Reviewer's report

Title: Agent-based simulation for a weekend-extension strategy to mitigate influenza outbreaks

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Reviewer: Erin Elizabeth Rees

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Review of BMC Public Health manuscript:
“Agent-based simulation for a weekend-extension strategy to mitigate influenza outbreaks” by Liang Mao

Dr. Liang Mao’s paper is generally well-written and presents an interest studying testing the effects of different non-pharmaceutical intervention scenarios against human influenza in an urban centre. Mao uses an agent-based spatially explicit simulation model to determine if extending weekends, as per three continuous or three discontinuous extension scenarios, reduces the attack rates for seasonal and pandemic influenza events. Mao finds the continuous weekend scenarios to be most effective and discusses the advantages of this non-pharmaceutical intervention.

Suggested text edits are indicated in capital letters.

Discretionary Revisions

1. Page 1: Change to “...few strategies have considered THE reductive effect...”
2. Page 1: Change to “...The purpose of this study is to explore SIX weekend-extension...”
3. Page 1: Change to “THEIR effectiveness IS EVALUATED USING AN ESTABLISHED agent-based spatially explicit simulation model in the urbanized area of Buffalo, NY, USA.”
4. Page 2: Provide more context describing what constitutes a high rate of spread for the new “highly pathogenic” influenzas in the opening paragraph (e.g., number of people infected per unit time and area) to give more support underlining the urgency of an appropriate response.
5. Page 3: Change to “This paper PROPOSES a new...”
6. Page 4: Remove “but relevant studies are scant”
7. Be consistent in the naming convention: “agent-based spatially explicit” on Page 1 differs from “spatially-explicit agent-based model” on Page 4
8. Page 4: Change to “and articulates the implications of modelling outcomes.”
9. Page 4/5: The 3-day discontinuous strategy is really the 2-day continuous strategy with the addition of a discontinuous element (i.e., Wednesday as a “weekend”). I recommend highlighting this distinction in the methods and
discussing implications of this “blended” scenario when interpreting model results.

10. Page 6: The Appendix describing the three zones is unnecessary. The zone descriptions are not too detailed or complex, therefore, include this information in the Methods section.

11. Page 8: The model does not allow for school-aged individuals to visit neighbours or other services on weekends (and weekend-extensions) without their parents. For the teenage component of the school-aged cohort, this is not a realistic behaviour for American teenagers. What is the justification for homogenous behaviour of school-aged individuals? Would the model outcomes be sensitive to accounting for unique behaviours of teenagers?

12. Page 8: An appendix for Table A1 is unnecessary and should be included as a Table 2 within the Methods section.

13. Page 8: Change to “…gain its momentum to rise EXPONENTIALLY TO PEAK INCIDENCE.” Remove text “as shown in Figure 4 and 6” because it is unconventional to introduce these figures at this time since Figure 3 has yet to be introduced; furthermore, the suggested edit #13 provides a sufficient explanation.

14. Page 9: Change to “…and serve as a REFERENCE for…”

15. Page 9: Change to “To validate the model, THE OUTCOMES ARE COMPARED WITH CDC weekly reports of laboratory confirmed specimens from the 2004-5 influenza epidemic in THE study area [26].”

16. Page 9: Remove “apparently”

17. Page 11: In the “Discontinuous weekend-extension strategies” section substitute the “but”(s) for “and”

18. Page 12: Change to “…travel restriction strategies MORE difficult…”

19. Page 13: Change to “…loss from work absenteeism IS A POTENTIAL problem FOR implementing…”

20. Page 14: Change to “…and learning are not feasible, THESE OCCUPATIONS COULD HAVE A HIGHER PRIORITY FOR RECEIVING pharmaceutical strategies…”

Minor Essential Revisions

1. Page 1: Change to “…overall attack rates and MAPS OF THE INFECTION INTENSITY”.

2. Page 2: Change to “…if appropriate extensionS of normal…”

3. Page 2: Use of “effective” in last sentence of the Abstract Conclusion section is inappropriate. Presence or absence of vaccine resources does not affect the mechanisms influencing the effectiveness of the weekend-extension strategy.

4. Page 3: Change to “…compliance of people and ARE difficult to…”

5. Page 3: Provide a further explanation or give examples of the “ethical and legal issues”

6. Page 3: Change to “…few mitigation strategies have EVALUATED the
reductive...”

7. Page 3: Remove text “has” to read “...European countries, reported a 10-20%...”

8. Page 3: Change to “Research by both Lee et al. and Cooley et al. attribute variance in influenza incidence to the weekdays/weekends effect”

9. Page 3: Change to “… weekend contacts is 2-4 TIMES less than DURING weekdays”

10. Page 4: Change to “The effectiveness of a weekend-extension strategy is tested using AN ESTABLISHED spatially-explicit agent-based model for the urbanized area of Buffalo, New York, USA.”

11. Page 5: Include in the methods that schools are also closed during the additional weekend days, and if they are not, the author should justify the reasoning.

12. Page 5: Cite examples of past studies using weekend-extension strategies “...been intensively studied before (citations),...”

13. Page 5: The first point differentiating the weekend-extension strategy from past studies is not clear. What constitutes a “majority of affected and unaffected businesses”? This is a key assumption in the modelling strategy that needs to be transparent to the readers. For instance, are 60, 70, or 80% of businesses closed?

14. Page 5: The inset of a on a map is the smaller map contained within. Therefore, for Figure 1a the inset is the map of small map of NY state in the upper left corner. Remove text “the inset map of”

15. Page 6: Define the year for data on the business locations

16. Page 7: Define age range of “school-aged individuals”

17. Page 7: Define that the “recovered” individuals become immune to future transmission events.

18. Page 8: Change to “…examine the effectiveness of a weekend extension...”

19. Page 8: Remove comma to read “…to be successfully suppressed if the total...”

20. Page 8: Change to “…is controlled below 5%, SINCE reported influenza epidemics often have AN attack rate #5%”

21. Page 8: Change to “…is expected to produce a lower epidemic peak...”

22. Page 8: “An effective mitigation strategy is expected to produce a lower epidemic peak and fewer infections”, yes, but by how much? One fewer case would not be a success. So how big of an effect size is a success? A reduction in the attack rate to below 5%?

23. Page 9: Change to “point locations to 50m x 50m grid cells”

24. Page 9: Remove sentence “This map estimates…” and Change to “The cumulative infection density from 200 days of simulation is estimated for every cell”
25. Page 9: Change to “Both the epidemic curve and infection intensity map show the mean of 50 runs to average out the variation caused by the stochastic simulation.”

26. Page 10: Change to “A possible reason for this result is that individuals have significantly fewer contacts because of a reduced weekday schedule.”

27. Page 10: Change to “...are not capable of suppressing the outbreak...”

28. Page 11: In reference to “200 infections/km2” include a citation for Figure 5. Also, is 200 infections/km2 a correct translation from the geographic resolution of 50 x 50 m grid cells? Is this the scale at which Kernal estimation was used to interpolate disease intensity? If so, indicate in the methods.

29. Page 11: Change to “…which would make it easier to apply…”

30. Page 11/12: The explanation at the end of the “Discontinuous weekend-extension strategies” section is not sufficient to explain (identify the mechanisms) causing the differences in epidemic when using a continuous or discontinuous intervention. Please develop.

31. Page 13: The sentence reads more clearly to include “…such as case isolation, household quarantine and long-term workplace closure.”

32. Page 14: More clearly write the ideas expressed in the second last paragraph of the Conclusion section starting at “With the help of additional strategies…” and the final paragraph.

33. Figure 1b: Do not include this figure unless the information it portrays (household density, transportation network, business locations) is being used to describe the modelling approach or provide insight into the interpretation of results.

34. Figure 3: Change caption to “…compared to the influenza epidemic reported by the CDC in the same area for 2004-5”

35. Figure 4 and 6: Add to caption “…extension strategies for the seasonal (A) and pandemic (B) influenza”

36. Figure 5: Change caption to “…extension strategies for a seasonal influenza scenario (R0=1.4). The 50 x 50 m cell values indicate the estimated…”

37. Figure 7: Change caption to “…extension strategies for a pandemic influenza scenario (R0=2.0). The 50 x 50 m cell values indicate the estimated…”

38. Figure 5 and 7: Data interpretation would be easier by delineating the three zones (CBD, transition, suburbs). If this is done, Figure 1A becomes unnecessary. Also, define on the legend the density units (i.e., # of cases per unit area) and remove the <VALUE> text.

Major Compulsory Revisions

1. How sensitive are model outcomes to the number of businesses closed during
a weekend-extension strategy? The proportion of closures is a key assumption in the simulations. Therefore, the author needs to be transparent as to the proportion of closures used in the model and the sensitivity of this parameter.

2. The paper needs to include more information about model stochasticity and its implications for interpreting data. For example, are there any other sources of stochasticity in the model beyond the process of defining a successful transmission event? Also, in the Methods section it is necessary to define the sample size of simulations run per weekend-extension scenario, and justify whether or not this sample size is sufficient to capture outcome variation. The author uses the mean to summarise and compare the attack rates under the different scenarios, which fails to account for the variance in the data, as could be done by using the coefficient of variation. Alternatively, the author could calculate an effect size for each scenario, relative to the scenario with no-intervention, to quantify the effect of using an intervention, relative to the sample size of the simulations. Another potential approach is to calculate the averaged number of contacts for a typical individual. This average could be calculated relative to “weekend” and “weekday” activity and then multiple regression can be used to assess for the effects of the scenarios. Furthermore, accounting for model variation is necessary to appropriately interpret the “oscillations” noted by the author in the attack rates among the different scenarios, as can be done using spectral, Fournier or wavelet analysis. In essence, this paper’s descriptive interpretation of the results fails to account for how outcome variation may cloud the data interpretation.

3. The part in the “Simulation results and discussion” beginning with the sentence “To display the spatial dispersion of influenza...” describes methodology, so should be moved to the Methods section. Regarding these methods, the paper should include a rationale for interpolating disease intensity from data with a geographic resolution of 50 m x 50 m grid cells. Also, the paper should include an explanation for calculating this intensity over the entire 200 days of simulation – because, since the epidemic changes in intensity over time, can it also change spatially over time? For instance, does the 200-day intensity map differ from maps created at different time intervals during the epidemic (e.g. growth phase, peak, waning phase)? Furthermore, how sensitive is the spatial distribution of disease intensity to the seeding of influenza at random locations within the study area? These answers may not contribute to the point of this paper, but in the least, it is important to define the rational for using data accumulated over 200 days for mapping disease intensity.

4. The two-day continuous strategy is identical to the three-day discontinuous strategy except for lacking the Wednesday “weekend” day (i.e., the three-day discontinuous “nests” the 2-day continuous scenario within). The author should drop the comparison between the continuous and discontinuous at that 3-day level and refer to the 3-day discontinuous strategy as a blend of the continuous and discontinuous. Given that differentiation, the author should expand the discussion and conclusions to comment on this type of strategy.

5. The Conclusion section needs to be further developed to explain how the current study results compare to previous studies. For instance, Mao refers to
using the weekend-extension strategy in developing countries. Is there any literature available to discuss the implications of using this strategy in developing countries, or for commenting on whether this strategy has been tried in these areas? Also, a more in-depth discussion is needed about the mechanisms of disease transmission that are affected by the different weekend-extension scenarios, and the mechanisms causing higher disease intensity in the central business district; and then, discuss how these factors relate to findings from other studies. Overall, the conclusion section is not as well written as the rest of the paper, and does not leave the reader with strong impression of the contributions from this paper’s research.

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests