Reviewer's report

Title: PRIMEtime CE: a multistate life table model for estimating the cost-effectiveness of interventions affecting diet and physical activity.

Version: 0 Date: 14 May 2018

Reviewer: Petros Pechlivanoglou

Reviewer's report:

This is a well written paper describing a simulation model that could estimate the value for money of public health interventions in the UK as well as the cost-effectiveness of two hypothetical interventions on salt reduction and increase in physical activity. The model is comprised of a number of steps and relies heavily on a number of assumptions. In fact, I think that the study is so ambitious that it is trying to explain too many things at the same time. I believe that the work would benefit greatly if separate publications for the model the PRIMEtime CE model and the CE of interventions were to be pursued. In that way, a lot of the material currently in supplementary appendices that have vital information to the structure of the model would be possible to be presented in the main text of the manuscript and properly peer-reviewed. As the authors mention in the limitations section, there are many assumptions in the model that affect the final estimates. These assumptions would need to be clearly presented in the main manuscript rather than the appendix. Below I provide specific comments throughout the manuscript:

1. The rationale for focusing on these two interventions is missing. Is it that the interventions serve only as an illustration? Have there been identified because of their potential for impact? what is the literature base for the effectiveness and cost-effectiveness of these two interventions? e.g. are there any other studies that look at the CE of salt reformulation?

2. The estimates are presented as inclusive of 95% confidence intervals. Given the fact that a number of the input parameters did not include an estimate of uncertainty around them, or that the shape of the uncertainty for some estimates had to be imputed (e.g. through a triangular distribution) I am doubtful as to whether this uncertainty represents the real range of uncertainty around the estimates. In addition, no information on the methods underlying the uncertainty analysis is being described in the main manuscript. I would suggest that you move any discussion on methods of uncertainty analysis in the main manuscript

3. There is very little information on the effectiveness of the interventions in the manuscript. Regarding the salt reformulation, it is assumed that the intervention will bring salt consumption to the 2017 salt targets, however no assumption is being made on the compliance to such an intervention. In fact if I understand correctly the implicit assumption
is that of perfect compliance. In addition, the governmental and industry costs are assumed to be lasting for three years, however, implementation of the salt reform would likely require long-term monitoring to ensure that the reform is actually taking place.

4. Furthermore, the salt reformulation intervention needs to be placed better in context of the other studies on CE of salt reduction where a recent sys review indicated that the vast majority of past studies detected cost savings. doi:10.1017/S1368980017000593

5. The Be Active intervention is informed by data that are quite different in nature by the salt reduction intervention. In particular, the BE Active intervention is accompanied by a measured relative effectiveness estimate that is directly associated to the intervention and not a hypothetical change to the effect modifier (salt or physical activity). In other words, this means that the observed finding in the Be Active intervention is more likely to be lower, given possible compliance issues but at the same time closer to a real world estimate. This discrepancy amplifies the notion that comparison across public health interventions are harder to be made given the heterogeneity of the input data.

6. Information on the PRIMEtime multistate lifetable model is minimal. The authors cite the supplementary file of a different paper, which itself does not describe in great detail the structure of the model exactly, as well as the sources used for the model to be fitted. How well did the PRIMEtime model predict the incidence of disease in the UK? Is it a validated model? In my opinion the multistate model and how this becomes a CE model needs to be article no 1 before the evaluation of the interventions.

7. In the results section the authors report a negative ICER for the salt reformulation. A negative ICER can be misleading as it can imply either cost-savings or a dominated strategy. Also, the magnitude of a negative ICER is not easily interpretable. Please consider switching to a net benefit framework.

8. The authors describe an intervention that is applied on a closed cohort. Given that the impact of the intervention is likely to affect more cohorts that the one alive when the decision of implementation will be taken, would there be value in applying the model on an open cohort instead?

9. The comparison to a 20/30K threshold is somewhat irrelevant once societal costs are taken into consideration.

10. There are a number of sentences in the results section (e.g. line 337) that belong to the methods instead of the results.
10. I think it would be informative for the reader if you were to report a per person cost and QALY estimate next to the totals (e.g. line 296 table 2)

11. In line 261 in the sensitivity analysis, would you consider sensitivity analysis on the utility estimates? given the long term nature of these chronic conditions a small decrement difference in utility might have important implications to the CE estimates.

12. Along the same lines as above, the results of the sensitivity analysis in 1,374 should in my opinion be in the main manuscript and not in the supplementary materials.

13. In line 191, how does this method capture costs in the presence of multi-morbidity do you double or triple count costs? is there a way to avoid it?

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Unable to assess

Does the work include the necessary controls?
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