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: 29 May 2018

Reviewer: Lennert Veerman

Reviewer's report:

This paper uses a lifetable model to compare the potential health and economic impact of two preventive interventions in England. It is well-written and addresses an important topic that is of interest to the readership of BMC Health Services Research. It highlights the large differences in the likely return on investment between various options for prevention of non-communicable disease, and in the comparison with the study by Emma Frey et al, the enormous influence that choices in data and model structure can have on the findings, which elegantly points to the need for further development of guidelines and for comparative studies. I have a number of comments, but am generally very positive about this paper.

General comments

My first comment is that throughout the paper, negative ICERs are reported. That is a big no-no according to standard economic evaluation methods (see Drummond's textbook). Negative ICERs make no sense: an intervention that saves 1 life year and saves GBP10,000 has the same ICER as one that saves 100 life years and saves GBP 1,000,000, but clearly the latter is preferable. Since both health and costs are benefits here, they should properly be added, not one divided by the other. (And then there is the issue that the ICER for an intervention that costs 1 life year and costs GBP10,000 would also have the same ICER!) Generally, negative ICERs are reported as 'dominant' or 'dominated'. I would suggest relying more on the 'return on investment' (RoI) metric, and using those for both interventions. I don't see why that couldn't also be reported for the 'Expanding Be Active' scenario, even though it does not turn out to be cost-saving.

Except that, secondly, the RoI seems to have been calculated only on the monetary components of the results, ignoring the health gains. That is unusual: the health gains represent an economic value, which is usually included in the RoI. Else, it is an incomplete metric. If you want to stick with that, it should be made clear in the methods and perhaps also in the discussion. Alternatively (and preferably), the health gains can be included. This requires quantifying the value of a QALY in monetary terms.

The third general comment I have regards the choice of the time horizon. In the base case, this is 10 years. However, as line 116-7 points out, "the time horizon should be long enough to
incorporate all important costs and effects”. I would recommend adhering to the quoted NICE reference case as the base case. I understand that the stakeholders unfortunately did not have such a long-term perspective, but this choice of time horizon does prevention no favours. For example, by this yardstick, don't bother preventing youth from taking up smoking. Very unfavourable ICER. And in this case, since the physical activity intervention benefits older people less than the salt intervention, this time horizon skews the comparison to the detriment of the former, the low 1.5% discount rate notwithstanding. If you do want to stick to this short time horizon, a stronger discussion of the implications of this choice should be included in the paper.

Specific comments

Please make clear in the main document that 'cancer' was breast and colorectal, separately modelled. (And not all cancers.)

Line 166: Because the definition of 'case fatality' in DisMod II may not be clear to all, best define this (annual mortality rate among prevalent cases, or something similar). Else it could be mistaken for the proportion that dies within 28 days of incidence.

Line 192: Was the 'cost per prevalent case' also applied to cancers? In ACE Prevention, cost per incident case was used, as cancer-related costs mostly occur in the first years (after which cure or death has taken place, in many cases). With a short time horizon, this matters (though assigning all costs to incidence risks over-estimating gains, with a 10-year time horizon).

Line 216: "Productivity gains and wider societal costs are included as sensitivity analyses." I thought productivity gains were part of the wider societal costs?

Additional data file:

Page 5: Correct definition of MET to 3.5 ml, per minute.

Page 7 "The parameters were unadjusted for obesity as this is assumed to act on the causal pathway": This is correct if no impact of physical activity on BMI was modelled. If that was the case, I suggest making that explicit by adding a sentence here.

Table S7: These values are generally low. Even lung cancer leads to a decrement of 12% of quality of life. Is that relative to prior quality of life (which on average is less than 100% at any age), or are these percentage-points? The utility loss from breast cancer is particularly low, at 1.9%. Is there any explanation for that? To compare, the lowest value for breast cancer in the GBD 2016 set of DWs is 0.049 (0.031-0.072) for the controlled phase ('has a chronic disease that requires medication every day and causes some worry but minimal interference with daily activities'). Is this because prevalence is defined as 'ever having been diagnosed in the lifetime',
in combination with a high rate of cure (without mastectomy, which comes with a DW of 0.083 in GBD)?

Table S13: Again, remove negative ICERs, and add a RoI for 'Expanding Be Active' for comparison.

Figures S8 and S9: What does 'Primary analysis' refer to?

Figure S10: Please remove negative ICERs. Best put it all in RoI. Consider doing the same for S12, or add a new graph with RoI for comparison.

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

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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