Reviewer's report

Title: Simulation Studies of Age-Specific Lifetime Major Depression Prevalence

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Reviewer: Jan J Barendregt

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Re: Simulation Studies of Age-Specific Lifetime Major Depression Prevalence
Authors: Scott B. Patten & Lee Gordon-Brown

This article looks at an important epidemiological measure, the lifetime prevalence (LTP) of major depression (MD). This measure is the lead variable in the CIDI questionnaire, and much of the value of the CIDI with respect to the epidemiology of MD depends on the validity the LTP is measured with.

The LTP as measured with the CIDI shows a distinct age pattern: a rise at younger ages, followed by a decline at older ages. This pattern can be explained by three factors: 1) increasing incidence in younger birth cohorts; 2) mortality selection; and 3) recall bias (and of course any combination of these).

Many psychiatric epidemiologists root for cause 1, with dire implications for the future prevalence of MD. Personally, as the authors know since they cite my publication, I think recall bias is the reason. The question cannot be settled easily because it is virtually impossible (and would take a very long time) to measure it empirically.

The article tries to get a handle on the problem by constructing a simulation model that mimics individual life histories under various conditions of changes in incidence, mortality selection, and forgetfulness. By varying these conditions, the authors establish under which circumstances the observed age pattern occurs.

As such this is a valid way of addressing an otherwise intractable problem, and I think the broad conclusions that are drawn are correct. However, I do have some concerns.

1. Validity of the model. The authors present some cursory test results, and conclude from them the model is valid. But I see odd 5 year patterns in the figures (eg 3 & 4) that are not explained, and from what I understand of the model specification, should not be there.

Also, I find it odd that the model needs more than 100 years of burn in to get stable LTPs: surely with constant incidence and mortality selection, replacing the entire population should do.

2. The specification of the incidence function. The function used allows incidence to either increase, decline, or stay constant over the entire age range. A likely pattern is an increase at young ages, followed by a decline after ~ age 30. Some evidence suggests that this is followed by an increase at old age. The incidence
function used seems far too simplistic.

Some more minor concerns:

1. Fig 1 needs CIs.
2. P8: age-specific mortality. Why not convert the age-specific mortality to a survival curve, and use a single draw from it to get age at death?
3. P10: RR mortality. Was the mortality rate of the non-depressed population recalculated?
4. Fig 2: colourful, but quite unclear.
5. P13: only 100 runs! To get stable 95% CIs I would think that you need at least 1000 runs.
6. P13: the animation is not accessible.
7. Fig 5: it would be helpful to have the real LTP in the graph as well.
8. P14: an RR of 2 is extremely high for LTP. It might be appropriate when people are in an episode, but fortunately most people with a history of MD are not in an episode most of the time.
9. Figs 9 & 10 are not discussed at all (and they are certainly not self-explanatory).
10. P17: staring should be starting.

**Declaration of competing interests:**

I declare that I have no competing interests