

SECTION 1

RESPONSES TO EDITORS AND REVIEWERS COMMENTS (6 FEBRUARY, 2021)

Editors comments

1. Please address the editors' comments in the 6 Jan decision letter to reframe/restructure the paper so that it is not focused on the GVP. In your response to the editors you note the reduced focus on the GVP but it is still mentioned at least 17 times in the paper. At the moment the messages hang off the GVP and not the other way around. We suggest the paper be restructured so that it makes a clear argument for and against a global surveillance system and what it might do in practice. The GVP can be one example within this.
2. The paper would benefit from a shorter introduction. Please see the attached as we have proposed some edits as a start with this.
3. Please keep the revised manuscript within the word count of 1800-2000 words.

Authors response

1. We have reframed/restructured the paper so that it does not focus on GVP. However, we have referenced the GVP in the context of its value in the context of the proposed viral surveillance network.
2. The paper has now a shorter introduction.
3. We have reduced the paper to just below 2000 words

Reviewers comments:

1. The authors talk about the power to “prevent, detect, and respond” after a global viral surveillance atlas is created. I don’t really know how that will work. We can document viruses in the wild, but we still have no clues why viruses emerge and begin transmitting in humans. Will the global atlas help that? The authors need to talk about what is possible specifically, and how an atlas would actually help.
2. Can the authors talk concretely about what a global surveillance network would actually take? How are we going to get multiplex diagnostics to these hotspots when we cannot even get malaria rapid diagnostic tests? I would love the authors to theorize on the operationalization of their envisioned surveillance network.

Authors response

1. In the revised article we have removed the reference to the power to “prevent, detect, and respond” after a global viral surveillance atlas is created. However, we have alluded to the fact that virus information generated from virus discovery projects (e.g. GVP) as well as the metadata provided from this research will contribute to generation of new diagnostic tools as well as improvement of the location of hot-spots in the field, and thus enable better targeting of the viral surveillance programmes in humans and domestic animals.
2. We agree that it is not possible to predict when novel viruses will emerge in humans and animals, and how they would behave once they made their jump. Precisely

because of this we propose a targeted, longitudinal viral surveillance system in humans and domestic animals that aims to detect new spillover events as and when they emerge.

3. We have briefly described the key elements of the envisioned viral surveillance system, and have also outlined some of the challenges, particularly in under-resourced hot spot regions where health capacities are poor.
4. We also state that the main target for viral surveillance will be humans and livestock in the hot spot regions of the world, precluding the need to conduct viral surveillance in every country in the world.
5. We have also proposed that the network will require political commitment from majority of the countries in the global south and north, a governance structure, and long-term financing mechanism, and accelerated efforts of strengthen existing global health capacities for its sustainability.
6. Given the global health, social and economic cost of pandemics, and likelihood of more to come, we state that there is an opportunity to rethink globally surveillance systems to prevent future pandemics.

Editors comments:

1. Provide a standfirst and key messages at the start of the paper. 1-2 sentences in italics to describe the articles central message. No more than 2-4 bullet points, to be included in the Abstract field.

Authors response:

Standfirst and key messages are:

1. COVID-19 has exposed the weaknesses in the existing global surveillance systems and overall health apparatus in their ability to detect early an emergent pathogen, and respond effectively to mitigate its impact.
2. Building on the existing surveillance systems and platform, establishment of a new, longitudinal viral surveillance systems in high risk areas at the interface of wild animals, humans and domestic animals. Such a system would focus on detecting detection of novel viruses in humans and domestic animals in hot-spot regional of the world, and enable the national and global health systems to disrupt their transmission before they manifest into significant outbreaks.
3. Such a system is envisioned to be coordinated through a global surveillance network to be managed and governed either under the aegis of the existing UN system, or a stand-alone body that be aligned with the UN system. Strong political commitment, sound governance structure and long-term financing mechanism will be necessary for its sustainability.
4. Dennis Carroll suggests that the ongoing COVID-19 provides an opportunity to initiate a high-level discussion to address how such a system can be established and operationalized.

SECTION 2

Comments from reviewers on the original submission and our responses in the context of the revised article:

Reviewer 1:

Reviewer comment:

1. This paper advocates the use of global viral surveillance networks for the prevention of future pandemics.

Although this is a valid suggestion, there are several comments to this paper:

Page 3, Line 49: That statement that most pandemic viruses have a zoonotic origin is true, but it should also be mentioned that the persistence of these viruses in animal reservoirs is far from being clear. We do not know the main reservoir species for many of these zoonotic viruses.

Authors response

We have removed the reference to persistence of viruses in animal reservoir.

Reviewer comment:

2, Page 5 Line 3: The statement that a multi-sector perspective is needed for future surveillance has already been stated in 2012 by the Worldbank and should be cited (World Bank, 2012. People, pathogens and our planet: Volume 2: The economics of one health. Report No. 69145-GLB, 50.).

An integrated surveillance system spanning from wildlife to domestic animals and humans is not new and has been published and should be cited: i.e. Paternoster, G., Babo Martins, S., Mattivi, A., Cagarelli, R., Angelini, P., Bellini, R., Santi, A., Galletti, G., Pupella, S., Marano, G., Copello, F., Rushton, J., Stark, K.D.C., Tamba, M., 2017. Economics of One Health: Costs and benefits of integrated West Nile virus surveillance in Emilia-Romagna. PLoS One 12, e0188156 or Zinsstag, J., Crump, L., Schelling, E., Hattendorf, J., Maidane, Y.O., Ali, K.O., Muhummed, A., Umer, A.A., Aliyi, F., Nooh, F., Abdikadir, M.I., Ali, S.M., Hartinger, S., Mausezahl, D., de White, M.B.G., Cordon-Rosales, C., Castillo, D.A., McCracken, J., Abakar, F., Cercamondi, C., Emmenegger, S., Maier, E., Karanja, S., Bolon, I., de Castaneda, R.R., Bonfoh, B., Tschopp, R., Probst-Hensch, N., Cisse, G., 2018. Climate change and One Health. FEMS microbiology letters 365.

Zinsstag, J., Utzinger, J., Probst-Hensch, N., Shan, L., Zhou, X.N., 2020. Towards integrated surveillance-response systems for the prevention of future pandemics. Infectious diseases of poverty 9, 140.

Reviewer comment:

We have included the above references in the latest submission.

3. Page 5 line 28: The citation of Jones uses superscript, while other citations are in brackets. The citations should be uniform.

Authors response

This was corrected in our last submission.

Reviewer comment:

4. Page 13, line 23: I disagree, consider the reference of Paternoster above for integrated West Nile Virus surveillance.

Authors response

We have now modified this sentence to acknowledge the presence of a multi-sectoral surveillance system in Italy for West Nile virus citing Paternoster et al, 2017.

Reviewer comment:

5. Page 15 Line 6: The authors should mention the International Health Regulations (IHR 2005) that more and more report on One Health surveillance.

Authors response

Agreed and the sentence modified appropriately mentioning IHR.

Reviewer comment:

6. General comment: We surely welcome support for integrated surveillance systems including wildlife, domestic animals and humans and an overall viral watchlist is useful. But this will not prevent zoonotic transmission if there is not a massive improvement of the biosecurity and humane standards of livestock production, transport and marketing worldwide. This has been stated already in 2005 in the framework of the H5N1 HPAI outbreak and should be cited (Zinsstag, J., Schelling, E., Wyss, K., Mahamat, M.B., 2005. Potential of cooperation between human and animal health to strengthen health systems. Lancet 366, 2142-2145).

Authors response

This reference has now been included in the last paragraph of the paper, and the sentence modified to reflect the importance of improvement in the livestock production systems including enhancement of biosecurity along the livestock value chains.

Reviewer 2

Reviewer comment:

The authors have written about the need for global viral surveillance. It's a timely topic, but I do think the authors need to tighten their arguments. They continually talk about predicting viral emergence, but provide zero evidence that it is even possible. (They also do not acknowledge in the paper that we are a long way from being able to predict viral emergence). Further, the article feels like it's been cut and pasted too many times. It doesn't have much flow, with lack of specifics in important places and too specific in others.

1. Throughout the paper the authors conflate infectious disease surveillance with the ability to predict which viruses emerge from the animal kingdom. Infectious disease surveillance is currently event based (page 13) and needs to be able to identify when something odd is happening that could lead to an epidemic or even pandemic. The global virome project, while commendable, may or may not lead to the ability to predict pathogen emergence. I am concerned that the authors are claiming that simply cataloguing and monitoring pathogens in the animal kingdom will somehow prevent the next pandemic. It can certainly help us create tools like the diagnostics mentioned in page 15, but until we are able to predict emergence or how a pathogen might spread after it emerges then it's simply a catalogue. It will be nice to name the pathogen raging in the pandemic, but in reality we won't know what pathogen it is until somebody sequences it, i.e. after event-based infectious disease surveillance has identified that something is wrong.

Authors response:

The paper does not claim that it is possible to predict viral emergence. However, the paper argues that with an improved, targeted, longitudinal viral surveillance in domestic animals and humans in high risk areas enhances the ability for the health sectors to detect viral spillover events early before it causes any harm. Once a spill over event is detected it is possible for the global community to put in place appropriate measures to restrict or stamp out the emergent pathogen thus preventing further expansion and transmission. It is suggested that the products of GVP such as a catalogue and partial molecular sequences of all the unknown zoonotic viruses that exist in wild life population, the metadata data generated, and the one health capacity developed, will contribute to implementing improved viral surveillance for early spillover events in domestic animals and humans in the pre-defined 'hot spot' regions.

Reviewer comment:

2. I recommend revising the second sentence in the first paragraph. We already have a good understanding of viral hotspot locations, as well as species that are particularly problematic. I also think we had great warning, with the virus's genome sequenced in 2019 before it spread widely. The ideas presented in this sentence need more nuance. I suggest the authors break this sentence down into two separate thoughts, one being how much more interconnected the global population is and the other being how new infectious diseases can emerge and spread.

Authors response:

In the third paragraph of the revised paper we have mentioned key drivers of disease emergence and spread with appropriate references (References numbers 1, 2 and 3). I

Reviewer comment:

3. In the second paragraph, first line I suggest changing “first pandemic” to “first emerging pathogen”.

Authors response:

We had revised the sentence to reflect this.

Reviewer comment:

4. In the second paragraph I suggest changing “All these epidemic and pandemic viruses jumped from wild animals”, to “All these emergent viruses jumped from transmission in non-human animals to transmission among humans”. Influenza particularly can emerge from domesticated animals, and camels likely served as a more important reservoir host than bats for MERS.

Authors response:

Modified as proposed.

Reviewer’s comment:

5. Second paragraph needs some change on “once they have made the inter-species jump...”. It’s not accurate that they tend to persist and evolve in the human systems. Most emergent pathogens actually don’t establish themselves for human transmission, including many the authors list in this paragraph. I suggest striking this sentence.

Authors response:

We have removed this sentence.

Reviewer comment:

6. On page four, the last paragraph the authors introduce the “upgrading of the health security apparatus”. Can the authors give a bit more introduction to this – what is the upgrading of the health security apparatus? It seems to me that it was a lot of talk about this, but we actually became worse with increasing nationalistic tendencies in the US and Europe.

Authors response:

We have given two references related to IHR and the Global Health Security Agenda that have contributed to upgrading of the health systems. However, the global health apparatus is far from adequate to deal with a pandemic like COVID-19 as has been aptly demonstrated.

Reviewer comment:

7. Beginning of page 5, the authors state that “Key is building a global surveillance system spanning... to identify geographic “hot spots”. Here the authors present this idea as if we don’t already know where these hotspots are. The authors need to revise this paragraph to present what is already known about viral emergency hot spots.

Authors response:

We have given two references (Jones et al, 2008 and Allen et al, 2017) in the paper that acknowledge the fact that geographic hot spots have been identified (see page 4 line1, and lines 12 to 15).

Reviewer comment:

8. Same paragraph as comment six, but last sentence. Current efforts in the US and Europe were largely ineffective, but Asia and Australia did amazingly well. I suggest striking this sentence, or at least revising so that it acknowledges that the current tools we have were highly effective when applied well.

Authors response:

This not relevant now as this thought is not expressed in the revised manuscript.

Reviewer comment:

9. Last paragraph on page six, beginning of page 7. The authors talk about the power to “prevent, detect, and respond” after a global viral surveillance atlas is created. I don’t really know how that will work. We can document viruses in the wild, but we still have no clues why viruses emerge and begin transmitting in humans. Will the global atlas help that? The authors need to talk about what is possible specifically, and how an atlas would actually help.

Authors response:

See our revised response in Section 1 above related to the new shortened revision of the manuscript.

Reviewer comment:

11. I enjoyed the section on GISRS. Can the authors maybe give more detail on how GISRS does or does not overlap with viral hotspots.

Authors response:

We had responded earlier saying that as far as we know the GISRS does not overlap with already identified viral hotspots.

Reviewer comment:

12. Last paragraph (page 16) the authors need to acknowledge domesticated animals’ role in pathogen emergence.

Authors response:

This was done in the last submission.