Author’s response to reviews

Title: Estimating the cost-effectiveness of salt reformulation and increasing access to leisure centres in England, with PRIMEtime CE model validation using the AdViSHE tool.

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RE BHSR-D-19-00881

Editor Comments:

In addition to the reviewers’ comments below, please address the following editorial points:

1. Section headers
   - change "abbreviations" into "list of abbreviations"
   - Change made.

2. Clean version
   At this stage, please also upload a clean version of your manuscript without any tracked changes/highlighted text, as this may interfere with the production process.
   - We have uploaded both a clean version and one with tracked changes

Reviewer reports:

Valentina Lorenzoni (Reviewer 1):
No additional comments, authors adequately resolved almost all issues raised in the previous revision.

- Many thanks.

Lennert Veerman (Reviewer 2):

1. This paper uses the new PRIMEtime CE model to compare the health impact of two interventions, one targeting salt consumption and one that enhances physical activity, when rolled out across England. It then goes on to use the results, and extensive additional analyses, to validate the model.

It is an interesting paper, especially from a methodological point of view, and considerable effort went into the exercise. I do find that the separation of this material from the model description leaves a few questions, as some of the detail in methods and input sources has now been removed. I have some question marks around some of the choices made, and did not understand a few issues, as per my comments below.

- Many thanks for these comments, the additional time you’ve put in to reviewing this manuscript is really appreciated.

2. Please explain in the methods section how you calculated your economic output parameters. Specifically the return on investment, where I find it un-intuitive (and undesirable) that the value of health is ignored (as I explained in my review of the first draft of this paper). You do mention this straight up in the results, which is helpful.

- Apologies for not including this in the methods as well (as per your comment on the previous review) – we have now done so. We do not include the value of health when calculating RoI as this would then be inconsistent between the presented cost effectiveness results and RoI results. It also appears to be inconsistently applied in the public health economic literature – for example it is not used by either Frew et al. or Collins et al., against which the model is validated. Furthermore, there is a lack of agreement about what the value of health should be, with the National Institute for Health and Care Excellence (NICE) using £20,000 in their return on investment tool (see https://www.nice.org.uk/about/what-we-do/into-practice/return-on-investment-tools/tobacco-return-on-investment-tool), the UK Department of Health recommend using £60,000 (see https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/216003/dh_120108.pdf), and Claxton et al. suggest it should be £13k (https://www.ncbi.nlm.nih.gov/pubmed/25692211). We have therefore made it explicit in the
methods, results and discussion that the value of health is not included in our calculations, and we say how this would impact results.

We have added the following paragraph to the methods section listing the input parameters for the primary analyses, the equations used for calculating cost-effectiveness and return on investment, and that direct economic costs of QALYs are not included when calculating RoI.

“The primary outcome is cost-effectiveness over a 10-year time horizon - or return on investment in circumstances where interventions are cost-saving - from health and social care perspective in England. The time horizon and perspective where chosen following stakeholder feedback (see Briggs et al.[1]). In the primary analyses, costs to government and industry are included, with all costs and health outcomes discounted at 1.5%. Cost-effectiveness is: \((Cb - Ca) / (Eb - Ea)\); \(Cb\) = sum of 10-year intervention costs and expenditure on health and social care; \(Ca\) = 10-year health and social care costs with no intervention; \(Eb\) = total QALYs in 10 years following the intervention; \(Ea\) = 10-year QALYs with no intervention. In the case where \((Cb - Ca)\) is negative, return on investment is calculated as: \((Cb - Ca) / Ci\); \(Ci\) = cost of the intervention. No direct economic value is attributed to QALYs when estimating return on investment. The potential impact of using different model parameters is explored with a range of sensitivity analyses.”

3. Likewise, can you please explain what the social care costs are? Large savings in the salt scenario, so I gather at least part are related to disease (in parallel to health care costs), as the old age pension would have the opposite effect. I am therefore puzzled by the explanation that 'Women were responsible for more social care savings due to living longer'. Why is that? Living costs money. Death is cheap.

- We have added a sentence to the first paragraph of the methods section explaining social care costs. The rationale behind women leading to more social care savings due to living longer is that if they have a better quality of life, then their social care costs reduce (because they are a function of quality of life) and the savings have longer to accrue with longer life expectancy. We have added an explanation of this to the results section.

4. The choice of a 10-year time horizon needs explanation, in the methods section. As I wrote previously, this disadvantages interventions targeting the young, compared to the old, and I consider it a bad choice for preventive interventions. The discount rate also merits mention in the methods section. I recommend using the CHEERS checklist to ensure the reporting is complete.

- Thank you for pointing out both of these omissions. We have added both the time horizon and discount rate to the methods, and have added a statement on the impact of using a short time
horizon to the strengths and limitations section. We have also added to the methods that the 10-year time horizon was chosen by stakeholders as a compromise between allowing long enough for health outcomes to manifest whilst still being relevant to the relatively short political cycles that politicians have to work within (this is the same reason why the NICE Return on Investment tools also use 3, 5 and 10yr time horizons).

5. Line 278: "Intervention costs per participant in 2014 after adjusting for inflation were £53.80 (triangular distribution 43.50, 53.80, 85.90)" A drawback of the triangular distribution is that in your model, the mean costs will be much higher than £53.80. See for example Briggs et al in 'Decision Modelling for Health Economic Evaluation'. You refer to Frew et al, but why copy someone else's less-than-optimal methods? A skewed distribution like gamma, Weibull or lognormal would not have this problem, and you can fit those using the parameters Frew et al give. As things stand, it seems that your central estimates of cost are too high, which negatively biases your C/E results.

- Many thanks for this comment. The rationale for referring to Frew et al. are two-fold. Firstly it is because Frew et al. represents the direct collection of data from the intervention and therefore these parameters are copied where possible, and secondly, because it means that our results are more directly comparable to those produced by Frew et al. We have therefore not changed distribution (which would also not materially change the paper’s key messages as it would not make the intervention cost effective). We have added this to page 9 of the additional data file, and included the following explanation in the additional data file under the section, Strengths and limitations of modelled interventions:

“Intervention costs were assumed to have a triangular distribution (also taken from Frew et al.) which means that our mean costs will be higher than the £53.80 cost per participant. Using a skewed distribution would reduce the mean cost to be closer to £53.80 and reduce the total cost per QALY estimate, but would mean that results were less directly comparable to Frew et al.”

6. Table 2: Why no RoI?

- Return on investment is not presented because the intervention is not dominant.

7. Line 128: typo 'are'

- Thank you, corrected.
8. Line 518-522: That is indeed a dramatic difference. Which of the parameters made the greatest difference on the cost per QALY estimates, between your assumptions and those of Frey et al?

We do not know exactly which parameters are making the greatest difference – although we do highlight the differences between the parameters used by each model in the additional data file.

- As we mention in the text, there are large differences in input costs and utilities between the two models, and the difference in results are likely to be a combination of these effects (no single difference between the two sets of model input parameters particularly stands out). Repeat runs of the model to identify the relative impact of changing each disease cost and utility value independently would require a significant investment in computing time and resources, and we do not think it would meaningfully change the key message of this part of the paper – that input costs and utilities greatly impact results. We have changed the text in line 544 to make this slightly clearer.

9. Additional data, page 6: MET is per minute.

- Change made.

10. Additional data, page 29, "the baseline annual incidence rate of breast cancer among those aged 16 years and over used in PRIMEtime CE was 0.0008." I assume this varied by age? Still, this seems too low. Cancer Research UK gives an incidence of around 80 per 100,000 for ages 35-39 years, rising to >400 for age 70+. It would take a very young population to arrive at an average of 80 per 100,000, which England does not have. Are you sure about this number? Where is it from?

- Well spotted, this is an error and should be 0.0021 – have made the change, including that the figure varies by age.

11. Figures S6 and S7: What does 'Primary analysis' stand for? Intervention effect on exposure to salt/PA?

- This has been changed to ‘main analysis’ so as to be consistent with the rest of the text.