Author’s response to reviews

Title: Spatial heterogeneity of environmental risk in randomized prevention trials: consequences and modeling

Authors:

Abdoulaye GUINDO (abdouguindo@icermali.org)
Issaka SAGARA (isagara@icermali.org)
Boukary OUEDRAOGO (boukary.ouedraogo@univ-amu.fr)
Kankoe SALLAH (kankoe.sallah@univ-amu.fr)
Mahamadoun ASSADOU (mmaiga@icermali.org)
Sara HEALY (sara.healy@nih.gov)
Patrick DUFFY (patrick.duffy@nih.gov)
Ogobara DOUMBO (okd@icermali.org)
Alassane DICKO (adicko@icermali.org)
Roch GIORGI (roch.giorgi@univ-amu.fr)
Jean GAUDART (jean.gaudart@univ-amu.fr)

Version: 2 Date: 16 May 2019

Author’s response to reviews:

Ezra Gayawan (Reviewer 1):

Quest 1 - Please include all comments for the authors in this box rather than uploading your report as an attachment.

Answer 1 - Thank you for this remark. Indeed, we had attached the cover letter as an additional file. We have considered your suggestion in this submission.

Quest 2 - Please only upload as attachments annotated versions of manuscripts, graphs, supporting materials or other aspects of your report which cannot be included in a text format.
Answer 2 - Following this recommendation, we have uploaded only the manuscript, graphs and supporting materials. Neither the cover letter nor the answer to reviewers have been uploaded.

Quest 3 - The authors have improved on the earlier draft and this is commendable. There is however the need for a careful language editing before publishing.

Answer 3 - We thank the reviewer for this encouraging comment. The text has been corrected for language errors by a professional editor.

Quest 4 - A minor issue I would point is that I do not see the review in lines 491 to 496 necessary.

Answer 4 - Following this recommendation, we have deleted this paragraph and added the former references #56, 57, 58 to the introduction section (page 4, line 93 to 95).

“Moreover, the SPDE model implemented using the INLA (Integrated Nested Laplace Approximation) algorithm is now used in an ever-wider range of contexts [21–23].”

Christian Heumann (Reviewer 2):

Quest 1 - My questions were adequately answered and my proposals were implemented (simulations for the theoretical model)

Answer 1 - We thank the reviewer for this comment.

Quest 2 - The authors should have a look on "Appendix 1.doc", line 15: the formula makes no sense as presented.

Answer 2 - Following this recommendation, we have deleted the formula (Appendix 1, line 13).

Quest 3 - In the text they write that the true model has nearly always a coverage rate of 100%. Looking in the appendix, this is not correct and I think this statement should be changed "...has nearly always the desired coverage rate.", which was 95%.

Answer 3 - Following this recommendation, we have corrected the sentence in the results section (page 11, line 273 to 276). Please note that following the recommendation of the third reviewer, we have replaced the “theoretical model,” or “true model” with the “Data-Generating Model (DGM).”
“Data-Generating Model (DGM)”

“The DGM was the simulation model, which took into account environmental risk. As expected, biases and MSEs were almost null and nearly always had the desired CR, regardless of the scenario (Appendix 2).”

T. Alex Perkins (Reviewer 3):

Quest 1 - The authors have done a good job addressing my comments. I only have a couple of minor suggestions to improve the clarity of the writing.

Answer 1 - We also thank the reviewer for this encouraging comment.

Quest 2 - Lines 42-45: Sentence does not make sense. What is the theoretical model? Not well written.

Answer 2 - We acknowledge that the term “theoretical model” lacks precision. Following the recommendation of the previous reviewer, we have analyzed the dataset using the Data-Generating Model (DGM), i.e. the model used for simulations.

In the manuscript and in the figures, we have replaced the term “True-M” (true model or theoretical model) with the term “DGM” (Data-Generating Model).

We have modified the sentences accordingly (page 2, lines 42-45):

“The performances of the following five statistical models were assessed: a non-spatial Cox Proportional Hazard (CoxPH) model and four models accounting for spatial heterogeneity—i.e., a Data-Generating Model (DGM), a Generalized Additive Model (GAM), and two Stochastic Partial Differential Equation (SPDE) models, one of which modeled survival time and the other the number of events.”

Quest 3 - Change all instances of environment-borne to environmentally influenced or some other wording.

Answer 3 - We have modified the passages, as per this recommendation.

Quest 4 - Lines 76-77 are a repeat of what is said 2 sentences previously

Answer 4 - We have deleted the sentence, as per this recommendation (page 3, line 73)
Quest 5 - Lines 91-93 reword sentence Line 104- again, what is "the theoretical model?" Aren't these all theoretical models?

Answer 5 - Lines 86-94 (page 4) have been corrected. We fully agree that all models are theoretical. As mentioned previously, we have replaced the “theoretical model” with the Data-Generating Model (DGM).

Quest 6 - 123-124: What does this mean?

Answer 6 - This sentence introduces the different simulated scenarios, i.e. the risk situations. These scenarios were simulated before the treatment randomization. Each factor involved in the scenario simulation has been detailed below this sentence. We have also modified the sentence to make it clearer (page 5, line 119 to 121).

“Before the treatment randomization was simulated, different risk situations (scenarios) were simulated according to location (spatial distribution of individuals), baseline risk, and heterogeneity of environmental risk (location and density of breeding sites) (see description below).”

Quest 7 - Line 441: Does this mean <0.6?. It is assumed they are in relative risk, but this is never explicitly mentioned.

Answer 7 - We are grateful to the reviewer for noticing this error! You are right. We have corrected this mistake and added mentions of relative risk (page 19, line 439).