOR): 1.70 (95% CI: 1.19, 2.43), stroke 1.41 (1.08,1.86), and on heart disease in non-smokers exposed to others smoking aOR 1.40 (1.06,1.86) were significantly and positively associated with smoking cessation….” **Page 3.**

**- Abstract: you give lots of aORs but it is not clear what is being compared with what.  For example "knowledge of health effect of tobacco smoking" compared to what gives the aORs provided?  Do you mean better knowledge versus worse knowledge and how is this stratification achieved and was it pre-specified?  Same comments for the health actions**

RESPONSE: We have added the comparator to make it clear. See the revised texts below:

“Among current and former smokers, having knowledge of health effect of tobacco smoking on heart disease [Adjusted Odds Ratio (aOR): 1.70, 95% CI: 1.19, 2.43)], stroke (1.41, 1.08,1.86), and on heart disease in non-smokers exposed to others smoking (1.40, 1.06,1.86) were significantly and positively associated with smoking cessation compared to those who were not aware of health effects. Knowledge of the importance of reducing dietary salt aOR 1.62 (1.23,2.13), dietary fat aOR 1.56 (1.17,2.08) and exercising more aOR 1.48 (1.22,1.80) to prevent heart disease or stroke were positively associated with taking anti-hypertensive medication compared to those who were not aware of preventative actions.” **Page 3.**

**- Abstract conclusion: I think you mean "Better health knowledge is associated with greater adoption of heart healthy behaviours.**

RESPONSE: Thank you for the suggestions to improve abstract conclusion. See the revised texts.

“Better health knowledge is associated with greater adoption of heart healthy behaviours such as smoking cessation and taking anti-hypertensive treatment even after accounting for baseline education and wealth.” **Page 3.**  
  
**- Introduction: should be limited to 1 page.  Anything essential can probably be incorporated in discussion**

RESPONSE: Thank you. We felt that our study needs an detailed introduction to establish research gaps, define concepts and state research aims/objectives; therefore kept the length of introduction section as it is.

**- Introduction: state the research question or hypothesis to be tested**

RESPONSE: The research objectives are presented in the last paragraph in the Introduction section in Page 6. Also copied below:

“The primary research question of this study is to examine the relationship between two aspects of health knowledge: i) awareness of health of effect of tobacco smoking among current and former smokers and ii) awareness of preventive actions for heart disease and stroke among those diagnosed with hypertension and their relationship with adoption of heart healthy behaviours such as smoking cessation and utilisation of antihypertensive treatment using a large cross-cohort study that has collected consistent data from low and middle-income countries.”

**- Methods: Overall these were reasonably clear**

RESPONSE: Thank you.

**- Methods: Suggest provide a table of the health knowledge questions asked and the expected correct responses to help the reader.  Some of the questions like coffee drinking don't appear to have a direct cardiovascular effect so I am not sure there is a "correct" answer for some of these questions.  Perhaps a comment on strength of evidence for the answer expected might help**

RESPONSE: We have already incorporated visualisation showing correct responses for each question by countries in **eSupplementary Figure 3**.

For ‘Drinking more coffee’, we used those who answered ‘No’ as a ‘correct’ response. This has been presented as ‘Drinking less coffee’ in Figure 1. **Page 25.**

**- Methods how was the cut-off for "better health knowledge versus worse health knowledge" derived and was this pre-specified?**

RESPONSE: Cut off for health knowledge scores were not prespecified. For each individual, we created a categorical knowledge score variable (3 categories: high, medium, low health knowledge) based on tertiles of scores; each tertile contributing to a third of the population. A tertile divides a dataset into three equal parts, each representing one-third of the population or distribution.

* The lowest tertile represents the bottom third of scores (lowest health knowledge).
* The middle tertile represents the middle third of scores (medium health knowledge).
* The highest tertile represents the top third of scores (high health knowledge).

See our methods texts in page 10, for further information.

“For each individual, we created a categorical knowledge score variable (3 categories: high, medium, low health knowledge) based on tertiles of scores; each tertile contributing to a third of the population.” **Page 10.**

**- Methods page 9 in the formula (Pr (yij=1), the i and j are so small I missed them suggest enlarging.**

RESPONSE: Thank you. Corrected.

**- Methods please state who carried overall responsibility for the statistical analysis it is not possible to tell from the author list and authors' contributions are not provided**

RESPONSE: We have added a detailed author’s contribution section in page 16.

“CK and SRM contributed to the conception or design of the study. SM performed data cleaning and statistical analysis of the dataset for the study with feedback from Simone Marschner. SM drafted the manuscript. CK provided supervision. All authors critically reviewed and provided feedback on the final manuscript. All authors contributed to the final article and approved the submitted version. CK is the guarantor of this work.”

**- Methods: "taking anti-hypertensive medication" probably some more explanation - how was this defined?**  
RESPONSE: We have revised methods texts in page 8, to provide more explanation on how this variable was defined:

“Taking anti-hypertensive medication is defined as those who responded taking anti-hypertensive medication in baseline.” **Page 8.**

**- Results please make sure all ratios are labelled e.g. on page 12  taking antihypertensive medication (2.58, 95% CI: 1.57,4.22) - the ratio is not labelled**

RESPONSE: We have added label to results presented in page 12. See below:

“Similarly, in those with hypertension or CVD, high health knowledge of actions to prevent CVD was significantly and positively associated with taking antihypertensive medication (aOR 2.58, 95% CI: 1.57,4.22) in model 1; the effect size only decreased marginally after adjusting for education and household wealth in model 3 (Table 4). “ Page 12  
  
**- Discussion: this seemed thin with just one paragraph on putting the findings into context of other research and existing knowledge - this should be expanded with an additional page or so explaining how the current findings add value.  Most of the Discussion focusses on strengths and limitations although those sections are fine.**

RESPONSE: We have revised the discussion section to explain how the current findings add value. See the revised texts below:

“Our findings are consistent with previous studies which showed effect of health knowledge on health behaviours on both short (high blood pressure, hyperglycaemia) and long term health outcomes (hospitalization, mortality) (35-38) and health-related quality of life.(39) For example, Isa et al suggested that health literacy has a notable effect on blood pressure outcomes, with consistently poorer control among people with lower health literacy.(38) Nevertheless, Du et al suggested that the evidence regarding the influence of health literacy on clinical and behavioural outcomes, such as self-care and self-efficacy, is insufficient, underscoring need for future studies.(40) Aligning with this idea, we quantified the association as well as the shape of the relationship with two aspects of heart health behaviours: smoking cessation and taking anti-hypertensive treatment in appropriate subgroups. We also quantified whether health knowledge is independently associated with these outcomes after considering education and wealth. Our analysis further confirmed that those with lower health knowledge, lower educational attainment and lower household wealth were less unlikely to stop smoking and or take anti-hypertensive medication. Our findings support the statement of the American Heart Association which highlights lack of knowledge as a barrier to improving cardiovascular health.(19) This is consistent with other social determinants of health; those with lower educational attainment and wealth status were least likely to adopt healthy behaviours. (41) Further studies are needed to assess the broader effect of health knowledge and literacy on both short- and long-term health outcomes and health system costs for diseases including and not limited to cardiovascular diseases. “ Page 14.  
  
**- Tables and figures (including supplement) please make sure all abbreviations are explained in the footnotes included OR**

RESPONSE: Thank you. Abbreviations are added to the footnotes of each figure and tables.

- Table 4 the formatting for the square borders seem to have moved

RESPONSE: Thank you. Revised!

**- Forest plot figures (all including supplement) please label the horizontal axis and indicate what the ratio either side of one means (e.g. "favours smoking cessation", "favours smoking continuation" or whatever is appropriate**

RESPONSE: Thank you. Revised!

**- for the figure titles it would help to summarise the main finding of the figure contents "This figure shows...." including figures in the supplement as it is not obvious in many cases.**

RESPONSE: Thank you. We have incorporated in text references for these figures with summary of main findings. See results texts.  
  
**REVIEWER #2:**

**Thank you for giving me the opportunity to review this manuscript. This study examined the association between health knowledge and the adoption of heart-healthy behaviors, such as smoking cessation and the use of antihypertensive medication. The researchers assessed two aspects of health knowledge: awareness of the health effects of tobacco smoking and awareness of preventive actions for heart disease and stroke. The study found that greater knowledge of the health effects of smoking and the importance of reducing dietary salt, fat, and increasing exercise to prevent heart disease and stroke were positively associated with smoking cessation and the use of antihypertensive medication, respectively.**

RESPONSE: Thank you. No response needed.  
  
**1.More detailed subgroup analysis could be conducted, such as the impact of different income countries (low-income or high-income countries) or different regions (Europe, Asia, etc.) on health knowledge and behavior.**

RESPONSE: Thank you for suggestion regarding analyses showing regional differences. Indeed, we have shown the distribution of correct responses on knowledge variables by countries in Figure 1. This graph shows the variation in correct responses (%) by income regions; with LIC showing low awareness on knowledge of health effect of tobacco smoking and lesser knowledge on health actions to prevention health attack or stroke. Further, we have added individual graph/visualisation showing percentage of correct response for each country in PURE EPOCH dataset (see eSupplementary Figure 3).

2.Why focus on studying smoking cessation and blood pressure medication use among heart health behaviors instead of other heart health behaviors?

RESPONSE: Smoking cessation and taking blood pressure medications are two health behaviours contributing to a large reduction in premature cardiovascular events and deaths. Therefore, we prespecified our analysis plan looking at the role of health knowledge on adoption of these health behaviours. Further information on why these research questions are important is addressed in our introduction section in page 5.

“Research on disease-specific knowledge has largely focused on chronic conditions. There is an incentive for those affected to invest in obtaining information, although they are not always better informed than those without the condition, as seen with cardiovascular disease in one German study.(15) However, greater knowledge has been linked to better outcomes for several conditions, including chronic airways disease,(16) irritable bowel disease,(16, 17) and rheumatoid arthritis.(18) …Thus, if measures are to be adopted that improve knowledge of health and disease then it will be important to have information on how this varies with markers of socio-economic status such as education or household wealth in different settings, and how it correlates with cardiovascular health behaviours.” Page 6.