PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Policies to prevent zoonotic spillover: protocol for a systematic scoping review of evaluative evidence
AUTHORS	Clifford Astbury, Chloe; Lee, Kirsten M.; Aguiar, Raphael; Atique, Asma; Balolong, Marilen; Clarke, Janielle; Labonte, Ronald; Ruckert, Arne; Togño, Kathleen Chelsea; Viens, A.M.; Wiktorowicz, M; Yau, Amy; Penney, Tarra

VERSION 1 – REVIEW

REVIEWER	Warwick, Clifford Emergent Disease Foundation
REVIEW RETURNED	23-Nov-2021

GENERAL COMMENTS	Page 3, Line 1, title and throughout.
	The title seems a bit awkward, and could be reworded. Also, I think that some clarification is need on the use of the term 'spillover of zoonotic disease'. 'Spillover', in my mind usually refers to pathogens rather than disease; the pathogens spillover, disease results. Perhaps the authors can spell out how they use their term in their paper.
	Page 4, Line 3
	Zoonoses are not just from vertebrate animals, invertebrates are also involved.
	Page 4, Lines 4 - 5 Read: 'ecological, behavioural and socioeconomic change' Not all are issues of change, some are ongoing habits. Suggest reads through document out as: 'ecological, behavioural habits and socioeconomic change' Page 4, Line 23 Reads 'as the study' Suggest reads: 'Because the study' Page 6, Lines 53-56 Suggest add keeping of exotic pets Page 7, Lines 8-18 It may be worth mentioning here that vested interest stakeholders are often wrongly given weight or priority over objective independent scientific entities/experts, who really ought to be the primary advisors to government. Page 7, Lines 31-35 Bans are the gold standard regulatory measure set by governments globally. Overall, no means of control are more effective than bans. The argument that bans 'force trade underground' are frequently poorly, selectively or subjectively

	evidenced. There are many well evidenced examples of the effectiveness of bans on both regarding agricultural and wildlife trade and zoonotic implications. One can say that murder has been pushed underground because it is banned, but all that is lacking is stronger enforcement. Almost all zoonoses in history have arisen from legal markets. It is highly misleading to imply bans involved weaknesses. Page 8, Line 15 Reads: 'contract' Should read: 'contact'

REVIEWER	Bhaumik, Soumyadeep BioMedical Genomics Centre
REVIEW RETURNED	27-Dec-2021

GENERAL COMMENTS	The protocol of the scoping systematic review (ScR) is on a relevant topic of global health importance. It is a complex issue and as such the use of ScR as a starting point as the authors propose is apt. Authors might consider the following comments : 1. The introduction has Sub-headings. This is rather unusual and authors might focus on making one shorter and more coherent narrative in the introduction without any sub-headings. The issue of focussing on preventing EIDs might be better framed as "One Health Approach" instead of using terminology around preventive medicine. The transdisciplinary and multi-sectoral approach which One Health provides - a framework focussing on human, environmental and animal health with intersections therein. This would also operate at several levels - individual, community, sub-national, national, regional and global. The study should entierely be reframed using a One Health Approach(only a cursory mentions is there in (P8L26). This also extends to the objectives which talk about population health policies alone. This is quite a reductionist way of doing a scoping review on EID prevention policies. One additional objective that might be attained through a scoping review of this nature is to develop a logic model . This will be highly useful in conduct of future effectivness systematic reviews (Chapter 17: Intervention complexity - Cochrane Handbook) on individual policies. This is a complex domain and as such, a ScR is fit for this purpose. In the current form it says "population health policies" - which is presumably focussing on human health only and at population level. Working definitions and boundaries of the term "populaition health policies" and "evaluations" need to be provided. 2. The PICO framework is not suitable for this current ScR. Authors need to use other framework relevant to the review question to define eligibility. 3. It is grossly inadequate to search policy evaluations in electronic databases . Authors should handsearch websites of Ministries , international bodies and societies.This is mentioned as a limitation but is so major for this topic that it biases the data and makes the study relevant. 4. Data charting form might be moved to appendix. More elements to align with final research objectives is needed . This includes but is not limited to capturing theoretical framework for the evaluations, use of quantiative evaluations and logic models within, intervention complexity and implementation issues. 5. It is strongly recommended that authors involve patients and public to answer this policy focussed SR through and advisory commitee. Resource: https://www.invo.org.uk/wp-content/uploads/2012/10/INVOLVEPublicInvolvementSystematicReviews2012.pdf 6. Authors need to use PRISMA-ScR or the 2020 version of PRISMA 7. The search strategy is incorrect and basic elements like use of MeSh terms (controlled vocabulory) along with key words is not provided. As such involving an information retrieval specialist to develop a search strategy Without a working definition and typology of what constitutes" preventive health policy interventions" it is not possible to check for search strategy robustness and comprehensiveness either. Having that will make the ScR very robust and authors might consider developing one.

Reviewer: 1
Dr. Clifford Warwick, Emergent Disease Foundation

Comments to the Author:
bmjopen-2021-058437
Reviewer comments

I have read the manuscript and supplementary files. The protocol has merit, and I should like to suggest the following considerations:

Page 3, Line 1, title and throughout.

The title seems a bit awkward, and could be reworded. Also, I think that some clarification is need on the use of the term 'spillover of zoonotic disease'. 'Spillover', in my mind usually refers to pathogens rather than disease; the pathogens spillover, disease results. Perhaps the authors can spell out how they use their term in their paper.
Thank you for this comment. As the reviewer suggests, we define zoonotic spillover as the transmission of a pathogen from an animal to a human, and have updated the manuscript to use this language consistently throughout. We have changed the title to:

Policies to prevent zoonotic spillover: protocol for a systematic scoping review of evaluative evidence

Page 4, Line 3

Zoonoses are not just from vertebrate animals, invertebrates are also involved.
Thank you for this clarification. We have changed this to simply 'animals'.

Page 4, Lines 4 - 5
Read: 'ecological, behavioural and socioeconomic change'
Not all are issues of change, some are ongoing habits.
Suggest reads through document out as: 'ecological, behavioural habits and socioeconomic change'
Thank you for this suggestion. We have reworded throughout to 'behavioural practices and ecological and socioeconomic change'.

Page 4, Line 23
Reads 'as the study'
Suggest reads: 'Because the study'
We have made this change.

Page 6, Lines 53-56
Suggest add keeping of exotic pets
This has been added.

Page 7, Lines 8-18
It may be worth mentioning here that vested interest stakeholders are often wrongly given weight or priority over objective independent scientific entities/experts, who really ought to be the primary advisors to government.
We have added this statement:

However, we acknowledge that non-government actors, including vested interest stakeholders, can play a powerful role in shaping government decisions.

Page 7, Lines 31-35
Bans are the gold standard regulatory measure set by governments globally. Overall, no means of control are more effective than bans. The argument that bans 'force trade underground' are frequently poorly, selectively or subjectively evidenced. There are many well evidenced examples of the effectiveness of bans on both regarding agricultural and wildlife trade and zoonotic implications. One can say that murder has been pushed underground because it is banned, but all that is lacking is stronger enforcement. Almost all zoonoses in history have arisen from legal markets. It is highly misleading to imply bans involved weaknesses.
Thank you for outlining the state of the evidence on this topic. We have removed this example, leaving the remaining examples around how policies in this space can have unintended consequences.

Page 8, Line 15
Reads: 'contract'
Should read: 'contact'
We have corrected this error.

Reviewer: 2
Dr. Soumyadeep Bhaumik, BioMedical Genomics Centre

Comments to the Author:
The protocol of the scoping systematic review (ScR) is on a relevant topic of global health importance. It is a complex issue and as such the use of ScR as a starting point as the authors propose is apt. Authors might consider the following comments :
1. The introduction has Sub-headings. This is rather unusual and authors might focus on making one shorter and more coherent narrative in the introduction without any sub-headings. The issue of focussing on preventing EIDs might be better framed as "One Health Approach" instead of using terminology around preventive medicine. The transdisciplinary and multi-sectoral approach which One Health provides - a framework focussing on human, environmental and animal health with intersections therein. This would also operate at several levels - individual, community, sub-national, national, regional and global. The study should entirely be reframed using a One Health Approach(only a cursory mentions is there in (P8L26). This also extends to the objectives which talk about population health policies alone. This is quite a reductionist way of doing a scoping review on EID prevention policies. One additional objective that might be attained through a scoping review of this nature is to develop a logic model. This will be highly useful in conduct of future effectivness systematic reviews (Chapter 17: Intervention complexity - Cochrane Handbook) on individual policies. This is a complex domain and as such, a ScR is fit for this purpose. In the current form it says "population health policies" - which is presumably focussing on human health only and at population level. Working definitions and boundaries of the term "population health policies" and "evaluations" need to be provided.

Thank you for these helpful comments around the introduction section. We have revised the section headings to be more succinct to improve flow and better reflect the content and distinctiveness of each sub-section, however feel that they are an important part of helping the reader navigate a complex set of paragraphs. We have removed reference to preventive medicine, and put greater emphasis on One Health in framing our review. We also agree that 'population health policies' is not the best way to refer to the policies we are including, as these focus on health in both animal and human populations, as well as interactions between wildlife, livestock and human populations, which is well-framed by the One Health lens. We have revised our objectives to refer to policies targeting the

factors located along Plowright et al.'s spillover pathway (i.e. animal and human health and interactions).

Thanks also for the suggestion to develop a logic model as part of this review. The purpose of the review is to map aspects of the evaluative evidence base reflected in our research questions. One aspect of that will be to consider policy effectiveness, which may lend itself to summarizing using a logic model approach. Our initial scoping of evidence has suggested that there is a great deal of heterogeneity in the design and context of different policies. It is unclear at this stage whether a logic model would be a useful approach to summarize the evidence and therefore would prefer to not commit to the approach at the protocol stage. However if the results are amenable, we would consider this as an option for synthesising and presenting our review findings.

2. The PICO framework is not suitable for this current ScR. Authors need to use other framework relevant to the review question to define eligibility.
Thank you for this comment. In developing this review, we also considered other frameworks, such as the Population-Concept-Context framework frequently used in scoping reviews, and the SPIDER framework. However, these seemed less appropriate for the review objectives and framing. We have altered the manuscript to highlight how the search strategy was built around the core concepts in the review (spillover pathway, public policy, prevention and zoonotic pathogens) without reference to the PICO framework (p. 7 l.19-21). Supplementary file 1 demonstrates how specific terms used in the search strategy map onto these concepts, using an example search strategy, as well as including the full search strategies used in each of the databases.

3. It is grossly inadequate to search policy evaluations in electronic databases . Authors should handsearch websites of Ministries, international bodies and societies. This is mentioned as a limitation but is so major for this topic that it biases the data and makes the study relevant.
We recognise this as a key limitation in our study, however feel that to do ad hoc handsearching is likely to be inadequate in this space (the grey literature is vast and multi-lingual) and should be informed by the appropriate methodology for identifying and assessing grey literature (Adams et al. 2016). As with other evidence reviews and synthesis, the scope is a balance of answering a scientifically and practically useful question with reasonable boundaries. The proposed review is an area of evidence synthesis that has yet to be conducted and given the standard of evidence and systematic approach we are able to employ for peer-reviewed evidence, we feel it is important to start by answering our question using electronic databases while citing that limitation. To conduct a robust grey literature review in this domain would require a different search strategy and overall approach, and therefore is beyond the scope of this piece of work. We have made many design decisions that have ensured that this evidence based will be broad, not only in terms of types and level of policy evaluations, but also the global scope. For example we do not limit our included studies by language. We have recruited a multi-lingual research team to screen and analyse papers in different languages, and are prepared to translate articles where necessary. This process has been added to the protocol (p.8 l.22-24). While limiting to peer-review articles bounds our study, we feel it is an appropriate boundary given the focus of the review.

Adams, J., Hillier-Brown, F.C., Moore, H.J. et al. Searching and synthesising 'grey literature' and 'grey information' in public health: critical reflections on three case studies. Syst Rev 5, 164 (2016). https://doi.org/10.1186/s13643-016-0337-y

4. Data charting form might be moved to appendix. More elements to align with final research objectives is needed . This includes but is not limited to capturing theoretical framework for the evaluations, use of quantitative evaluations and logic models within, intervention complexity and implementation issues.

We have moved the data charting form to Supplementary file 2, and have added theoretical framework and logic models to our data charting form. We will additionally extract barriers and facilitators to policy implementation, where these are mentioned, when thematically analysing included evaluations. We already plan to extract whether the evaluation is an impact or process evaluation, and for impact evaluations we will extract outcome measures and quantitative change in the outcome measure.

5. It is strongly recommended that authors involve patients and public to answer this policy focussed SR through and advisory committee. Resource: https://www.invo.org.uk/wp-content/uploads/2012/10/INVOLVEPublicInvolvementSystematicReviews2012.pdf

Thank you for this comment. While we do not engage patients or the public in this review as the focus is on policy, systems and prevention of spillover events, we are engaging relevant policy level stakeholders. The scoping review is being undertaken as part of a larger project involving policy actors at both national and international levels as research team members, participants and knowledge users. Project-level insights from these stakeholders have informed the development of this protocol and will inform the interpretation and synthesis. We are also planning dissemination events and interactive workshops involving policy stakeholders, which findings from this review will feed into alongside other project findings. The patient and public involvement statement has been revised to reflect this (lines 10-15).

6. Authors need to use PRISMA-ScR or the 2020 version of PRISMA

Thank you for this comment. We will use PRISMA-ScR to guide reporting our full review manuscript. We have now specified this in the protocol (p. 8 l.22-24).

7. The search strategy is incorrect and basic elements like use of MeSh terms (controlled vocabulary) along with key words is not provided. As such involving an information retrieval specialist to develop a search strategy Without a working definition and typology of what constitutes" preventive health policy interventions" it is not possible to check for search strategy robustness and comprehensiveness either. Having that will make the ScR very robust and authors might consider developing one.

We believe this critique can be clarified. The included search strategy is for Scopus only, as an exemplar, which does not have controlled vocabulary. MeSH terms were used where this was an option (Medline). To clarify this in the manuscript, we have now included complete search strategies for all databases (see Supplementary File 1), in line with guidance from PRISMA-2020. We have provided additional detail in the methods section to explain how the search strategy was developed (p.7 l.25-27):

The search strategy was developed iteratively, informed by existing systematic reviews focused on related concepts (23,43–47) and known indicator papers meeting inclusion criteria.

VERSION 2 – REVIEW

REVIEWER	Warwick, Clifford
	Emergent Disease Foundation
REVIEW RETURNED	13-Mar-2022

GENERAL COMMENTS	This is a much improved text, and I have no further comments or suggestions.

REVIEWER	Bhaumik, Soumyadeep
	BioMedical Genomics Centre
REVIEW RETURNED	10-Mar-2022

GENERAL COMMENTS	The author has given some justifications to comments raised but some of these do not adequately address methodological concerns raised in the previous review. The authors have reworked the objectives based on comments. This is helpful to understand things.
	As mentioned the PICO framework is only useful for effectivness review which is objective 2 and 3. How will Objective 1 studies meet eligibility criteria? This needs some other framework.
	The author mentions that the purpose of the review is to map the evidence base reflected from research questions and mention consideration of policy effectiveness.(Objective 2 and 3) This is not possible without a logic model and the heterogeneity and difference in contexts (which authors mention as justification for not doing logic model) is in fact the very reason why logic model is required. It is a complex intervention. Authors should be ready to commit to answer the research questions and lay down appropriate methods for the same. Handsearching of websites in a systematic and thorough manner is not ad hoc and is essential for answering the question(Obj1). Policies (Obj1)are not published in peer-reviewed journals and searching for them in electronic databases is not helpful. This is not comparable to review of research evidence where searching peer-reviewed is standard. I think the key thing is the methods are focussed on Obj 2 and 3 only overall.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 2

Dr. Soumyadeep Bhaumik, BioMedical Genomics Centre

Comments to the Author:

The author has given some justifications to comments raised but some of these do not adequately address methodological concerns raised in the previous review. The authors have reworked the objectives based on comments. This is helpful to understand things.

As mentioned the PICO framework is only useful for effectiveness review which is objective 2 and 3. How will Objective 1 studies meet eligibility criteria? This needs some other framework.

Response:

Before explaining the framework (cited in the paper) which we used to bound the scoping review, we wanted to highlight something that may be causing confusion. Our review is focused on evaluative evidence. However, we are targeting an unknown range of potential policies that have been evaluated across a very wide domain (prevention of zoonotic spillover events). While there is some overlap with

more narrowly focused systematic reviews in terms of the type of evidence we are targeting, our scope and purpose are much broader. It is also important to point out that this broad research question makes the use of a scoping review methodology appropriate (which we explain further below). Therefore, we could have used PICO, as we were identifying evaluative evidence, however we would have needed to leave each of these characteristics open to the point of not being helpful. We therefore replaced this with a different approach based on the reviewer's initial suggestion. We also want to clarify that the objectives therefore should be interpreted within the context of the scoping review methodology: if we report the results of the evaluation (i.e. effectiveness, fidelity etc.), it is as one descriptive element of the evidence base. It is not the sole purpose of the review.

In order to determine whether studies meet eligibility criteria, we defined evaluations as being eligible for inclusion if they operationalise one of the stages of the spillover pathway – defined by Plowright and colleagues – as the main outcome of their evaluation, or as a key concept or variable for process evaluations. Where we previously referenced Plowright's work, we have now included a figure representing the spillover pathway to provide more emphasis as it represents the main conceptual framework guiding the scoping review (p.8 l.1-2):

Figure 1 Spillover pathway adapted from Plowright et al. (8,22)

We also included a more in-depth description of how we used this pathway in our data charting process (p.8 l. 22-26):

"Data charting focused on characteristics of the study, the policy and the evaluation. For each policy, this included identifying which determinant of zoonotic spillover situated along the spillover pathway was being targeted. For the purpose of this study, we used a model of the spillover pathway adapted from Plowright et al.'s work (8,22), in which we differentiated between wildlife and domesticated animals (Figure 1). This differentiation is important in the policy context, as the wildlife-domesticated animal interface is an important site for intervention, as well as the human-animal interface."

Comments to author:

The author mentions that the purpose of the review is to map the evidence base reflected from research questions and mention consideration of policy effectiveness.(Objective 2 and 3) This is not possible without a logic model and the heterogeneity and difference in contexts (which authors mention as justification for not doing logic model) is in fact the very reason why logic model is required. It is a complex intervention. Authors should be ready to commit to answer the research questions and lay down appropriate methods for the same.

Response:

We feel there might be a misunderstanding around the study methodology given the reviewer comments that logic models will allow us to examine heterogeneity in context, that they are essential for our review approach and that we are not following the appropriate methods. We want to emphasize that this review is a scoping review, and is following established methodology, which is cited extensively in the manuscript and justified given the body of evidence we are looking to examine. Scoping reviews are intended to cast a wide net - and for our study - to identify and

synthesize some essential elements of the existing literature base related to the evaluation of policies that have the potential to prevent zoonotic spillover. The purpose is not to aggregate the evidence base related to a single set of highly related policies that are heterogenous because of their populations or contexts, which would be better suited to a more traditional systematic review.

Given the breadth of policies that will span the spillover pathway, the heterogeneity we are contending with is in the types of evaluated policies themselves. A logic model is designed to allow one to describe a program or policy in detail, its activities, outputs and intended outcomes, to unpack pathways of influence, but not to synthesize policies designed around different mechanisms or outcomes, even if ultimately, they may contribute to the prevention of zoonotic spillover events. As we are not focused on a single set of policy evaluations, but on a range of evaluated policies, each policy within that evaluative evidence is likely to have its own underlying 'logic' and intended outcomes. It would be akin to an expectation that a logic model could help to summarize all policies that may prevent poverty which could span all behavioural, social, economic and environmental determinants. We could develop higher level theory for this, but at the level of a policy or program, this is less illuminating. This approach would therefore not provide clarity on policy effectiveness; it would cloud and overwhelm the purpose of our review – which is to map the breadth of types of policy evaluations and explore insights around policy instruments, unintended consequences and challenges related to implementation and evaluation.

Perhaps the reviewer is judging this review against best practice for traditional systematic reviews, where a single or similar set of intervention(s) or policy(s) are examined. In that case, we agree, a logic model could help to build program-level theory to support a better understanding for how that program or policy works. However, this is not a theory-driven review nor is it a traditional systemic review – it is a scoping review with a systematic search. If the reviewer wants to push back further, we encourage them to provide us with a much stronger case for the appropriateness of logic models to be used with our review purpose and method, and share specific examples as to how and why a logical model is essential in a scoping review context.

We have re-worded our objectives to more clearly reflect the scope of our review and our approach (p.6 l.18-21):

1. Identify evaluations of policies that target the determinants of zoonotic spillover included in the spillover pathway (8) (i.e. human and animal health and interactions);

2. Identify insights around policy success and failure, and unintended consequences of policy implementation; and

3. Describe approaches to evaluation and key barriers and facilitators to evaluating policies to reduce the risk of zoonotic spillover.

Comments to author:

Handsearching of websites in a systematic and thorough manner is not ad hoc and is essential for answering the question(Obj1). Policies (Obj1)are not published in peer-reviewed journals and searching for them in electronic databases is not helpful. This is not comparable to review of research evidence where searching peer-reviewed is standard.

Response:

Again, we feel there might be some misunderstanding with the focus of this review. Our scoping review is not intended to catalogue policies themselves; it is looking to examine the breadth of the evidence base related to a wide range of evaluated policies that are relevant to pandemic prevention, along the conceptual pathway we have articulated. We provided a well-considered response related to why we are hesitant to include a grey literature each as part of this scoping review, which is sound. Unfortunately, the reviewer has not provided us with a rebuttal addressing our concerns around the significant lack of consistency of evaluations in peer-review and non-peer reviewed journals, which creates significant challenges for coherent synthesis, nor have they addressed our concerns around the challenges in conducting a robust, replicable search to identify appropriate evaluations. However, we have proposed a middle ground, where we conduct directed hand searching where relevant policy evaluations are mostly likely to be found via relevant organizations, an accepted approach for searching grey literature (Adams et al. 2016).

We will hand search websites of organisations known to be operating in this space for public policy evaluations. Given our global scope, it is challenging to identify all of the public, private and civil society organisations operating at the national and sub-national level. In a parallel study being undertaken as part of this project, we have identified over 80 organisations working at the global level (defined as global, regional, or working across multiple countries) on the prevention and control of emerging zoonoses. We have selected 18 of these organisations as being most relevant to the research questions, focusing on central UN agencies and a purposive selection of organisations with a highly relevant focus, covering topics such as One Health, emerging zoonoses, and health in wild and domesticated animal populations. We will search these organisations' websites for publications (e.g. reports, conference proceedings) that meet our inclusion criteria of primary empirical evaluations of government policy. We have described this process in our manuscript (p.7 l.24-27):

"We also searched the websites of 18 organisations involved in the prevention of zoonotic spillover to identify relevant grey literature. See Supplementary File 1 for details of search strategy and websites searched."

We have also included the list of organisations whose websites we will search in Supplementary File 1:

List of organization websites searched for grey literature

1. World Organization for Animal Health (formerly OIE)

2. Food and Agriculture Organization

3. World Health Organization

4. Wildlife Disease Association

5. International Alliance against Health Risks in Wildlife Trade

6. United Nations Environment Program

7. United Nations Office for Drugs and Crime

8. Global Alliance for Rabies Control

9. EcoHealth Alliance

10. Network for EcoHealth and One Health

11. International Livestock Research Institute

12. Preventing Pandemics at the Source

13. World Veterinary Association

14. CITES

15. TRAFFIC

16. One Health Commission

17. World Wildlife Fund

18. World Trade Organization

Adams, J., Hillier-Brown, F.C., Moore, H.J. et al. Searching and synthesising 'grey literature' and 'grey information' in public health: critical reflections on three case studies. Syst Rev 5, 164 (2016). https://doi.org/10.1186/s13643-016-0337-y

Reviewer: 1

Dr. Clifford Warwick, Emergent Disease Foundation

Comments to the Author:

This is a much improved text, and I have no further comments or suggestions.

Thank you, we appreciate your comments on both versions of our manuscript.

Reviewer: 2

Competing interests of Reviewer: None

Reviewer: 1

Competing interests of Reviewer: None.