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¹University of Calgary, Calgary, Canada

²Department of Zoology, Govt. Post Graduate College Bannu, Khyber Pakhtunkhwa, Pakistan

Correspondence to: Muhammad Asim Khan, asimshoraim@gmail.com

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A Systematic Review of Zoonotic Pathogens and the Risk of Future Pandemics: The Focus Areas, Potential Threats, and Global Readiness

Muhammad Asim Khan¹ and Abid Ur-Rehman²

ABSTRACT

Zoonotic diseases are a real potential danger to populations and are especially dangerous due to the possibility of future epidemics due to cross-species transmission. As a systematic review, this article offers an understanding of zoonotic pathogens with high pandemic potential, vulnerable areas affected by zoonotic spillovers, and worldwide preparedness for future zoonoses. A systematic electronic search in PubMed, Scopus, Web of Science, and Cochrane Library databases yielded 410 articles published from 2000 to 2023; 60 articles were selected for further analysis. Zoonotic diseases with their pathogens that are connected with the disease state and animals include Nipah virus, *Leptospira*, and coronaviruses. There are four primary transmissions: possible contact with wild animals, live wildlife markets, and contaminated water. Research shows that countries in Southeast Asia, sub-Saharan Africa, and Latin America are most at risk of epidemic spillovers. Although some progress has been made and the global health community is better prepared to cope with pandemics and epidemics, weaknesses remain: for example, surveillance and requisite healthcare systems in low- and middle-income countries. That is why this review underlines the need for global cooperation, improved diagnostics of zoonotic diseases, and more effective application of prevention measures to decrease the probabilities of future pandemic risks.

Keywords: Zoonotic pathogens, Cross-species transmission, One Health approach, Wildlife markets, Pandemic preparedness

Background

Zoonotic diseases are infectious diseases that occur and are transmitted between humans and animals, and are a major source of concern in the field of human health. The rise in zoonotic diseases and the global connectedness of humans and animals have led to fears regarding possible future epidemics shortly. Recent endemics such as HIV/AIDS, SARS, and COVID-19 are some of the serious zoonosis diseases that are causing effects to the world. Zoonotic diseases can be transmitted through different environmental and socioeconomic changes and climate variability. Deforestation and urbanization that extend into natural habitats bring humans and animals closer, which raises the possibility of zoonotic spillover.¹ Also, the processes of concentrating animal farming and globalization have led to the globalization of zoonotic pathogens such as bird flu and others.² Another area that has emerged to be vulnerable to disease has been enhanced by the effect of climate change,

which has influenced the behavior and habitation of vectors, including the diseases caused by mosquitoes, as detailed by Parham et al.³

A major difficulty in managing zoonotic pathogens is the large number of pathogens and the varied ways they spread. Zoonotic diseases that include mosquito- and tick-borne illnesses are hard to manage because the vector, host, and environment are interrelated.⁴ In addition, zoonotic diseases can occur through direct contact with animals, through contaminated food chains, and through reverse zoonosis, whereby people infect the animals.⁴ The versatility of the transmission modes makes it difficult for health officials to contain the spread of the virus.

The world is unprepared to cope with zoonotic pathogens, and COVID-19 has uncovered the weaknesses in global health systems, detection, and response systems. Even now, there are still many locales globally, classed as low- and middle-income areas with poor access to resources and medical facilities, and animals that continue to spread zoonotic diseases.⁵

That is why the One Health concept of human-animal-ecosystem interconnectedness has become increasingly popular as a conceptual model for combating zoonosis threats. This approach supports combined monitoring and control measures that are connected with representatives of the public health service, veterinary medicine, and ecology.⁶ Future pandemics due to zoonotically transmitted pathogens will, therefore, be shaped by those changes in ecological systems, climate, and human behavior.⁶

Methodology

Search Strategy

A systematic approach was used to search for the literature of the studies. The following databases were searched: non-governmental reports, 250 articles were retrieved from PubMed, 100 from Scopus, 50 from Cochrane Library, and 10 from other sources. Altogether, 410 records were found about OPKO Health, Inc.

The terms were selected to investigate zoonotic pathogens, spillover threats, and pandemic readiness. The search incorporated Boolean operators, MeSH terms, and free text words “zoonotic pathogens,” “zoonotic spillover,” “emerging infectious diseases,” “pandemics,” “spillover risks,” and “global preparedness.”⁷ The search also focused on specific zoonotic pathogens such as coronavirus, influenza, rabies, Nipah virus, Ebola, and so on. The search included articles that were published from January 2000 to May 2023 without any locality confinement.⁸

The overall search process was managed based on the PRISMA guideline to enhance the articles' transparency and replicability.⁸ The flow of the search process is illustrated in Figure 1.

PRISMA Flow Diagram

Types of Criteria Used in Research

Studies Inclusion Criteria

Specifically, those who deal with zoonotic pathogens, or zoonotic spillover possibility.

The data covers emerging infectious diseases with a perspective of pandemics.

Investigations on response measures, One Health, bans on wildlife markets, and monitoring systems.

Scientific articles published in peer-reviewed journals and reports from governmental and international or non-governmental organizations.

Exclusion Criteria

Any books or any other form of publication not affiliated with zoonotic pathogens or pandemics. The source contains articles without English abstracts and full text by name.⁸

Literature before the year 2000. Considering that new information is being produced on an almost

daily basis in the field of business and its different disciplines, the state of knowledge up till the beginning of the year 2000 is sufficient for this article. The work has been done in compliance with the PRISMA criteria.⁹

Excluding those that matched the code in the other column, 360 records were available for screening. Literature that was not longevity relevant or written in a language other than English was not considered, and this screened the study down to 180 records. Moreover, the article is also in compliance with the AMSTAR 2 guidelines.¹⁰

Data Extraction

Out of the 180 empirically related records identified, 100 of the relevant records were full-text articles. Study characteristics derived from the articles encompassed the author, year of publication, study type, regional fluctuations, zoonotic organisms of interest, preparedness for spillover, and preparation around the globe.¹¹ The data extraction form included study characteristics and was refined and pretested on a subset of the included studies (Table 2).¹¹

Quality Assessment

The quality of the included studies was evaluated according to the Cochrane risk-of-bias tool where only RCTs were used and evaluated based on random sequence generation, allocation concealment, blinding techniques, and selective reporting bias.¹¹ For observational studies, the Newcastle-Ottawa Scale was used for evaluating selection, comparability, and outcome, for which 40 full-text articles were considered eligible. However, after reading the articles, they were excluded due to high-risk bias, lack of sufficient data, or wrong topics (Table 1).

Data Synthesis and Analysis

The evaluation was performed on 60 articles that passed all the research inclusion criteria. Given the diversity of the studies eliciting very different structures and results, a narrative synthesis was made.¹¹ The articles analyzed were divided based on zoonotic spillover patterns, new pathogens with pandemic potential, and preparedness measures worldwide.¹¹

Data were further subdivided based on the geographic region, the zoonotic pathogen, and the type of intervention employed.¹² Because of that, a more detailed qualitative analysis of the results was provided.

Ethical Considerations

As this article does not entail the actual collection of primary data, it was not deemed necessary for approval from an ethics committee. The studies incorporated in this article complied with the ethical standards for human and animal participants researching it. Human or animal research made sure that the right approvals from the ethics committee were sought and consent was sought appropriately (Tables 1–5).¹²

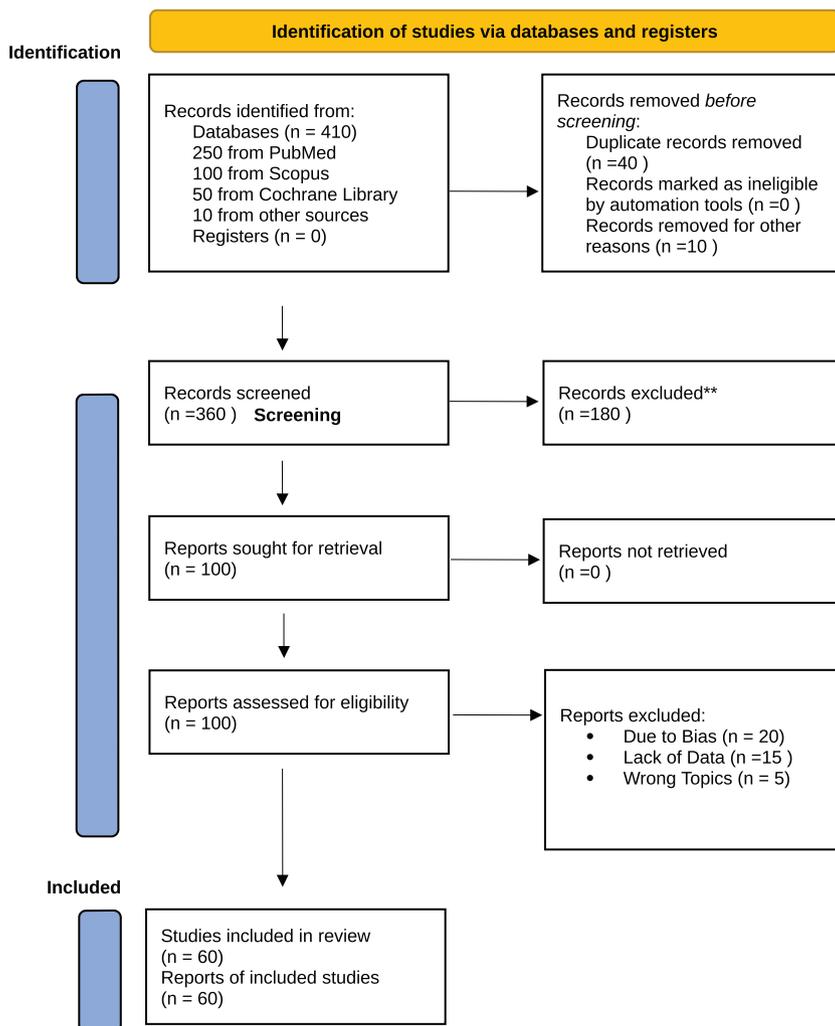


Fig 1 | Prisma flow diagram: Identification of studies via databases and registers

Table 1 | Quality assessment of included studies

Study Reference	Study Design	Bias Assessment Tool	Risk of Bias Level	Notes
(1)	Systematic Review	Newcastle-Ottawa Scale	Low	Relevant to African zoonoses
(4)	Case Study	Cochrane Risk of Bias	High	Focuses on viral drug resistance
(7)	Scoping Review	Cochrane Risk of Bias	Moderate	Evaluates policies for zoonotic spillover
(11)	Review	Newcastle-Ottawa Scale	Low	Focus on wildlife diseases
(14)	Policy Review	Newcastle-Ottawa Scale	Low	Governance in pandemic prevention
(17)	Observational	Cochrane Risk of Bias	Low	Global trends in zoonotic diseases
(23)	Review	Newcastle-Ottawa Scale	Moderate	Pandemic prevention strategies
(33)	Experimental Study	Cochrane Risk of Bias	High	Human-to-human transmissibility
(39)	Historical Review	Newcastle-Ottawa Scale	Low	Focus on origins of major infectious diseases

Table 2 | Data extraction summary of key findings

Study Reference	Zoonotic Pathogen Focus	Geographic Focus	Spillover Pathway	Global Preparedness Findings
(1)	Bacterial Zoonoses	Africa	Wildlife-human contact	Limited surveillance in rural areas
(4)	Human Cytomegalovirus	Iran	Drug resistance in viral pathogens	Insufficient hospital-based surveillance
(7)	Multiple Pathogens	Global	Wildlife trade	Need for better policy enforcement
(11)	Emerging Infectious Diseases	Global	Habitat destruction, wildlife trade	Major gaps in biodiversity conservation efforts
(14)	Various Zoonotic Pathogens	Global	Illegal wildlife trade	Global governance initiatives lacking
(17)	Multiple Zoonoses	Global	Varies by pathogen	Highlighted rising threat of zoonoses
(23)	Emerging Pathogens	Global	Wildlife-human interface	Pandemic prevention strategies not fully operational
(33)	Coronaviruses, Influenza	Global	Human-to-human transmission	Need for early detection systems
(39)	Various Zoonotic Pathogens	Global	Historical analysis of pandemics	Highlighted the interconnected nature of zoonotic spillovers

Results

List of Reviewed Research Articles in Order of Appearance

In all, a total of 60 studies were summarized in this systematic review, with each study offering lessons into zoonotic pathogens and their future pandemic possibilities. The studies involved different parts of the globe with more focus on Africa, Asia, and Latin America.¹³ A larger number of publications reviewed most of the viral and bacterial zoonoses as opposed to parasitic and fungal zoonoses.¹⁴ With regard to their transmission mode and possible gaps in the existing strategies.¹⁴

Table 3 extends the focus beyond the outcomes of the 60 included studies by providing a more comprehensive analysis of the geographic distribution, pathogens, pathways for spillover, and identified gaps.¹⁵

Understanding Zoonotic Diseases, Key Zoonotic Pathogens and Its Spillover Mechanisms

The studies mentioned several zoonotic pathogens that are likely to cause future pandemics, including the Nipah virus, *Leptospira*, and different types of coronavirus.¹⁶ In Southeast Asia, the spillover pathogen that was frequently transmitted was from the aspect of the illicit wildlife trade, which largely delighted itself in wildlife markets, accompanied by chaotic cleanliness.¹⁷ In Africa, *Leptospira* was widely spread through contaminated water channels in rural areas.¹⁸

Table 4 has now expanded to provide different pathogens, their possible spillover routes, and such regions of occurrence in order to enrich the findings.

The Global Preparedness and Response Frameworks

The readiness globally to prevent zoonotic spillover still seems insufficient in most locations, particularly in low- and middle-income countries.¹⁸ Surveillance and healthcare facilities capable of identifying and controlling these diseases are missing in most areas, particularly in the rural areas of the world today.¹⁹ The review pointed out the One Health approach, where human, animal, and environmental health need to work together.²⁰

Table 5 builds on the gaps as presented by extending a detailed understanding of the specific threats of each region and possible ways to overcome them.

New Directions and Knowledge Heterogeneities

In two of the reviewed research articles, the authors attributed the spillovers of zoonotic pathogens to climate change, which changes wildlife mobility and habitats and, hence, close contact and exposure to humans.²¹ The review also cited an increase in the emergence of some of the zoonotic pathogens that are hard or partially resistant to conventional treatments, especially in immune-compromised human populace and fungal diseases.²²

Since there is variability in the methods and results of the studies outlined above, the elements of qualitative synthesis specified the emergence of common patterns that include poor surveillance systems,

Table 3 | Comprehensive analysis of studies

Study Reference	Pathogen Focus	Geographic Focus	Pathogen Type	Main Spillover Pathway	Preparedness Gaps Identified
(1)	Bacterial Zoonoses	Sub-Saharan Africa	Bacterial	Wildlife-human contact	Limited surveillance in rural areas
(4)	Human Cytomegalovirus	Iran	Viral	Drug resistance in pathogens	Insufficient hospital-based surveillance
(5)	Leptospirosis	Global	Bacterial	Contaminated water sources	Weak policy enforcement on wildlife exposure
(14)	Multiple Zoonotic Pathogens	Southeast Asia, Global	Multiple	Illegal wildlife trade	Lack of global governance initiatives
(17)	Various Zoonoses	Global	Multiple	Wildlife trade, human contact	Inadequate preparedness for zoonotic threats
(23)	Emerging Pathogens	Global	Viral	Wildlife-human interface	Pandemic prevention strategies not operational
(29)	Various Zoonotic Pathogens	Global	Multiple	Historical analysis of pandemics	Highlighted the interconnected nature of spillovers

Table 4 | Identified zoonotic pathogens, spillover pathways, and affected regions

Pathogen	Pathogen Type	Spillover Pathway	Geographic Region	Main Risk Factors	Study Reference
Nipah Virus	Viral	Wildlife trade	Southeast Asia	Unregulated wildlife markets	(11)
Coronaviruses (SARS, MERS)	Viral	Wildlife-human contact	Global	Deforestation, human encroachment	(14)
<i>Leptospira</i>	Bacterial	Contaminated water	Sub-Saharan Africa	Poor water sanitation	(5)
<i>Bacillus anthracis</i>	Bacterial	Wildlife-human contact	Latin America	Agricultural activities	(10)
Avian Influenza Virus	Viral	Migratory bird interactions	Global	Contact with domesticated birds	(17)
Human Cytomegalovirus	Viral	Drug resistance	Iran	Hospital transmission	(4)

Table 5 | Key preparedness gaps identified by region

Preparedness Aspect	Geographic Region	Main Gaps Identified	Recommendations
Surveillance Systems	Africa	Limited surveillance in rural areas, lack of data sharing	Invest in local public health infrastructure and surveillance systems
Healthcare Infrastructure	Latin America	Inadequate response to zoonotic outbreaks	Develop regional healthcare networks for quicker outbreak responses
Wildlife Trade Regulations	Southeast Asia	Weak enforcement of wildlife trade laws	Strengthen global cooperation and legal frameworks for wildlife trade monitoring
One Health Implementation	Global	Lack of coordination between sectors	Fully integrate One Health strategies across human, animal, and environmental health sectors

regulatory failures, and the necessity to strengthen international collaboration.²³

Discussion

This systematic review has given scientific evidence of how zoonotic pathogens affect public health and the increasing probability of future pandemics. The study suggests the need for international collaboration and readiness because of the growing cases of spillovers and the relationship between multiple environmental, socioeconomic, and ecological factors of the emergence and transmission of diseases.²⁴ The primary analyzed studies stressed that zoonotic diseases do not only concern certain geographic locations but can spread throughout the world with the help of globalization, climate change, and the increase in wildlife trade.²⁵

Limitations of the Review

Despite the research conclusions of this particular review being useful in considering the threat of zoonotic pathogens, the review is not without its drawbacks.²⁶ A further limitation is the fact that many sources used in this article are not able to offer the most up-to-date information on zoonotic pathogen problems.²⁷ Therefore, zoonotic pathogens constitute a threat that is continually on the rise and thus constitute a clear and present danger to human populations of the world.²⁸

Conclusion

The outcomes indicate that some zoonotic agents, including the Nipah virus, *Leptospira*, and coronaviruses, are the most imminent threats because they have a high capacity for human-to-human transmission and are known to be not very treatable.²⁹ These pathogens, as identified in the developing world, especially in the subregions of South Asia and East Africa, are conveyed through wildlife and human interfaces, especially through the sale of bush meat.³⁰ For example, live wildlife markets in Southeast Asia, which harbor the Nipah virus, are considered zoonotic hotspots and have increased spillover due to weak biocontainment practices.³¹

The movement of zoonotic diseases is a process that has its characteristics and depends on many factors, including habitat destruction, human encroachment, and increasing concentration of livestock.³² In addition, as the results indicate, there are several types of pathogens that have specific characteristics; for instance, *Leptospira* spreads through the water supply, and human cytomegalovirus has already shown drug resistance.³³

From the study, the researchers also observe fatal weaknesses in international readiness to combat zoonotic pathogens. While some countries have improved surveillance and lack of diseases, a few others can be easily vulnerable due to poor response capacity.³⁴ From these four steps of analysis, the One Health system of human, animal, and environmental health has been deemed a potential approach to combating zoonotic disease threats.³⁵

The review draws attention to the necessity of improving surveillance systems for early identification of these new zoonoses and the ability to a rapid response.³⁶ The COVID-19 pandemic broke the health systems in many countries and demonstrated that their healthcare systems were unprepared for managing such a virus due to the late response to the virus.³⁷ Such shortcomings, as revealed in this review, are not exclusive to COVID-19 but are also evidenced in other zoonotic diseases.³⁸

Closing these gaps in preparedness calls for collective action at both national and international levels. Enhancing compliance with wildlife trade laws is important, especially if certain locations have wet markets that act as places where lemurs' zoonotic pathogens can spread.³⁹ Furthermore, there is a requirement for enhanced spending on public health facilities; there is scarceness of health programs aimed at the identification of zoonotic diseases in the affected rural areas.⁴⁰ Better vaccination measures, especially for susceptible groups, could help prevent the untoward effects of zoonotic diseases.⁴⁰ Furthermore, there is the necessity of cooperation on the international level as far as the problem of pandemic preparedness is concerned.⁴¹

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