PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	A study protocol for projecting the effects of tobacco control policies in the United States through microsimulation
AUTHORS	Tam, Jamie; Levy, David; Jeon, Jihyoun; Clarke, John; Gilkeson, Scott; Hall, Tim; Feuer, Eric; Holford, Theodore; Meza, Rafael

VERSION 1 – REVIEW

REVIEWER	Chris Kypridemos MD, MPH, PhD Research Associate in Public Health Modelling University of Liverpool. Department of Public Health & Policy, Institute of Psychology, Health & Society. Whelan Building, Quadrangle, Office 220 LIVERPOOL, L69 3GB United Kingdom
REVIEW RETURNED	22-Sep-2017

GENERAL COMMENTS	Thank you for the opportunity to review this excellent study protocol. SimSmoke is a well-known and widely-used tobacco-control model. With this update and the fusion with the SHG, the methodological part of the model gets freshen-up, strengthen, and becomes up-to-date. In addition, the new web user interface (UI) is excellent and will greatly increase the usability of the model when officially released. I have only minor comments below, aiming to further improve the readability and transparency of this protocol. 1. In figure 1, please describe all graph elements in the caption. Some are not self-explanatory, i.e. the first initiation and first cessation dashed lines. Also, please consider rewording the term first cessation because it may confuse some readers by implying that the model allows for multiple cessation attempts. 2. The assumption that smoking cessation of more than two years equates lifetime smoking cessation is understandable. However, I have an intuition that this may be a highly influential assumption. Please add a few words in this protocol to describe your plan for a sensitivity analysis of this assumption or your justification why sensitivity analysis is not relevant and/or feasible in this case. 3. The main assumption and limitations of the model are now scattered throughout the text. Please consider summarising them in a table. 4. The decay rate of the impact of taxation value, now seems like it was chosen completely arbitrarily. Please, consider adding some justification. If it was indeed chosen arbitrarily then please mention any sensitivity analysis or calibration plans.

	5. As above for the smoke-free air laws relative effects by place. 6. Please describe how smoking-attributable deaths are estimated in this SimSmoke version. Although I can vaguely recall a probably 20-year-old publication describing this, it is not cited here. In any case, I would strongly recommend adding this section here for completeness even if nothing has changed in this aspect over the last 20 years.

REVIEWER	Adam Briggs The Dartmouth Institute for Health Policy and Clinical Practice Lebanon, NH. USA
REVIEW RETURNED	02-Oct-2017

GENERAL COMMENTS	Many thanks for the opportunity to see this protocol, it describes a very neat (and important) piece of modelling research that aims to estimate the impact of different policy options on smoking initiation and cessation rates in the US. I have a couple of major points that I would like to make and although they may not result in major changes to the manuscript, I think they should be addressed. Major points: 1. I am not entirely sure why this is being published as a protocol. Although specifying a model's a priori intention is important, part of the process of developing public health models is that they are often iterative in nature and scope, with feedback between model developers and stakeholders, and results of literature searches helping to refine the model's boundaries (for some of the discussion around this from an economic perspective, see Squires et al. Value in Health 2016;19(5):588). Secondly, I was invited to review this manuscript on the 8th Sept by which time results are already available on the quite fantastic website that is linked to this model. Therefore, it may be more appropriate for this paper to be written as a full research paper reporting results rather than as a protocol followed by results. I therefore think that both the editor and authors should justify whether or not this protocol should be published in light of these points. 2. In terms of replicating the model described, the descriptions of the interventions are excellent however I am unable to find a reference or link to the SHG model itself. Is it free to download or can it be requested from the original developers? If so, this should ideally be added to the manuscript or made more clear if already there. 3. I think that there needs to be more explanation of the rationale underlying some of the parameters used for specific interventions simulated. For example, it seems as though the cessation and initiation elasticities used for the cigarette tax scenario are assumed rather than empirically derived. It is unclear exactly where the numbers are taken from and if there is any uncertainty around them. The same can be said of the decay rate used for each intervention, the non-specific 'approximately 60-70% of reductions' and reductions in smoking prevalence of '9-10%' for the smoke free air laws, and the effect of raising the MLA on initiation rates.

	For these parameters and others, is any uncertainty in effect size going to be quantified, or are any sensitivity analyses planned? These estimates and assumptions could have significant implications on results over time. Minor comments First paragraph of methods and analysis, sentence two. Should this be 'transition to Never smokers...' rather than 'to ever smokers...'?

REVIEWER	Laura Webber UK Health Forum, UK
REVIEW RETURNED	04-Oct-2017

GENERAL COMMENTS	This is a well written and interesting paper about the development of a microsimulation model to test the impact of tobacco policies in the US. The paper would benefit from a few minor adjustments/additions: - Please place the model in context by providing information about other, existing microsimulation models for tobacco and how this model differs. - Please clarify why such historic data is used, presumably this would bias estimates due to cohort effects since more recent data has a much lower smoking prevalence. -It would be useful to note the language that the model is written in - How many individuals are simulated in the model? - How is uncertainty handled in the model? Are 95% CI produced around the projections/outputs? - Will the project provide some sensitivity analysis? - line 21, p5 - subject = subjects OR a subject -It would be useful to include a note saying why morbidity is not quantified (just mortality), since morbidity is costly to the health system and wider society (e.g. lost productivity). Is this considered at all ? Perhaps as a future development? - the authors might comment on differences by social group and how this may/may not be incorporated into the model, and may be a limitation of the proposed model

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Chris Kypridemos MD, MPH, PhD
Institution and Country: Research Associate in Public Health Modelling, University of Liverpool. Department of Public Health & Policy, Institute of Psychology, Health & Society. LIVERPOOL, United Kingdom
Competing Interests: None

Comment: Thank you for the opportunity to review this excellent study protocol. SimSmoke is a well-known and widely-used tobacco-control model. With this update and the fusion with the SHG, the methodological part of the model gets freshen-up, strengthen, and becomes up-to-date. In addition, the new web user interface (UI) is excellent and will greatly increase the usability of the model when officially released. I have only minor comments below, aiming to further improve the readability and transparency of this protocol.

Response: We thank the reviewer for their encouraging feedback. Although the SHG policy module is a microsimulation and different from the SimSmoke model, it relies on many of the same policy assumptions that have been used by SimSmoke in the past. We are delighted to hear that they are pleased with the model application, its methodological strengths, and the design of the user interface.

1. In figure 1, please describe all graph elements in the caption. Some are not self-explanatory, i.e. the first initiation and first cessation dashed lines. Also, please consider rewording the term first cessation because it may confuse some readers by implying that the model allows for multiple cessation attempts.

Response: Thank you for this suggestion. We have changed “Youngest Cessation” to “Cessation” and “Youngest Initiation” to “Initiation” in the Figure to avoid potential confusion. We have also added the following caption to Figure 1. Population covered by the NHIS and the Smoking History Generator status quo scenario.

“Caption: Schematic diagram for data sources for Smoking History Generator Parameters: years and ages with available National Health Interview Survey data (yellow), and projection estimates (green), earliest (1890) and latest (1997) cohorts with available data, and youngest initiation (8 years) and cessation ages (15 years).”

2. The assumption that smoking cessation of more than two years equates lifetime smoking cessation is understandable. However, I have an intuition that this may be a highly influential assumption. Please add a few words in this protocol to describe your plan for a sensitivity analysis of this assumption or your justification why sensitivity analysis is not relevant and/or feasible in this case.

Response: Our definition of a current smoker includes recent quitters who quit less than two years ago, which results in an inflated overall smoking prevalence estimate compared to other definitions of smoking that do not include those who recently quit. This assumption was made for simplicity, since incorporating all future relapse would greatly add to the complexity of the model, without, in our opinion, adding to its capabilities. Although it does not capture complex relapse behavior, we believe that it provides a reasonable approximation for permanent quitting.

Because of high relapse rates among those who quit within the first two years, and since we are not modeling relapse, we used this definition of 2-yr quit from within the National Health Interview Surveys (NHIS) to calibrate the SHG, relabeling and censoring former smokers with less than two years since quit as current smokers at their reported quit age. Based on this data, the SHG is able to produce annual cessation probabilities that represent approximately ‘true’ quitting. The CISNET Smoking History Generator (SHG) has been validated against NHIS data on smoking prevalence using a revised 2-yr quit definition [Figure 2. SHG adult smoking prevalence projections under the status quo scenario, 1965-2060].

We now include the following language in the Methods section to accompany a new figure: “We validated the SHG smoking prevalence estimates against NHIS data using a revised definition for current smoking that includes those who quit less than 2 years ago. Figure 2 compares SHG smoking prevalence projections under the status quo scenario with NHIS using the 2-year quit definition.”

This shows the close correspondence between NHIS data on smoking prevalence using the revised 2-year quit definition and the SHG baseline estimates.

Caption: SHG = Smoking History Generator. NHIS = National Health Interview Surveys. SHG and NHIS estimates shown above use an adjusted definition for smoking where 'current smoking' is defined as having smoked at least 100 cigarettes in their lifetime, currently smoking every day or some days, or having quit smoking less than two years ago."

3. The main assumption and limitations of the model are now scattered throughout the text. Please consider summarising them in a table.

Response:The reviewer makes an excellent suggestion. We have added an additional table (Table 4) that describes the model estimates, assumptions, and limitations for each of the policies.

4. The decay rate of the impact of taxation value, now seems like it was chosen completely arbitrarily. Please, consider adding some justification. If it was indeed chosen arbitrarily then please mention any sensitivity analysis or calibration plans.

Response: We model a decay rate to reflect findings in the tobacco control literature that a permanent tax increase has an immediate effect that tapers off over time. This parameter was estimated during calibration to match the target effects of a tax increase on smoking prevalence over a twenty year period. We have added the following language to the protocol:

"A 0.2 decay rate was estimated during model calibration, so that in conjunction with the SHG cessation probabilities, the model reproduced reported policy effects on smoking prevalence over time. This reflected the immediate impact with continued effects over time, as indicated by studies of price increases on smoking prevalence.44 These time patterns are also consistent with results from the validated SimSmoke model."
44International Agency for Research on Cancer. IARC Handbooks of Cancer Prevention, Tobacco Control, Vol 14: Effectiveness of Tax and Price Policies for Tobacco Control. Lyon, France, 2011.

"A 0.2 decay rate was also calibrated to reflect evidence of the effects of [smoke-free air laws] on smoking prevalence over time."

"We assume the same decay rate for [TC expenditures policy] as for smoke-free air laws and for tax increases."

We appreciate the reviewer's suggestion and will include plans on additional sensitivity analyses around this decay rate. We note this in a newly added paragraph describing our plans for sensitivity analyses:

"We plan to conduct sensitivity analyses to assess the extent to which parameter uncertainty may influence the model results. Table 4 summarizes model estimates, assumptions, and limitations for each tobacco control policy as previously described. For each parameter (e.g. policy decay rate, price elasticities), we will develop plausible ranges for the numerical estimate. Then for each simulated tobacco control policy, we will use standard techniques, such as latin hypercube or joint multivariate methods, to jointly sample from within those sets of parameter ranges during simulation. By varying all the parameters simultaneously for a given scenario, we will produce a range of possible outcomes and quantify the degree of uncertainty in the modeling. This additional analysis ensures a more rigorous assessment of the model, assumptions, and their implications for policies."

5. As above for the smoke-free air laws relative effects by place.

Response: The relative impacts for smoke-free air laws are based on an extensive review of the literature conducted for the original SimSmoke smoke-free air module, which was recently updated. Based on this literature on the impact of comprehensive smoke-free air laws, including research specifically on worksite restrictions and a smaller evidence-base on restaurants, the relative effects sizes were distributed across the different venues and reviewed and approved by an expert panel.

To make this clearer in the protocol, we have added new language to explain this and include three additional citations referring to the validated SimSmoke smoke-free air law modules on which the relative effects are based.

“These relative effects were reviewed by an expert panel as part of an extensive assessment of the literature conducted for a previously validated model of smoke-free air laws.”
- Levy DT, Friend K, Polishchuck E. Effect of clean indoor air laws on smokers: the clean air module in the SimSmoke computer simulation model. Tob Control. 2001 Dec;10(4):345-51. PMID: 11740026. PMCID: PMC1747628
- Levy DT, Friend K. The effects of clean indoor air laws: what do we know and what do we need to know? Health Educ Res. 2003 Oct;18(5):592-609.
- Levy DT, Meza R, Zhang Y, et al. Gauging the Effect of U.S. Tobacco Control Policies From 1965 Through 2014 Using SimSmoke. American Journal of Preventive Medicine 2016;50(4):535-42. doi: https://doi.org/10.1016/j.amepre.2015.10.001

6. Please describe how smoking-attributable deaths are estimated in this SimSmoke version. Although I can vaguely recall a probably 20-year-old publication describing this, it is not cited here. In any case, I would strongly recommend adding this section here for completeness even if nothing has changed in this aspect over the last 20 years.

Response: We estimated the smoking-attributable deaths by using the methodology reported in the appendix of the IOM Report on the Public Health Implications of Raising the Minimum Age of Purchase of Tobacco Products, which is now cited in the revised protocol. The following language has been added under the ‘Model outcomes’ section: “Using the same methodology previously used by the IOM committee on raising the minimum age of legal access to tobacco, total smoking-attributable deaths are calculated...”

Reviewer: 2
Reviewer Name: Adam Briggs
Institution and Country: The Dartmouth Institute for Health Policy and Clinical Practice, Lebanon, NH. USA
Competing Interests: None declared

Comment: Many thanks for the opportunity to see this protocol, it describes a very neat (and important) piece of modelling research that aims to estimate the impact of different policy options on smoking initiation and cessation rates in the US.

Response: We are grateful to the reviewer for their encouraging comments.

I have a couple of major points that I would like to make and although they may not result in major changes to the manuscript, I think they should be addressed.

Major points:
1. I am not entirely sure why this is being published as a protocol. Although specifying a model's a priori intention is important, part of the process of developing public health models is that they are often iterative in nature and scope, with feedback between model developers and stakeholders, and results of literature searches helping to refine the model's boundaries (for some of the discussion around this from an economic perspective, see Squires et al. Value in Health 2016;19(5):588). Secondly, I was invited to review this manuscript on the 8th Sept by which time results are already available on the quite fantastic website that is linked to this model. Therefore, it may be more appropriate for this paper to be written as a full research paper reporting results rather than as a protocol followed by results. I therefore think that both the editor and authors should justify whether or not this protocol should be published in light of these points.

Response: The reviewer is correct that public health models are iterative in nature and scope. Our modeling work is ongoing and we plan to continue making refinements to the methodology based on feedback, new data, and improvements to the underlying microsimulation model. While the website was made public on September 15th we plan to update it with more accurate estimates as they become available over the next few years. The data currently on the website represents our best available estimates, and it was released for public and expert feedback. For example, we have since received feedback about the lack of uncertainty quantification with the model. In addition, we are planning to conduct sensitivity analyses that will allow us to better understand the potential effects of policies. Once these are completed, we will produce a research manuscript with a more rigorous assessment of the modeling and its implications for policy. The purpose of this study protocol submission is to describe in extensive technical detail our modeling approach to date.

As described in BMJ Open guidelines: “Publishing protocols in full also makes available more information … and increases transparency, making it easier for others (editors, reviewers and readers) to see and understand any deviations from the protocol that occur during the conduct of the study.”

Because of the nature of this type of work, most research papers do not allow for sufficient discussion of the methodology. Our goal in publishing this open access protocol is to make the methods accessible and transparent to all, as well as document our original methodological approach so that future efforts that may differ from this approach are made apparent to all. When we report final conclusions and analyses in a future publication, we expect to cite this study protocol in those manuscripts.

2. In terms of replicating the model described, the descriptions of the interventions are excellent however I am unable to find a reference or link to the SHG model itself. Is it free to download or can it be requested from the original developers? If so, this should ideally be added to the manuscript or made more clear if already there.

Response: Great suggestion. We have added this sentence to the Methods section: “A version of the SHG microsimulation model is available upon request from the CISNET lung group.” We are still in the process of developing a public website that makes the current SHG available for others to directly download.

3. I think that there needs to be more explanation of the rationale underlying some of the parameters used for specific interventions simulated. For example, it seems as though the cessation and initiation elasticities used for the cigarette tax scenario are assumed rather than empirically derived. It is unclear exactly where the numbers are taken from and if there is any uncertainty around them. The same can be said of the decay rate used for each intervention, the non-specific 'approximately 60-

70% of reductions' and reductions in smoking prevalence of '9-10%' for the smoke free air laws, and the effect of raising the MLA on initiation rates. For these parameters and others, is any uncertainty in effect size going to be quantified, or are any sensitivity analyses planned? These estimates and assumptions could have significant implications on results over time.

Response: We have added Table 4 summarizing the major modeling assumptions and estimates, which also clarifies how parameter estimates are used in the modeling. in addition, we have added further explanation regarding the smoke-free air law and tax effects in the manuscript in response to comments #3, 4, and 5 from Reviewer #1.

We have not yet conducted sensitivity analysis, but such analyses are part of our future plans, which we now describe in the protocol. While the website contains results from the baseline model simulations, a more rigorous assessment regarding parameter uncertainty is still needed. A new paragraph under “Future developments” has been added to the protocol describing our plans to explore uncertainty around the effect sizes. As discussed in our response to comment #1, this study is not a completed study and analyses are still ongoing.

Minor comments
First paragraph of methods and analysis, sentence two. Should this be 'transition to Never smokers...' rather than 'to ever smokers...'?

Response: Thank you for noting this. We have changed the sentence as follows: “Parameters for the microsimulator were derived by fitting a compartment model for smoking history in which individuals transition from never to current to former smokers based on initiation and cessation rates developed using the National Health Interview Survey (NHIS).”

Reviewer: 3
Reviewer Name: Laura Webber
Institution and Country: UK Health Forum, UK
Competing Interests: None declared

Comment: This is a well written and interesting paper about the development of a microsimulation model to test the impact of tobacco policies in the US.

Response: Thank you.

The paper would benefit from a few minor adjustments/additions:

- Please place the model in context by providing information about other, existing microsimulation models for tobacco and how this model differs.

Response: Excellent suggestion. We now cite a systematic review of US tobacco policy models (Feirman, 2017) and include this additional context in the Introduction section:

“A recent systematic review identified computational models of US-based tobacco control policies; most used population-level approaches (e.g. system dynamics or compartmental models) when evaluating different types of policies. (Feirman, 2017)

In contrast with previous work, we use a novel individual-level approach to evaluate the effects of tobacco policies through microsimulation. The advantage of this method is that it integrates detailed historical information about smoking patterns by birth cohort, age, and gender. Furthermore, we

develop an adaptable policy module that allows the microsimulation framework to readily integrate policy effects specific to each selected tobacco control policy."

- Please clarify why such historic data is used, presumably this would bias estimates due to cohort effects since more recent data has a much lower smoking prevalence.

Response: We have added more clarifying language to the Methods section: "We use comprehensive historical data to reconstruct cohort patterns of smoking that have changed over time. The data used in the model to project future patterns initiation and cessation rates were generated using an age-period-cohort statistical model that specifically allows for age, period and cohort effects in recent years."

To further clarify, we have added a new figure to show how the Smoking History Generator, which integrates survey data from 1965-2015, corresponds closely to actual estimates from the National Health Interview surveys. [Figure 2. SHG adult smoking prevalence projections under the status quo scenario, 1965-2060]

It would be useful to note the language that the model is written in
We have added sentences to state: "The Smoking History Generator (SHG) was developed in C++." and "The SHG policy module was developed in python and the mortality and life year calculations in R version 3.1.3."

- How many individuals are simulated in the model?

Response: 100,000 were simulated per birth cohort. We have changed language in the Methods section to state this explicitly: "Smoking initiation and cessation rates under the baseline scenario are applied to hypothetical cohorts of 100,000 men and women born in the years 1910 to 2060 for a total of 30 million individuals simulated per policy scenario."

- How is uncertainty handled in the model? Are 95% CI produced around the projections/outputs?

Response: The modeling process is an ongoing effort. While the website's numerical estimates are stable qualitatively, we play to investigate how parameter uncertainty could influence our results. For the current web interface, we simplified what users are able to see in order to reduce potential confusion among the public and non-researcher audiences. However we have added a new section to describe our future plans to assess this uncertainty, pasted directly below:

"Future developments

We plan to conduct sensitivity analyses to assess the extent to which parameter uncertainty may influence the model results. Table 4 summarizes model estimates, assumptions, and limitations for each tobacco control policy as previously described. For each parameter (e.g. policy decay rate, price elasticities), we will develop plausible ranges for the numerical estimate. Then for each simulated tobacco control policy, we will use standard techniques, such as latin hypercube or joint multivariate methods, to jointly sample from within those sets of parameter ranges during simulation. By varying all the parameters simultaneously for a given scenario, we will produce a range of possible outcomes and quantify the degree of uncertainty in the modeling. This additional analyses ensures a more rigorous assessment of the model, assumptions, and their implications for policies."

- Will the project provide some sensitivity analysis?

Response: Yes. We have added a new paragraph on sensitivity analysis to the protocol (see response above). Thank you for this suggestion.

- line 21, p5 - subject = subjects OR a subject

Response: Thank you. We have revised the sentence to state “subjects” as: “Parameters for the microsimulator were derived by fitting a compartment model for smoking history in which individuals transition from never to current to former smokers based on initiation and cessation rates developed using the National Health Interview Survey (NHIS).”

-It would be useful to include a note saying why morbidity is not quantified (just mortality), since morbidity is costly to the health system and wider society (e.g. lost productivity). Is this considered at all ? Perhaps as a future development?

- the authors might comment on differences by social group and how this may/may not be incorporated into the model, and may be a limitation of the proposed model

Response: Thank you for these suggestions. We are already in the process of extending the model to consider additional health outcomes and differences by social groups. To highlight this, we added a new section titled “Future developments” to the protocol that includes the language below:

“We also plan to extend this model to consider additional health outcomes and different subpopulations across the US. As one example, the current model simulates the impact of policies on the number of deaths due to any cause; we will eventually evaluate the impact of policies on deaths due to lung cancer specifically. Future work may also include considering the impact of policies on morbidity in addition to mortality.

Patterns of smoking are known to differ by geographic region and sociodemographic characteristics, with important disparities in smoking initiation, cessation, and prevalence across the population. Although the current model is based on national-level data, and a rescaling approach based on state-level population and smoking prevalence, we will use additional data to develop state-specific smoking parameters in future work. We also plan to extend the underlying SHG to simulate differences by level of educational attainment.”

VERSION 2 – REVIEW

REVIEWER	Chris Kypridemos MD, MPH, PhD University of Liverpool, UK
REVIEW RETURNED	14-Nov-2017

GENERAL COMMENTS	Thank you. The authors addressed all my comments in the revised version of the paper. Therefore, I recommend it for publication.

REVIEWER	Adam Briggs The Dartmouth Institute for Health Policy and Clinical Practice, Lebanon, NH. USA
REVIEW RETURNED	28-Nov-2017

GENERAL COMMENTS	Many thanks for letting me see this manuscript again and for all the work you've done to address my initial comments. I would just suggest that on page 7 a reference is provided for the exact location of the SHG model (i.e. how to contact the CISNET lung group), and also on page 9, I am still unclear as to why the authors use '60-70%' and '9-10%' when describing their input parameters. Given the quantitative nature of the work, unless there is good reason not to, I suggest that the authors state the parameters they plan to use in the model (66% and 9%). Table 4 is a welcome addition. Under the future developments, I think it would also be worth stating that based on future feedback on the model and its results following its online publication, input parameters and uncertainty estimates may change with any deviation from the protocol being made clear in subsequent peer-reviewed publications of the model's results.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1
Thank you. The authors addressed all my comments in the revised version of the paper. Therefore, I recommend it for publication.

- We are pleased to hear this. Thank you.

Reviewer: 2
Many thanks for letting me see this manuscript again and for all the work you've done to address my initial comments.
I would just suggest that on page 7 a reference is provided for the exact location of the SHG model (i.e. how to contact the CISNET lung group), and

- We revised the reference on page 7 as follows : "A version of the SHG microsimulation model is available upon request from the CISNET lung group. For requests please send a message to shg-distrib@lung.cisnet-group.org."

Response: Also on page 9, I am still unclear as to why the authors use '60-70%' and '9-10%' when describing their input parameters. Given the quantitative nature of the work, unless there is good reason not to, I suggest that the authors state the parameters they plan to use in the model (66% and 9%).

- Done. We changed "60-70%" to "66%" and "9-10%" to simply "9%."

Response: Table 4 is a welcome addition. Under the future developments, I think it would also be worth stating that based on future feedback on the model and its results following its online publication, input parameters and uncertainty estimates may change with any deviation from the protocol being made clear in subsequent peer-reviewed publications of the model's results.
- The following two sentences have been added under 'Future developments': "The input parameters and uncertainty estimates presented here may change based on future feedback on the model and its results. In subsequent peer-reviewed publications of the model’s findings, we will note any deviations from this protocol."