Elasticity and substitutability of food demand and emerging disease risk on livestock farms

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▶ **To cite this version:**

Alexis Delabouglise, Guillaume Fournié, Marisa Peyre, Nicolas Antoine-Moussiaux, Maciej Boni. Elasticity and substitutability of food demand and emerging disease risk on livestock farms. Royal Society Open Science, 2023, 10 (3), 10.1098/rsos.221304 . hal-04067339

HAL Id: hal-04067339
https://hal.inrae.fr/hal-04067339v1

Submitted on 25 Apr 2023

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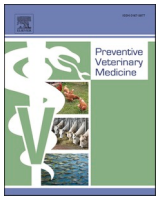
Preventive Veterinary Medicine 213 (2023) 105867

Contents lists available at ScienceDirect

Preventive Veterinary Medicine

journal homepage: www.elsevier.com/locate/prevetmed



Risk of rinderpest virus re-introduction 10-years post-eradication

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ARTICLE INFO

Keywords:
Risk assessment
Risk analysis
Eradication

1. Introduction

Rinderpest was a viral disease that affected cattle, domestic buffalo, and several wild ruminant species until its eradication, which was jointly declared by the Food and Agriculture Organization of the United Nations (FAO) and the World Organisation for Animal Health (WOAH) in 2011.

A risk assessment was conducted in 2012 (hereafter referred to as the 2012 study) (Fournié et al., 2014) to assess the risk of rinderpest virus re-introduction post-eradication, specifically to estimate the probability of at least one host becoming infected and infectious with rinderpest virus outside a laboratory anywhere in the world within a one-year period. The probability was estimated to range from 'Negligible' to 'High', with a median of 'Very Low'. Over the past ten years, thanks to the coordinated efforts of the FAO, WOAH, and member countries, to destroy rinderpest virus-containing material (RVCM) or to transfer these materials to designated rinderpest holding facilities (RHFs), the number of laboratories identified as holding RVCM has reduced from 44 in 2011 (Fournié et al., 2013) to 14 in 2021 (Budke et al., 2022). It is therefore timely to re-evaluate the risk of rinderpest virus re-introduction to assess progress and inform future risk mitigation efforts.

2. Methods

For this study (hereafter referred to as the 2022 study), the same semi-quantitative risk assessment model as in the 2012 study was used, with only the model input parameters being modified: the number of laboratories holding different types of RVCM and the conditional probabilities of pathway steps. The risk assessment model is described in Fournié et al. (2014). Briefly, the risk was defined as the probability of at least one susceptible host becoming infected and infectious with rinderpest virus outside of a laboratory anywhere in the world within a ten-year period. We considered the following risk pathways: 1) deliberate use of virus held in laboratories, 2) accidental use of virus held in laboratories, 3) deliberate use of vaccine, 4) accidental use of vaccine, 5) anti-animal biological warfare and 6) exposure to an environmental source (Fig. 1). Each pathway consisted of a series of inter-dependent steps, with their associated risk being obtained by combining the conditional probability of each pathway step occurring. The overall risk estimate was obtained by combining the probabilities π_i of at least one host becoming infectious through pathway i as follows: $1 - \prod_i (1 - \pi_i)^y$, with y being the considered time period in years.

In the 2012 study, step probabilities were assessed by expert opinion elicitation. We conducted another expert consultation in March-May

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https://doi.org/10.1016/j.prevetmed.2023.105867
Received 2 September 2022; Received in revised form 11 January 2023; Accepted 29 January 2023
Available online 31 January 2023
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2022, to reassess the conditional probabilities associated with selected steps. We focused on 1) steps where a change was likely because their occurrence was influenced by human behaviour, 2) steps that were influential for the overall risk estimate based on sensitivity analysis in the 2012 study, and 3) steps that depended on the number of laboratories holding RVCM. The probabilities associated with other steps were assumed to remain the same as in the 2012 study. Four experts assessed the abovementioned laboratory- and vaccine-related pathways, and two of them also assessed the anti-animal biological warfare pathway, as they had relevant expertise on this topic. All four experts had knowledge and expertise in virology and/or transboundary and emerging animal diseases. Two of them had extensive experience in rinderpest diagnostics and were members of the FAO-OIE Rinderpest Joint Advisory Committee, and one of them participated in the expert opinion elicitation in the 2012 study. Note that none of the step probabilities associated with the risk of rinderpest re-introduction through environmental sources were re-assessed, the resulting risk was therefore unchanged, ranging from "Negligible" to "Extremely Low" with the median being "Negligible" (see Table 1 for the interpretation of risk categories). This pathway is not described below but was taken into account in the computation of the overall risk estimate.

First, experts were asked to independently select a single risk category for each selected step (i.e. the probability of an event occurring in a one-year period), and a single uncertainty category (Tables 1 and S1). They were provided with the description of those steps, the estimates generated in the 2012 study, and information about the laboratories identified as holding RVCM in 2021 (Budke et al., 2022), including their country, RHF category, biosafety level and the RVCM type they held. The results from all experts were collated, and steps for which there was a diversity of opinion were identified, specifically those for which risk estimates spanned more than two risk categories. A virtual meeting was then organised during which the experts were given the opportunity to discuss and justify their estimates for the identified steps, after which a poll was conducted, and each expert was asked to re-estimate the step probabilities. This poll was conducted simultaneously and anonymously for all experts, and the results were recorded. The probability associated with each pathway step could thus be described by a single probability category if the experts all selected the same category, or by a set of

Table 1
Probability categories and their associated numerical range.

Category	Numerical range	Interpretation	
Negligible	$[0;10^{-9}]$	Event is so rare that its probability cannot be differentiated from zero, and in practical terms can be ignored	Close to 0
Extremely Low	$]10^{-9};10^{-4}]$	Event is extremely rare but cannot be excluded	Occurs less often than 1 in 10,000 (10^{-4})
Very Low	$]10^{-4};10^{-2}]$	Event is very rare	Occurs between 1 in 10,000 (10^{-4}) and 1 in 100 (10^{-2})
Low	$]10^{-2};10^{-1}]$	Event is rare	Occurs more often than 1 in 100 (10^{-2}) up to 1 in 10
Moderate	]0.1;0.5]	Event occurs sometimes	Occurs more often than 1 in 10 up to 5 times out of 10
High	]0.5;0.8]	Event occurs often	Occurs more often than 5 times out of 10 up to 8 times out of 10
Very High	]0.8;1]	Event occurs almost always	Occurs more often than 8 times out of 10

The qualitative categories are adapted from (EFSA Panel on Animal Health and Welfare, 2006), and the numerical ranges are as defined in Fournié et al. (2014).

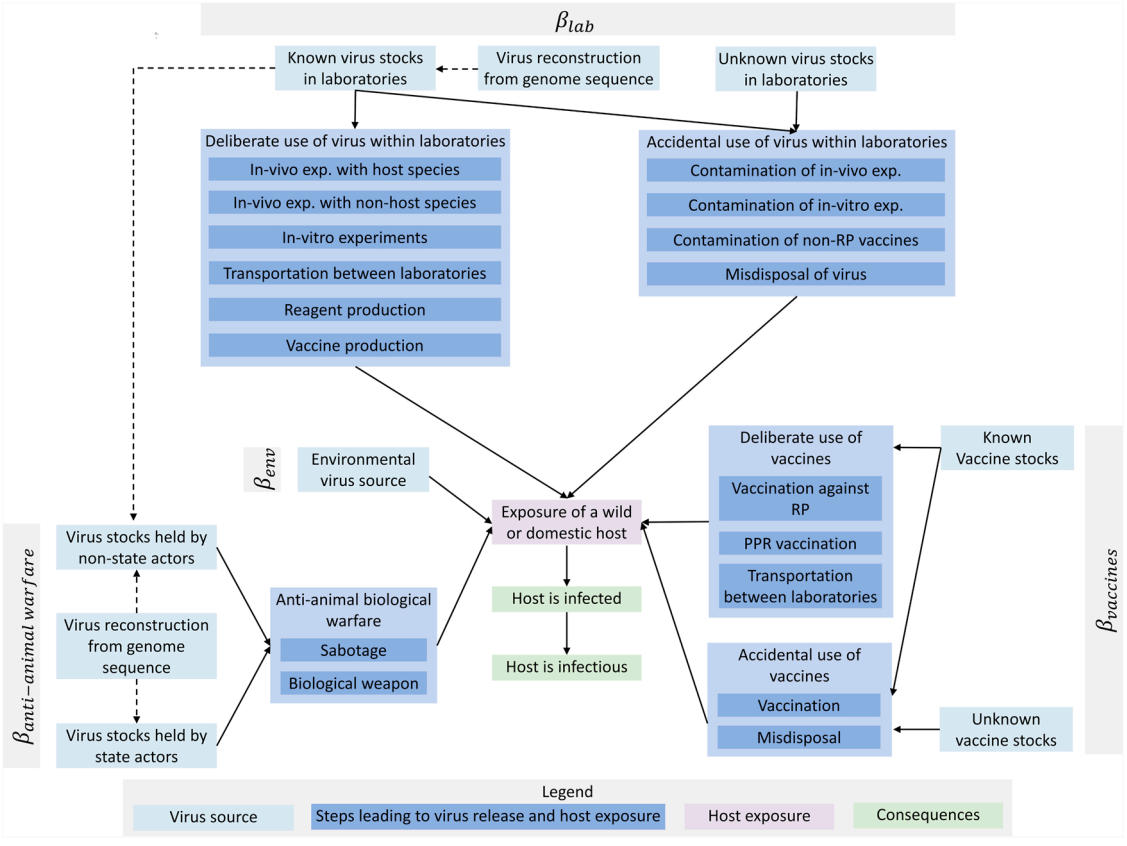

Fig. 1. Rinderpest virus sources and risk pathways (Fournié et al., 2014). Dotted arrows: creation of new virus sources

probability categories if they differed in their selection.

The types of RVCM held in each laboratory, and under what conditions, was assessed through a review of progress with rinderpest sequestration and destruction over the past 10 years (Budke et al., 2022). There was a reduction in holdings for all types of virus stocks since 2011 (Table 2). The number of laboratories holding field strains and diagnostic samples halved. The number of laboratories holding attenuated strains and repositories holding vaccines decreased by about 3-fold. This reduction was more pronounced for biosafety level-2 (BSL-2) facilities than for BSL-3 and BSL-4 facilities.

Ten-year risk estimates were assessed for each pathway, according to the virus type—laboratory-attenuated or field virus—and according to some other factors recognised as influencing probabilities associated with some risk pathway steps, such as laboratory biosafety level (low: BSL-2, high: BSL-3 or 4) and geographical location by continent. As in the 2012 study, scenarios involving low-and high-biosafety laboratories (1 or 5 labs) deliberately using virus stocks for different purpose (in-vivo and in-vitro experiments, vaccine production) over different periods of time (1–20 years) were explored. Similarly, scenarios involving accidental uses of laboratory virus stocks were explored assuming different time periods (1–20 years) and sequestration conditions: 1) the number of virus stocks is as reported; 2) destroying all field strains held in low-biosafety laboratories; 3) destroying all viruses held in low-biosafety laboratories; 4) upgrading these laboratories from low to high-biosafety; 5) only 5 laboratories hold virus stocks; and 6) only 1 laboratory holds virus stocks. Finally, for each risk pathway, the uncertainty was equal to the maximum uncertainty estimate among the individual steps of the pathway.

3. Results

3.1. Overall estimate

The overall risk of rinderpest virus re-introduction over a ten-year period for all pathways combined was estimated to range from “Very Low” to “Moderate” with a median risk of “Low” (Fig. 2A) (see Table 1 for the interpretation of risk categories), indicating that the median risk was unchanged from the 2012 study, but the maximum risk reduced from “Very High” to “Moderate”. Assuming that other conditions remained the same during a given time period (i.e., step probabilities, type and number of virus sources), the maximum risk estimates increased to “High” for longer periods of 15 and 20 years, but the median risk estimates did not change (Fig. 2A).

3.2. Individual pathway estimates

While the median overall risk estimate remained the same, risk estimates for individual pathways showed different patterns for the 2012 and 2022 studies (Fig. 2B). The uncertainty associated with each risk pathway was “High”.

Table 2
Number of laboratories holding virus and the number of repositories holding vaccines. The number of laboratories and repositories used in the 2012 study are shown in brackets.

Types of virus stocks	Laboratories/vaccine repositories		
	Low-biosafety BSL-2	High-biosafety BSL-3, 4	Total
Laboratory-attenuated strains (excluding vaccines)	4 (25)	11 (24)	15 (49)
Vaccine seeds	4 (18)	7 (17)	11 (35)
Reagents seeds	2 (8)	5 (10)	7 (18)
Field strains	1 (6)	7 (10)	8 (16)
Diagnostic samples	1 (5)	3 (5)	4 (10)
Vaccines	-	-	7 (25)

3.2.1. Deliberate use of virus

The maximum estimate of the 10-year risk of rinderpest re-introduction through deliberate use of laboratory virus stocks decreased from “Low” in the 2012 study, to “Very Low” in the 2022 study (Fig. 2B). The median risk estimate remained unchanged at “Extremely Low”. Most probabilities associated with laboratories deliberately engaging in experiments involving rinderpest viruses were estimated to be lower in the 2022 study than in the 2012 study. Only the transportation of viruses between laboratories, and the production of vaccines (including the subsequent inoculation of non-host species), were assessed to be more likely to occur in the 2022 than in the 2012 expert elicitation. This reflected the expected relocation of some virus stocks, and the ongoing production of vaccine to maintain contingency stocks. In relation to the deliberate use of virus for experiments, different scenarios were explored with different numbers of laboratories and time periods (Fig. 3), but the 2012 and 2022 risk estimates remained unchanged, except for vaccine production in low biosecurity laboratories, for which the maximum risk decreased for most scenarios from “Very Low” to “Extremely Low”, or from “Low” to “Very Low”.

3.2.2. Accidental use of virus

The median estimate of the risk of rinderpest re-introduction through accidental use of laboratory virus stocks over a 10-year period decreased from “Low” in the 2012 study, to “Very Low” in the 2022 study, and the maximum risk estimate decreased from “High” to “Moderate” (Fig. 2B). These reductions were partly explained by the experts estimating the probability that unknown virus stocks were viable to be lower in 2022 compared with 2012. If only virus stocks known to laboratory staff were considered, the median risks were similar between the 2012 and 2022 studies (Scenario 1 in Fig. 4). Destroying all field strains held in low-biosafety laboratories (Scenario 2) was enough to reduce the median risk estimate to “Extremely Low”, even for a 20-year period. However, even allowing only one (Scenario 6) high-biosafety laboratory to hold virus stocks could not reduce the maximum risk estimate below “Very Low” for periods of 5–20 years (Fig. 4).

3.2.3. Deliberate use of vaccine stocks

In the 2012 study, the 10-year risk of rinderpest re-introduction through deliberate use of vaccine stocks ranged from “Negligible” to “Very High” with a median of “Very Low”, while in the 2022 study, the range reduced to “Negligible” to “Low” and the median decreased to “Extremely Low”. This was because the experts considered that the use of vaccines in the field for routine rinderpest vaccination or against peste des petits ruminants was less likely in 2022 than in 2012.

3.2.4. Accidental use of vaccine stocks

In contrast, the 2012 and 2022 median risk estimates associated with the accidental use of vaccine stocks did not change, but the maximum estimate decreased from “Moderate” to “Low”. If the number of vaccine repositories is reduced from seven to five or less, the associated risk estimate ranged from “Negligible” to “Very Low”, with a median of “Extremely Low” for all investigated time periods of 1–20 years (Fig. S1).

3.2.5. Anti-animal biological warfare

The anti-animal biological warfare pathway was the only pathway for which the risk estimate increased between 2012 and 2022 (Fig. 2). The median risk estimate increased from “Extremely Low” to “Low”, and the maximum risk increased from “Very Low” to “Moderate”. This was due to the clandestine use of rinderpest virus by state actors for acts of sabotage being considered by experts to be more likely to occur in 2022 than in 2012, which was likely influenced by the international events over the ten-year period and at the time the expert elicitation was conducted (May 2022).

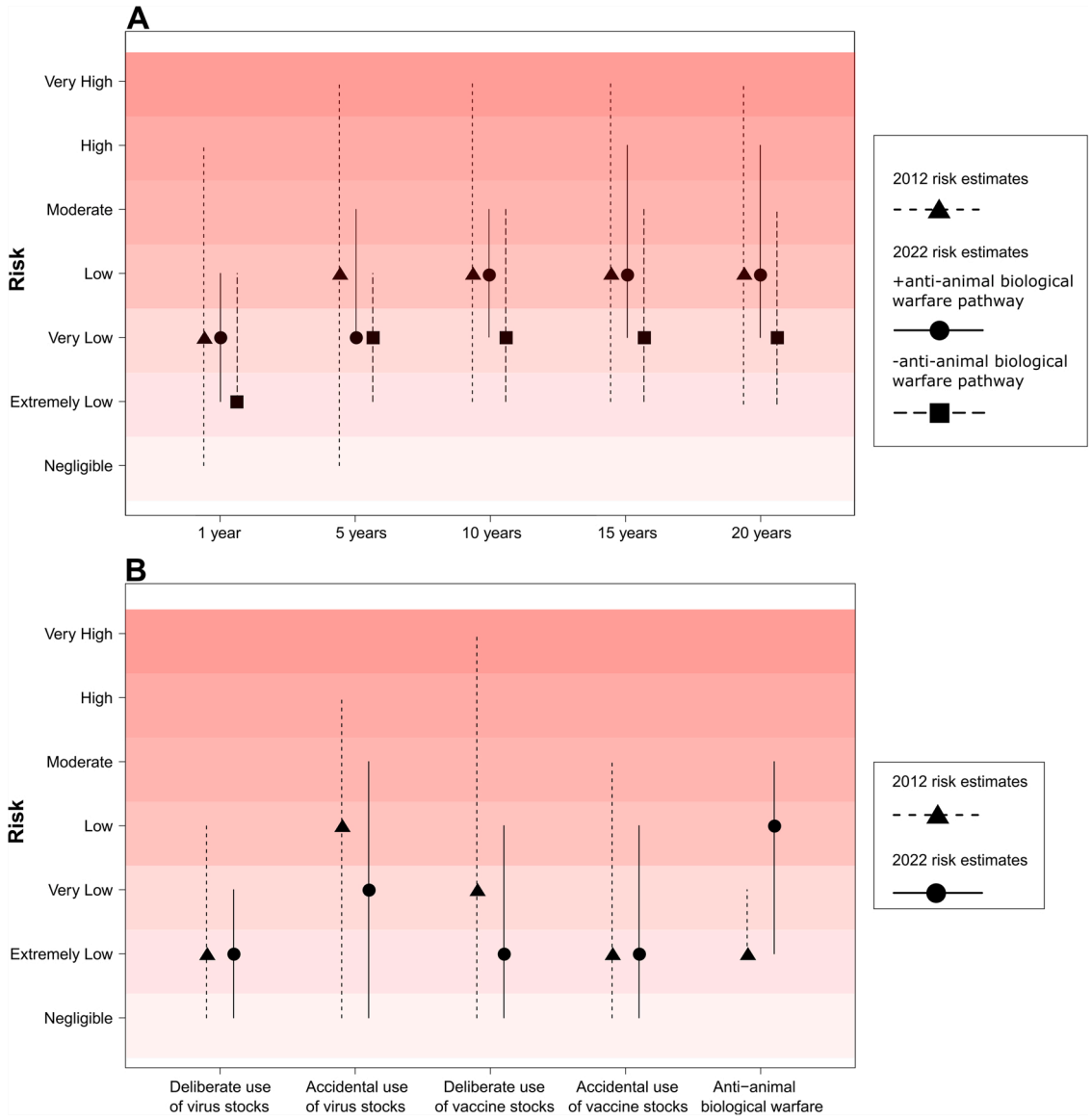

Fig. 2. The risk of rinderpest re-introduction. The overall risk is presented for different time periods (A), and the 10-year risk is split by pathways (B); for (A), time periods of 1 year, 5 years, 10 years, 15 years and 20 years were explored; the median, minimum and maximum risk estimates are shown for the 2012 (triangle and dashed line) and 2022 studies, when including (circle and solid line) or not the anti-animal biological warfare pathway for the latter (square and dashed line).

3.2.6. Effect of individual pathways on the overall risk estimate

The accidental use of laboratory virus stocks and deliberate use of vaccine stocks were the main contributors to the overall risk variability in the 2012 study, whereas the anti-animal biological warfare pathway had the most influence on the 2022 risk estimate. If this pathway is excluded from the model, the median overall risk estimate reduced from "Low" to "Very Low", with the maximum risk showing a decreasing pattern under scenarios assuming different time periods (Fig. 2A).

4. Discussion

Over the past ten years, the number of laboratories identified as holding RVCM has decreased, especially the number of low biosecurity laboratories, and the likelihood of deliberately using virus and vaccine stocks has also reduced. These factors have contributed to a reduction in the risk of rinderpest re-introduction, as estimated by this study. Our analysis suggests that continued efforts to limit the number of laboratories holding RVCM and requiring those that do hold RVCM to be high biosecurity, would be expected to decrease further the risk associated with accidental use of viruses. Such efforts would also reduce the likelihood of the rinderpest virus being used experimentally for research and teaching purposes.

However, it should be noted that although the viability of unknown virus stocks was expected to have decreased over the past ten years, some laboratories could still unknowingly hold viable rinderpest viruses, such as unlabelled or mislabelled virus stocks or diagnostic samples collected for another purpose that are infected with rinderpest virus. In addition, rinderpest virus may be also held at establishments without the knowledge of national veterinary authorities, and it is therefore difficult for these authorities to ensure that all stocks are destroyed or transferred to designated RHFs. Furthermore, rinderpest viruses could be re-created using publicly available genetic sequences.

The increase in the estimated risk associated with anti-animal biological warfare reflects how external events could influence the risk of rinderpest re-introduction. While it is important to maintain emergency preparedness, the production of contingency vaccine stocks requires the manipulation of attenuated virus and efficacy testing, which also contributes to the risk of re-introduction. Continuing to coordinate the

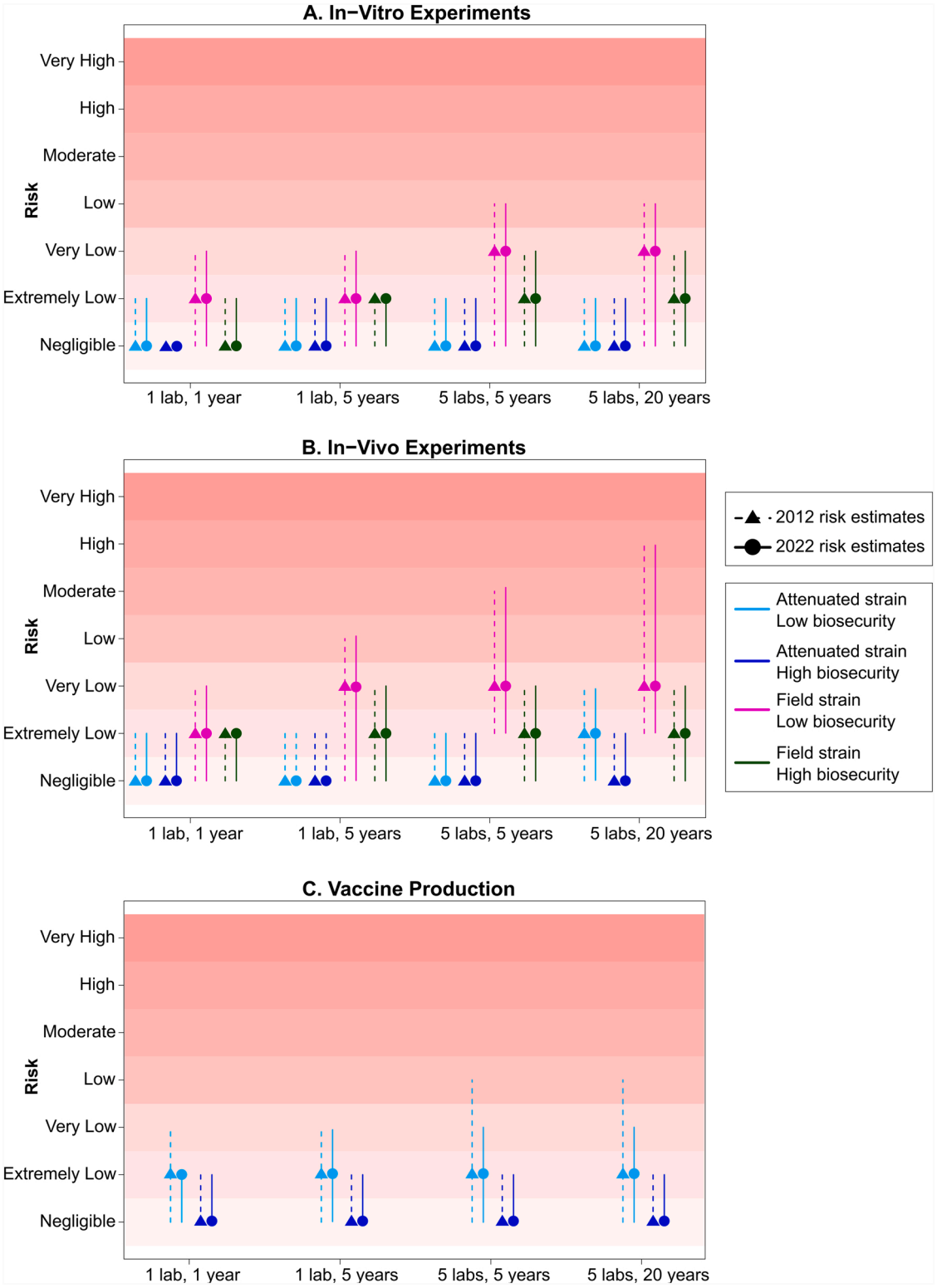

Fig. 3. Risk of rinderpest re-introduction through various scenarios involving deliberate uses of laboratory virus stocks. The median, minimum and maximum risk estimates are shown for the 2012 (triangle and dashed line) and 2022 studies (circle and solid line).

production and management of vaccines and diagnostic capacity at the international level will limit the number of production units and repositories and hence the associated risk.

Similar to the 2012 study, several limitations should be noted for the 2022 study. The elicitation was conducted with a small number of experts. It was similar to the number of experts assessing each pathway in the 2012 study. Involving more experts might have resulted in a more diverse set of probability categories being selected for each pathway step, and therefore in wider ranges for the estimated risk. As the step probabilities estimated in 2012 were considered as our baseline, these were provided to experts. However, it should be noted that such prior knowledge could have biased the estimation towards no or small

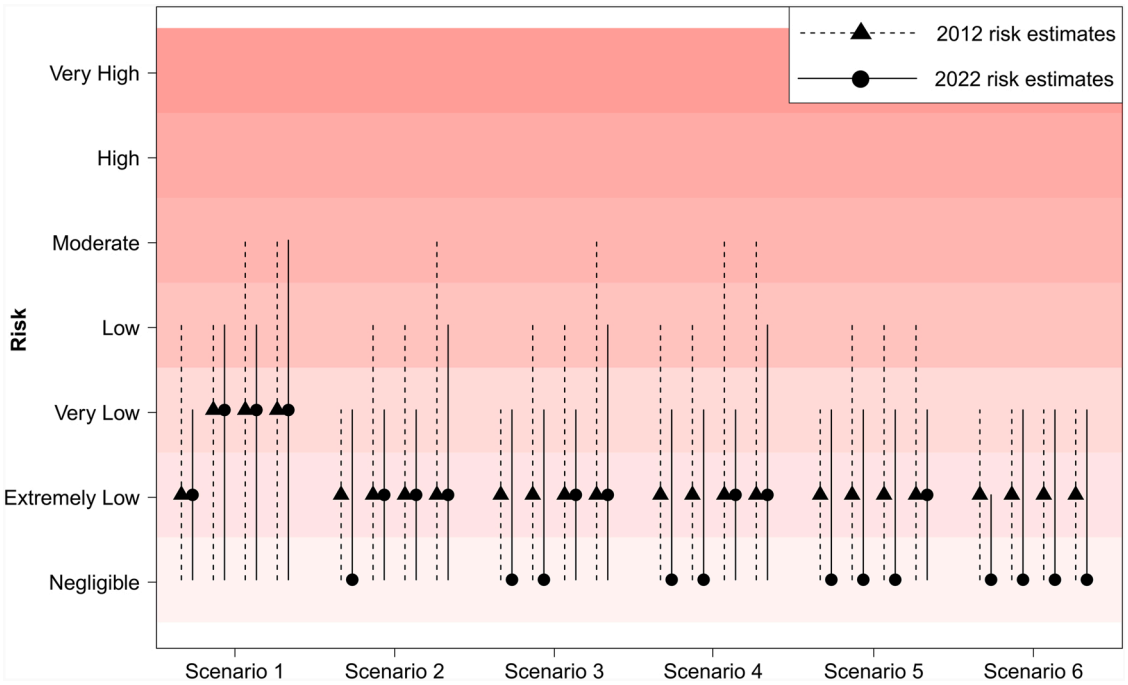

Fig. 4. Risk of rinderpest re-introduction through various scenarios involving accidental uses of laboratory virus stocks. Four time periods – 1 year, 5 years, 10 years and 20 years – were explored and are shown for each scenario; only the accidental use of virus stocks recognized as such by laboratory staff was considered; the median, minimum and maximum risk estimates are shown for the 2012 (triangle and dashed line) and 2022 (circle and solid line) studies; Scenario 1: the number of virus stocks is as reported in Table 1; Scenario 2: destroying all field strains held in low-biosafety laboratories; Scenario 3: destroying all viruses held in low-biosafety laboratories; Scenario 4: upgrading these laboratories from low to high-biosafety; Scenario 5: only 5 laboratories hold virus stocks; Scenario 6: only 1 laboratory holds virus stocks.

changes in step probabilities. Most pathway steps are rare events with little data available, so expert opinion elicitation is prone to systematic error, for instance the over-reporting of rare events in the media potentially resulting in the overestimation of some step probabilities, and, consequently, of the overall risk of rinderpest re-introduction (Burgman et al., 2012; van der Meer et al., 2019). The influence of human behavior on the occurrence of many steps further increased the difficulty in estimating associated probabilities. As mentioned above, risk estimates were based on the assumption that present conditions remained unchanged over the time periods considered. Given that the model was sensitive to expert estimates for several pathway steps (Fournié et al., 2014), expert opinion elicitation should be repeated to revise risk estimates if further information about the likelihood of the occurrence of some pathway steps becomes available, or if this likelihood is expected to have changed over time for many pathway steps, as was observed between the 2012 and 2022 studies.

5. Conclusion

In conclusion, the risk of rinderpest re-introduction was estimated to have decreased compared to the previous estimation in 2012 but still had a high uncertainty. This risk could be further reduced by continuing the efforts to relocate and destroy virus stocks, to limit their use, and to restrict the production and storage of vaccine stocks. However, even with such measures, the maximum risk is unlikely to become negligible, so ensuring commensurate response preparedness remains important.

Acknowledgements

This work was commissioned by the World Organisation for Animal Health through a grant from the United States Department of Defense, Defense Threat Reduction Agency. The content of the information does not necessarily reflect the position or the policy of the Federal Government of the United States, and no official endorsement should be inferred. The views expressed in this publication are those of the authors and do not necessarily reflect the views or policies of the World Organisation for Animal Health.

We would like to express our gratitude to the experts involved in this work, namely Michael Baron, Alfonso Clavijo, Genevieve Libeau, and Barbara Martin, and also contributions from Vincent Michaud. We also thank Emma Snary for reviewing the manuscript before submission. Finally, the authors thank the members of the Rinderpest Holding Facility Network and other laboratories interviewed during this process and recognise the contribution of the Food and Agriculture Organization of the United Nations.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.prevetmed.2023.105867.

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