

Reviewers' comments:

Reviewer #1 (Remarks to the Author):

The authors extend their "MIR" epidemic model, already published in Nature Physics, to shed light on the interplay between population density and mobility in determining the spread of epidemics in cities. In particular, they claim that population density alone is not sufficient to determine the vulnerability of cities to epidemic spreading, and that non-pharmaceutical interventions should be tailored to a more detailed analysis that involves population flows between hotspots. The problem of finding "signatures" about many phenomena in cities with different characteristics is timely and very interesting in several fields of science and technology, and this paper surely advances the state of the art in this respect.

In general, I have found the paper well written and agreeable to read, and I would deem it already acceptable for publication. However, I have some comments for the authors that they may want to tackle in the discussion, or with additional analyses.

1. If I understood correctly, the authors consider cities as isolated entities, considering population flows only within cities and not between neighboring cities. Considering the wide extent of inter-city commuting, the authors may want to put in context this observation, considering if this could constitute a limitation of their study. Also, the hypothesis that people return to their patch at each time step may be restrictive, as the authors are discarding flows with longer time scales that may be present in cities, and more evidently, between cities. To what extent these considerations may constitute a limitation= Is there a way to include these aspects in an enhanced version of the paper?

2. To what extent the hypothesis of homogeneous mixing within each patch is restrictive? Several studies point out the limitations of homogeneous mixing in populations, the authors may want to consider this point of discussion and also shed some light on perspective improvements of their work along these directions.

3. With reference to points 1. and 2., the authors may want to check for example the model and results of <https://royalsocietypublishing.org/doi/full/10.1098/rsif.2020.0875>, which debates and try to consider observations in points 1 and 2.

4. The authors use a SIR model. An intense debate has been held in these months about the role of asymptomatic, yet contagious individuals. Considering these individuals may be crucial for the outcome of their model. This would make at least a SEIR model the most parsimonious selection to include this phenomenon. What is the authors opinion about this consideration? Would such a choice affect the epidemic threshold or the model outcome in general? How could this phenomenon be accounted for in the model?

5. The authors use the compartment R for the recovered individuals. Actually, according to the typical SIR dynamics, the compartment R contains both the recovered and the deceased individuals. Considering COVID19 dynamics and the goals of the study, I think the authors can still keep a single R compartment, clarifying that it contains both kinds of individuals, and adjusting the μ parameter accordingly, toward a comprehensive rate that may include both death and recovery rates.

6. The paper needs an accurate polish of typos and other little mistakes.

Reviewer #2 (Remarks to the Author):

In this manuscript, the authors investigate the joint role of population density and mobility in determining epidemic spread in cities. In particular, they focus on the epidemic threshold, computed in the context of a SIR metapopulation model with recurrent mobility, as a proxy for vulnerability. By comparing the epidemic threshold across a large collection of cities, the authors

show that cities with mobility fluxes that are more localised in high-density hotspots are generally more vulnerable to epidemics. In addition, they introduce a new aggregate quantity, κ , that nicely summarises this last result. Analysis of SARS-CoV-2 epidemic growth rates provides an interesting confirmation of author's predictions. Finally, the authors show how their theoretical insights could be leveraged to inform new policies that are less restrictive compared to blanket lockdowns, while retaining some degree of efficacy.

Overall, I think that this is an interesting paper that tackles a challenging question. Both theoretical investigations and data-analysis techniques appear appropriate and solid to me. I particularly appreciate the general character of some of the authors' main results, e.g. the information content vehiculated by κ in the context of epidemic spread. For these reasons, I believe that this journal would be a nice venue for this manuscript; however, I have a few remarks that I believe the authors should address before the manuscript is accepted for publication. Please find my comments below.

MAJOR COMMENTS

- I feel slightly confused by the interpretation of parameter p . According to the authors, p is the probability to travel, but in fact when $p > 0$ people may still stay in their home area (perhaps because they commute within the same area). At the same time, p is interpreted as a parameter interpolating between a static model and a model where people move according to the R matrix. However, these two interpretations seem to be quite different. My confusion might also have been exacerbated by the fact that the authors consider only the extreme cases $p = 0$ and $p = 1$. Why not considering a different parametrisation where p is the probability to move to a different patch (according to R_{ij} , $i \neq j$)?
- In addition to the previous comment, I am not entirely convinced by the ratio $\lambda_c(p = 1) / \lambda_c(p = 0)$ *removing* the effect of population density. Perhaps this is just a consequence of phrasing, but I find that the rationale behind this choice is only hinted in the paper and a more convincing argument should be given. At the same time, it is not clear to me which alternative comparisons should be made (e.g. homogenising population density across patches?). Also, what about intermediate values of p ? Is the relationship between vulnerability and p monotonic?
- As mentioned earlier, I found the information content vehiculated by κ quite interesting, particularly in the context of epidemic spread. The authors acknowledge that κ may not all complex features at play. While investigating these additional features would require a new manuscript, I believe it would be interesting for the authors to discuss what is "left out" by κ in terms of network structure (e.g. residual heterogeneity). Please see also my comment below, which I think is linked somewhat to this comment.
- The authors employ a null model where fluxes between hotspots are set to zero and the corresponding weights are re-assigned to remaining edges in order to preserve the total mobility volume. If I understand correctly, this reshuffling is performed by splitting the removed volume evenly across remaining edges, shifting them by some constant C . If this is the case, I am wondering whether this would be the most appropriate null model for the question at hand. My concern is that shifting the remaining weights by an additive constant affects the distribution of weights significantly. In my opinion, it would feel more natural to consider a more conservative null model in which the remaining weights are multiplied by some constant C' .

MINOR COMMENTS

- Why is the average population density computed as a simple average over cells' individual population densities?
- P.12 "experience a (???) something seems to be missing here.
- P.17 "to to".
- Multi-panel figures should have each panel labelled with letters as in the caption. Please fix this.
- I found Fig. 2B slightly confusing at first sight since the coloured background made me think of stacked histograms. I suggest the authors to make the distinction between histogram and background more net.
- I wonder if insets in Fig. 3 are really necessary. I think it is sufficient to show the correlation coefficients after removing NYC.

Reviewer #3 (Remarks to the Author):

In this paper, the authors develop a model based on real data to study how the mobility network of flows and the distribution of resident populations affect the epidemic spread. The results show that, in all the studied countries, the epidemic threshold decreases as the flow of individuals between hotspots increases. In addition, their results show that at the beginning of the COVID-19 outbreak, U.S. cities with higher flow between hotspots tend to have a higher growth rate in the number of infected cases. Finally, the authors study different strategies to halt the spread of the virus and find that reducing the flow from suburbs to hotspots is the most effective strategy to increase the epidemic threshold. Overall, the paper is well structured, and the results are relevant not only for the current COVID-19 pandemic but also for future diseases.

I only have a few questions/suggestions:

- 1) It is not clear how to compare Fig. 3 and 2. Please, include a figure showing λ_c vs. κ for the COVID model as in Fig. 2A.
- 2) In Fig. 2B and 2C, the authors find that the reshuffling process is detrimental for a small number of cities. Could you please provide the name of these cities, and their thresholds λ_c and λ_c^{MOD} in the supplementary information?

Note: All changes to the manuscript are marked in red.

Reviewer 1

The authors extend their "MIR" epidemic model, already published in Nature Physics, to shed light on the interplay between population density and mobility in determining the spread of epidemics in cities. In particular, they claim that population density alone is not sufficient to determine the vulnerability of cities to epidemic spreading, and that non-pharmaceutical interventions should be tailored to a more detailed analysis that involves population flows between hotspots. The problem of finding "signatures" about many phenomena in cities with different characteristics is timely and very interesting in several fields of science and technology, and this paper surely advances the state of the art in this respect.

In general, I have found the paper well written and agreeable to read, and I would deem it already acceptable for publication. However, I have some comments for the authors that they may want to tackle in the discussion, or with additional analyses.

RESPONSE: We thank the very positive evaluation of our work. We are happy that the referee finds our results timely and an advance of the state of the art in the field of network epidemiology applied to real systems, in this case cities. Below we answer the referee's comments and point out the changes that we have done to improve the manuscript.

1. If I understood correctly, the authors consider cities as isolated entities, considering population flows only within cities and not between neighboring cities. Considering the wide extent of inter-city commuting, the authors may want to put in context this observation, considering if this could constitute a limitation of their study. Also, the hypothesis that people return to their patch at each time step may be restrictive, as the authors are discarding flows with longer time scales that may be present in cities, and more evidently, between cities. To what extent these considerations may constitute a limitation= Is there a way to include these aspects in an enhanced version of the paper?

RESPONSE: The referee is correct pointing out the possible extensions of our study. Our study concentrates in intra city mobility and population density, with the aim of classifying different cities with respect to epidemic spreading within these cities. Certainly, a multi-scale approach that considers inter-cities flows is an important issue that should be addressed in the future when extending our formalism to regional or national scales.

Regarding the limitation of the kind of commuting trips duration, we restricted to the most simple assumption and focused our analysis on the impact of back-and-forth movements. We think that this scheme represents the minimal approach to model daily urban mobility and allows for incorporating readily mobility data from other sources such as those provided by census surveys.

Nevertheless, we made an attempt to incorporate the existence of different visiting times in reference [32], but it turned out to be very challenging. Including different trips duration poses an important computational problem: the residents in a given area are no longer statistically equivalent and the set of the equations, and therefore the size of the critical matrix, should be enlarged. In particular, while the complexity of the proposed formalism scales quadratically with the number of patches in the metapopulation, the formalism with tunable trips duration scales with the number of flows in the mobility matrices. This fact entails a much higher computational cost of the latter compared with the former, which becomes especially relevant when the spatial resolution of the mobility data is very refined.

At the light of these computational issues and given the general scope of the manuscript aimed at simplifying at most the structure of the metapopulation, we found keeping the back-and-forth mobility scheme the more balanced approach.

CHANGES: We have added a brief discussion on these two limitations in the concluding part of the manuscript to illustrate possible avenues for improving the analysis presented here. We have added new ref [66] to support the discussion.

2. To what extent the hypothesis of homogeneous mixing within each patch is restrictive? Several studies point out the limitations of homogeneous mixing in populations, the authors may want to consider this point of discussion and also shed some light on perspective improvements of their work along these directions.

RESPONSE: We agree that this limitation, which most (with few exceptions as noted in point 3) of metapopulations models have, is restrictive. In principle, one could extend the current formalism to a more realistic framework in which the heterogeneity in the interaction patterns is captured. However, in the same spirit as in point 1, we wanted to keep our analysis as doable as possible since, currently, we do not have access to accurate and homogeneous data about human interaction networks within patches for the broad spectra of cities covered in the work.

CHANGES: We have commented on this assumption in the concluding part of the manuscript.

3. With reference to points 1. and 2., the authors may want to check for example the model and results of <https://royalsocietypublishing.org/doi/full/10.1098/rsif.2020.0875>, which debates and try to consider observations in points 1 and 2.

RESPONSE: We thank the referee for pointing out this reference. In fact this article, together with Cota et al. [arxiv:2102.10614], are the few works that try to incorporate the heterogeneity of the interactions within patches in metapopulation frameworks. As noted above, this is a promising research avenue that will advance the field of network epidemiology in the near future.

CHANGES: We have added these two works with the discussion about the limitations of the homogeneous mixing hypothesis mentioned in point 2.

4. The authors use a SIR model. An intense debate has been held in these months about the role of asymptomatic, yet contagious individuals. Considering these individuals may be crucial for the outcome of their model. This would make at least a SEIR model the most parsimonious selection to include this phenomenon. What is the authors opinion about this consideration? Would such a choice affect the epidemic threshold or the model outcome in general? How could this phenomenon be accounted for in the model?

RESPONSE: The referee points out a very interesting point, that concerns the choice of the compartmental model. Although the SEIR could seem to better approach the existence of asymptomatic individuals, it is not. The Exposed compartment in SEIR, makes the agents not to infect others, while asymptomatic do infect. Then the best consideration we found is to assume that the compartment Infected in the SIR includes any agent with capability to infect. A better approach could be to consider a SAIR, susceptible-asymptomatic-infected-recovered compartmental model, however in the particular set up we are describing, this makes no difference at all in the critical properties and outcome of the model in any case. The reason is that the main factor controlling the critical properties of the model is mobility, and given the mobility of agents in our Infected compartment will account identically for the mobility of Asymptomatic agents, no difference in the outcome and critical properties are possible.

Nevertheless, more refined models distinguishing symptomatic and asymptomatic courses of a disease will be extremely useful to evaluate the response to particular epidemics. In fact, we addressed this issue in two formalisms tailored for Dengue and COVID-19 (Refs. 36 and 39 respectively) since asymptomatic infections play a relevant role in the propagation of these particular communicable diseases, while symptomatic cases are severe enough to make individuals stay at home (at best).

CHANGES: We have incorporated a brief discussion about the issue of asymptomatic and severe cases when dealing with the mobility of infectious agents highlighting the importance of incorporating this distinction for particular diseases.

5. *The authors use the compartment R for the recovered individuals. Actually, according to the typical SIR dynamics, the compartment R contains both the recovered and the deceased individuals. Considering COVID19 dynamics and the goals of the study, I think the authors can still keep a single R compartment, clarifying that it contains both kinds of individuals, and adjusting the μ parameter accordingly, toward a comprehensive rate that may include both death and recovery rates.*

RESPONSE: We agree with the referee that a more complex description of the clinical course of patients contracting COVID-19 is needed if one aims to reproduce the infection curves or retrieve the evolution of the fatalities in a given region. Having said this, we would like to stress that the manuscript does not aim at doing such a thing. Instead, here we seek those structural features of the underlying metapopulations which characterize how a given city is going to react upon the arrival of a given pathogen, which is fully-characterized by the value of the epidemic threshold. Note that this indicator is independent of the composition of the R compartment as long as the parameter μ is equivalent for all cities.

6. *The paper needs an accurate polish of typos and other little mistakes.*

RESPONSE: Thanks. We have revised the manuscript thoroughly, to correct typos and mistakes.

Reviewer 2

In this manuscript, the authors investigate the joint role of population density and mobility in determining epidemic spread in cities. In particular, they focus on the epidemic threshold, computed in the context of a SIR metapopulation model with recurrent mobility, as a proxy for vulnerability. By comparing the epidemic threshold across a large collection of cities, the authors show that cities with mobility fluxes that are more localised in high-density hotspots are generally more vulnerable to epidemics. In addition, they introduce a new aggregate quantity, kappa, that nicely summarises this last result. Analysis of SARS-CoV-2 epidemic growth rates provides an interesting confirmation of author's predictions. Finally, the authors show how their theoretical insights could be leveraged to inform new policies that are less restrictive compared to blanket lockdowns, while retaining some degree of efficacy.

Overall, I think that this is an interesting paper that tackles a challenging question. Both theoretical investigations and data-analysis techniques appear appropriate and solid to me. I particularly appreciate the general character of some of the authors' main results, e.g. the information content vehiculated by kappa in the context of epidemic spread. For these reasons, I believe that this journal would be a nice venue for this manuscript; however, I have a few remarks that I believe the authors should address before the manuscript is accepted for publication. Please find my comments below.

RESPONSE: We thank the referee for his/her very positive assessment on the validity and general applicability of our study to understand the unfolding epidemic scenarios in large cities. Below we answer all the points raised by the referee and comment on the changes made to the revised manuscript.

MAJOR COMMENTS

- I feel slightly confused by the interpretation of parameter p . According to the authors, p is the probability to travel, but in fact when $p > 0$ people may still stay in their home area (perhaps because they commute within the same area). At the same time, p is interpreted as a parameter interpolating between a static model and a model where people move according to the R matrix. However, these two interpretations seem to be quite different. My confusion might also have been exacerbated by the fact that the authors consider only the extreme cases $p = 0$ and $p = 1$. Why not considering a different parametrisation where p is the probability to move to a different patch (according to R_{ij} , $i \neq j$)?

RESPONSE: We thank the referee for pointing out this issue. One of the most typical problems that one faces when aggregating mobility data from fine to more coarse-grained scales is the existence of a large volume of trips remaining in the same geographical area where they originated. In mathematical terms, this implies that the resulting OD matrices contain self-loops, which force some individuals to stay inside the origin patch although moving, thus being indistinguishable (from the point of view of modeling) from the fraction $(1-p)$ of inhabitants of the patch that do not commute. Importantly, these self-loops are very heterogeneous across the different patches, for they depend on the characteristics of the aggregated flows.

The heterogeneities observed in the self-loops prevent us from adopting a parameterization as the one suggested by the referee without losing information about the real spatial distribution of agents. For this reason, we opted for leaving the mobility network as it is, containing the information about the heterogeneities in the different self-loops, and propose the global indicator $\$p\$$ which allows for determining the fraction of the population following their usual commuting patterns. Therefore, a scenario with $\$p=0\$$ always corresponds with the static case in which all the agents remain in their associated patch. In contrast, $\$p=1\$$ encodes the situation in which the population follows the commuting patterns contained in the OD matrix.

CHANGES: We have added a brief comment about the limit $\$p=1\$$ and the existence of self-loops in the mobility matrices.

*- In addition to the previous comment, I am not entirely convinced by the ratio $\lambda_c(p = 1) / \lambda_c(p = 0)$ *removing* the effect of population density. Perhaps this is just a consequence of phrasing, but I find that the rationale behind this choice is only hinted in the paper and a more convincing argument should be given. At the same time, it is not clear to me which alternative comparisons should be made (e.g. homogenising population density across patches?). Also, what about intermediate values of p ? Is the relationship between vulnerability and p monotonic?*

RESPONSE: We agree that the statement about the removal of the population density was wrong and misleading. The definition of the normalized threshold is made to have a quantitative indicator to highlight the role of the mobility network in determining the spread of diseases. This impact is indeed determined by how mobility shapes the underlying population density distribution, which is the fact that the normalized epidemic threshold aims at capturing. In this sense, unlike the unnormalized threshold, the dependence of the normalized epidemic threshold on the mobility is equal in two cities with the same OD matrices and density profiles, despite possible differences in the average population density in both cases.

Regarding the effect of homogenizing the population density, unfortunately the classification of patches as hotspots or suburbs does not allow us to account for the heterogeneities of the density profile within each class of patches, so no clear statements can be made about this intervention. Nonetheless, this fact has been widely explored in previous works (see e.g. ref. [28]) showing that the homogenization of the underlying population distribution hinders the beneficial effect of mobility.

Finally, we agree that it is insightful to represent how the epidemic threshold varies as increasing the mobility from $p=0$ to $p=1$. Having said this, the behavior of the epidemic threshold for intermediate p values is the outcome of a nontrivial combination of the two mechanisms at play in this work. Namely, the redistribution of individuals driven by mobility and the initial distribution of residents across the city. This outcome is highly influenced by the heterogeneities in terms of the densities of the hotspots, something which cannot be characterized with the approach proposed here. Given this complexity, we believe that analyzing the relationship of the parameter κ with some indicators, such as the position of the peak of the epidemic threshold, lies beyond the scope of this manuscript.

CHANGES: Following the referee's comments we have better motivated the need for introducing the normalized epidemic threshold in the revised version of the manuscript. Furthermore, we have included a new Figure in the Supplementary material (Fig. S6) classifying each of the studied cities as a function of the qualitative dependence of the epidemic threshold observed when increasing mobility.

- As mentioned earlier, I found the information content vehiculated by κ quite interesting, particularly in the context of epidemic spread. The authors acknowledge that κ may not all complex features at play. While investigating these additional features would require a new manuscript, I believe it would be interesting for the authors to discuss what is "left out" by κ in terms of network structure (e.g. residual heterogeneity). Please see also my comment below, which I think is linked somewhat to this comment.

RESPONSE: This is a very interesting point and, as the referee states, would deserve a new work to be addressed in detail. In our opinion one possible avenue is to use a more detailed ranking of hotspots (as the one provided in Ref. 47) in which different levels of hotspots are identified resulting in a hierarchical characterization of urban areas. This will be beyond the analysis provided here, since only the top level of hotspots is used to define parameter κ . Instead, with a hierarchical ranking composed of different levels one would explore more refined versions of κ to better capture the skeleton of human flows and its distribution connecting areas belonging to different levels. Furthermore, the inclusion of different hierarchies within suburbs would allow the formalism to better account for the density heterogeneities observed across the city.

CHANGES: As suggested by the referee we have briefly commented on this possible generalization of the parameter κ in the discussion.

- The authors employ a null model where fluxes between hotspots are set to zero and the corresponding weights are re-assigned to remaining edges in order to preserve the total mobility volume. If I understand correctly, this reshuffling is performed by splitting the removed volume evenly across remaining edges, shifting them by some constant C . If this is the case, I am wondering whether this would be the most appropriate null model for the question at hand. My concern is that shifting the remaining weights by an additive constant affects the distribution of weights significantly. In my opinion, it would feel more natural to consider a more conservative null model in which the remaining weights are multiplied by some constant C' .

RESPONSE: We thank this very interesting suggestion. Our proposal of adding evenly the removed inter-hotspot flows to the links connecting each hotspot to its neighboring suburbs is based on the absence of any preference regarding the new suburb destination for those hotspot's residents whose original (before the intervention) commuting trip has been forbidden.

Nevertheless, we find the proposal of the referee very interesting. Indeed, the random reallocation of those inter-hotspot flows removed among the links connecting with neighboring suburbs can (specially in the case of large κ , i.e. when the amount of flows between hotspots is much larger than the flows from

hotspots to suburbs) lead to the removal of the heterogeneities in the distribution of flows between hotspots and suburbs.

CHANGES: Following the suggestion of the referee we have replaced the former reshuffling approach by a new version of the reshuffling intervention preserving the heterogeneity. We do so by partitioning the removed flows from a hotspot to others preserving the original distribution. For instance, suppose that a hotspot is connected with another hotspot and two suburbs A and B (three neighbors in total) and the % of flows with these patches are 90%, 7% and 3% respectively. Then, after removing the flow towards the hotspot neighbor the partition of flows will be 0%, 70% and 30% respectively.

The results of this new implementation of the reshuffling intervention are shown in new Figures 2 and 4, being highly consistent with the results obtained for the previous null model.

MINOR COMMENTS

- *Why is the average population density computed as a simple average over cells' individual population densities?*

RESPONSE: We thank the referee for this valuable comment. We wanted to compute the average population density in the residential patch of one individual randomly chosen within the population. However, we are aware that this might not be the most conventional way of capturing the population density in our city, typically computed as the total population in the city divided by the total land area.

CHANGES: We have changed the expression for the average population density and remake Fig S3 accordingly.

- *P.12 "experience a (???) " something seems to be missing here.*

RESPONSE: Thank you for pointing out this typo, now it is corrected.

- *P.17 "to to".*

RESPONSE: Thanks again for pointing out this typo, now it is corrected.

- *Multi-panel figures should have each panel labelled with letters as in the caption. Please fix this.*

RESPONSE: We have redone the corresponding figures with labels as suggested.

- *I found Fig. 2B slightly confusing at first sight since the coloured background made me think of stacked histograms. I suggest the authors to make the distinction between histogram and background more net.*

RESPONSE: We totally agree with the referee that the background color is misleading since the plot appears, at first sight, as a phase diagram with three phases (being one of these regions the bars of the histogram). We have redone this panel to avoid any misunderstanding.

- *I wonder if insets in Fig. 3 are really necessary. I think it is sufficient to show the correlation coefficients after removing NYC.*

RESPONSE: We had the same idea (showing only the correlation coefficients without NYC and not the trend without this city) but we think that it is useful to keep the insets (since the free space in these plots allows us to do so) in order to better showcase the trend of the data without NYC.

Reviewer 3

In this paper, the authors develop a model based on real data to study how the mobility network of flows and the distribution of resident populations affect the epidemic spread. The results show that, in all the studied countries, the epidemic threshold decreases as the flow of individuals between hotspots increases. In addition, their results show that at the beginning of the COVID-19 outbreak, U.S. cities with higher flow between hotspots tend to have a higher growth rate in the number of infected cases. Finally, the authors study different strategies to halt the spread of the virus and find that reducing the flow from suburbs to hotspots is the most effective strategy to increase the epidemic threshold. Overall, the paper is well structured, and the results are relevant not only for the current COVID-19 pandemic but also for future diseases.

RESPONSE: We thank the referee for his/her very positive assessment on the validity and applicability of our study. Below we answer the points raised by the referee and comment on the changes made to the revised manuscript.

I only have a few questions/suggestions:

1) It is not clear how to compare Fig. 3 and 2. Please, include a figure showing λ_c vs. κ for the COVID model as in Fig. 2A.

RESPONSE: We thank the referee for this comment. We have realized that the motivation for changing the linear function governing the contacts to include a more realistic dependence was not properly illustrated in the previous version of the manuscript. Unfortunately, we cannot include the latter function for the rest of the countries, for infection data is required to calibrate its free parameter.

CHANGES: To address the comment raised by the referee, we have included a new Figure in the supplementary information, now Fig. S1, comparing the information represented in Figs. 2a) and 3a) by choosing either the linear function or the alternative and more realistic expression of the function relating the contacts to the density in each area. There we observe that the new function is able to better capture the cities' vulnerability to COVID-19 when preserving the inverse dependence of the epidemic threshold on the flow between hotspots.

2) In Fig. 2B and 2C, the authors find that the reshuffling process is detrimental for a small number of cities. Could you please provide the name of these cities, and their thresholds λ_c and λ_c^{MOD} in the supplementary information?

RESPONSE: Thank you for this suggestion. We agree that this information is interesting, since these few cities seem to be outliers of the whole set of cities analyzed.

CHANGES: We have followed the advice of the referee and added the list of these outlier cities together with the corresponding values of λ_c and λ_c^{MOD} in the supplementary information.

REVIEWERS' COMMENTS:

Reviewer #1 (Remarks to the Author):

The authors made an effort in adding more perspective and context the their work, toward better highlighting the aim of the submitted work, its context, strengths and limitations. I think that the paper is now in good shape and I deem it acceptable for publication.

Reviewer #2 (Remarks to the Author):

I am satisfied with the authors' replies.

Reviewer #3 (Remarks to the Author):

All my comments have been adequately addressed in the revised manuscript. I recommend this manuscript for publication in Communications Physics.