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Dear Editor Hailey Banack and Editor-in-Chief Timothy Lash,

We would like to submit the second revision to our article, “Unexpected Transmission Dynamics in a University Town: Lessons from COVID-19,'' again for publication in *Epidemiology*. After receiving helpful comments from both Reviewers, we have greatly refined our manuscript. In the first revision, we clarified the subpopulation sizes and how these values were estimated per Reviewer 1, and we also added an entire section to the Supplement, Appendix C: Model Diagnostics, in response to the concerns of Reviewer 2. In the second revision, we address the comments from Reviewer 2 in the detailed responses below.

We believe the two revisions have strengthened our manuscript and we still believe that our work will be of broad interest to the readership of *Epidemiology* because our results offer insights into the management of publish health regulations for higher education for future outbreaks of respiratory disease. We confirm that this work is original and has not been published, nor is it currently under consideration for publication elsewhere. We have no conflicts of interest to disclose. Please address all correspondence concerning this manuscript to erin.clancey@wsu.edu. Thank you for again considering our manuscript.

Sincerely,

Dr. Erin Clancey, on behalf of all authors

Reviewer #2 Comments and Responses:

Main comment: In my initial report, I pointed out that the assumptions made by the authors that the reproduction number was constant and close to 1 during the whole study period (i.e. including week 34) was inconsistent with the clear rise in cases observed between week 34 and week 35 and the authors' estimate of Rt over time with Rt much higher than 1 over this time period.

In this comment, Reviewer #2 is misrepresenting the assumptions of our model. We DO NOT assume that the reproductive number is constant and close to 1 during the whole study period. Explicitly, we estimate R0 for the total population and for each subpopulation. This is stated in lines 155-156, and the results from the estimation are shown in Figure 3 and Table 2. To help make this clearer, we have revised the text in lines 138-139 to explain that we calculate each R0 using the estimates of each transmission parameter and the subpopulation sizes.

In response to this comment, authors have now included the possibility of having imported cases on weeks 34-35. However, the small number of imported cases estimated for this period still does not allow to properly explain what is observed during weeks 34-35.

Per Reviewer 2’s request that we demonstrate that our model fits the data, in Appendix C.1 we now show that our model does indeed fit the data. The imported cases during weeks 34-35 do explain what we observe in the data. The additional cases increase the rate of transmission without creating susceptible depletion. This is described in more detail below.

Indeed:  
- In the data, we observe an important rise in cases between weeks 34 and week 35, from 75 cases on w34 to 275 on w35, so it's +200 cases in 1 week, and an increase by a factor x 3-4.  
- Two phenomena could explain such a rise:  
o a lot of local transmission (i.e. R>>1 and around 3-4);  
o or, a large number of imported cases on week 35.  
- However, none of these phenomena appears in the model since:  
o The model assumes that R is close to 1 throughout the epidemic;

Very importantly, the model makes NO ASSUMTIONS about R0. R0 is estimated.   
o Only 8 cases are estimated to be imported on week 35; so it is far from the +200 observed in the data.

The additional 8 cases estimated to be imported change the *rate* at which cases increase in the mass action term βSI. Notably, I increases without susceptible depletion because cases are imported.   
So, the model cannot currently describe the important rise observed between week 34 and week 35.

The Reviewer seems very focused on the number of cases but is not considering how the additional cases change the model dynamics (e.g. as the number of infected goes up the *rate*, βSI, goes up). Because of this increase in rate, the model can indeed explain the rise in cases.

Following one of my requests, authors now compare to data to simulated runs of their model in Supplementary Figure C1. However, again, I don't think that this indicates that the model can reproduce the important rise seen between w34 and w35. Current initialization settings of the algorithm allow very high numbers of cases on week 34 (i.e. up to more than 400) even though there were only 75 cases on week 34; and so, having simulations that start very high mean that some of them will get 300 cases on week 35. But it does not mean that the model can reproduce the important rise observed between week 34 and week 35.

Reviewer 2 claims that we initialize our model with “up to more than 400” cases. We initialize the model with exactly 103 cases in the student population and 2 cases in the community population. The calculations for the initial values are given in Table 1, and we have now added the number of case reports at initialization to the text in lines 137-138. We apologize, but we do not fully understand this comment.

In summary, I don't think that author's statement that R0 was close to 1 for the whole study period is supported by the current model if the study period includes w34 and w35. This statement also appears inconsistent with author's own estimates of Rt that is above 1 early one.

In lines 211-213, we explain that Rt estimates from EpiEstim are sensitive to imported cases and this would account for the differences in the two reproductive number estimates. Since arrival testing was not mandated at WSU, we did not have this data to add imported cases to the analysis with EpiEstim. The estimates of R0 from our epidemic process model and Bayesian estimation demonstrate that R0 was in fact near 1. In the next comment we explain the difference between R0 and Rt.

I note that it would be fine if authors were to describe "estimates of R close to 1 from w36". Alternatively, they could have a model with a different R on week 34-36 or estimate separately importations on w34 and w35 (if the observed rise is due to importations, it's likely most of them occurred on week 35 rather than 34).

It seems that Reviewer 2 is confusing R0 with Rt. R0, the basic reproductive number, is the expected number of cases generated by one case in a population where all individuals are susceptible to the pathogen. Equations (1) and (2) describe R0 (i.e. a pathogen spreading through a completely susceptible population). Notice we use the total population sizes to make this calculation. It would be incorrect to follow the Reviewer’s suggestion to simply say that R0 is close to 1 only after week 36. In contrast, Rt, estimated from EpiEstim, is the time-varying reproductive number and decreases as the number of susceptibles in the population are depleted.

We give explicit definitions of each of these parameters in the main text. In lines 94-95 we define the basic reproductive number and in lines 102-103 we define the time-varying reproductive number. We would like to note that these definitions have remained unchanged since the original version of the manuscript.

Other comments:  
- Authors compares simulated trajectories with the observed epidemic on Figure C1, and the observation falls in the range of the simulations. But I have questions about the way these simulations were done. In the simulations, the number of cases on week 34 can be between 0 and 500. I don't get why authors would start simulations assuming there could be so many cases on week 34 given that there were <100 cases on week 34. Authors should plot the average simulation curve so that we can understand the expectation (which presumably will be flat at about 200 cases for a few weeks).

We agree with the Reviewers that we can add more detail to clarify how we have performed these simulations. We have added these sentences to Appendix C1: “Specifically, we sampled the 3,125 rows making up the joint posterior without replacement to make 1,000 synthetic epidemics using our two-population ODE process model in Equation (A1) using the same initial values given in Table 1 in the main text. From each synthetic epidemic, we then used Equation (B1) to make negative binomial draws and generated the simulated case report time series data represented in Figure C1.”

To address the Reviewer’s concerns, the starting values are the same in every single simulation – 103 in the students and 2 in the community and these calculations are documented in Table 1. The reason there is so much variation in simulated case reports is because the variation from the Poisson draws in the Tau Leaping algorithm used to stochastically solve the system of ODEs is summed with the variation generated by the negative binomial distribution when we make random draws to simulate case counts. First author, EC, has verified this model behavior is normal via personal communication with Arron King, one of the developers of the pomp R package and professor at the University of Michigan.

- The fit should be shown in the main text and these discrepancies should be discussed.

We respectfully disagree. We believe that Figure C1 should remain in the Appendix as it is not part of the main results of the paper.

- "R0u was estimated to be significantly less than 1, and Rt estimates for the WSU students dropped to 1 quickly and remained near 1 for the duration of the fall semester". EpiEstim estimates show that it was >1 early on. Authors cannot just pick 1 of their 2 estimates. If the authors theory is that Rt was always close or below 1, it is strange to show the estimates of Rt that demonstrate the opposite. Authors seem to want to make the point that Rt was always close to 1 even on week 34-35; but estimates of Rt say the opposite.

Here again the Reviewer appears to be confusing R0 with Rt. In a comment above we explain the distinction and give line numbers where to find each definition in the main text. DEAL WITH THIS

- Notation k : When reading this article, most modeler may wrongly interpret parameter k as the measure of individual heterogeneity in infectiousness. Since this is not the case, my suggestion would just be to change the notation, i.e. replacing k with another letter.

Per the Review’s suggestion we have changed the notation “k”. We now use the same exact notation used in the paper King at al. 2016, which describes the method and the pomp package. We also now call the parameter the “size” parameter instead of the overdispersion parameter. These changes can be found in section B1 of the Appendix.

- Line 138: "To approximate the initial values for Ru0 and Rc". Please clarify what is meant by initial values. Is it the values at iteration 0 of the algorithm?

We are happy to clarify. We have made changes to line 138 and we have also added that “or values used at the first time point of the simulation” in line 135-136.

- Figure 2: good to indicate in the legend that Rt estimates are obtained with EpiEstim

We have added this to the legend of Figure 2.  
- Figure 2: It is confusing not to have the same scales for the epidemic curve (left hand side in weeks) and the estimates of R (right hand side in days) as it means we cannot compare the dynamics of Rt and of the epidemic curves. Authors need to ensure that we can compare the 2 for example putting Rt above the epidemic curve rather than on the side; and ensuring appropriate alignment between the 2.

In lines 106-112 we explicitly explain that EpiEstim can estimate daily Rt from weekly case reports. The fact that we present weekly case reports and daily Rt estimates precisely follows the analysis. We think this is clear and we would like to keep our figures consistent with the inputs and outputs of EpiEstim.   
- "sustained transmission of COVID-19 was likely very weak during fall 2020 in Pullman, WA". I'm sorry but I still don't understand what this sentence means. Transmission can be sustained (i.e. R>1). Transmission can also be "very weak" (R<<1). It's unclear what "very weak sustained transmission" means. Authors should clarify this statement (this was already a request in my previous report).