Author’s response to reviews

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

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Author’s response to reviews:

Dr Maria Zalm

BMC Health Services Research

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Dear Dr Zalm,

RE: BHSR-D-18-00710R2

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

Many thanks for your consideration of this manuscript. We are very grateful both to you and to the reviewers for the time that you will have spent on this. Further to your email on 30th April, 2019, below are the response to reviewer comments that relate only to this manuscript.

The original submission requested that we split the manuscript into two separate papers. This is the first of those papers. The second is BHSR-D-19-00881 (Estimating the cost-effectiveness of salt reformulation and increasing access to leisure centres in England, with PRIMEtime CE model validation using the AdViSHE tool). As requested, in this submission we now only include this manuscript (BHSR-D-18-00710R2) and not the second paper.
We have responded to each of the reviewer’s comments below and have uploaded a clean copy of the manuscript. Please let us know if you have any further question or concerns.

Yours sincerely,

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Response to editor and reviewers RE: BHSR-D-18-00710R2

Editor’s comments

We have made the essential changes to abstract headings, manuscript headings, authors contributions, figure legends, and additional file lists as requested. We have also paid particular attention to reviewer number 2’s discretionary comments, as suggested.

Lennert Veerman (Reviewer 2): You have responded well to the previous round of comments, and the work described in the two papers remains impressive. The comments below are minor, and suggestions only.

Paper 1, Table 2: Some of the units of change for fruits and vegetables are per 106g/day, others for 100g/day. Units change for serum cholesterol and SBP are negative (and most RRs <1), others positive. I assume that stays true to the sources, but it does hinder interpretation (comparison). Some of the values could be converted to form a more consistent set.

You are correct that this is because of the source data, plus this is how the parameters are used in the model. It would be possible to convert the parameters however this would then be inconsistent with other publications of PRIME and PRIMEtime that have published a similar table (e.g. Cobiac et al., ref 30), and inconsistent with the source data themselves. We feel that
this has the potential to mislead readers of the paper and potential users of the model. Therefore, we would rather not change the parameters in the table.

Table 2, page 25-26, 'Mediation factors': Does this require a new set of headers? The final column does not seem to be about RRs.

Yes – well spotted. The same is true for the theoretical minimum risks and risk factors operating through intermediate variables. These have now all been changed.

Table 9, 'No unrelated disease costs included': In the MSLT, fully removing all 'unrelated' disease costs is not possible. It cannot be done for the diseases in the model, which are influenced by the risk factors in the model, but which also act to add health care costs in added years of life.

You are correct, this has been clarified to say that this means that costs potentially accruing from diseases not modelled by PRIMEtime CE are not estimated. We have made this change in both paper 1 (and the supplementary file of paper 2).

Line 360-1: As currently described, PRIMEtime CE only has limited power to address the issue of impact on inequalities; it only presents results for the aggregate population of England (by age and sex), not inequalities by socio-economic position or ethnicity.

We have changed the text to remove the line regarding inequalities.

Line 412-3: Please mention the set of disability weights that was used. These were the Dutch DWs: Stouthard, M., Essink-Bot, M., Bonsel, G. & Group., D. D. W. (2000) Disability weights for diseases - A modified protocol and results for a Western European region, European Journal of Public Health, 10, 24. Or see http://dro.deakin.edu.au/eserv/DU:30046702/stevenson-burdenofdisease-2003.pdf. I recognize that is not as well-documented as it should have been. These weights were then applied to what the team judged to be the most likely distribution across stages/conditions within the prevalent pool of each disease.

This change has been made.
Valentina Lorenzoni (Reviewer 3): Modelling and estimating the cost-effectiveness of public health policies is of paramount importance to appropriately choose, prioritize, target and understand interventions while being extremely challenging from a methodological point of view because of the difficulties in being at the same time comprehensive and "simple" to properly estimate costs and consequences at large.

Splitting the original manuscript in two different works according to previous revision has improved understanding of the works, but further improvements are needed. It is still quite evident that the two papers are not born as stand alone works.

Given the challenges posed by the modelling of public health policies, the First paper is still lacking of details enabling a full understanding and clarity.

General comments to paper 1. The authors provide a detailed discussion of model limitations related to the assumptions used and the type of model used that, in particular imply independence among stated (that is introduced to simplify modelling but it will strongly impact on model outputs), some of the assumption used should be better presented in the methods section that is still not detailed enough to qualify the paper as stand alone. In common practice and when possible, assumptions used in models are considered in sensitivities analyses or even addressed introducing scenario analyses, I think these section are not comprehensively described.

Thank you for these comments. We agree that it is important to ensure that assumptions are appropriately stated. In lines 443-493 we describe the main limitations of PRIMEtime CE, including its principal assumptions and the potential impact of these on results. Furthermore, the sensitivity analyses listed in table 9 (which are also reported in paper 2) test the potential impact of these assumptions on results. We take on board your comment that the language around assumptions and limitations needs to be more explicit and we have made additions to various sections of the methods to expand on this – including in the section on adding physical activity as a risk factor, estimating costs, estimating utilities, and to the strengths and limitations section in the discussion.

For the original submission, reviewer 1 suggested that the manuscript would be better presented as two discrete papers, and we redrafted both as suggested. Although reviewer 1 was unable to review our revision, reviewer 2 (who was relatively positive about the original article and didn’t suggest dividing it into two papers) is now positive about both manuscripts and - save for some minor revisions - is happy with its format.

We are in agreement with reviewer 2 (and reviewer 1’s original assessment) in that we think that the manuscripts provide sufficient detail to stand alone – indeed, both papers are over 6,000
words long with substantial additional data files. We therefore do not think that substantially more detail beyond that added is likely to improve the paper nor benefit the reader.

Specific comments to paper 1.

Please check model description and risks factors considered, the presentation seems confusing citing somewhere 12, 13 or 14 risk factors.

Thank you for identifying this, we agree that it is confusing and have updated the text to try to make this easier to follow. To clarify, PRIMEtime CE includes 14 risk factors: physical activity plus 13 dietary risk factors (line 132), PRIME includes 13 behavioural risk factors (line 139), and PRIMEtime included 14 dietary risk factors (lines 147-149). We have added to lines 185-186 why this discrepancy occurs.

Costs estimation too seems not so clear or appropriate, for NHS costs (i.e costs related to the diseases included) did the authors consider just prevalent costs or even costs related to the acute phase?

We included prevalent costs only. You are right that costs will vary depending on time since diagnosis or proximity to end-of-life. It is not possible to estimate incident/end of life costs with the method used. The top down method for calculating costs (using NHS England programme budgeting data) was chosen because the disease costs are then directly comparable – having the same limitations, assumptions, and potential biases. This is expanded on in more detail in reference 84 which describes the costing method’s benefits and limitations in considerable detail. The cost per prevalent case is an average across all individuals with disease irrespective of time since diagnosis – it is then applied to all those in PRIMEtime CE with a disease to estimate total costs. This might over or underestimate costs, particularly if an intervention prolongs or shortens time with disease (case-fatality rate changes). We have added this limitation to the strengths and limitations section of the discussion.