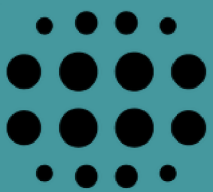
Rational Policy Over Panic

Re-evaluating Pandemic Risk within the Global Pandemic Prevention, Preparedness and Response Agenda

A report on zoonosis spill-over risk assessments within global pandemic preparedness policy prepared by the Re-Evaluating the Pandemic Preparedness And REsponse agenda (REPPARE) research group at the University of Leeds.

Version 2 | July 2024



REPPARE

UNIVERSITY OF LEEDS

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Version 2 corrects minor errors and typos within Version 1, and adds a section: 4.3. The WHO Priority Disease List

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Glossary

AFRO	World Health Organization African Region (Regional Office)
CGD	Center for Global Development
COP	Conference of Parties
DALYs	Disability-adjusted life years
DRC	Democratic Republic of Congo
EID	Emerging infectious diseases
EMS	Emergency Management System
EU	European Union
G7	Group of Seven (governments)
G20	Group of Twenty (governments)
HIV/AIDS	Human immunodeficiency virus / Acquired Immunodeficiency Syndrome
HLIP	High-Level Independent Panel (of the G20)
IHR	International Health Regulations
INB	Intergovernmental Negotiating Body (of WHO)
IPPPR	Independent Panel for Pandemic Preparedness and Response
IPSN	International Pathogen Surveillance Network
JID	Journal of Infectious Diseases
LMIC	Low- and middle-income country (s)
MCP	Medical countermeasures platform (of WHO)
MERS	Middle East Respiratory Syndrome

ODA	Official Development Assistance
PCR	Polymerase chain reaction (diagnostic technology)
PHEIC	Public Health Emergency of International Concern
PNAS	Proceedings of the National Academy of Sciences
PPR	Pandemic Preparedness and Response (often interchanged with PPPR)
PPPR	Pandemic Prevention, Preparedness and Response (often interchanged with PPR)
QALYs	Quality-adjusted life years
SARS1	Severe Acute Respiratory Virus -1
SMU	Standardized Mortality Units
UHC	Universal Health Coverage
UN	United Nations
WGIHR	Working Group on amendments to the International Health Regulations (of WHO)
WHA	World Health Assembly
WHO	World Health Organization

Executive Summary

Background

International health institutions are emphasizing an urgency to prioritize prevention and response to pandemics.

Pandemic risk is characterized as an "existential threat to humanity" and has been used to justify proposed amendments to the International Health Regulations and ongoing negotiations for a new legally binding Pandemic Agreement. It also underlies unprecedented annual financial requests to support this agenda, including over $10 billion in new Overseas Development Assistance and over $26 billion in LMICs investment, with additional funds for One Health interventions.

Although the World Health Assembly adopted the International Health Regulations (IHRs) in May 2024, they are still subject to ratification by member states, with many details to be determined through ongoing governance processes. The Pandemic Agreement, however, failed to find consensus, resulting in the decision to continue negotiations until the WHA in May 2025. As a result, important political and public health discussions on pandemic preparedness continue within highly compressed timeframes, with many key policy areas still undetermined.

Problem

The urgency and unprecedented scope of this agenda is based on interpretations of evidence claimed to demonstrate increasing pandemic frequency and burden. It is therefore essential that this evidence is correct, and its interpretation appropriate and objective. Any investment must be weighed against competing health, social and economic priorities, and therefore carries broad implications for global health, and risks to, global health.

Objective

This report investigates the evidence base supporting the assumption that natural pandemics constitute a significant health burden, and will increase in frequency and severity. By doing so, the report seeks to better determine to what degree the associated risk supports the trajectory of current Pandemic Prevention, Preparedness and Response (PPPR) policy.

Method

This report analyzes the data and evidentiary material cited within 8 key G20 (n=3), World Bank (n=2) and WHO (n=3) policy documents used to support current policy assumptions about

pandemic risk. Our analysis included key secondary citations (n=2) and academic sources (n=6) directly referenced in the policy documents to support these claims. Additional third-level academic references (n=15) found within these secondary citations were also considered as part of the overall analysis in this report. Our analysis focused on reported mortality and outbreak frequency to determine trends in risk and demonstrated harm.

Result

The report finds that the data and evidence is poorly supportive of current pandemic risk assumptions, suggesting that the urgency is unwarranted and that more time is required to formulate policy that reflects the true risk of pandemics in the wider healthcare context.

In contrast, the data suggests that an increase in recorded natural outbreaks could be largely explained by technological advancements in diagnostic testing over the past 60 years, while current surveillance, response mechanisms and other public health interventions have successfully reduced burden in the past 10 to 20 years. COVID-19, if indeed of natural origin, appears as an outlier rather than part of an underlying trend.

Implications

Most data underlying the WHO, World Bank and G20 reports demonstrate a flattening of the increase in outbreak reporting over the past two decades, with a reduction in mortality, and some in outbreak frequency, over the past 10 years. In this context, their claims regarding pandemic risk indicate that diverting investment to this risk is of lesser urgency than claimed, while the evidence supporting the scope of investment is weak. Any new investment should therefore be carefully weighed against investment in diseases of greater burden, particularly in low-resourced settings. This raises concern that escalated urgency based on weak evidence could undermine both.

Overall, mortality from these outbreaks is also historically low, and low in contrast to other current health burdens. Analyses indicating annual mortality in the millions include pre-antibiotic era Spanish Flu and the multi-decade HIV event. Both influenza and HIV have extensive international mechanisms already in place (although there is room for improvement), with mortality trends reflecting improved management.

In this context, the analyses of WHO, the World Bank and the G20, and in certain cases the sources they cite, are disappointing in terms of scholarship and balance. They raise concern that a desire to address a perceived threat is driving analysis, rather than analysis objectively determining the extent of threat. However well intentioned, this seems unlikely to effectively

address the needs of public health or the populations it serves. Disease outbreaks harm people and shorten lives and must be addressed. This is best achieved on the basis of well-compiled evidence and scholarly analysis if we aim to achieve effective pandemic preparedness and global health policy coherence.

The evidence, assessed objectively, paints a picture of an increasing ability to identify and report outbreaks up to the period 2000 to 2010, followed by a reduction in burden consistent with an increasing ability to successfully address these relatively low-burden events through current public health mechanisms. Whatever the underlying mechanisms, the data on which the major international agencies base their claims strongly indicate that the imperative of using health resources wisely in the context of overall public health and economic need should temper the current prioritization of health threats that are poorly defined and almost certainly overstated.

Recommendations

There is a clear need to commission better evidence to accurately determine the scale and urgency of pandemic risk.

An appropriate determination of pandemic risk must account for recent advancements in diagnostic capacity, information sharing, and improving disease control mechanisms.

Understanding relative disease burden is crucial for identifying the cost-benefit of pandemic investment and how to best select interventions and promote overall public health outcomes.

Given the poor evidence underlying risk assessment, it is prudent not to rush into or finalize new pandemic initiatives such as the proposed WHO pandemic instruments until underlying assumptions receive proper assessment based on robust evidence, recognized need, and overall benefit.

WHO Member States should support proportional pandemic preparedness efforts based on substantiated evidence, careful deliberation, and rational reflection.

1. Background

The pandemic preparedness, prevention, and response (PPPR) agenda is currently dominating international public health, and prevalent in deliberations of multilateral bodies including the Group of 20 (G20), Group of 7 (G7), United Nations (UN), European Union (EU), and World Bank. The World Health Organization (WHO) is the primary focus for coordination of this agenda. Supporters are seeking, and receiving, substantial funding from international official development assistance (ODA) budgets, whilst domestic research agendas and spending are being similarly directed.

These evolving priorities are having a major impact on global health financing. Although COVID-19 era ODA budgets saw an increase since 2019 in overall dispersals for health, 63.9% of that increase was for COVID-19 response with another one billion dollars disbursed for infectious disease control. Contemporaneously, ODA for basic health care fell from $3.4 billion in 2019 to $2.3 billion in 2020, a drop of 34.5 %, while nutrition declined by 10.1%. Although ODA for basic health rose again in 2022, it has not recovered to 2019 funding levels, while ODA for COVID-19 and infectious disease control saw additional increases of $1 billion and $500 million respectively in 2022. Furthermore, there is evidence indicating that national budgets are reallocating existing resources to PPPR, resulting in increased vulnerabilities for universal health coverage (UHC) and threatening to reverse positive health outcomes (Brown et al., 2022).[1,2]

The World Health Assembly (WHA),[3] the governance council of WHO, is currently pursuing two significant PPPR instruments. These instruments are intended to bring substantial changes to the management of future pandemics and threats of pandemics, and other health emergencies.

The first instrument is a set of over 300 proposed amendments to the International Health Regulations (IHR) with the intent of strengthening the role of WHO in declaring and directing responses to public health emergencies of international concern (PHEIC).[4] The aim of strengthening the IHRs is to address perceived failures experienced during COVID-19 related to cooperation, policy alignment, and compliance. As stated in the IHRs, countries will *undertake* to comply with WHO recommendations, treating WHO as the *authority* on these matters (Article 13A). The revised IHRs were adopted by the WHA in May 2024 and are now being ratified by Member States. In addition, many last-minute items were included into the IHRs (such as a new Coordinating Financing Mechanism) in which details are to be determined by May 2025.[5]

[1] https://www.oecd.org/dac/financing-sustainable-development/ODA-2022-summary.pdf
[2] https://www.brookings.edu/articles/global-health-financing-after-covid-19-and-the-new-pandemic-fund/
[3] https://www.who.int/about/accountability/governance/world-health-assembly
[4] https://apps.who.int/gb/wgihr/pdf_files/wgihr1/WGIHR_Compilation-en.pdf
[5] https://apps.who.int/gb/ebwha/pdf_files/WHA77/A77_ACONF14-en.pdf

A second instrument, a new Pandemic Agreement (sometimes referred to as the 'pandemic treaty') intended to have force under international law,[6,7,8] is still under negotiation with a WHA vote postponed until May 2025. The new Pandemic Agreement seeks to establish a new governance body (Conference of Parties - COP) with extensive mandate to develop new PPPR requirements and regulations, funding mechanisms and implementation mechanisms to support WHO in preparedness activities and response when a PHEIC is declared.[9]

Financial requirements to support current proposals for PPPR are high in terms of prior spending on ODA for health. Estimates used by the World Bank, WHO and G20 propose approximately $31.5 billion in total annual funding for PPPR, including $26.4 billion in annual PPPR investments by low-and middle-income countries (LMICs) and $4.7 billion required in new ODA funding to shore-up international efforts. These estimates assume that 25% of existing ODA already covers international PPPR efforts and further assumes that LMICs will only require $7 billion in extra ODA to fill national budget shortfalls. Thus, the total estimated ODA requirement for PPPR is currently $3.5 billion + $7billion = $10.5 billion.[10,11]

WHO, in its IHR amendments and proposed Pandemic Agreement, envisions increased regular financial contributions and potentially a mechanism for acquiring further 'surge' resources on request during a PHEIC. The World Bank has already established the Pandemic Fund to make further funds available for surveillance, diagnostics and related human resources. Compared with approximately $3.8 billion in current annual funding to WHO, and $3 billion in total estimated funding globally for malaria, $10.5 billion in ODA for PPPR would constitute a major increase and redirection in international public health funding.

As is claimed in the G20 High Level Independent Panel report 'A Global Deal for our Pandemic Age':

> *"without greatly strengthened proactive strategies, global health threats will emerge more often, spread more rapidly, take more lives, disrupt more livelihoods, and impact the world more greatly than before."*

Moreover,

[6] https://www.who.int/news-room/questions-and-answers/item/pandemic-prevention--preparedness-and-response-accord
[7] https://www.whitehouse.gov/briefing-room/statements-releases/2022/11/16/g20-bali-leaders-declaration/
[8] https://www.consilium.europa.eu/media/66739/g20-new-delhi-leaders-declaration.pdf
[9] https://inb.who.int/
[10] https://thedocs.worldbank.org/en/doc/018ab1c6b6d8305933661168af757737-0290032022/original/PPR-FIF-WB-White-Paper.pdf
[11] https://pandemic-financing.org/report/foreword/

> *"…countering the existential threat of deadly and costly pandemics must be the human security issue of our times. There is every likelihood that the next pandemic will come within a decade…"*

In other words, the G20's report claims that: 1) there will be increasing infectious disease outbreaks (epidemics), driven largely by escalating risk of major "spillover" from pathogens from animals (zoonosis), and; 2) some of these outbreaks will be severe, posing an "existential threat" to humanity.

1.1. Detecting outbreaks

A disease outbreak may be detected by the spread of an unusual or characteristic illness (set of symptoms and signs) in a population, or by detection of a specific pathogen in the presence of non-specific symptoms and signs. To be recorded, there must be communication channels, recording mechanisms and an accessible record, and institutional interest and resources that ensure these mechanisms are applied.

Symptom recognition depends on sufficiently trained people recognizing the patterns of disease involved. Pathogen detection requires specific tests that detect signs of pathogen presence that are accessible to the point of care or linked through sample transport mechanisms. There must be both resources and human interest available to apply such tests, on the part of the provider and the affected population.

Prior to the development of microscopy two centuries ago, there was no way of detecting and recognizing pathogens directly. Proteins (antigens) characteristic of pathogens and immune responses mounted against them by the host have only been detectable within the past century, and detectable at point of care in the past few decades. Basic tests are still unavailable for common outbreak diseases in many populations.

PCR tests, critical to detect and distinguish between many human pathogens, were only developed in the 1980s.[12] Versions of PCR (and other nucleic acid amplification tests) suitable for point-of-care use have only become available within the past 20 years, remain limited in scope, and too expensive or resource-dependent for widescale use in many geographical settings. Lateral flow tests for rapid detection of antigens and antibodies have been rolled out widely for more common diseases such as malaria,[13] but remain inaccessible for many less common pathogens.

Reporting of disease is dependent on electronic or paper-based reporting systems, and human willingness or capacity to use them. Reporting thoroughness has been transformed over the past century by electronic communications, road networks, rising human population density, literacy, and health service funding.

Therefore, when we discuss frequency of disease outbreaks in human populations, we depend on a range of requirements being in place to record an event as having occurred, and these requirements have changed dramatically over time and at different rates in different geographies. The probability of an outbreak being detected and recorded now is greatly

[12] https://www.future-science.com/doi/10.2144/btn-2020-0057
[13] https://www.nature.com/articles/nrmicro1525

increased compared to a few decades ago in many geographies, and to a century ago in all settings. This empirical reality must be understood in the interpretation of all data regarding trajectories of disease outbreaks in human populations and is critical to understanding this report.

1.2. Burden and balance

The justification for the PPPR agenda rests on pandemics constituting a major and growing threat to human wellbeing. This needs to be understood, therefore, both in terms of what constitutes human wellbeing, and the significance of the threat itself.

WHO defines health as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity."[14] There is no hierarchy of importance implied between these aspects of health. The WHO definition is important when considering responses to outbreaks of infectious disease. Manifestations of infectious disease are predominantly physical, though sickness and death have obvious mental and social consequences. However, any response also has direct social and potentially mental health consequences. Quarantine, travel restrictions, workplace closures and restrictions on social activities are obvious examples.

Any public health intervention must involve a balance of risk versus benefit. If restricted to physical disease, this is somewhat simpler to assess. Local travel restrictions have potential benefits in slowing the spread of a pathogen, with immediate physical risks limited to, perhaps, inability to seek care for another ailment. However, they may have huge economic, mental and social consequences related to inability to work, obtain education, socialize with family or friends, or attend important life events such as graduations, weddings and funerals.

While mental and social wellbeing are harder to quantify, several well accepted methods are used to estimate relative physical burdens imposed by disease. The simplest of these are case numbers and death counts. The former is poor beyond a very rough measure of spread of a pathogen in a community. Obviously, severity and duration are critical to the impact of a disease, as is long-term disability versus rapid and complete recovery.

Mortality alone can also give only a poor measure of overall impact, as death of a young child will foreshorten life far more than death of an elderly person. If most death from a disease occurs in old age and in those with comorbidities expected to shorten life, such as with COVID-19, recorded deaths may be high but the impact on average life expectancy will be small. Most would likely have died due to age and/or comorbidities within a few years if COVID-19 had not occurred. In contrast, most deaths from malaria occur at an age less than 5 years, with perhaps 70 years of life lost per child. The death of a middle-aged woman, such as from HIV/AIDS or cervical cancer, may also leave orphan children and a reduced family income, exposing them in turn to higher health risks.

[14] https://apps.who.int/gb/bd/PDF/bd47/EN/constitution-en.pdf?ua=1

To address discrepancies in age, measures involving life-years lost are commonly used.[15] Though not widely used for COVID-19, these are standard metrics used by WHO and other agencies and are as relevant to outbreaks and pandemics as they are to endemic and non-communicable disease. Disability-adjusted life years (DALYs) combine life-years lost with measures of impact of illness (years of disability or lost healthy life years) on daily life, while quality-adjusted life years (QALYs) combine life-years gained by an intervention and the quality of life (lack of disability) during those years.[16,17]

Appropriate metrics of disease burden are vital to determining the relative risks and benefits of any intervention. Directly, they allow estimation of the benefits of PPPR in terms of projected reduction in burden of projected outbreaks against the projected impact of the measures taken to avert or manage them. Indirectly, they allow this disease burden to be weighed against the opportunity cost of diverting resources to projected outbreaks rather than applying them to reduce the burdens of other diseases.

Opportunity costs can arise from reduction in resources available to address an alternate disease or health issue (*physical, mental and/or social*), or from economic costs that hinder the ability to reduce disease burdens more generally. Such economic costs will be most acute in lower income countries,[18] where readily avoidable disease burdens tend to be higher. Including such considerations in policy development is fundamental to good public health practice.

[15] https://www.who.int/data/gho/indicator-metadata-registry/imr-details/159
[16] https://www.who.int/data/gho/indicator-metadata-registry/imr-details/158
[17] https://onlinelibrary.wiley.com/doi/full/10.1111/j.1524-4733.2009.00515.x
[18] https://www.bis.org/publ/work910.htm

1.3. The imperative of reliable evidence

The opportunity costs of diverting $10.5 billion to fill PPPR financing shortfalls while reallocating considerable resources from other national and regional health, economic or other priorities are likely to be significant. These sums are far larger than expenditure on other high-burden infectious diseases such as malaria[19] and tuberculosis,[20] and may divert further funding from such diseases to achieve PPPR priorities. For example, in 2017 the combined LMIC national spending on high burden diseases such as HIV/AIDS and malaria equaled $25.3 billion,[21] just above the amount being asked from LMICs for more targeted efforts of PPPR. Moreover, in 2019 the total amount of ODA on PPPR was $374 million,[22] whereas the current ODA financial ask looks to be 28 times that amount. Investment in nutrition and sanitation are also important health alternatives, particularly given the spin-offs in this case, which include improving population resilience to viral outbreaks as well as having broad positive benefits in reducing the burden of other diseases and improving economic health (and accordingly future healthcare).

It is therefore vital that data on current risks from acute outbreaks of infectious diseases are reliable and provide adequate evidence to support the resource diversions that the PPPR agenda is proposing. Similarly, modeling of anticipated future burdens must be based on reliable data and defensible assumptions. One hallmark of evidence-based policy is that policy decisions should be substantiated by rigorously established objective evidence and not based merely on ideology, dogma or common belief. This enables appropriate allocation of resources among competing health and economic priorities. Global health resources are already scarce and stretched; there is little doubt that decisions about pandemic preparedness will have significant implications for global and local economies, health systems, and wellbeing.

The evidence supporting the PPPR agenda must therefore demonstrate that the resources being directed to the PPPR agenda are proportionate to the burden of disease these health threats pose, compared to other disease and health priorities. In other words, justification for large scale mobilization of financing and resources must be based on the burden of pandemic-causing pathogens, and the frequency with which such pathogens cause significant outbreaks of disease. The threat must justify the means and although it is prudent to prepare for public health emergencies and pandemic risk, it is also sensible to assure that these preparations are reflective of the best available evidence concerning pandemic risk, and that any policy response is proportional to that threat.

[19] https://www.who.int/teams/global-malaria-programme/reports/world-malaria-report-2022
[20] https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2022
[21] https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(20)30608-5.pdf
[22] Ibid.

The REPPARE project is investigating the relative disease burden of outbreaks and competing disease priorities in a separate series of reports. This current report investigates the assumptions and evidence-base underwriting the current PPPR agenda as it relates to the frequency and severity of pandemic threat. By doing so, the report seeks to better determine to what degree the associated risk supports the trajectory of PPPR policy.

The report will proceed by examining the key PPPR policy documents and reports in turn, highlighting where pandemic risk claims are made and the evidence upon which these claims are based. The report will then investigate key supporting studies individually to test the robustness of the underpinning research and to make initial determinations about its reliability as an evidence-base. To be clear, the motivation for this investigation is not to propose that no pandemic preparedness and response is necessary. Instead, this report aims to identify gaps and question the assumptions on which a huge shift in global health policy is being based and to stimulate better reflections about the urgency and scale of PPPR.

2. Methodology

2.1. Aims

This report has four research aims:

1) To locate and outline the major claims of pandemic risk within the main policy documents (below) involved with the Pandemic Prevention, Preparedness and Response policy agenda (PPPR).
2) To identify the evidence-base used within these policy documents to support these claims of pandemic risk, particularly evidence supporting claims of increased outbreak frequency and severity.
3) To analyze the robustness of this evidence-base.
4) To determine to what degree this evidence supports current PPPR assumptions and policy.

2.2. Approach

The four aims were addressed with the following methods:

1) Locating and outlining main policy documents

Key policy documents were identified through a series of rapid online searches.

- General searches of key intergovernmental organizations were conducted using combinations of search terms that included “zoonosis”, “spillover”, “pandemic risk”, “emerging infectious disease”, “pandemic threat”, “epidemics” and “acute health emergencies”.
- General searches of major institutional websites of the G7, G20, World Bank, World Health Organization and the United Nations were conducted.
- General internet searches (Google and other search engines) and alert requests were used to help identify wider policy discussions, media foci, and institutional references associated with pandemic risk.

Key selection criteria for inclusion were that the policy document or report:

- Explicitly gave pandemic risk assessments in support of policy recommendations;
- Was published after COVID-19, and;

- Was widely cited within the PPPR policy discourse.

2) Identification of the evidence base

This report analyzed the data and evidentiary material cited within 8 key G20 (n=3), World Bank (n=2) and WHO (n=3) policy documents / reports used to support current policy assumptions about pandemic risk. These documents represent the major post-COVID-19 PPPR policy initiatives where pandemic risk is explicitly reassessed, often in the context of the emergence of SARs-CoV-2, and were designed to explicitly provide evidentiary material for wider PPPR initiatives such as the Pandemic Agreement, revision of the International Health Regulations (IHRs), the Pandemic Fund, the International Pathogen Surveillance Network (IPSN), and the Medical Countermeasures Platform (MCP).

The policy documents and reports examined included:

- The G20 Bali Leaders Declaration (November 2022).
- A Global Deal for a Pandemic Age: Report of the G20 High Level Independent Panel on Financing the Global Commons for Pandemic Preparedness and Response (June 2021).
- Analysis of Pandemic Preparedness and Response (PPR) Architecture, Financing Needs, Gaps and Mechanisms. World Health Organization and World Bank. Prepared for the G20 Joint Finance & Health Task Force (March 2022).
- Future Surveillance for Epidemic and Pandemic Diseases: A 2023 perspective. World Health Organization (November 2023).
- Managing Epidemics: Key Facts about Major Deadly Disease. 2nd Edition. World Health Organization (2023).
- World Health Organization R&D Blueprint (2021).
- Putting Pandemics Behind Us: Investing in One Health to Reduce Risks of Emerging Infectious Diseases. World Bank (2022).
- World Bank Technical Report: Increasing Investments in One Health to Reduce Risks of Emerging Infectious Diseases at the Source (2022).

The study also included analysis of key secondary citations (n=2) and academic sources (n=5) directly referenced in the policy documents for key evidentiary support.

Non-Academic Documents

- Not the last pandemic: Investing now to reimagine public-health systems. McKinsey & Company (May 2021).
- Data on Non-Influenza Zoonotic Spillover Events. Metabiota (August 2021).

Academic Publications

- Bernstein, Aaron S., Amy W. Ando, Ted Loch-Temzelides, Mariana M. Vale, Binbin V. Li, Hongying Li, Jonah Busch et al. "The costs and benefits of primary prevention of zoonotic pandemics." *Science Advances* 8, no. 5 (2022): eabl4183. https://doi.org/10.1126/sciadv.abl4183
- Jones, Kate E., Nikkita G. Patel, Marc A. Levy, Adam Storeygard, Deborah Balk, John L. Gittleman, and Peter Daszak. "Global trends in emerging infectious diseases." *Nature* 451, no. 7181 (2008): 990-993. https://doi.org/10.1038/nature06536
- Marani, Marco, Gabriel G. Katul, William K. Pan, and Anthony J. Parolari. "Intensity and frequency of extreme novel epidemics." *Proceedings of the National Academy of Sciences* 118, no. 35 (2021): e2105482118. https://doi.org/10.1073/pnas.2105482118
- Morand, Serge, and Bruno A. Walther. "The accelerated infectious disease risk in the Anthropocene: more outbreaks and wider global spread." *BioRxiv* (2020): 2020-04. doi: https://doi.org/10.1101/2020.04.20.049866
- Smith, Katherine F., Michael Goldberg, Samantha Rosenthal, Lynn Carlson, Jane Chen, Cici Chen, and Sohini Ramachandran. "Global rise in human infectious disease outbreaks." *Journal of the Royal Society Interface* 11, no. 101 (2014): 20140950. https://doi.org/10.1098/rsif.2014.0950

Additional third-level academic references (n=15) found within the non-academic and academic secondary citations were also considered as part of the overall analysis in this report (see list here).

Analysis of the documents proceeded in four stages:

- Identification and categorization of documented pandemic risk assumptions, assessment and associated policy response;
- Exegesis of stated pandemic risk;
- Identification and mapping of cited evidence-base, and;
- Descriptive analysis of reported mortality and outbreak frequency within the reports.

3) Analysis of the evidence base

Analysis of the evidence-base focused on determining:

- Level of evidence used;
- Main conclusions and recommendations;
- Research methodologies;
- Overall coherency of argument / approach.

Critical analysis of the evidence-based further focused on determining:

- Any misrepresentations of cited evidence;
- Methodological errors or shortcomings;
- Faulty research assumptions;
- Limitations and methodological confounders;
- Reliability of data.

4) Determination of fit of evidence to policy

Each policy document and its supporting evidentiary material was then analyzed individually to determine to what degree the evidence supports current PPPR risk assumptions and policy. To make this determination, the evidence was first judged on its own merits in terms of whether it represents a robust risk assessment, whether there is appropriate research coherency, as well as the overall convincingness of its conclusion. In case of the former, this included weighing the evidentiary material against existing counterevidence and public health data as well as reassessing the urgency of pandemic risk assumptions against wider global health contexts and burdens.

3. The G20 evidence base

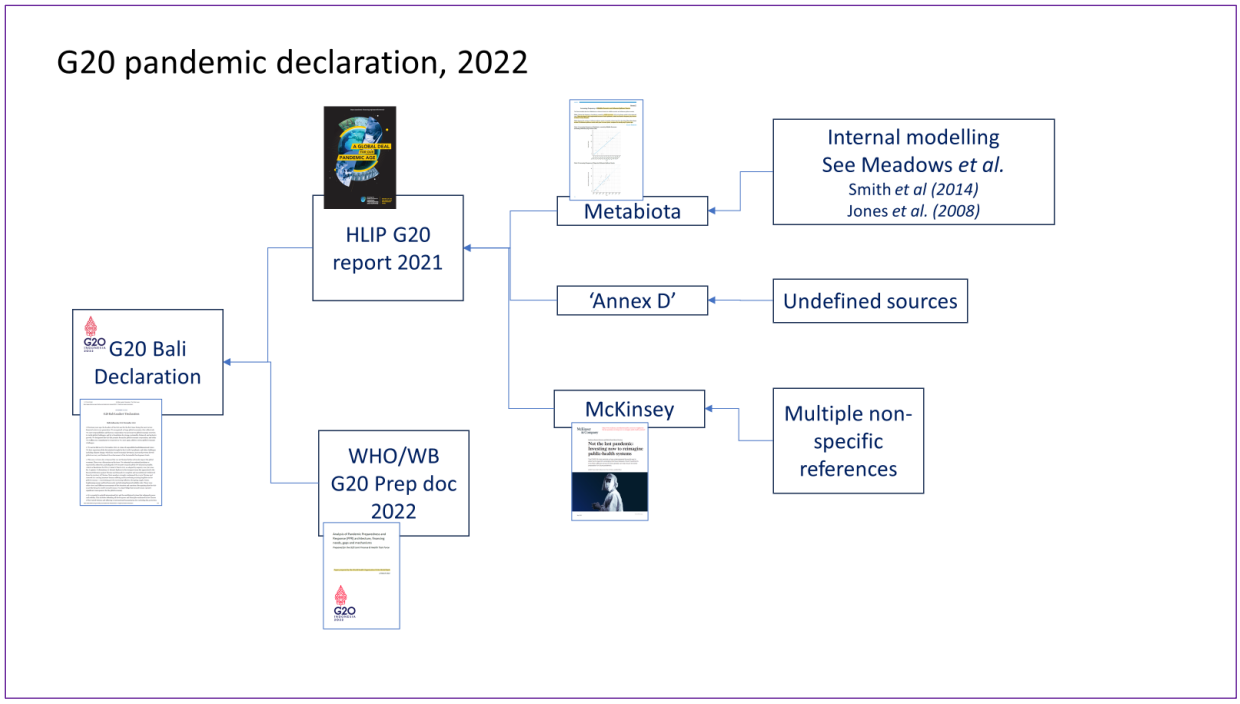
3.1. The G20 Bali Leaders Declaration, 15-16 November 2022.

Meeting in Indonesia in 2022, the G20 group of nations expressed support for the PPPR pandemic initiatives of WHO, the World Bank and partners to strengthen financial support for PPPR.[23] Prior to the meeting, the G20 commissioned two reports to help evidence its decision making on PPPR. The first report of the 'G20 High Level Independent Panel on Financing the Global Commons for Pandemic Preparedness and Response' (HLIP) was published in June 2021, with the specific mandate to "propose how finance can be organized, systematically and sustainably, to reduce the world's vulnerability to future pandemics."[24] The second report was commissioned from WHO and the World Bank as a gap analysis and preparation white paper on financing PPPR, titled 'Analysis of Pandemic Preparedness and Response (PPR) architecture, financing needs, gaps and mechanisms' (March 2022).[25]

Whereas the HLIP focused more on mobilizing financing, the WHO-World Bank report's aim was to better identify country, regional and global level gaps in PPPR and to estimate the cost of responding to those gaps. The first report had three independent co-chairs, multiple project leads from different organizations, and used external consultations to inform their conclusions. an analysis commissioned from McKinsey and Company contributed to the findings. As part of their remit, both reports were tasked to compile and analyze the evidence on outbreak risk and to provide some estimates on the social and economic costs of that risk. Both G20 reports were produced in under five months and relied heavily on existing reports and academic literature on pandemic risk and estimated gap costs (see Figure 1, below).

[23] https://www.whitehouse.gov/briefing-room/statements-releases/2022/11/16/g20-bali-leaders-declaration/
[24] https://pandemic-financing.org/report/foreword/
[25] https://thedocs.worldbank.org/en/doc/5760109c4db174ff90a8dfa7d025644a-0290032022/original/G20-Gaps-in-PPR-Financing-Mechanisms-WHO-and-WB-pdf.pdf

Figure 1. Derivation for evidence for the statements on PPPR of the G20 Bali Leaders Declaration.



The official G20 Bali Leaders Declaration,[26] released by the United States Government, devotes Paragraphs 19-24 to support the initiatives behind the PPPR and health emergencies agenda.[27] The Declaration states G20 backing for the WHO Intergovernmental Negotiating Body (INB) process to develop a "legally binding instrument" to strengthen PPPR,[28] and the work of the Working Group on amendments to the International Health Regulations (WGIHR).[29]

Of relevance to this report, the Declaration specifically mentioned COVID-19 and monkeypox PHEICs as examples of the need for these new WHO instruments. Monkeypox was declared a PHEIC by the WHO Director General (DG) in July 2022, after five recorded deaths globally after an equivocal determination of WHO's IHR emergency committee. The PHEIC was ceased in April 2023 after 120 deaths globally. In the context of the findings below, this reflects a tendency to include very low-burden events in the justification for funding, underlining the need to assess

[26] https://www.whitehouse.gov/briefing-room/statements-releases/2022/11/16/g20-bali-leaders-declaration/
[27] Ibid.
[28] https://inb.who.int/
[29] https://www.who.int/health-topics/international-health-regulations#tab=tab_1

these events in the broader public health context that seems poorly addressed in the reports on which the G20 and other international institutions have relied.

3.2. The Analysis of Pandemic Preparedness and Response (PPR) architecture, financing needs, gaps and mechanisms – Prepared for the G20 Finance and Health Task Force

In advance of the G20 in Indonesia, a PPPR gap analysis was conducted by the WHO and World Bank to estimate the costs of appropriate PPPR investment at country, regional and global levels.[30] The report concludes by suggesting that suitable PPPR requires $31.1 billion per year with an estimated gap of $10.5 billion a year needed in new ODA. As part of the justification for these investments the report laid out the following pandemic risks:[31]

> *"Pathogens will emerge and re-emerge with the potential to cause disease, death, and disruption of a magnitude equal to or greater than SARS-CoV-2. Outbreaks of infectious pathogens have been a defining feature of human history, and any analysis of prevailing trends strongly suggests that outbreaks of pathogens of pandemic potential are set to continue to increase in frequency for the foreseeable future."*

> *"The intensification of, and interaction between, factors such as ecological degradation, climate change, conflict and resource competition, mass population movement and displacement, urbanization, global travel and trade, and changes in agricultural practices continue to multiply the risks of emergence and re-emergence of epidemic and pandemic threats."*

To substantiate these claims the report cites a webinar organized by the Center of Global Development (CGD - also a project lead for the HLIP),[32,33] which included research from Metabiota Inc. Citing this webinar and the associated Metabiota research, the G20 report concluded that:

> *"Modeling suggests that the probability of a zoonotic event in which a pathogen with a pandemic potential similar to SARS-CoV2 jumps from another species into humans is between 2.5% and 3.3% annually, putting the chances of a similar outbreak between 47% and 57% within the next 25 years."*

As will be detailed below, Metabiota (a California-based consultancy now absorbed by Ginkgo Bioworks) and McKinsey & Company were the primary evidence sources used by the G20 within

[30] https://thedocs.worldbank.org/en/doc/5760109c4db174ff90a8dfa7d025644a-0290032022/original/G20-Gaps-in-PPR-Financing-Mechanisms-WHO-and-WB-pdf.pdf
[31] https://thedocs.worldbank.org/en/doc/5760109c4db174ff90a8dfa7d025644a-0290032022/original/G20-Gaps-in-PPR-Financing-Mechanisms-WHO-and-WB-pdf.pdf
[32] https://www.cgdev.org/event/whats-next-predicting-frequency-and-scale-future-pandemics
[33] https://www.cgdev.org/blog/the-next-pandemic-could-come-soon-and-be-deadlier

both commissioned pandemic preparedness reports.[34,35] These reports constitute the main evidence-base that underwrote the subsequent 2022 G20 Declaration.

[34] https://www.ginkgobioworks.com/
[35] https://www.mckinsey.com/industries/public-sector/our-insights/not-the-last-pandemic-investing-now-to-reimagine-public-health-systems#/

3.3. The G20 High Level Independent Panel (HLIP) Report

The HLIP of the G20 published a commissioned report 'A Global Deal for our Pandemic Age', in June 2021. Its findings regarding pandemic risk and the need for urgent action were primarily based on analysis by Metabiota Inc. and McKinsey & Company, with additional input from unspecified sources.[36]

Key findings of the HLIP report, which forms the basis for the G20 considering pandemics a major and increasing threat, are that pandemics and disease outbreaks are increasing in frequency and impact, with a high likelihood of recurrence of a major pandemic within one to two decades:

> "*without greatly strengthened proactive strategies, global health threats will emerge more often, spread more rapidly, take more lives, disrupt more livelihoods, and impact the world more greatly than before*.
>
> *…countering the existential threat of deadly and costly pandemics must be the human security issue of our times. There is every likelihood that the next pandemic will come within a decade…"*
>
> (High Level Summary. Page 5)

The Report claims that considerable increases in financial support are essential to avoid and mitigate outbreaks, including increased effort by low- and middle-income countries (LMIC):

> "*Low- and middle-income countries will need to add about 1% of GDP to public spending on health over the next five years.…*
>
> *Governments must collectively commit to increasing international financing for pandemic prevention and preparedness by at least US$75 billion over the next five years, or US$15 billion each year with sustained investments in subsequent years…*
>
> *The Panel assesses this to be the absolute minimum in new international investments required in the global public goods that are at the core of effective pandemic prevention and preparedness. The estimate excludes other investments that will contribute to resilience against future pandemics while benefiting countries in normal times.…*"
>
> (High Level Summary. Page 6)

[36] https://pandemic-financing.org/report/foreword/

The Report further asserts that such investment will reap major returns, based on its assessment of the costs and risks of outbreak:

> *"besides being a scientific and moral imperative. They will materially reduce the risk of events whose costs to government budgets alone are 700 times as large as the additional international investments per year that we propose, and 300 times as large as the total additional investments if we also take into account the domestic spending necessary."*
>
> (High Level Summary. Page 6)

The High-Level Summary recommends the establishment of commitments for such funding for countries, including expansion and greater financing for WHO. Below we examine the specific evidence base on which the above claims and recommendations are made. In doing so, several questions emerge regarding the reliability of the existing evidence-base, suggesting the need for a better understanding of pandemic risk and what assumptions should underwrite emerging PPPR policies.

In the Overview of the HLIP Report,[37] a basic claim is asserted:

> "*Even as we fight this pandemic, we must face the reality of a world at risk of more frequent pandemics*."

The support for this assertion is laid out on page 20 of the HLIP's report:

a) "*The last two decades have seen major global outbreaks of infectious diseases every four to five years, including SARS, H1N1, MERS and COVID-19*. (See Annex D.)"
b) "*There has been an acceleration of zoonotic spillovers over the last three decades. (See Annex E*.)"
c) "*Scientists attribute the increased frequency of infectious disease outbreaks to population growth and increased human encroachment on the natural environment; the loss of the world's biodiversity; the growth of the wildlife trade; increasing urbanization, crowded living conditions and increased mobility; and the broader consequences of a warming environment on the life cycle of pathogens and the geographical spread of insect-borne diseases*."

Claim 'c' will be discussed later in Section 4 and Section 6. Here we examine the assertions in 'a' and 'b'.

[37] Ibid.

3.4. HLIP Report, Annex D

Annex D lists “Major Infectious Disease Outbreaks in the Past Two Decades” (Figure 2A), as justification for the assertion of major infectious disease outbreaks every 4 to 5 years for the past 2 decades (HLIP report, page 20). No reference or attribution is provided, and no data sources given. Specifically, there is no associated mortality or other impact data provided, nor is the geographic location of the outbreak given.

Based on the largest outbreaks identifiable for each disease commencing in the year listed, we analyzed the impact of these listed outbreaks (Figure 2B). Sources for our assumptions are listed in Annex I. Annex D appears to contain errors, as some years listed were not the largest outbreaks recorded for the disease in the past two decades. For instance, the Enterovirus 71 outbreak presumably refers to the outbreak in Taiwan of that year. However, recorded mortality for this disease was far higher in mainland China in 2008-2012.

While the major West African Ebola outbreak is listed, a further outbreak in 2017 may be an error, as only 3 recorded deaths could be located in reports of that year. The intent may have been to refer to 2018, where two larger outbreaks occurred in the Democratic Republic of Congo. We have included these two outbreaks on the assumption that ‘Ebola 2017’ as listed in Annex D meant to refer to the more significant outbreaks in 2018 in the Democratic Republic of Congo (Figure 2B).

COVID-19 was included in the HLIP table. We have excluded this from analysis, as it is dealt with later, and the origins of the outbreak (natural spill-over versus laboratory-mediated) remain controversial.

Figure 2. (A) Annex D from the HLIP Report 'A Global Deal for our Pandemic Age', and (B) REPPARE assumptions for outbreaks listed and associated mortality. (See Annex I for sources of mortality estimates).

A

Table 1: Major Infectious Disease Outbreaks in the Past Two Decades

YEAR	OUTBREAK
2019	SARS-CoV-2
2018	Lassa
2017	Zika
2017	Ebola
2014	Chikungunya
2014	Ebola
2012	MERS
2010	Cholera
2009	H1N1 Influenza
2004	H5N1 Influenza
2003	SARS-CoV-1
2001	Enterovirus 71
2001	Nipah

B

Outbreak	Mortality
2019 SARS-CoV-2	…
2018 Lassa	114
2017 Zika	362
2017 Ebola	3
2014 Chikungunya	0
2014 Ebola	11,325
2012 MERS	858
2010 Cholera	9,792
2009 H1N1 Influenza	164,000
2004 H5N1 Influenza	32
2003 SARS-CoV-1	774
2001 Enterovirus 71	26
2001 Nipah	45
(2018 Ebola)	33
(2018-2020)	2287
TOTAL	**187331**
TOTAL Excl influenza	**23,299**

See Annex 1 for data sources

As Figure 2B demonstrates, the only outbreak in this list that killed over 20,000 people (prior to COVID-19) was the H1N1 influenza pandemic of 2009 (Swine Flu) with 163,000 deaths. Remaining mortality once this is excluded is dominated by the West African Ebola outbreak, which resulted in 11,325 deaths. The H1N1 influenza outbreak killed far less people than normal seasonal influenza does each year (approx. 290,000 to 650,000).[38] The next largest outbreak (Ebola, 2014) was largely confined to three countries. Ebola historically occurs in quite geographically confined areas due to its reliance on close contact for transmission and readily distinguishable illness.

For contrast, endemic diseases such as tuberculosis and malaria are responsible for approximately 1,380,000[39] and 620,000[40] deaths annually respectively, each dwarfing the combined total of all outbreaks listed in the HLIP report table (under 200,000, and under 25,000 excluding influenza – Figure 2B). In context, the West African Ebola outbreak, the largest in history, thus resulted in the equivalent of 4 days of global tuberculosis mortality, while the Swine Flu outbreak of 2009 had less than half the average mortality of seasonal influenza.[41]

The third largest outbreak listed by the G20 HLIP report was the cholera outbreak in 2010, which was confined to Haiti, and thought to have originated from poor sanitation in a UN compound.[42] Cholera once caused major outbreaks (peaking between 1852-1859) and was the subject of the first international agreements on pandemics.[43] Improved water and sewage sanitation, its impact has reduced greatly to a point where the Haiti outbreak was unusual, and there has been an decline in relative burden since the 19th century.

While there are many outbreaks overlooked in Annex D of the HLIP report, it contains most major events (see note on Enterovirus 71) and is the only evidence quoted for the Report's claim of major outbreaks every 4 to 5 years. This claim requires outbreaks with mortality equivalent to 1 to 3 days of tuberculosis mortality (approximately 3,800 deaths)[44] to be considered 'major outbreaks.'

[38] Iuliano AD, Roguski KM, Chang HH, Muscatello DJ, Palekar R, Tempia S, Cohen C, Gran JM, Schanzer D, Cowling BJ, Wu P, Kyncl J, Ang LW, Park M, Redlberger-Fritz M, Yu H, Espenhain L, Krishnan A, Emukule G, van Asten L, Pereira da Silva S, Aungkulanon S, Buchholz U, Widdowson MA, Bresee JS; Global Seasonal Influenza-associated Mortality Collaborator Network. Estimates of global seasonal influenza-associated respiratory mortality: a modelling study. Lancet. 2018 Mar 31;391(10127):1285-1300. doi: 10.1016/S0140-6736(17)33293-2. Epub 2017 Dec 14. Erratum in: Lancet. 2018 Jan 19;: PMID: 29248255; PMCID: PMC5935243.
[39] https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2022
[40] https://www.who.int/teams/global-malaria-programme/reports/world-malaria-report-2022
[41] https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(17)33293-2/fulltext
[42] https://www.ijdh.org/wp-content/uploads/2013/07/The-Cholera-Outbreak-in-Haiti_Where-and-How-it-Begin.pdf
[43] https://www.thelancet.com/article/S0140-6736(02)11244-X/fulltext
[44] https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2022

The assertions of the HLIP report based on this table are therefore poorly evidenced. However, the quality of data, and lack of referencing or indication of source data, also raises questions on the quality of underlying work involved in preparation of the report.

3.5. Metabiota data contributing to the HLIP Report

Metabiota Inc. was based in San Francisco, California, USA,[45] and specialized in data analysis including health-related data. It is no longer extant as an independent entity, but reports being acquired by Cameroon-based HEADA (a non-profit organization)[46] with Ginkgo Bioworks acquiring Metabiota's epidemiology and disease monitoring group.[47] The team of epidemiological data experts responsible for the analysis used by G20 was also integrated into Ginkgo Bioworks and is now present there.

Metabiota Inc. are listed as one of two major sources for outbreak data justifying proposed financing in the HLIP Report. Data in Annex E is sourced to Metabiota and is the basis of the assertion of "an acceleration of zoonotic spillovers over the last three decades." Annex E (Figure 3) itself makes an extraordinary epidemiologic claim for non-influenza wildlife zoonoses that:

> *"There has been a clear exponential increase of such epidemics, which increased in frequency by a factor of about 3 every 20 years."*

and for influenza, that there has been a dramatic change (worsening) of the threat:

> *"There have been around 10 influenza spillover events each year in recent years, compared to hardly any 25 years ago."*

Figure 3 illustrates a marked increase in frequency of outbreaks of both non-influenza and influenza zoonotic spillover events. The curves indicate one or less non-influenza events annually prior to 1960, and one or less influenza spillover events annually prior to 1995, but now more than 20 non-influenza and 10 influenza events annually.

The second chart on influenza 'spillover' events is difficult to interpret. Influenza deaths are trending down in the United States (where data is relatively good) over the past few decades. Furthermore, available global estimates are relatively flat, with around 600,000 deaths per year for the last few decades and despite increases in population. Thus, Metabiota's claim of an increase from 1 to 10 spill-over events per year from 1995 to 2000 seems unlikely to refer to a real change in seasonal influenza. It is possible that the increase refers to advances in detection. What is more, if only less common influenza variants are considered such as highly pathogenic avian influenza (HPAI) types H5 and H7, then mortality has greatly declined over the past

[45] https://web.archive.org/web/20230727112046/https:/www.metabiota.com/news
[46] https://web.archive.org/web/20230727112046/https:/www.metabiota.com/news
[47] https://www.prnewswire.com/news-releases/ginkgo-bioworks-announces-strategic-purchase-of-epidemiological-data-infrastructure-assets-301609075.html

century.[48] WHO equally notes that mortality from 'Bird Flu', of which we most frequently hear, has been declining (Figure 3).[49]

Unfortunately, the HLIP Report does not provide Metabiota's sources for the charts in Annex E (Figure 4). REPPARE contacted former Metabiota employees now at Ginkgo Bioworks who confirmed that the dataset used is the same as that used in a Metabiota presentation to the Center for Global Development (CGD) on August 25th, 2021, which was a source also cited in the HLIP.[50] Ginkgo Bioworks also confirmed that the dataset also appears in a more recent academic article in the British Medical Journal in 2023, co-authored by Metabiota personnel (Meadows et al., 2023).[51] In that article the authors analyzed the Metabiota database of 3150 outbreaks, including all outbreaks recorded by WHO since 1963 as well as "historically-significant" prior outbreaks (Figure 5). The data used in Meadows et al. (2023) is available in the article's supplementary information, and former Metabiota staff confirmed to REPPARE that the dataset used in that article, as in the earlier analyses, is now commercially available through Concentric by Ginkgo Bioworks.

[48] https://ourworldindata.org/influenza-deaths
[49] https://cdn.who.int/media/docs/default-source/global-influenza-programme/2023_march_tableh5n1.pdf
[50] https://www.cgdev.org/blog/the-next-pandemic-could-come-soon-and-be-deadlier
[51] https://gh.bmj.com/content/bmjgh/8/11/e012026.full.pdf?with-ds=yes

Figure 3. Annex E from the HLIP Report, intended to demonstrate an exponential increase in the frequency of epidemics (outbreaks) derived from zoonotic spillover.

ANNEX

Annex E

Increasing Frequency of Wildlife Zoonotic and Influenza Spillover Events

The Panel studied data from Metabiota on historical trends in wildlife zoonotic and influenza spillover events.

Chart 1 shows the frequency of epidemics caused by wildlife zoonoses. (It fits a log-linear model to the observed data.) **There has been a clear exponential increase of such epidemics, which increased in frequency by a factor of about 3 every 20 years.**

Chart 2 shows the number of influenza spillover events. (It applies a linear best fit to the data.) **There have been around 10 influenza spillover events each year in recent years, compared to hardly any 25 years ago.**

Source: Metabiota

Chart 1: Increasing Frequency of Epidemics caused by Wildlife Zoonoses (excluding Influenza) (log-normal scale)

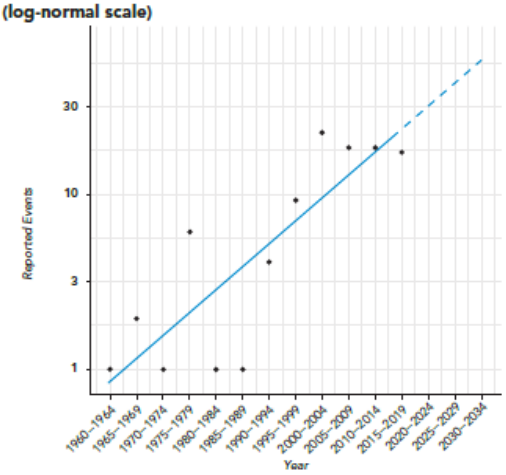
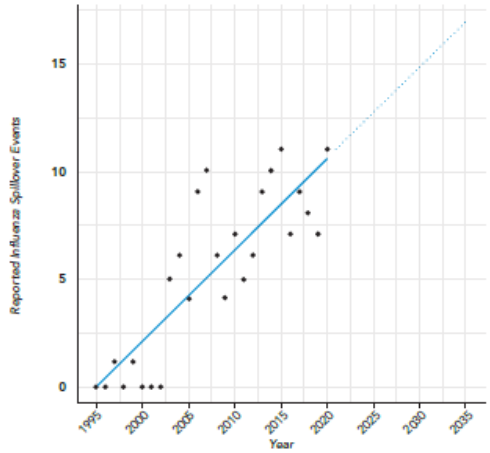


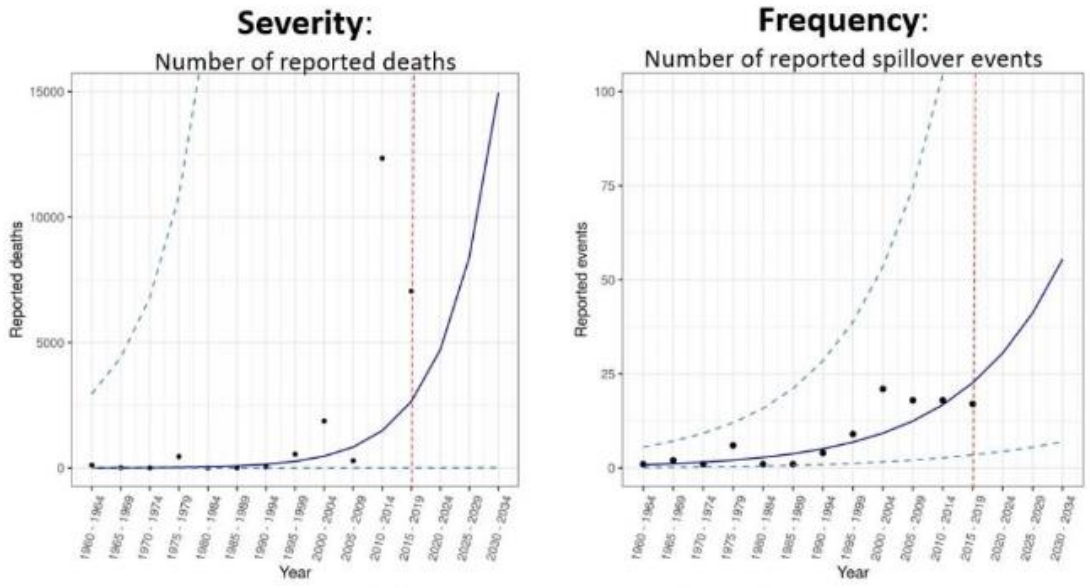
Chart 2: Increasing Frequency of Reported Influenza Spillover Events



73

Figure 4. Metabiota data on non-influenza zoonotic spillover events presented to the Center for Global Development, 25 August 2021, derived from the same dataset prepared for the HLIP report.[52]

Figure 1. Trend: frequency and severity of spillover events



Severity: $p < 0.001$; Frequency: $p = 0.02$; better fit than linear function

Source: A Global Deal for our Pandemic Age: Report of the G20 High Level Independent Panel on Financing the Global Commons for Pandemic Preparedness and Response, 2021

[52] https://www.cgdev.org/blog/the-next-pandemic-could-come-soon-and-be-deadlier

Figure 5. Reported non-influenza zoonotic spillover events and corresponding mortality, 1960 to 2020, from Figure 2 of Meadows et al., 2023.

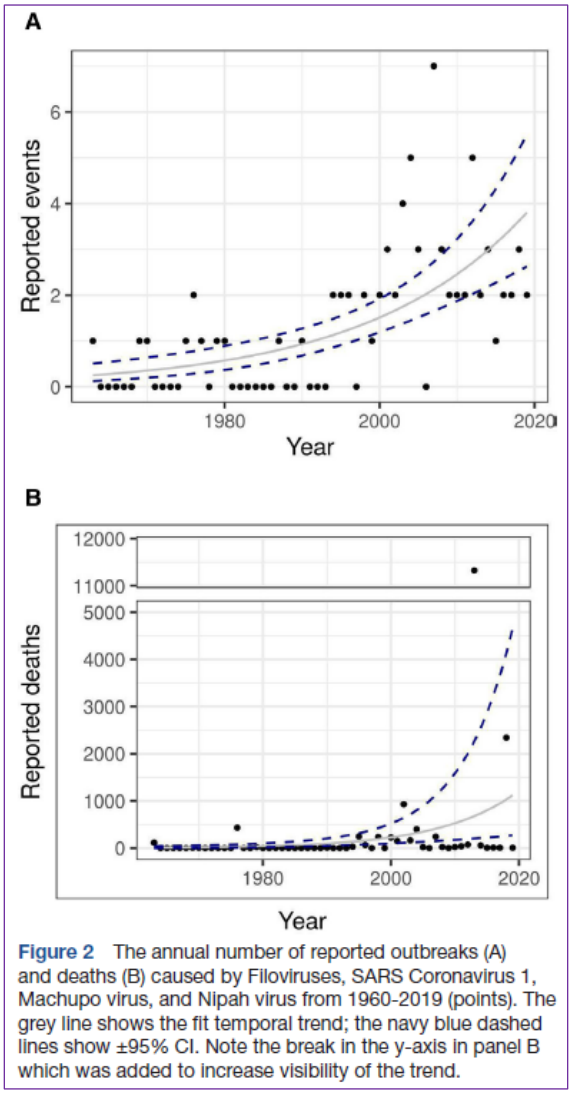


Figure 2 The annual number of reported outbreaks (A) and deaths (B) caused by Filoviruses, SARS Coronavirus 1, Machupo virus, and Nipah virus from 1960-2019 (points). The grey line shows the fit temporal trend; the navy blue dashed lines show ±95% CI. Note the break in the y-axis in panel B which was added to increase visibility of the trend.

3.6. Expansion on Metabiota data: Meadows et al. (2023) and Metabiota data presented to CGD.

Meadows et al. (2023) state that they (i.e. Ginkgo Bioworks, incorporating Metabiota's epidemiology team) have 3,150 outbreaks in their database, including those reported by the WHO since 1963, and prior "historically significant" outbreaks.[53] In the BMJ article, they concentrate on outbreaks of zoonotic origin from 1963 to 2019 that are not vector-borne, and of not more than 5 years duration (to exclude endemic diseases), with at least 50 deaths recorded for that pathogen, added over all outbreaks in the data (e.g. an Ebola outbreak with 10 deaths would be included because all Ebola outbreaks add up to more than 50 deaths). They further excluded influenza because specifically targeted surveillance programs increased detection. These exclusion criteria were considered to reduce reporting bias.

The outcome, and therefore the basis for the HLIP report data, is 75 outbreak events with 17,232 deaths in 24 countries, caused by Filoviruses (Ebola, Marburg), SARS Coronavirus 1, Nipah virus, and Machupo virus. Machupo virus causes localized outbreaks in Bolivia linked to an endemic species of mouse, while Nipah has been confined to Southeast Asia. Most of these outbreaks involved less than 50 deaths.[54]

The chart of frequency of events in Figure 5, and those in Figure 3 and 4 from the HLIP Report and Metabiota's CGD presentation respectively, demonstrate an obvious increase in event frequency. Applying models to this data shows an exponential increase in frequency. This could be explained by a rapid increase in actual events, which does not necessarily imply an increase in risk as it could simply reflect a rise in total population. However, the increase in reported events could also be explained, at least in part, by the following:

- Increased surveillance effort:
    - Economic growth – more labs, roads
    - Rising donor interest in outbreaks
    - Rising total donor funding
    - Rising emphasis on publication
- Expansion of diagnostic capacity:
    - Development of PCR (1983), and gradual expansion of PCR use
    - Development of improved and lower cost antigen tests
    - Expansion of access to lower cost serology tests
- Multiple other reasons for increased detection, reporting and recording.

[53] https://gh.bmj.com/content/bmjgh/8/11/e012026.full.pdf?with-ds=yes
[54] Ibid.

The curves produced by Metabiota indicate that very few outbreaks occurred before the 1970s. This seems to lend weight to the influence of the confounders listed above, particularly technological advancement in detection, rather than showing a true exponential increase. The potential for this confounder to be important is confirmed by Meadows et al. in the limitations section of their paper, where this increase in reporting frequency did not consider the development of new surveillance and diagnostic technologies, which would have enabled better (or in some cases any) detection. As outlined above, PCR testing was only developed in the 1980s and has steadily become more accessible in laboratories over the last 30 years.[55] Antigen and point-of-care serology tests were only widely available in the past couple of decades, and genetic sequencing only very recently.[56]

Since 1960, we also have had significant improvements in road transport, clinic access and digital information sharing. As a result, this limitation in the Meadows study raises questions about how advancements in detection technology could account for the large increase in reported outbreaks, since most small and localized outbreaks will have been missed 60 years ago. As just one example, HIV/AIDS was missed for at least 40 years before identification in the 1980s.[57]

What the above suggests is that there are certainly known spillover effects and that these do occur with some frequency. What is less reliable from the Metabiota data is the claim that there is an increased frequency of zoonosis and/or that the increase in reporting cannot be fully or partly explained by advancements in detection technologies. Determining the former would require further research that could control for this latter variable.

Analysis of the mortality trends for these diseases raises similar concerns. Meadows et al. indicate that the data represents an exponential increase of 8.7% annually, and that: "*If these annual rates of increase continue, we would expect the analysed pathogens to cause four times the number of spillover events and 12 times the number of deaths in 2050 than in 2020*."[58]

The mortality chart in Figure 6A on which Metabiota's team have based their conclusions shows 2 outlier points driving the upswing of the curve between 2010 and 2019. These are the West African Ebola outbreak of 2014 and the Democratic Republic of Congo (DRC) Ebola outbreaks of 2017 (which we have assumed are the 2018 and 2018-2020 DRC outbreaks). The 2014 outbreak in particular was unusual due to a relatively slow response by authorities and is by far the largest such recorded outbreak in history.[59]

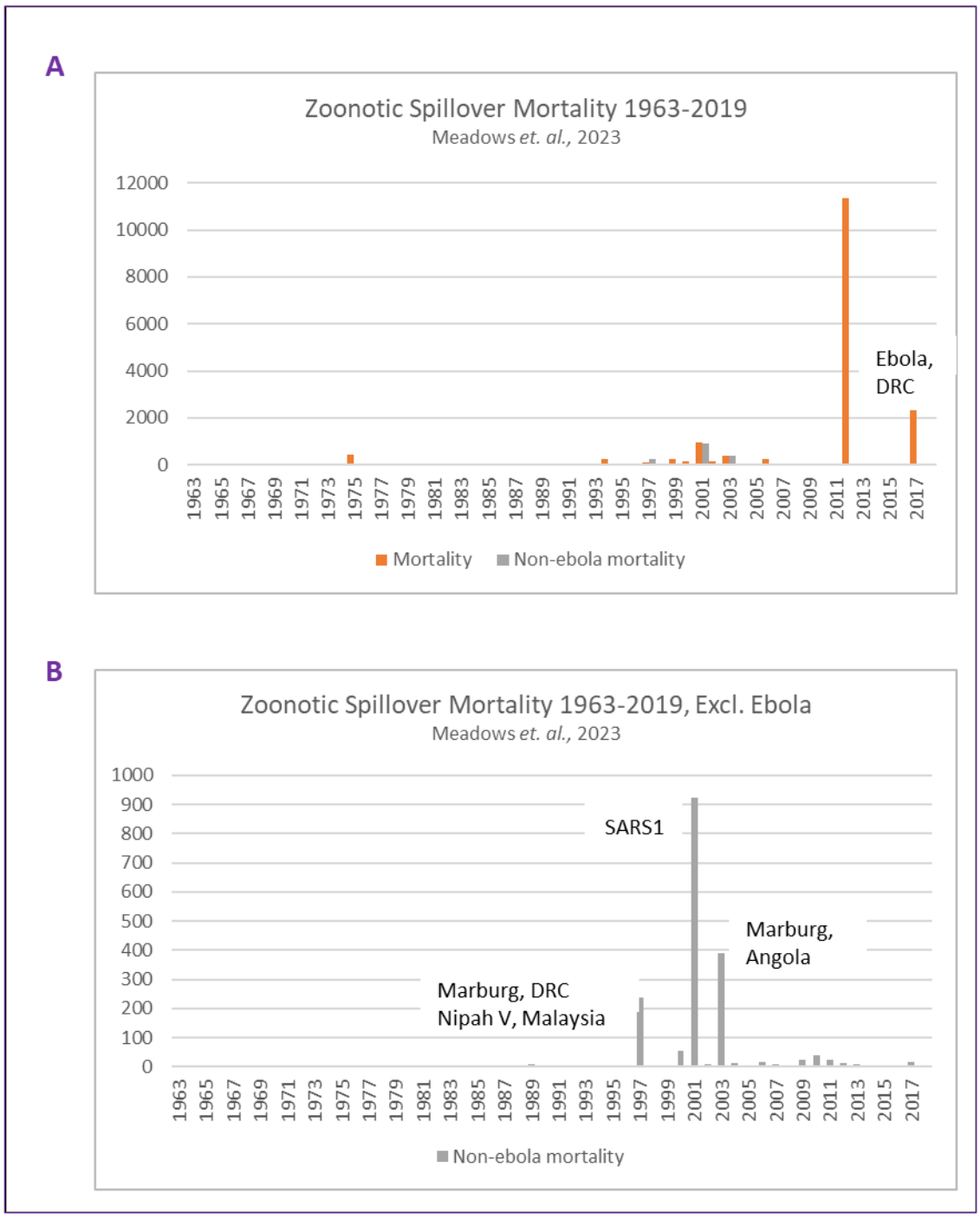
[55] https://www.future-science.com/doi/10.2144/btn-2020-0057
[56] https://www.nature.com/articles/nrmicro1525
[57] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3234451/
[58] https://gh.bmj.com/content/bmjgh/8/11/e012026.full.pdf?with-ds=yes
[59] https://speakingofmedicine.plos.org/2014/08/22/global-response-ebola-fever-epidemic-took-long/; https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(15)00946-0/fulltext

As a thought experiment, Figure 6B shows the Metabiota mortality data from the 75 outbreaks since 1963 with Ebola virus outbreaks removed. The trend is quite different when Ebola is excluded, showing three outbreaks, all with mortality well below 1000 people, dominating the data set. The figure illustrates a relative increase in mortality in the 1997 to 2003 period (SARS1, Marburg and Nipah virus outbreaks), and very little mortality since. It is clear that an exponential increase in mortality is no longer present when Ebola is excluded, and the data suggests that such zoonotic events may be becoming less serious in terms of mortality (consistent with Smith et al. (2014), discussed below).[60]

The reanalysis also illustrates the very low overall burden of mortality resulting from such events. In terms of annualized mortality over the 1963 to 2019 period, the 75 outbreaks produce an average of just 302 deaths per year in total, 34 if Ebola is excluded, and 17 if SARS1 is also excluded. As a result, in relative terms, the risk of mortality from these events, even when all events are included, is low and further suggests that perceptions of risk are disproportional to the historical disease mortality record.

[60] https://royalsocietypublishing.org/doi/10.1098/rsif.2014.0950?url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org&rfr_dat=cr_pub++0pubmed

Figure 6. Meadows et al. (2023) data recharted, (A) including Ebola outbreaks and (B) excluding Ebola outbreaks (note change in Y-axis intervals).



3.7. Supporting references in Meadows

Meadows et al. (2023) quote three studies to back their assertion of significant increases in the frequency of emerging infectious disease outbreaks; Smith et al. (2014)[61], Jones et al. (2008)[62] and the WHO Regional Office for Africa (2022).[63] Smith et al. and Jones et al., are discussed in more detail later in this report.

These studies are part of the wider literature on pandemic risk and will be examined in greater detail below. However, given that these studies are cited in the Meadows et al. article as corroboration of increasing outbreak frequency, which is the basis of the G20's evidence-base as cited from Metabiota, it is useful to summarize here.

In brief, the article by Smith et al. (2014) notes an increase in outbreak frequency of modest size compared to Meadows et al., but a reduction in mortality rate from such outbreaks once internet usage (as a proxy for communication access) is adjusted for.[64] Jones et al. (2008) show an overall increase in outbreaks from the 1940s to the year 2000, but a reduction from the 1980s to the 1990s.[65] They note that much of the increase is attributable to secondary infections in HIV-infected patients (immune-deficiency) and also due to antimicrobial resistance (each mutation is classed as a new outbreak in their analysis). The WHO AFRO reference cited in Meadows et al. is a blog stating a 63% increase in zoonotic outbreaks occurred in the African Region from 2001-2011 to 2012-2022.[66] No reference is given for this statement and no data provided, and REPPARE was unable to obtain responses from the WHO AFRO office to clarify this.

The supporting references quoted by Meadows et al. therefore do not support a rapid and consistent increase in risk of mortality from zoonotic outbreaks, (with the possible exception of unreferenced WHO data), though Smith et al. (up to 2010) and WHO (unreferenced) note an increase in frequency of reported events. As discussed elsewhere, this is likely to be significantly influenced by improved detection and reporting.

[61] https://royalsocietypublishing.org/doi/10.1098/rsif.2014.0950?url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org&rfr_dat=cr_pub++0pubmed
[62] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5960580/
[63] https://www.afro.who.int/news/africa-63-jump-diseases-spread-animals-people-seen-last-decade
[64] https://royalsocietypublishing.org/doi/10.1098/rsif.2014.0950?url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org&rfr_dat=cr_pub++0pubmed
[65] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5960580/
[66] https://www.afro.who.int/news/africa-63-jump-diseases-spread-animals-people-seen-last-decade

3.8. McKinsey and Co. report contributing to the HLIP report

The HLIP "primarily" relied on WHO and McKinsey for their financial assessments, summarized in Annex H of their report. As stated on Page 48 of that report:

> *"These are current best estimates based on WHO, McKinsey and others to size the various requirements for future pandemic prevention and preparedness".*

This statement makes reference (page 81) to the WHO and World Bank report to the G20 "Assessment of Gaps in Pandemic Preparedness" in 2020. This report was a "work-in-progress" and was "replaced" in March 2022 by a final report titled "Analysis of Pandemic Preparedness and Response (PPR) architecture, financing needs, gaps and mechanisms". It was this later report that was presented to the G20 in Indonesia.

As outlined earlier, this report solely drew upon the evidence provided by Metabiota and McKinsey & Company for its pandemic risk assessments. Thus, the assessments provided above for Metabiota and Meadows et al. holds for this WHO and World Bank report, since there is no new evidence provided. Aside from the Metabiota research examined above, the G20 relied significantly on the McKinsey & Company's report "Not the last pandemic: Investing now to reimagine public-health systems."

The report by McKinsey & Company bases its conclusions on important assumptions concerning pandemic and outbreak risk.[67] Yet, no data is provided in their report to support these conclusions, which were subsequently accepted by the HLIP. Moreover, McKinsey's 13-page report to the HLIP is non-specific regarding risk, referencing general media reports and WHO summaries rather than data. Therefore, it is not possible to draw firm conclusions on whether financial conclusions from McKinsey are well supported by evidence. However, major assumptions underlying them raise concerns on reliability.

The McKinsey report makes several assumptions regarding the COVID-19 outbreak that are important to their conclusions. Briefly, they claim increased costs for countries "*responding late*" to COVID-19, and "*difficulties in managing second and third surges*" as being evidence of the need for greatly increased investment. Such statements raise questions on the veracity of subsequent financial assumptions. For example, the OECD notes that Sweden, instituting relatively light restrictions, has the lowest all-cause mortality of any OECD country.[68] A lack of clear correlation between strictness of restrictions and health outcomes raises questions regarding whether 'improve response' of the type envisioned (e.g. lockdown-related approaches) are is an

[67] https://www.mckinsey.com/industries/public-sector/our-insights/not-the-last-pandemic-investing-now-to-reimagine-public-health-systems#/
[68] https://data.spectator.co.uk/covid-inquiry

investment with clear returns in terms of health, or whether former lower-cost approaches are preferable.[69] These issues require in-depth discussion and research, but are raised here to highlight the assumptions and lack of quantifiable data throughout the report.

On evidence for outbreak frequency and severity – the primary justification for investment, the McKinsey report is very sparse:

- On Page 2 the Independent Panel for Pandemic Preparedness and Response (IPPPR)[70] is quoted *"…if investment doesn't occur now, 'we will condemn the world to successive catastrophes.'"* Importantly, the IPPPR report does not provide data to support this assertion, but notes uncited opinions of an increase in outbreak frequency.
- Again, on Page 2 the McKinsey report justifies its investment case by claiming increased possibility of an outbreak with 25% mortality, which will disproportionately harm children. However, such an outbreak has not occurred at broad scale since bubonic plague in the 14th Century, with the exception of virus outbreaks (smallpox and measles) in immunologically-isolated populations of the Americas and Oceania in the 16th to 19th Centuries. The former is readily addressable through hygiene and antibiotics, while conditions for the latter (large, isolated populations) no longer exist. McKinsey do not offer an explanation as to how such an event would recur nor do they provide further evidence to support the 25% mortality claim.
- On page 8, the McKinsey report notes that "*zoonotic events, in which infectious diseases make the jump from an animal to a human, touched off some of the most dangerous recent epidemics, including of COVID-19, Ebola, MERS, and SARS*". Apart from COVID-19, these are the only outbreaks discussed as evidence. Based on the Metabiota dataset described above, these diseases resulted in 16,237 total deaths globally from 1963 to 2019 (average 290/year). Including COVID-19 will obviously increase this, yet it is important to factor that COVID-19 deaths occur predominantly in the unwell elderly and therefore cause relatively lower life years to be lost. [71,72,73] Furthermore, the origin of COVID-19 is important here, as McKinsey are referring to natural zoonotic spillovers, while the origins of COVID-19 are disputed.[74,75] If it is of natural origin, then based on the G20 data it could be understood as an isolated event and not part of a trend. If SARS-CoV-2 is laboratory-modified,[76] as some have argued,[77] then the massive effort underway to build surveillance for naturally occurring threats would not be justified nor appropriate to the task.

[69] https://apps.who.int/iris/bitstream/handle/10665/329438/9789241516839-eng.pdf?ua=1
[70] https://theindependentpanel.org/wp-content/uploads/2021/05/COVID-19-Make-it-the-Last-Pandemic_final.pdf
[71] https://www.sciencedirect.com/science/article/pii/S001393512201982X#bib42
[72] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9420458/
[73] https://covid.cdc.gov/covid-data-tracker/#demographics
[74] https://www.bmj.com/content/382/bmj.p1556
[75] https://www.dni.gov/files/ODNI/documents/assessments/Unclassified-Summary-of-Assessment-on-COVID-19-Origins.pdf
[76] https://www.bmj.com/content/382/bmj.p1556
[77] https://www.dni.gov/files/ODNI/documents/assessments/Unclassified-Summary-of-Assessment-on-COVID-19-Origins.pdf

- Evidence within the McKinsey report referenced by the HLIP therefore poorly supports the contention that PPPR investment on the scale of $85-130 billion over 2 years followed by $20-50 billion annually (HLIP report, page 13) is justified or urgent.

3.9. Summary of G20 evidence base

While actual outbreaks, including those arising from zoonoses, may or may not be increasing, the evidence of the HLIP report, forming the basis for the G20 Bali Leaders Declaration, does not strongly support either conclusion. The basis of the G20 recommendation, that "*without greatly strengthened proactive strategies, global health threats will emerge more often, spread more rapidly, take more lives, disrupt more livelihoods, and impact the world more greatly than before*" is not supported. Most importantly, it is not supported by the HLIP report provided, or other evidence from the entities this report relied on. It is inevitable that reporting of outbreaks will be influenced by changes in both the capacity and incentive to report. These include the development of, and increasing access to, major diagnostic platforms including PCR and point-of-care antigen and serology tests, as well as the development of communication infrastructure. Increased interest from funders and research groups in outbreak detection may also be influencing the frequency of recording.

COVID-19 has of course intervened, continuing through the publication of the HLIP report, as the first rapidly-spreading outbreak since 1969 to result in greater mortality than seasonal influenza does each year. This mortality has occurred predominantly in the elderly and those with significant co-morbidities in higher-mortality high-income countries,[78,79] a contrast to the predominantly childhood deaths from malaria and young to middle-aged adults who die from tuberculosis. Excess mortality rose over baseline but separating out COVID-19 mortality from mortality resultant from the 'lockdown' measures, reducing disease screening and management in high-income countries and diverting resources from poverty-related diseases in low-income countries makes actual burden estimates difficult.

However, if COVID-19 (for sake of argument here) is accepted as a natural event, then it should obviously be included when determining risk. There are meaningful debates about the accuracy of how deaths were recorded and attributed to COVID-19.[80,81] However, assuming the WHO is correct in its estimates, then the WHO records 7,010,568 deaths attributed to (or associated with) the SARS-CoV-2 virus over 4 years, with most in the first 2 years (Figure 2). Allowing for population increase, this is still higher than the 1.0 to 1.1 million deaths attributed to the influenza outbreaks in 1957-58 and 1968-69, and the largest since the Spanish Flu that inflicted a mortality several-fold higher over a century earlier. With an average mortality of 1.7 million per year over 4 years, COVID-19 is not greatly different from tuberculosis (1.3 million), but concentrated in a considerably older age group. Tuberculosis, however, continues before and will continue after

[78] https://covid.cdc.gov/covid-data-tracker/#demographics
[79] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9420458/
[80] https://www.bmj.com/content/382/bmj.p1556
[81] https://www.dni.gov/files/ODNI/documents/assessments/Unclassified-Summary-of-Assessment-on-COVID-19-Origins.pdf

COVID-19, whereas COVID-19 mortality remains low since mid-2023.[82] As the first event in 100 years of this magnitude, though little different from endemic tuberculosis over 4 years, and against a background that does not demonstrate an overall increase in mortality from outbreak events, it appears to be an outlier rather than evidence of a trend.

Given the above, there is poor support for a genuine exponential, rapid or continuing increase in mortality from zoonotic spillover-derived outbreaks in the data provided by Metabiota and other contributors to the HLIP Report. An apparent increase was driven by an exceptional outbreak of Ebola Virus in West Africa in 2014, and a later Ebola virus outbreak in the DRC. Ebola virus outbreaks have always been largely localized and time-limited, and due to the nature of the disease, are likely to remain so.

The basis for the large benefits predicted to accrue from the recommended investments must therefore be considered highly unreliable. Observations of increasing outbreaks are likely to be partly or largely due to causes other than an increase in zoonotic spillover, and mortality risk does not appear to have been increasing pre-Covid. The arguable exception is Ebola risk in Central and West Africa, but these outbreaks remain localized. The largest sustained transmission was in just 3 countries and resulted in the equivalent of 3 days mortality from endemic tuberculosis.

While COVID-19 has a higher recorded raw mortality, the evidence provided to the G20 Bali meeting does not provide strong support for this being part of a trend rather than an exception. Yet, outside general statements about globalization, increased speed of travel, urbanization, and increased ecological interfacing, there is nothing concretely offered to think COVID-19 constitutes the start of a new trend in zoonosis spillovers. This has important implications for assessing relative disease burden, which is a key factor to understanding risk. This will be discussed in detail in a further report on pandemic disease burden and relational burdens to other infectious and non-infectious diseases.

[82] https://data.who.int/dashboards/covid19/deaths?n=c

4. WHO evidence base for pandemic risk

The World Health Organization (WHO) has made several references for the pressing need to prevent, prepare and respond to pandemic threats. Most of these statements have been brief comments made during speeches by WHO personnel, in WHO memos, and in Director General reports.[83] The need for increased policy response to pandemic threat has also been articulated within key policy documents. Yet, as with the G20, these claims tend to lack citations and/or disclosure of the underlying evidence.

This section of the report will examine key WHO documents where pandemic risk is explicitly articulated and where those claims are supported with reference to some level of evidentiary material.

4.1. The WHO Future Surveillance Report

In late 2023 the WHO published its report "Future Surveillance for Epidemic and Pandemic Diseases: a 2023 Perspective."[84] The report was produced by the Strategic and Technical Advisory Group on Infectious Hazards with Pandemic and Epidemic Potential. The report starts with the claim that:

> *"Since the beginning of the 21st century, the world has experienced major epidemics and pandemics every four to five years."*

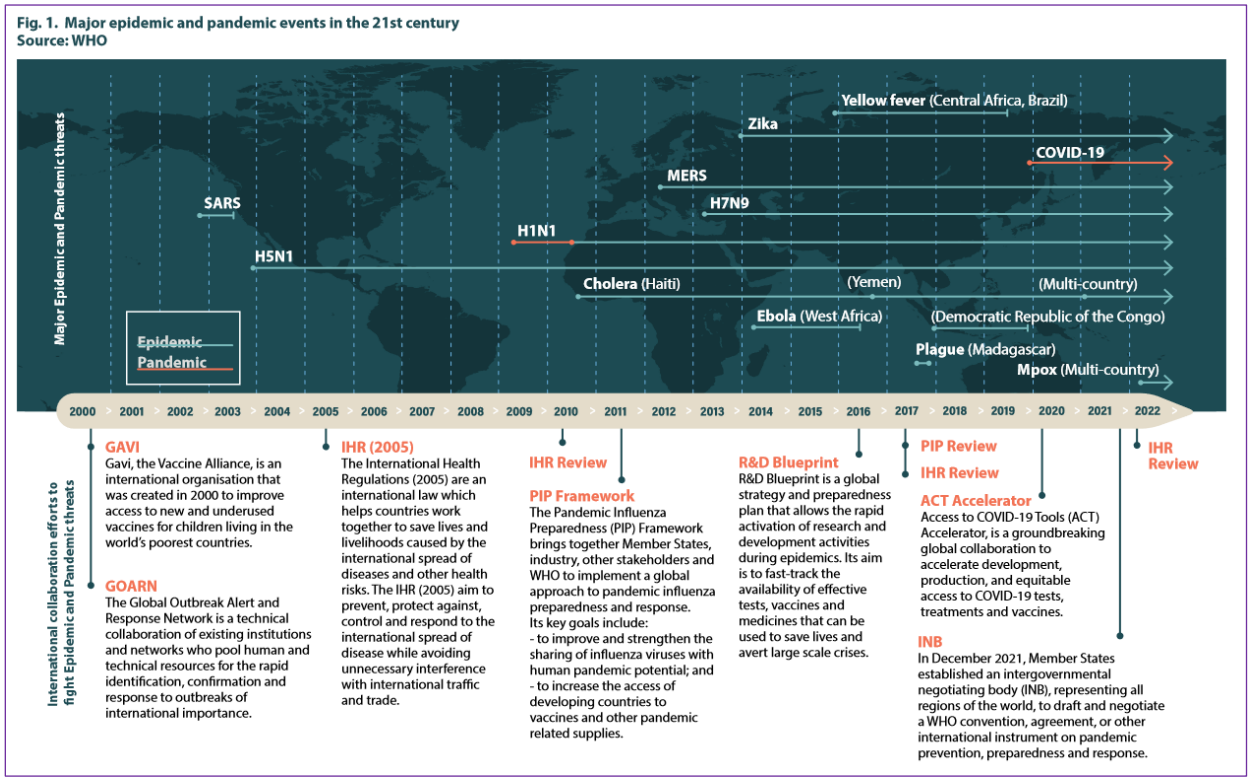
Citing a joint statement of UN organizations from April 2020, the report further claims that:

> *"The progression of COVID-19 has indeed proven that "no one is safe until everyone is safe" in this interconnected world."*

To substantiate the first claim the report provides a figure illustrating what the WHO suggests are major epidemics or pandemics (see Figure 7).

[83] https://apps.who.int/gb/ebwha/pdf_files/WHA76/A76_10-en.pdf
[84] https://www.who.int/publications/i/item/9789240080959

Figure 7. Figure 1 from WHO Report; 'Future Surveillance for Epidemic and Pandemic Diseases: a 2023 Perspective', showing "Major epidemic and pandemic events in the 21st century".



Of the mentioned diseases, COVID-19 is responsible for almost the entire death toll. If you exclude COVID-19 and the 2009 influenza pandemic (which is less severe than seasonal influenza) we can see that these two events are responsible for roughly 90 percent of combined deaths. Moreover, all listed diseases combined, including COVID-19, had an average death toll between the years 2000 and 2022 that is less than a fourth of TB mortality or that of traffic accidents.85,86 Mortality alone, as discussed above in Section 1.2 of this report, can give only a poor measure of overall impact, as death of a young child will foreshorten life far more than death of an elderly person. If most death from a disease occurs in old age and in those with comorbidities expected to shorten life, such as with COVID-19,[87,88,89] recorded deaths may be high but the impact on average life expectancy will be small.

As a visual tool to provide an impression of increasing outbreak risk, Figure 7 is compelling. However, the chart poorly reflects reality. Eight diseases are shown to be currently active in 2022, compared to zero in the year 2000. Of these eight, Zika virus, cholera, Ebola and Mpox

[85] https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2022
[86] https://www.who.int/news-room/fact-sheets/detail/road-traffic-injuries
[87] https://www.sciencedirect.com/science/article/pii/S001393512201982X#bib42
[88] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9420458/
[89] https://covid.cdc.gov/covid-data-tracker/#demographics

(monkeypox) had all been widely geographically distributed prior to the year 2000, with long histories of human infection. The three influenza sub-types reflect the normal genetic drift of this group of viruses. Only Covid-19, arguably a result of human interference, constitutes a truly new outbreak in this period. Of the four remaining short-term outbreaks in the figure, only SARS was unrecognized prior to 2000, with plague, yellow fever and cholera being long established endemic diseases that are greatly reduced in outbreak severity within the past century. Rather than demonstrating increasing risk, it demonstrates mostly low-level persistence of formerly more severe disease risks.

In terms of the claim that "*no one is safe until everyone is safe,*" the Future Surveillance report does not substantiate this claim nor does it lay out how such a broad claim might be proven. There is also concern about its factuality, since it has been clear since early 2020 that children are at low risk from SARS-CoV-2.[90] In addition, several of the events highlighted in Figure 7 do not pose a global spread risk, such as Ebola, which is largely confined to country and regional level outbreaks, and why the WHO has in the past not declared all Ebola outbreaks a PHEIC. What this suggests is that specific pathogens require specified approaches that respond to the individual characteristics of the pathogen as well as the context in which the outbreak occurs (i.e. the need to distinguish between epidemics and pandemics). Although preparedness is necessary to mitigate the threat of an outbreak, it is not immediately clear that all outbreaks should be treated as a uniform global threat, nor should they receive the same response in every case.

WHO further notes within Future Surveillance that "*300 to 400 infectious hazard events of public health concern are now detected annually*," apparently illustrating the prevalence of infectious disease. This number is from the 2021 Annual Global Report on Public Health Intelligence Activities[91], which is part of the WHO Health Emergencies Programme. This report notes an increase in substantiated public health events recorded in Emergency Management System (EMS) over the 20 years leading to the COVID-19 pandemic,[92] although the highest value thus far was reached in 2009. Yet, within that report the authors acknowledge that the overall increasing trend between 2013 and 2020 is "i*n part, due to an improved use of EMS and increased trainings for WHO Regions, along with systematic engagement with States Parties to improve national surveillance systems*". Despite this recognized confounder, the report goes on to assume that there is an increased trend of public health events, and that this trend will continue "*as climate change, (protracted) humanitarian crises, and disasters become more frequent*", none of which is further substantiated with evidence or citations to evidentiary sources.

[90] https://www.sciencedirect.com/science/article/pii/S001393512201982X#bib42
[91] https://cdn.who.int/media/docs/default-source/documents/emergencies/phi_2021_annual_report_web.pdf?sfvrsn=7482a7c9_2&download=true
[92] https://www.who.int/publications/i/item/WHO-HSE-GCR-LYO-2014.4

It is possible to find similar assumptions about environmental and social contributors repeated in the Future Surveillance report. In the Introduction, the report lays out several global trends that plausibly contribute to the future emergence and re-emergence of pandemics, including "*population and demographic changes, biodiversity and ecological changes, urbanization, livestock production and expanded and higher-volume transportation networks*" (p. 27). However, these claims are not supported by a citation to any source. As a result, there is an evidence gap and/or under-evidenced assumption about how these environmental and social changes translate into "exacerbating factors" of epidemic and pandemic risk. Moreover, it is important to note that there is contestation within the literature that explicitly examines the role of these factors. For example, there is evidence to support a positive relationship between basic nutrition and immune response to infections[93] as well as other adverse health effects from poor or contaminated food sources.[94] As a result, food production and land use can have important impacts on susceptibility to disease. Yet, this holds for most diseases. Thus, it is a mainstay of basic population health and not just relevant for infectious diseases. What the literature demonstrates is that the relationship between these variables and pandemic risk is highly complex and multivariant, and that these factors can both exacerbate and help mitigate pandemic risk depending on how these sectors are managed (see discussion below).

4.2. Managing Epidemics

In November 2023 the WHO released the 2nd Edition of the handbook Managing Epidemics: Key Facts About Major Epidemic Diseases.[95] In its Introduction, the handbook proclaims that:

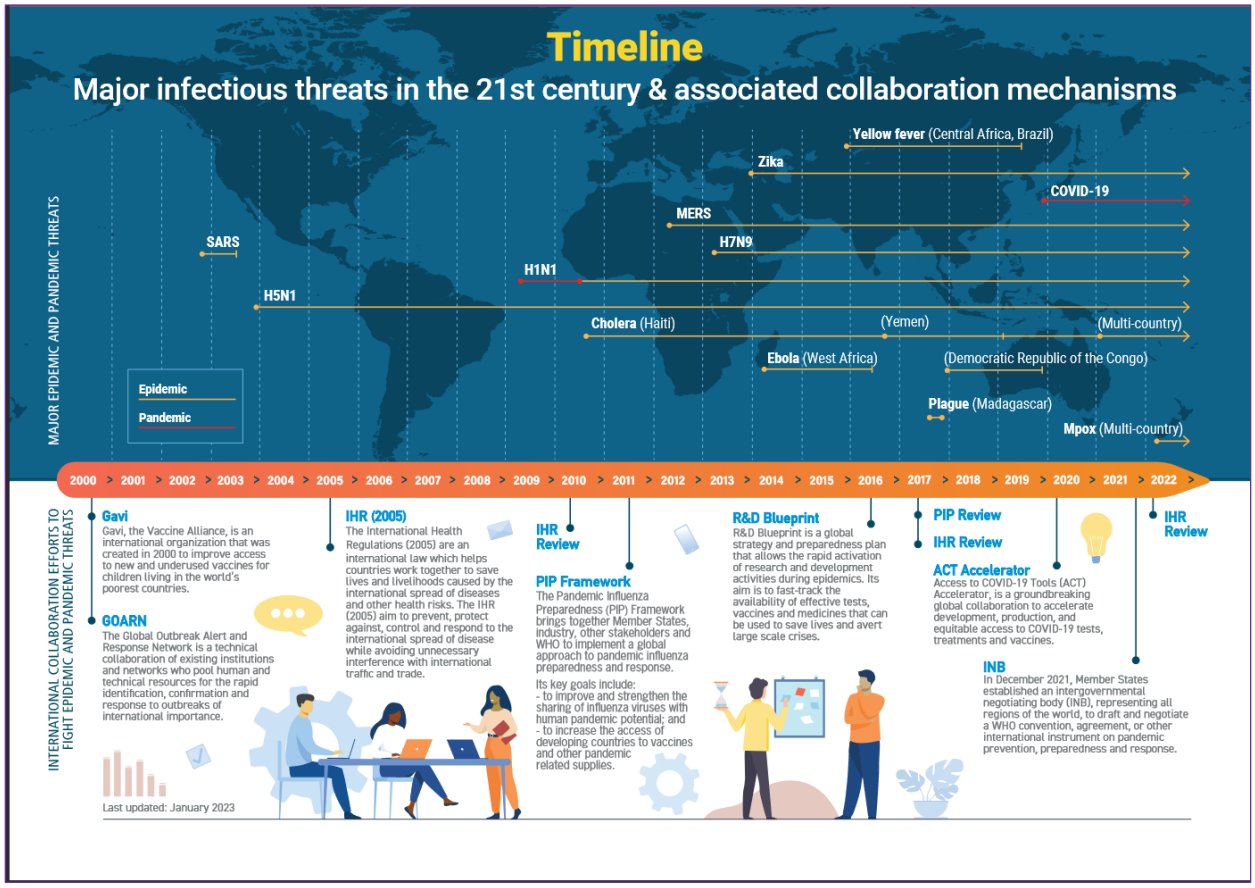
> *"Epidemics and pandemics of infectious diseases are occurring more often, and spreading faster and further than ever, in many different regions of the world. The background factors of this threat are biological, environmental and lifestyle changes, among others."*

The document goes on to describe that the "*early years of the 21st century have already been deeply scarred by so many major epidemics.*" To substantiate the claim the handbook lists several outbreaks, including, SARS, H1N1, MERS, Ebola, Zika, COVID-19 and a plague outbreak in Madagascar that killed 209 people in 2017. Repeating the claim from its Introduction, the handbook again asserts on Page 5 that "*epidemics in the 21st century are spreading faster and further than ever.*"

To visualize increased risk from outbreaks the following graphic is provided (Figure 8) which differs from Figure 7 only in formatting:

[93] https://pubmed.ncbi.nlm.nih.gov/18207566/
[94] https://pubmed.ncbi.nlm.nih.gov/28138818/
[95] https://www.who.int/publications/i/item/9789240083196

Figure 8. Fig. 1 from WHO handbook 'Managing Epidemics: Key Facts About Major Epidemic Diseases, Second Edition', showing "Major epidemic and pandemic events in the 21st century".



To demonstrate an increased risk in outbreak frequency the handbook provides the table of 'acute public health events' in Figure 9A. This is stated to be based on diseases from the WHO priority disease list (see Section 4.3).[96] Although these diseases correspond to those listed and tracked within the Blueprint as priorities, the Blueprint itself does not provide the associated data related to the relationship between outbreaks and 'health events,' or their impact. For example, sixty-three 'acute public health events' were reported for Zika virus in 2016. These presumably refer to multiple localities of the same outbreak(s) in South America that year, calling into question WHO's claim in Figure 9A that time and space linked reports were merged and counted as one event.

The numbers here in Figure 9A, being events a country chooses to report to WHO, are therefore quite arbitrary. Malaria killed roughly 600,000 in each of these years but is recorded as a few outbreaks per year. Measles remains endemic in many regions, as is yellow fever, while dengue has frequent outbreaks across the tropics. However, by charting event numbers by year (Figure

[96] https://www.who.int/activities/prioritizing-diseases-for-research-and-development-in-emergency-contexts

9B), the WHO document provides a visual impression of increasing outbreaks. The event numbers in Figure 9B don't match those in Figure 9A and so must include a broader spread of diseases, though the non-specific source, 'acute public health events reported to WHO,' is the sole basis. The reader is to take on trust from WHO that this represents a real increase in risk, though Figure 9A suggests that the vague methodology underlying these charts does not support this.

Figure 9. Acute public health events from WHO handbook 'Managing Epidemics: Key Facts About Major Epidemic Diseases, Second Edition.' (A) Acute public health events for selected diseases, and (B) infectious disease public health events by year.

A. Acute public health events* for selected infectious diseases (2011–2021)

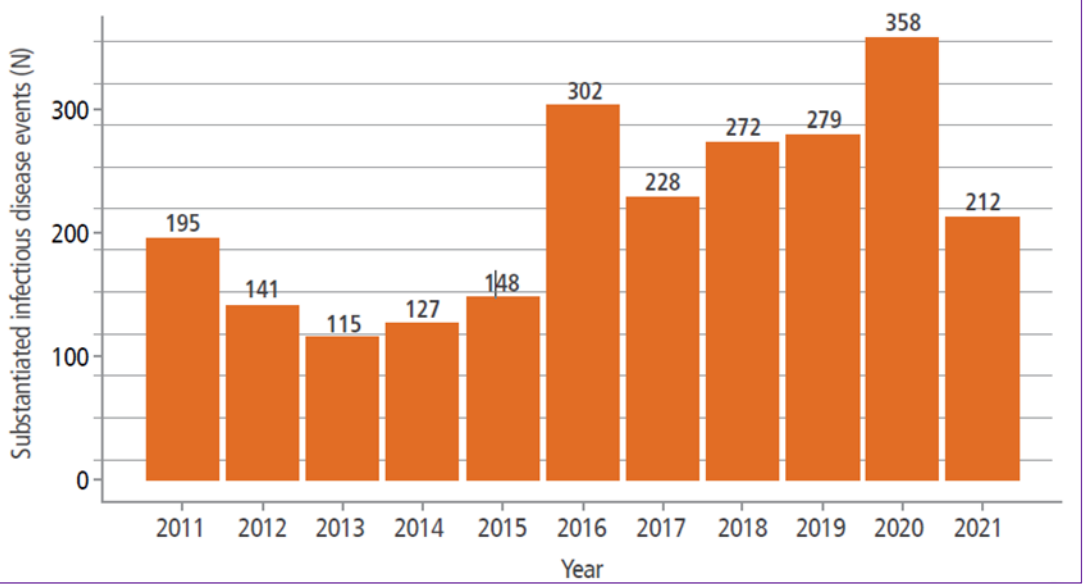
	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	TOTAL
Avian/Animal influenza	5	2	1	3		5	5	3	2	5	16	47
Chikungunya	1	3	4	24		5	3	3	2		1	46
Cholera	24	24	11	1	19	16	14	23	19	4	12	167
Crimean-Congo haemorrhagic fever	1		3		4	2	8	4	8	3	3	36
Dengue	8	10	7	6	7	5	12	13	16	4	10	98
Ebola virus disease	1	3		3				2	2		1	12
Lassa fever	2	1	2	1	2	2	7	3	6	1	4	31
Malaria	2	2			3	3	11	4	8	3	7	43
Marburg virus disease				1			2				1	4
Measles	19		7	11	13	7	15	25	15	3	5	120
Meningococcal disease/Meningitis	11	11	3	4	4	8	10	7	2	2	2	64
MERS		3	5	9	2	1	1	5	4	1	2	33
Nipah virus	1		1					1	2	1	1	7
Poliomyelitis	10	1	4	3	2	2	3	13	16	6	16	76
Rift Valley fever	2				2	3	3	3	3	1	2	19
Yellow fever	2	3	3		1	5	1	5	2	6	3	31
Zika				2	15	63	5	3	1		2	91

* A public health event is an outbreak of a disease reported to WHO. One event may consist of one or several case reports or clusters. Time and space linked reports are merged and counted as one event.

Heatmap for selected infectious diseases:
– Top 10 most commonly reported infectious diseases selected in the 11-year time period.
– Priority diseases in WHO R&D blueprint

Note:
Events of acute watery diarrhoea have **not** been included as cholera

B. Number of acute public health events* of infectious disease typology by year (2011–2021)



To explain WHO's claimed increase in outbreak frequency and scope the handbook outlines two key drivers: 1) The "*fast and intense mobility of people,*" and; 2) Increased land use and agricultural changes, namely, "*deforestation, urban sprawl and human encroachment into previously untouched*

habitats." According to the handbook, these latter changes "i*ntensify our interactions with wildlife and the pathogens they harbor. Changing and intensified food production, from live poultry and animal markets to deforestation for expanded large-scale agriculture, also leads to increased contact between people and wildlife. Some of the animals that humans are increasingly in contact with (bats for example) are likely sources of new pathogens.*" Again, as with the 2023 WHO Future Surveillance report, no evidence is cited to support these claims.

It is important to analyze these in turn.

First, it is unescapable that there is a direct connection between the increased volume of travel and a higher chance of a given pathogen spreading more quickly. For example, global airline passenger traffic increased fivefold between 1989 and 2019.[97] This will undoubtedly increase the speed in which a pathogen moves. However, increased travel also means that people have been exposed to a greater number of pathogens and over time have formed immunities. As a result, although speed of travel and volume is a risk factor for new zoonosis (that needs to be considered in any contingency planning), what is less likely is that reemerging pathogens will be reaching completely immune naïve populations.

Second, the evidence for land use change leading to increased disease emergence is less obvious. Deforestation has slowed down substantially in the past 2 decades[98]. The same goes for the claim that "*ever increasing climate-mediated disasters create humanitarian emergencies where infectious diseases can take hold and quickly spread.*" Actually, deaths from natural disasters have decreased massively compared to the first half of the 20th century,[99] disasters themselves have not increased[100] and the reason why economic losses have increased lies in societal change (larger, more wealthy populations) rather than climate change.[101] This suggests a more complicated story, which further suggests the need for additional investigation and research. Lastly, the relationship between climate change and health is a rather new field of study and the scientific data is now only starting to emerge.

Third, the claim that "unprecedented levels of urbanization and swelling populations of city dwellers inescapably pose greater risks of infectious disease transmission" is also not straightforward. Although urbanization accelerates speed of inflection by placing a greater number of human bodies in proximity, it can also facilitate a more targeted response. Moreover, urbanization often also coincides with economic development and depending on urban management, urbanization positively affects public health.[102] Finally, the handbook mentions the

[97] https://www.airlines.org/dataset/world-airlines-traffic-and-capacity/
[98] https://www.fao.org/3/ca9825en/ca9825en.pdf
[99] https://ourworldindata.org/natural-disasters#
[100] https://www.forbes.com/sites/michaelshellenberger/2022/01/10/why-disasters-have-declined/
[101] https://www.tandfonline.com/doi/full/10.1080/17477891.2020.1800440
[102] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9852986/

increased number of displaced people and how their often crowded and poor living conditions benefits the spread of epidemics. Depending on level sanitation, nutrition, housing, and humanitarian assistance, this is undoubtedly an exacerbating factor if poorly managed (e.g. Haiti cholera outbreak due to poor sanitation in UN facilities). Where risk persists is in cases where large and unexpected displacement occurs and where appropriate response to that crisis is unavailable or undelivered. The key word here is proper "managing" of situations where there is an increased risk of epidemics before conditions result in humanitarian disasters. Here, there is a clear role for the WHO and other UN agencies to act in the face of basic human health needs.

In sum, the WHO handbook Managing Epidemics paints an extremely bleak picture of a world that suffers with ever more epidemics, natural disasters, and other humanitarian emergencies. Most of the foundational claims within the handbook remain under-evidenced and presumptive. This points to the need for better evidence production to assess pandemic risk, but also in how to best respond to those risks. By not doing so, the handbook constructs a future narrative that contradicts several actual long-term trends while promoting a sense of urgency and unmitigated risk.

4.3. The WHO Priority Disease List

A further major document promoting action based on pandemic risk is the WHO Priority Disease List for Research and Development in Emergency Contexts.[103] Intended to accelerate research and development in public health emergencies, it lists non-influenza diseases considered by WHO to be potential major epidemic or pandemic threats; COVID-19, Crimean-Congo hemorrhagic fever , Ebola virus disease and Marburg virus disease, Lassa fever, Middle East respiratory syndrome coronavirus (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS), Nipah and henipaviral diseases, Rift Valley fever, Zika, and "Disease X".

The Priority Disease list is intended to be indicative of pathogens at high risk of causing naturally occurring pandemics. However, COVID-19 is widely considered to be the result of human manipulation rather than natural emergence,[104,105,106] and irrespective is rarely severe beyond the unwell elderly.[107,108] Lassa fever is an endemic disease confined to West African countries and kills around 5000 people per year,[109] whilst Ebola virus presents as mostly isolated outbreaks in West and Central Africa, with by far the largest outbreak, in West Africa in 2014, killing under

[103] https://www.who.int/activities/prioritizing-diseases-for-research-and-development-in-emergency-contexts
[104] https://oversight.house.gov/landing/covid-origins/
[105] https://www.bmj.com/content/382/bmj.p1556
[106] https://www.dni.gov/files/ODNI/documents/assessments/Unclassified-Summary-of-Assessment-on-COVID-19-Origins.pdf
[107] https://covid.cdc.gov/covid-data-tracker/#demographics
[108] https://www.medrxiv.org/content/10.1101/2022.10.11.22280963v1
[109] https://www.who.int/publications/i/item/introduction-to-lassa-fever

12,000 people.[110] None of the remaining diseases have killed more than 1000 people in recorded history. Of those of natural origin, this list therefore reflects diseases either highly geographically confined (and still of relatively low burden) or that have been widespread but with very low mortality. Tuberculosis, by contrast, kills an estimated 1000 people every six to seven hours.[111]

WHO lists "Disease-X" as a potentially highly transmissible and virulent disease that could arise and cause a far higher disease burden; however, the fact that a hypothetical disease must be included to represent such risk is significant. It seems sensible from a public health viewpoint to consider the possibility of such an event. However, if resource allocation is to remain proportionate, it ought to be informed by actual risk rather than speculation. The prominence given to Disease-X in the media and by entities cooperating with WHO suggests that the context of the priority disease list may not be widely understood.[112,113,114]

[110] https://www.who.int/emergencies/situations/ebola-outbreak-2014-2016-West-Africa

[111] https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2023

[112] https://www.weforum.org/agenda/2018/03/a-mysterious-disease-x-could-be-the-next-pandemic-to-kill-millions-of-people-heres-how-worried-you-should-be/

[113] https://apnews.com/article/fact-check-disease-x-davos-world-economic-forum-496804566435

[114] https://fortune.com/well/2024/01/12/what-is-disease-x-world-economic-forum-pandemic-planning/

4.4. Summary of WHO evidence base

Whilst outbreaks may or may not be increasing, the evidence from WHO documentation does not strongly support either conclusion. As a result, the foundation for the WHO's general claim that *"Epidemics and pandemics of infectious diseases are occurring more often, and spreading faster and further than ever, in many different regions of the world"* is not well supported.[115] In most cases the WHO does not cite evidence to support its claims, or cites other WHO documents that in turn lack evidence to support a specific claim.

Moreover, there is no evidence in the data provided by WHO to support what they call "exacerbating factors" such as climate change and increased urbanization. Although there is evidentiary material available that could shed light on these relationships, it is not cited in the WHO documentation. Moreover, the literature regarding these factors is complex and demonstrates that factors such as increased urbanization both enhances certain risks while mitigating others.[116,117] A more thorough analysis and presentation of how these factors affect pandemic risk is required before the information presented by WHO can be used to legitimately support increased investment.

[115] https://www.who.int/publications/i/item/managing-epidemics-key-facts-about-major-deadly-diseases
[116] https://link.springer.com/article/10.1007/s10393-014-0941-z
[117] https://www.frontiersin.org/articles/10.3389/fvets.2021.661063/full

5. World Bank Report (2022): Putting Pandemics Behind Us

5.1. The Report preface and overview.

The 2022 World Bank Group report '*Putting Pandemics Behind Us: Investing in One Health to Reduce Risks of Emerging Infectious Diseases*' was written with the intent of laying out a justification for, and costing of, a One Health Approach to prevent pandemics resulting from spillover events transferring pathogens from animal to human populations.[118] An accompanying technical report, 'Increasing investments in One Health to reduce risks of emerging infectious diseases at the source', is discussed later.

The Executive Summary lays out the general theme and basic claims to be elaborated later:

> *"We publish this report with a sense of urgency. As damaging as COVID-19 has been, the number of infectious disease outbreaks—from avian influenza to Middle East respiratory syndrome to Ebola—has been increasing dramatically. Every year, zoonoses cause more than a billion human infections and a million deaths —a trend that we must put an end to because it jeopardizes human development and breeds larger outbreaks such as COVID-19, bringing much higher death tolls."*

A phrase also similar across documents follows:[119,120,121,122]

> *"Effectively addressing the challenges posed by pandemics requires a departure from the old cycle of panic and neglect."*

It is unclear what this really means, as it suggests a frequent cycle of pandemics with a panicked response, whereas there seems little evidence of this in recent decades. Arguments have been made of a mishandled response to the 2009 Swine Flu pandemic,[123] but prior influenza pandemics listed by WHO, in 1957 and 1968, passed with relatively little notice.[124] The SARS (2003) and MERS (2012) were quite rapidly contained with mortality of each below 1000 people

[118] https://documents.worldbank.org/en/publication/documents-reports/documentdetail/099530010212241754/p17840200ca7ff098091b7014001a08952e
[119] https://blogs.worldbank.org/health/moving-away-panic-and-neglect-big-step-forward-pandemic-preparedness-and-response
[120] https://news.un.org/en/story/2018/05/1010641
[121] https://openknowledge.worldbank.org/entities/publication/32eceb2b-1f11-5c7b-9166-a62feec8e393
[122] https://reliefweb.int/report/world/panic-and-neglect-investing-health-security-financing-pandemic-preparedness-national
[123] https://link.springer.com/chapter/10.1007/978-3-319-68173-3_9
[124] https://apps.who.int/iris/bitstream/handle/10665/329438/9789241516839-eng.pdf?ua=1

globally,[125,126] while the West African Ebola outbreak was characterized by a relatively low mobilization of response but essentially then contained and managed similarly to other Ebola outbreaks.[127] Based on the disease burdens of listed outbreaks in this report, in comparison to the major causes of mortality globally, the case for 'neglect' is unclear. The concern here, as elsewhere in this analysis, is that a major global institution is appealing for increased funding for a program based, at least in part, on emotive language rather than evidence. In this case, the emotive language is echoed by multiple institutions and media, and may take on meaning by repetition that may not be justified through fact.

One Health is explained by the World Bank as an approach to "…*sustainably balance the health of people, animals, and Ecosystem*". This is an important definition, as it does not clearly put human health first, as public health traditionally has. This is important in phrasing that has been echoed elsewhere in wording specifically placing the welfare of humans and other species on an equal level.[128] It would be of concern to many as a justification of public funding, though this lack of clear prioritization of human health here is not discussed further and may not be the intent of the World Bank text.

Four approaches to reduce risk are mentioned, centering around reduced spillover of zoonotic pathogens, but nothing on building human resilience through nutrition or other approaches (shown so central in COVID-19). Rather, it focusses on building and strengthening technical agencies and financial institutions - risking a vertical and one-size fits all approach to fix a problem externally, rather than supporting populations to build resilience.

The last executive summary sentence repeats the phrase: "*Investing in One Health based prevention is the best way forward to break the cycle of panic and neglect*", but again – it is not clear in what way there is a cycle nor what dynamics are involved in this cycle. Consequently, the language of panic and neglect (or its sister phrase "panic and forget") looks to be more about motivating policy consensus than a description of an empirical condition. For example, pre-COVID-19, the last acute pandemic above the level of normal influenza deaths was the 1968-1969 influenza pandemic (1 million deaths)[129] and there are now influenza surveillance programs and systems in place aimed to mitigate against flu outbreaks.

[125] https://www.who.int/publications/m/item/summary-of-probable-sars-cases-with-onset-of-illness-from-1-november-2002-to-31-july-2003
[126] https://www.who.int/health-topics/middle-east-respiratory-syndrome-coronavirus-mers#tab=tab_1
[127] https://link.springer.com/chapter/10.1007/978-3-319-68173-3_9
[128] https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(23)00090-9/fulltext
[129] https://apps.who.int/iris/bitstream/handle/10665/329438/9789241516839-eng.pdf?ua=1

5.2. An important note on the term 'emerging infectious diseases' (EIDs)

The sub-title of this report, and the accompanying technical report, raises a significant terminology issue underlying the approach currently common in public health regarding infectious disease outbreaks. 'Emerging disease' implies a pathogen that has newly evolved or crossed from other hosts (e.g., a zoonosis) to humans, rather than considering changes in technology or approaches that may simply have enabled a pre-existing disease (or pathogen) to be detected and characterized. In the context of rapidly evolving diagnostic technology, the term 'emerging disease' should generally be used with caution, unless a clear origin can be demonstrated, or the clinical picture is relatively unique.

HIV is an example of a pathogen that is likely to have newly emerged, though perhaps a generation before it was recognized. It thus illustrates the importance of both size of outbreak (related to human population size), the geographical context in which it occurs, and the development and subsequent availability of methods to detect a pathogen. While probably arising in areas in Africa that were remote from modern diagnostics and before recent advances in molecular biology upon which much modern diagnosis depends,[130] it was only detected several decades later when it caused illness in more technologically advanced communities where newly developed laboratory techniques could be employed to identify and characterize the virus.

Small outbreaks such as those now attributed to Nipah Virus infections or Mpox (formerly Monkeypox) are therefore likely to have persisted for centuries, associated with limited, localized disease clusters with clinical features poorly distinguishable from other illnesses, in areas where reporting was poor. They are therefore not necessarily 'emerging', but 'newly characterized'.

Terminology matters here, as much of the urgency around pandemic preparedness hinges on a perception that new diseases are rapidly emerging. If infectious disease outbreaks are actually relatively stable, then the approach, and certainly the urgency, will be very different.

[130] https://perspectivesinmedicine.cshlp.org/content/1/1/a006841.full

5.3. Concerns with the introduction in the Report

The Introduction to the World Bank's report makes bold claims regarding the need for action in addressing pandemics and One Health needs. These set a tone for the report but fit poorly with the evidence provided and lack objectivity. The outbreaks under consideration by the World Bank are generally very mild in terms of disease burden:

> *"Before COVID-19, HIV/AIDS, Nipah virus disease, avian influenza, Ebola virus disease, severe acute respiratory syndrome (SARS), Middle East Respiratory Syndrome (MERS), and Zika were among the diseases that emerged from animals in contact with humans over the last few decades, and several of these fully realized their pandemic potential."*

HIV/AIDS is clearly a major disease and fits some 'pandemic' definitions in that it arose as a new disease and spread worldwide, but probably took decades to become noticeable.[131] It is not necessarily justified to suggest such a situation would be repeated today – HIV spreads slowly compared to respiratory viruses (such as SARS-CoV-2) and by direct human contact involving exchange of body fluids, while the ability to detect the virus and diagnose the disease has been transformed throughout most of the world since HIV emerged.

Ebola virus has never maintained transmission beyond three countries in an outbreak (the West African outbreak, which killed less than 12,000 people, is the only outbreak to achieve this).[132] MERS and SARS killed less than 900 people each,[133,134] Zika less than 400.[135] The largest Nipah virus outbreak (Malaysia in 1998) caused under 110 deaths.[136] Avian influenza mortality is less than 80 annually for the past two decades, and near zero for the past 6 years.[137] For context, tuberculosis, a major endemic infectious disease, kills approximately 1.3 million people annually (or over 3,500 daily).[138]

So, the Report's contention that

> *"several of these fully realized their pandemic potential"*

does not apply beyond COVID-19 and HIV (a several decades event) unless we accept that pandemics are generally mild events with little or no impact on overall mortality. If the latter is true, the question arises of whether this is indeed a major health issue and being addressed

[131] Ibid.
[132] https://www.who.int/emergencies/situations/ebola-outbreak-2014-2016-West-Africa
[133] https://www.who.int/health-topics/middle-east-respiratory-syndrome-coronavirus-mers#tab=tab_1
[134] https://www.who.int/publications/m/item/summary-of-probable-sars-cases-with-onset-of-illness-from-1-november-2002-to-31-july-2003
[135] https://www.nejm.org/doi/pdf/10.1056/NEJMoa2101195
[136] https://www.frontiersin.org/articles/10.3389/fmicb.2021.811157/full
[137] https://cdn.who.int/media/docs/default-source/global-influenza-programme/2023_march_tableh5n1.pdf
[138] https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2022

proportionately, or whether other drivers are influencing the prioritization of the PPPR agenda.[139] Adoption of a calm and more low-key response might be a more appropriate approach to PPPR in the context of these outbreaks – reflecting previous approaches such as the WHO pre-2020 guidance for pandemic influenza,[140] rather than promoting unfounded concern regarding health burden.

A further statement adds to this confusion regarding the report's evidence base:

> *"Every year, zoonotic diseases sicken billions of people, killing millions, with low- and middle-income countries being most vulnerable."*

Pre-COVID-19, HIV/AIDS is the only claimed zoonotic spillover associated with over a million deaths annually over the past half century. It is unclear what other diseases are referred to, as mortality is low for other zoonotic spillover outbreaks listed in Section 3.4. of this report. The statement presumably refers to seasonal influenza, for which international mechanisms are already in place.

The Introduction then outlines the driver, repeated throughout the report, for the claimed increase in outbreaks:

> *"As humans extend their footprint on the planet, encroaching into natural habitats and altering them, the potential for diseases to emerge has increased exponentially.",*

causing (later):

> *"…an accelerating trend of outbreaks…"*

As discussed below, these claims are not supported by the data cited. As a note, it is also not well demonstrated in other main PPPR documents examined earlier in this report.

Finally, the phrase: *"risk anywhere becomes risk everywhere"* appears derived from the WHO COVAX slogan "No one is safe, until everyone is safe",[141] but again seems inappropriate and unevidenced when referring to disease outbreaks (this slogan is reproduced again in the 2023 WHO Future Surveillance report – see above). Outbreaks over the past century have been highly heterogenous in impact across populations. Most are defined by local ecology and host susceptibility. As an example, people outside of Africa are not at risk from Ebola (nor are most Africans), and Nipah virus is highly geographically defined (Figure 12, p. 71). The severity of respiratory viruses such as SARS-CoV-2 (COVID-19) are highly dependent on age and comorbidities.[142] The statement is

[139] https://www.tandfonline.com/doi/full/10.1080/13563467.2024.2304180
[140] https://apps.who.int/iris/bitstream/handle/10665/329438/9789241516839-eng.pdf?ua=1
[141] https://www.who.int/initiatives/act-accelerator/covax
[142] https://covid.cdc.gov/covid-data-tracker/#demographics

therefore illogical and seems inappropriate for a serious report, again potentially aimed to influence policy consensus and compliance based on emotive triggers rather than analysis of data.

5.4. Concerns regarding the importance of One Health reforms

The report claims on page 14 that One Health approaches successfully combated River Blindness. River Blindness (Onchocerciasis) is not a zoonosis, but spreads from human to human through a blackfly insect vector. Control has been achieved predominantly through insecticide use (particularly DDT) and mass drug treatment (predominantly with ivermectin).[143] This is a strange example of what the World Bank seeks to promote as One Health but does illustrate that health services have long addressed environmental influences on disease (malaria is another example).

Further examples suggested as amenable to the One Health approach include COVID-19 (for which a natural spillover origin is widely questioned),[144] and Avian flu, Mpox and Langya virus. Avian Flu and Mpox have a combined global mortality below 1000 over the past two decades,[145,146,147] while Langya virus has been reported from a few dozen human cases in Asian countries, as a probable spillover from shrews or bats.[148]

The urgency for investment in One Health is then referenced to a report by the Independent Panel on Pandemic Preparedness and Response (IPPPR),[149] which itself does not cite quantitative data but describes the views of its expert contributors. The evidence base provided to support the urgency and scope of World Bank's proposed One Health approach is, therefore, weak.

[143] https://www.sciencedirect.com/science/article/pii/S0001706X10002111
[144] https://www.dni.gov/files/ODNI/documents/assessments/Unclassified-Summary-of-Assessment-on-COVID-19-Origins.pdf
[145] https://cdn.who.int/media/docs/default-source/global-influenza-programme/2023_march_tableh5n1.pdf
[146] https://iris.who.int/bitstream/handle/10665/365630/WER9803-29-36.pdf?isAllowed=y&sequence=1
[147] https://www.who.int/news-room/fact-sheets/detail/monkeypox
[148] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10129132/
[149] https://theindependentpanel.org/wp-content/uploads/2021/05/COVID-19-Make-it-the-Last-Pandemic_final.pdf

5.5. Questions on outbreak frequency

On page 17, the Report opens its discussion on pandemic frequency by stating:

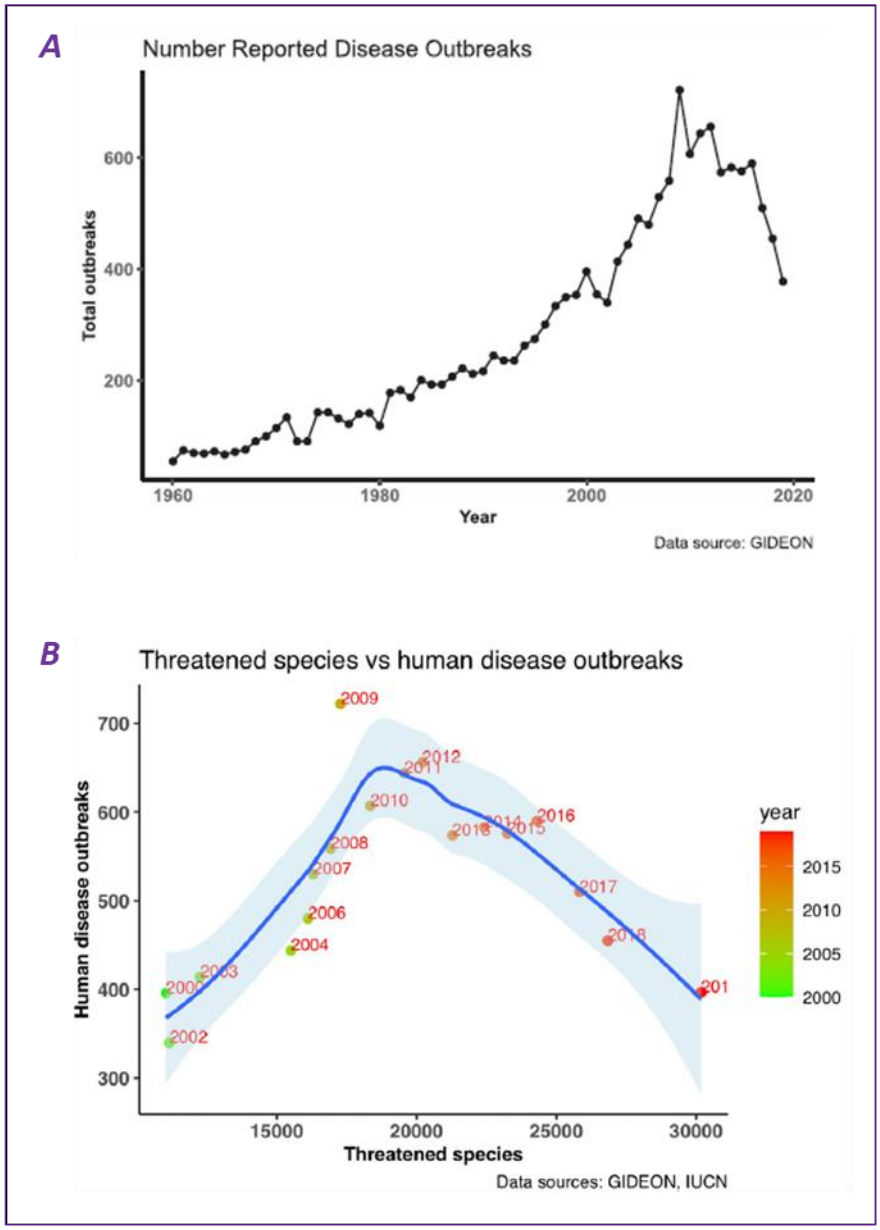
> *"The pace of EIDs [Emerging Infectious Diseases] has accelerated at an annual rate of 6.7 percent from 1980, with the number of outbreaks growing to several hundred every year since 2000 (Morand 2020)."*

The cited study, Morand (2020),[150] presents a more nuanced picture. Outbreak frequency decreases after 2010, while a later analysis of the same Global Infectious Disease and Epidemiology Network (GIDEON) dataset by Morand, in Morand and Walther (2023),[151] shows *disease frequency* in 2018 returning to 1960 levels. As Figure 10A illustrates, Morand (2020) does show an accelerating increase to several hundred per year from 1960, peaking around 2009. It then consistently decreases over the subsequent (most recent) decade.

The reported risk per capita of becoming a case in an outbreak has been declining based on the same GIDEON dataset (Smith et al., 2014).[152] The overall increase since 1960 in reported outbreak frequency forming the basis of GIDEON data takes no account of improved communications, road networks, development and expansion of PCR and other diagnostics (e.g. point of care serology and antigen tests) and laboratory capacity. Reporting of outbreak diversity is heavily dominated by more highly developed countries, expanding in less developed countries later, reflecting expectation if the probability of detection and reporting are major drivers of an apparent increase in outbreak frequency (Figure 11).

[150] https://www.sciencedirect.com/science/article/pii/S0006320720307655
[151] https://www.biorxiv.org/content/10.1101/2020.04.20.049866v2
[152] https://royalsocietypublishing.org/doi/10.1098/rsif.2014.0950?url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org&rfr_dat=cr_pub++0pubmed

Figure 10. Extracts from Morand (2020) [153] Figures 3 and 4, showing (A) reported outbreak frequency 1960 to 2020, and (B) relationship between outbreak frequency and animal species density.



Smith et al. (2014) are then quoted as suggesting that

> *"the richness of microbes causing diseases also increased significantly over that period."*

[153] https://www.sciencedirect.com/science/article/pii/S000632072030765

However, the World Bank authors fail to note that Smith et al. went on to show a per capita reduction in cases (i.e., risk per person) once internet use (as a proxy for improved communications) was taken into account.

The World Bank continues:

> *"…and the yearly probability of an occurrence of large outbreaks could increase up to threefold in the coming decades (Marani et al. 2021)."*

The reference here (Marani 2021) is discussed elsewhere in this report. Yet here it is important to note that the claimed 3x increase in outbreak frequency is a modelling result that ignores reasons for increased detection and identification over the past few decades. Two studies are then cited as supporting this finding; Jones et al (2008) and Daszak et al. (2001).[154,155] These studies do not cover the past two decades and do not lend direct support for this assumption (see below, for a more detailed discussion of Jones et al.).

[154] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5960580/
[155] https://doi.org/10.1016/S0001-706X(00)00179-0

Figure 11. Diversity of reported outbreaks over time in the GIDEON database, reported by Smith et al. (2014).[156]

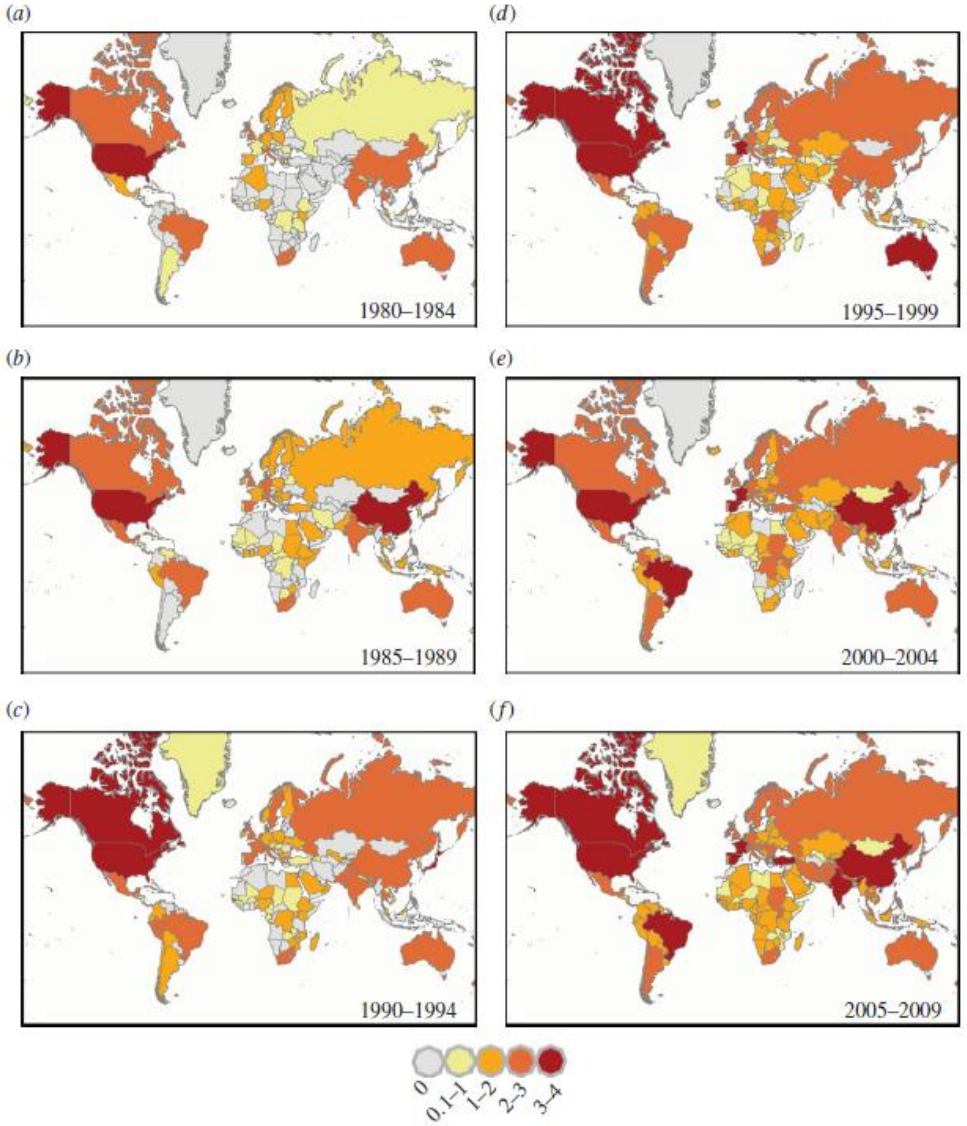


Figure 2. Global outbreak diversity for the nations of the world over time. Diversity is calculated for each nation using Shannon's diversity index (SDI) as described in the methods. Nations with the highest diversity of outbreaks are represented by larger values and darker shading. (Online version in colour.)

[156] https://royalsocietypublishing.org/doi/10.1098/rsif.2014.0950?url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org&rfr_dat=cr_pub++0pubmed

5.6. The Example of Nipah Virus Disease

The World Bank Report illustrates its concerns regarding pandemic risk through a section on the Nipah Virus (*A Cautionary Tale – The Story of Nipah Virus Disease*. [page 17]). Analysis of the claims here regarding Nipah Virus, a cause of recurrent severe encephalitis outbreaks, is important in illustrating the overall approach taken within the Report.

The discussion starts with:

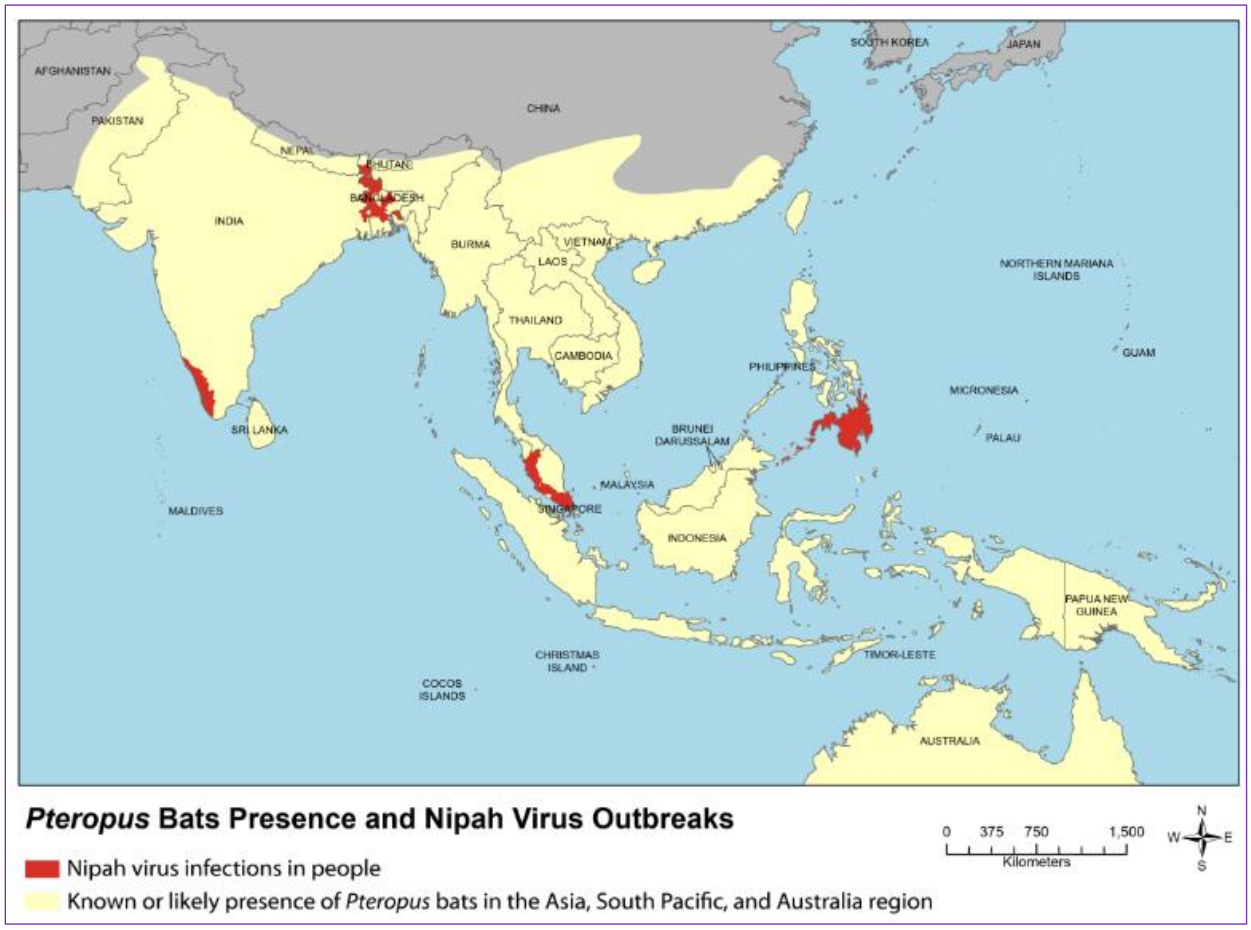
> *"Events started in 1998 in Nipah, a suburb of Ipoh, Malaysia, when villagers experienced febrile encephalitis for which there was no cure or treatment. Young people would be healthy one day and the next day their brains would swell up. They couldn't walk or talk. About half the patients died."*

It is then noted that the outbreak was initially misdiagnosed as Japanese Encephalitis (a mosquito-borne illness). It was soon recognized that the illness was associated with contact with, and preceded by an unusual illness in, pigs. The report postulates that environmental changes including deforestation promoted increased movement of fruit bats (that carry the virus) into fruit orchards near pig farms (perhaps implausibly, as fruit bats commonly fly to orchards to eat irrespective of deforestation, and to the increased density of pig rearing, promoting transmission within farms). The Malaysian government culled approximately one million pigs during the response, with considerable economic impact on rural communities.

Mortality from the Malaysian Nipah virus outbreak, the first and largest such outbreak recorded, killed 105 people out of 376 total cases by 2014.[157,158,159] Subsequent outbreaks elsewhere have recorded human to human transmission within villages and health facilities.[160,161] No further outbreaks have been recorded in Malaysia, and outbreaks have been confined to very limited geographical areas, despite the wider range of the major fruit bat species associated with spreading the virus (Figure 12). The World Bank Report notes 412 deaths in total globally at time of publication (unreferenced in the supporting technical report).[162] The virus is carried by other bat species in Asia and Africa, but without recognized transmission to humans.[163]

[157] https://link.springer.com/article/10.1007/s11908-006-0036-2#preview
[158] Looi LM, Chua KB. Lessons from the Nipah virus outbreak in Malaysia. Malays J Pathol. 2007 Dec;29(2):63-7. PMID: 19108397
[159] https://www.frontiersin.org/articles/10.3389/fmicb.2021.811157/full
[160] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2878219/
[161] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3373078/
[162] https://documents1.worldbank.org/curated/en/099042023145037128/pdf/P17840202eae520aa0ab910137cb6f1a142.pdf
[163] https://www.who.int/news-room/fact-sheets/detail/nipah-virus

Figure 12. Areas of known human Nipah Virus infections, and range of the bat species harbouring the virus.[164]



Reconsidering the evidence, the Nipah Virus story suggests a quite different scenario than the one suggested by the World Bank. The geographic spread of identified infections strongly suggests that the virus is not newly emerged, as does its presence in other bat species. The lack of any recurrence in Malaysia since its initial identification therefore suggests that this was an unusual spillover of an endemic zoonotic agent rather than a newly emerged virus.

It took several months for the causative pathogen to be identified in Malaysia as there was no test available for a previously unrecognized virus. PCR tests, the main form of identification, were invented less than 20 years earlier, and genomic sequencing barely available. It's similarity to Japanese Encephalitis, relative rarity and relative remoteness of most outbreaks suggest that

[164] https://www.cdc.gov/vhf/nipah/outbreaks/distribution-map.html#print

prior unrecognized outbreaks are likely to have occurred across the current range without being characterized as a separate disease.

Nipah Virus infection causes a clinically serious disease, with high case fatality rate.[165] However, no recorded outbreak has caused more than 105 deaths. The lack of recurrence in Malaysia suggests it is readily avoidable once its epidemiology is understood and mitigation mechanisms are in place, though outbreaks are more common in India and Bangladesh.[166] The main change regarding Nipah Virus in recent decades is likely our ability to recognize it, rather than it emerging de-novo.

The World Bank Report finishes its discussion on Nipah with:

> *"But the Nipah story is also a tale of a changing climate, changing use of land and food systems, lack of adequate biosecurity on farms, urbanization, social inequities and tensions, human activities driving disease emergence, and total blindness to prevention."*

While more intensive farming seems a likely factor in promoting pig-pig, and therefore pig-human spread (pigs are infected by proximity to fruit bats or bat excrement), the argument that forest degradation would increase bat-pig interaction is poorly evidenced, and not well supported as a general underlying cause of increased zoonotic spillover.[167,168] The link between Nipah Virus disease and climate change remains unexplained in the Report, as do links to social inequities and tensions. "Total blindness to prevention" may refer to a lack of ability to detect a disease if no test, or understanding of its epidemiology, is available. The example in the Report surely demonstrates that Nipah Virus Disease is largely an example of a newly recognized problem being, after an initial large outbreak, quite well addressed through existing mechanisms.

The story of Nipah Virus is perhaps best suited as an example of the improved differentiation of diseases as diagnostic capacity expands, and the ability to manage and contain such health threats within existing health system capacity.

[165] https://www.cdc.gov/vhf/nipah/symptoms/index.html
[166] https://www.cdc.gov/vhf/nipah/index.html
[167] https://www.nature.com/articles/s41893-019-0293-3
[168] https://link.springer.com/article/10.1007/s10393-014-0941-z

5.7. Discussion on investments.

The World Bank Report quotes the G20 High Level Independent Panel (HLIP) and a joint report of the World Bank and WHO to summarize the initial financial requirements for PPPR:

> *"The G20 High Level Independent Panel (HLIP) estimated the amount in international financing for pandemic preparedness that would be required every year for five years at $15 billion, along with significant increases in domestic spending, to address current gaps."*
>
> *"Recently, WHO and the World Bank estimated the total amount at US$31.1 billion annually, of which US$10.5 billion of international financing is needed annually for the next five years (WHO and World Bank 2022)."*

The Report (on page 27) then suggests this does not fully cover costs of the One Health approach. As a response the report advocates, adding $2.1 billion for veterinary public health systems, $5 billion for farm biosecurity, and $3.2 to $4.4 billion to reduce deforestation; in total adding a further $10.5 to $11.3 billion/year (it should also be noted that the $31.1 billion estimate from the 2022 report does not cover pandemic response financing and capacity building, which if pegged to the WHO Joint Evaluation Exercise (JEE) is estimated to add another $124 billion over five years to the total amount").[169]

The claim on deforestation promoting pandemic risk is repeated in Box 3 on page 34, and again on page 36 of the Report. The costing of mitigation of deforestation cites Allen et al. (2017). Allen et al. re-examined the data[170]. The authors found that the main associations with high EID outbreaks were broadleaf evergreen (i.e., tropical) forests and high mammalian species richness. This is not consistent with deforestation, where tree cover and mammalian species richness are expected to be reduced.

While forest preservation is desirable for many reasons, its use here to justify billions of dollars in funding to mitigate pandemic risk appears poorly supported by evidence.

Country ownership and equity.

Page 38 of the World Bank report discusses COVID-19 costs and country ownership. The approach outlined here raises concerns. The report justifies a need to "mainstream" One Health with its associated costs on the basis that:

[169] https://gh.bmj.com/content/8/1/e011172
[170] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5654761/

> *"Once the SARS-CoV-2 virus started spreading, it reached every corner of the globe, and no country was spared COVID-19's health and economic losses. Pandemic risk may have been perceived as hypothetical and a concern for high-income countries, while endemic diseases already burden lower-income countries. However, the burden of pandemics is heavy also in low- and middle-income countries along many dimensions,..."*

This statement seems at odds with the direct health costs of COVID-19 in many low-income countries, and the costs of diverting resources from other priorities (e.g., other health priorities and economic development) to PPPR. In most sub-Saharan African countries, the burden of COVID-19 paled beside other higher burden, and currently increasing, endemic disease burdens.[171] The economic costs of lockdowns and imposed income loss in the COVID-19 public health response cannot reasonably be included in the pandemic burden in these countries without demonstrating that such measures as school closures, market closures and closing of employment in such situations were a necessary response.[172,173,174,175]

The health burden of COVID-19 was clearly heterogenous, affecting predominantly older populations with metabolic diseases who are predominantly in higher-income countries.[176,177,178] True country ownership and equity would therefore seem to mitigate against low-income countries having to contribute or divert resources to this area, whilst higher burden health priorities persist. The Report does not seek to refute this but leaves the issue unaddressed. In this context of "country ownership", the subsequent note that the proposed amendments to the IHR, intended to strengthen PPPR, will be:

> *"...enforcing minimum standards for what constitutes One Health spending..."*

also suggests an emphasis against country ownership and control.

In finishing this section, the Report repeats the need to:

> *"...correct the prevailing panic and neglect cycle..."*

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[171] https://www.ajtmh.org/view/journals/tpmd/aop/article-10.4269-ajtmh.21-0899/article-10.4269-ajtmh.21-0899.xml
[172] https://apps.who.int/iris/bitstream/handle/10665/329438/9789241516839-eng.pdf?ua=1
[173] https://www.who.int/teams/global-malaria-programme/reports/world-malaria-report-2022
[174] https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2022
[175] https://www.unaids.org/en/resources/fact-sheet
[176] https://www.sciencedirect.com/science/article/pii/S001393512201982X#bib42
[177] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9420458/
[178] https://covid.cdc.gov/covid-data-tracker/#demographics

This claim remains confusing in the context of PPPR, as no examples of panic are provided and, aside from the COVID-19 event, it is unclear when such conditions have been widely suggested to have prevailed in recent decades. Certainly not widely and consistently.

5.8. Summary of World Bank Report

In summary, the World Bank's report is poorly evidenced and provides no solid support for rapidly increasing pandemic risk. The references cited within the report to support this contention are selectively cited and appear sometimes to be mis-interpreted. There is no solid recognition of competing priorities and potential opportunity costs of the resource allocation proposed, beyond a general recognition that LMICs have a higher endemic infectious disease burden than high income countries.

Fundamentally, both the report and its references, which rely heavily on analysis of the GIDEON database, fail to take account of the development and expansion of diagnostics, and provide only limited allowance for improving communications and surveillance, and funding for the same. Claims of rising risk, together with emphasis on a perception of panicked historical responses, are used to paint a picture of urgency and chaotic or absent response from current health system models. However, the examples provided, such as Nipah Virus outbreaks, could equally serve to illustrate current success in mitigating potential harm, with acute outbreaks resulting in low disease burdens and COVID-19 (predominately affecting older people in high income countries) being an outlier. The argument for spending a further $10 billion annually on One Health approaches, not included in previous budgeting, and the over $31 billion previously proposed, are therefore poorly supported.

6. World Bank Technical Report (2022): Increasing investments in One Health to reduce risks of emerging infectious diseases at the source.

6.1. Overview

The World Bank Technical Report was produced to support the 2022 Report 'Putting Pandemics Behind Us'.[179,180] The report covers evidence for pandemic risk and reasons for emergence, and then the financial implications. Here we discuss the first two issues, in the initial sections 'What is the trend in emergence of infectious diseases?', and 'What drives emergence of infectious diseases?' and critique the assumptions and claims.

The report states in the first paragraph of the introduction that:

> *"The burden of infectious diseases continues to grow, and humanity faces more outbreaks, some with the potential to become pandemics."*

and

> *"The One Health approach offers a practical and successful framework to reduce pandemic risks at the source."*

The first claim requires scrutiny. It is well recognized that the main improvements in life expectancy in both high- and low-income countries has been achieved through reduction in the risk of infectious diseases.[181,182] This has occurred primarily through prevention and through building host resilience, improved sanitation, nutrition and general living conditions. Other aspects of modern medicine; antibiotics and to a lesser extent vaccines, have also played a major role.[183] Life expectancy increase is continuing globally, with a 6.6-year increase recorded by WHO between 2000 and 2019.

Non-communicable diseases are now globally the main cause of mortality, as the share from infectious disease continuously declined for decades before the COVID-19 pandemic.[184] For an institution such as the World Bank to claim the opposite is highly misleading and misrepresents

[179] https://documents.worldbank.org/en/publication/documents-reports/documentlist?qterm=P178402
[180] https://documents1.worldbank.org/curated/en/099042023145037128/pdf/P17840202eae520aa0ab910137cb6f1a142.pdf
[181] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2836340/
[182] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7404362/
[183] Ibid.
[184] https://ourworldindata.org/burden-of-disease

information in a way that weakens the evidence pool and its ability to provide suitable insights for decision-making.

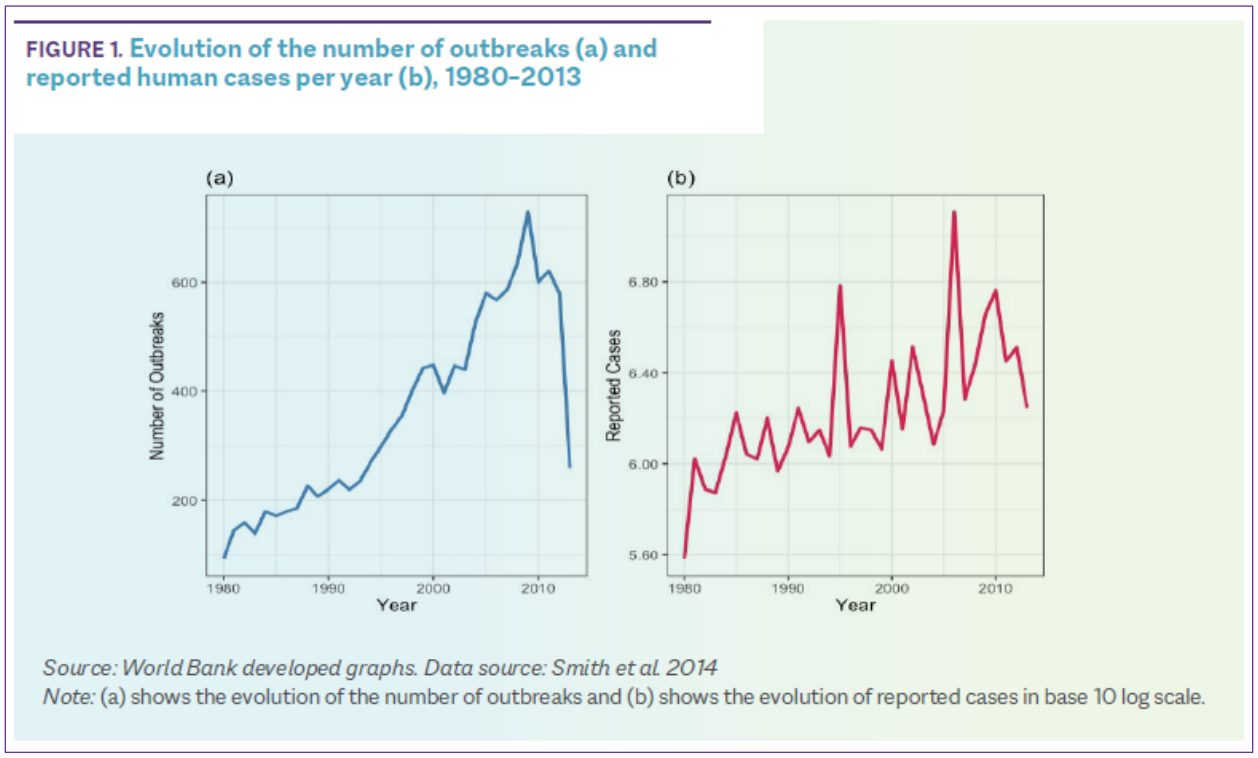
The emphasis of One Health approach is that it *"recognizes that human and animal health are interdependent and bound to the health of the ecosystems…"* From this it forms the justification for subsequent recommendations.

Section One of the Report, "trends in emergence of Infectious Diseases," begins with:

> *"Since 1980, the number of outbreaks per year has been steadily increasing (Figure 1a). Between 1980 and 2012, the number of outbreaks increased at an average of 6.7 percent per year."*

This is based on Smith et al (2014),[185] who found that while the number of reported outbreaks increased, the overall mortality rate (i.e., risk) from outbreaks was declining (Figure 13). Moreover, Smith et al. do not take into account changing detection and reporting capacity over this period (see Section 7.3 of this report).

Figure 13. Evolution of outbreaks in the World Bank technical report, based on Smith et al. (2014).



[185] https://royalsocietypublishing.org/doi/10.1098/rsif.2014.0950?url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org&rfr_dat=cr_pub++0pubmed

Smith et al. based their analysis on the GIDEON database.[186] The World Bank authors note that Morand et al. (2020),[187] extending the same database to 2020, demonstrated that outbreak frequency then declines. As presented by the World Bank,

> *"Although not seen in our dataset, graphs from Morand (2020) show a stagnation of the yearly outbreaks between 2013 and 2016, followed by a decline."*

This note is important, as the report was published in 2022 and there is no obvious reason not to present a more recent dataset.

The GIDEON data is also reproduced in Stephens et al. (2021),[188] another source cited within the World Bank report. This study demonstrates the major reduction in reported medium (>100 cases) and large (>1000 cases) outbreaks over the period 2009 to 2017 (Figure 14).

Therefore, the World Bank's opening sentence that "*the burden of infectious diseases continues to grow, and humanity faces more outbreaks, some with the potential to become pandemic*" is contrary to what the datasets within the cited research shows.

[186] https://www.gideononline.com/
[187] https://www.biorxiv.org/content/10.1101/2020.04.20.049866v2
[188] https://royalsocietypublishing.org/doi/10.1098/rstb.2020.0535

Figure 14. Figure 1 from Stephens et al. (2021), one of five key references for the World Bank analysis, reproducing GIDEON data and demonstrating a reduction in recent reported outbreaks.[189]

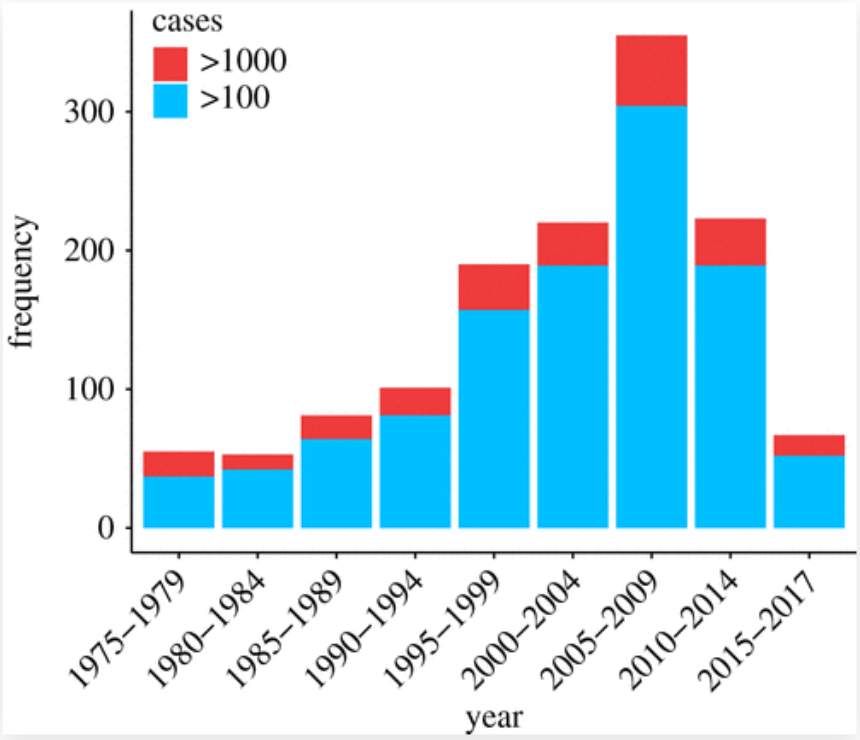


Figure 1. Global numbers of outbreaks with a minimum of 100 cases. Depicts potentially zoonotic outbreaks with at least 100 reported cases and start dates between 1975 and 2017 from Gottdenker *et al.* [11]. Based on these data, it seems most likely that the frequency of large outbreaks is either stable or increasing over time. However, reporting effort, detection capabilities and human population density are all also increasing in many regions over time [12], and a previous study showed that apparent temporal trends in outbreak frequency can vary considerably depending upon the potentially confounding covariates and types of outbreaks (e.g. pathogen taxa) considered [7]. (Online version in colour.)

Figure 14 also underlines the danger of assuming that the increases in outbreak frequency seen in Figure 11 (p. 69) and derived from the GIDEON database represent a true increase. An increase of approximately 6 times from 1980 does not sound biologically likely without quite dramatic ecological changes. The major reporting areas in Smith et al. are North America and Europe and these remain relatively stable, with Asia and later Africa becoming significant only in recent years. In 1980 to 1984 North America accounted for 35% of global reports (page 6), which then reduced relative to other regions over time. These trends strongly suggest that detection and reporting capacity spreading to lower-income settings are major drivers (see discussion of Smith below). A relative increase in viral versus bacterial outbreaks over time also supports this assumption, as

[189] https://royalsocietypublishing.org/doi/10.1098/rstb.2020.0535

techniques to detect viruses, particularly PCR and antigen detection, have been developed with access expanded more recently (see Section 1.1 of this report).

The authors of the World Bank report recognize the issue of reporting capacity on a geographic basis (page 9):

> *"As with all data on infectious diseases, a potential limitation is that some regions are overrepresented in global incidence of infectious diseases because of better reporting and monitoring and more frequent testing. In that sense, when looking at the baseline and evolution of outbreaks and deaths based on region, it is likely that numbers for Africa and South America are underestimated."*

This raises a key question with the underpinning methodology of the report, since it is inconsistent for the authors not to recognize that the same relationship must apply on a temporal basis, having noted that the relative share of reporting from higher income areas reduced over time in keeping with growing capacity in lower income settings. This is shown clearly in Figure 2 of Smith et al. (2014),[190] based on the same dataset and reproduced in Figure 11 above.

Section Two of the World Bank report, "What drives emergence of infectious disease?", lays out the basis for the proposed One Health response to perceptions of increasing risk. While listing a wide range of drivers of infectious disease, including host susceptibility, the report focuses on three:

> *…land use change, agriculture industry change, and international travel and commerce were the top three primary drivers.*

and these form a basis for subsequent financial calculations.

The first, land use change, is discussed here, as the report emphasizes additional spending on forest preservation as a method of reducing outbreak risk:

> *… increases in outbreaks of zoonotic and vector-borne diseases from 1990 to 2016 were associated with deforestation in tropical areas as well as reforestation in temperate countries (Morand and Lajaunie 2021).*

The cited paper of Morand and Lejaunie illustrates this (Figure 15). When assessed at a country level as shown in Figure 16, this reveals an association with latitude, but with similar areas under the curve indicating similar frequencies of association of outbreaks with both deforestation and reforestation. As tropical areas are undergoing most rapid deforestation and are also

[190] https://royalsocietypublishing.org/doi/10.1098/rsif.2014.0950?url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org&rfr_dat=cr_pub++0pubmed

characterized by lower income countries,[191,192] the association may be explainable by a relative increase in detection capacity incidental to deforestation in these countries.

Figure 15. Figure 5 from Morand and Lejaunie (2021), demonstrating the associations at a country level of change in forest cover and infectious disease outbreaks.[193]

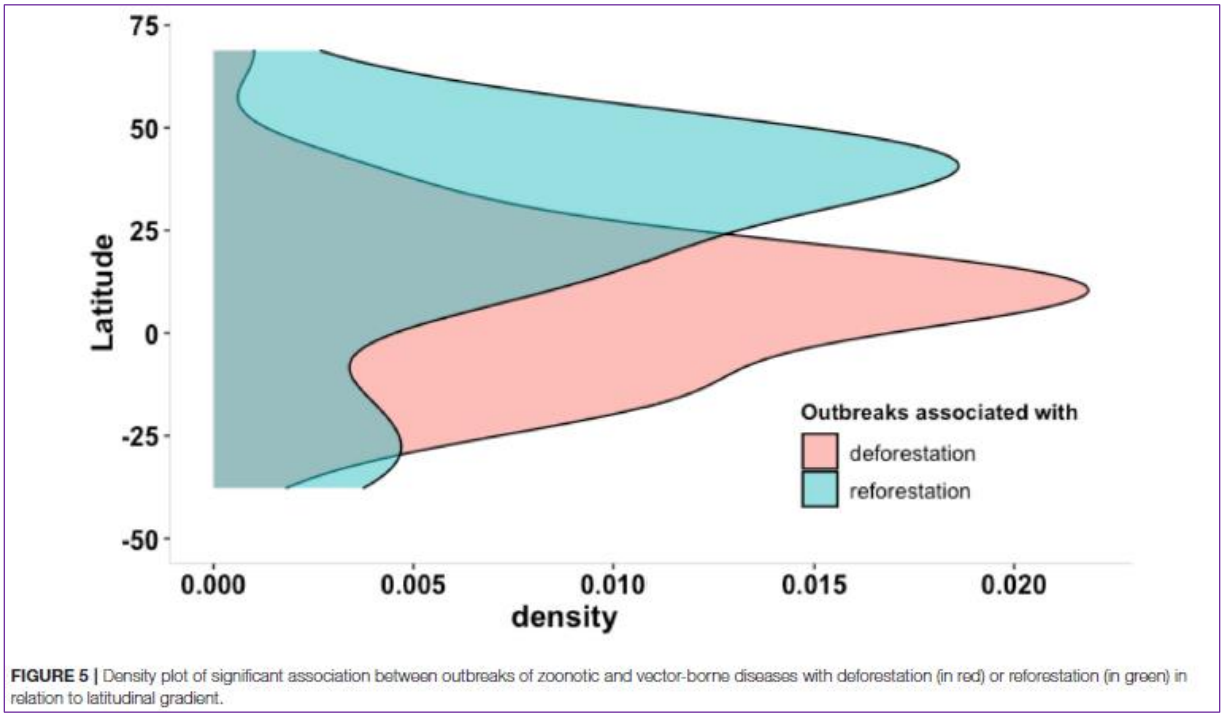
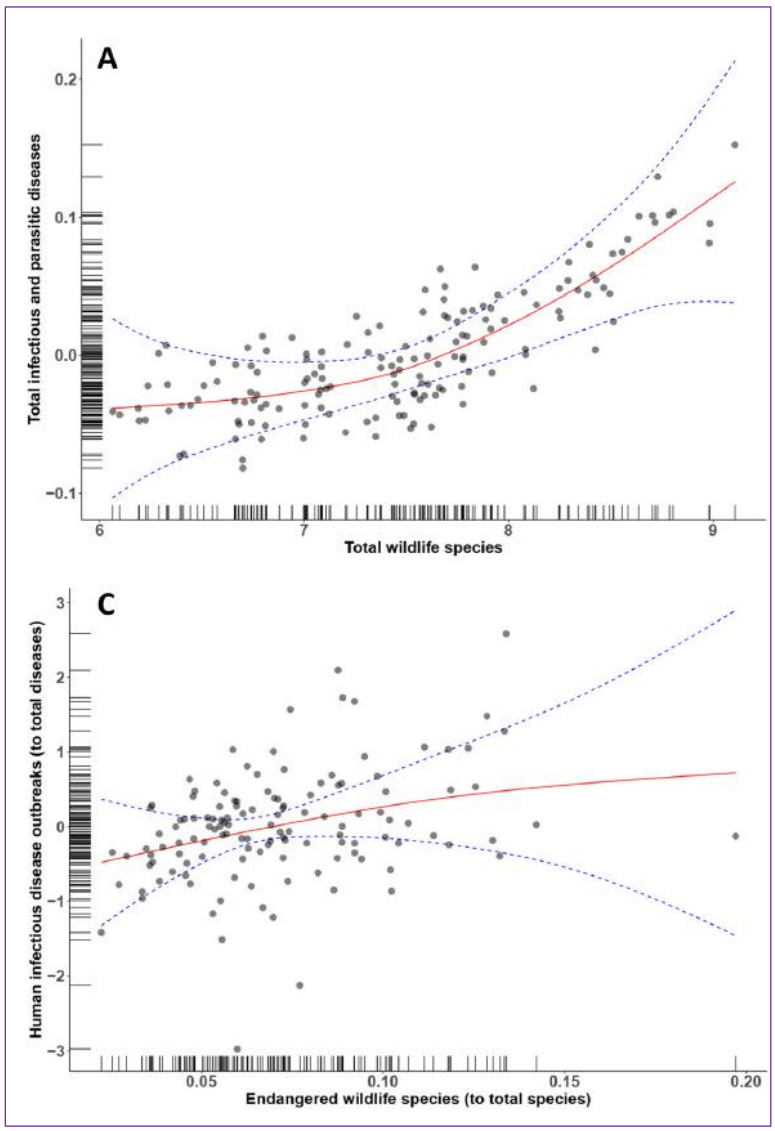


FIGURE 5 | Density plot of significant association between outbreaks of zoonotic and vector-borne diseases with deforestation (in red) or reforestation (in green) in relation to latitudinal gradient.

Morand (2020),[194] also cited by the World Bank report, reinforces the argument that in some circumstances, species richness is associated with human outbreak frequency, suggesting that more intact ecosystems may be associated with a higher rate of zoonotic spillover events, at least in some circumstances (Figure 16). A weaker correlation exists between the number of threatened wildlife species associated with outbreak frequency (Figure 16), but extrapolating this to forest degradation would rely on several assumptions that require more in-depth analysis.

[191] https://www.science.org/doi/10.1126/science.1244693?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed
[192] https://www.nature.com/articles/sdata20184
[193] https://www.frontiersin.org/articles/10.3389/fvets.2021.661063/full
[194] https://www.sciencedirect.com/science/article/pii/S0006320720307655

Figure 16. Extract from Fig. 2 in Morand (2020), illustrating human outbreak frequency in the GIDEON dataset with wildlife species diversity and number of endangered species in a country.[195]



The example of Nipah Virus in Malaysia is discussed in Section 5 of this report. The Nipah Virus example is also repeated in Annex 1 of the report, failing to apportion any significance to the fact that it was initially misdiagnosed, and only identified through use of newly developed diagnostic technologies. The argument that it newly emerged is therefore poorly supported.

[195] Ibid.

The discussion on the relationship between land degradation and outbreaks is extended to financial returns in Section 3 (page 23):

> *"wildlife to humans are likely to occur overlays deforestation risk, high biodiversity, and accessibility data. We estimate the annual cost of avoided deforestation for each of the zoonotic spillover risk groups developed by Allen et al. (2017) (see Appendix 1 for more details on the approach developed by Allen et al. 2017)."*

Allen et al. (2017)[196] showed the highest spillover events occurred in areas of tropical rainforest (evergreen broadleaf trees) with high mammalian species density (i.e., potentially intact forest ecosystems rather than deforested or degraded areas). Their findings are therefore significantly mischaracterized in the report, where they are associated with 'land use changes', while Allen et al. rather note the presence of 'wildlife species richness, concluding that "*Rather* [than biodiversity loss increasing risk*], it is consistent with previous suggestions that the relationship between biodiversity and disease risk is complex, context-specific and idiosyncratic*."[197] Moreover, while there are other good reasons to retain healthy tropical forest ecosystems, the findings of Allen et al. actually signal perverse outcomes that may contribute to, not reduce, outbreaks arising from wildlife spillover events. For example, the main policy recommendation made in this area is to preserve 50% of broad leaf (mostly tropical) forest that would otherwise be degraded – the habitat associated with the highest rate of spillover events by Allen et al. Under this logic, the World Bank seeks health-sector investments to maintain pools from which the greatest level of wildlife spillover events occur.

[196] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5654761/
[197] Ibid.

6.2. Annex 1. Classification of EID risk

The Authors of this technical report note reliance on Jones et al. (2008) and Allen et al. (2017) to determine the main drivers of Emerging Infectious Diseases (EIDs).

> *"There are two key papers that classify EIDs. Jones et al. (2008) analyze a database of 335 EID events (origins of EIDs) between 1940 and 2004. Allen et al. (2017) builds on Jones et al. (2008)."*

Jones et al. (2008) is discussed in detail elsewhere. Their main finding was an increase in reported EIDs from the 1940s, peaking in 1980-1990, and reducing somewhat in the 1990s. They found that:

> *"human population density was a common significant independent predictor of EID events in all categories, …. Wildlife host species richness is a significant predictor for the emergence of zoonotic EIDs with a wildlife origin."*

They did not find land degradation as the major driver, but rather conditions where more intact ecosystems support high mammalian diversity.

Annex 1 states, regarding Allen et al.'s findings:

> *"They find that the risk of disease emergence is elevated in tropical forest regions experiencing anthropic land use changes related to agricultural practices and where mammal biodiversity is high."*

This is a significant mischaracterization of the cited reference. Allen et al. state, at the start of their Results section:

> *"After factoring out reporting effort (in the weighted model), evergreen broadleaf trees (median 7.6% of the model's predictive power), human population density (6.9%), Global Environmental Stratification (climate) (5.9%), and mammal species richness (an aspect of biodiversity) (5.6%) had the largest relative influence over the distribution of EID events (Fig. 1)."*

Figure 1 from Allen et al. (Figure 17, below) illustrates their findings.

Figure 17. Fig. 1 from Allen et al. (2017), illustrating identified major drivers of emerging infectious disease events, after adjustments for reporting bias. 'Global envir. Strat.' Refers to climate.[198]

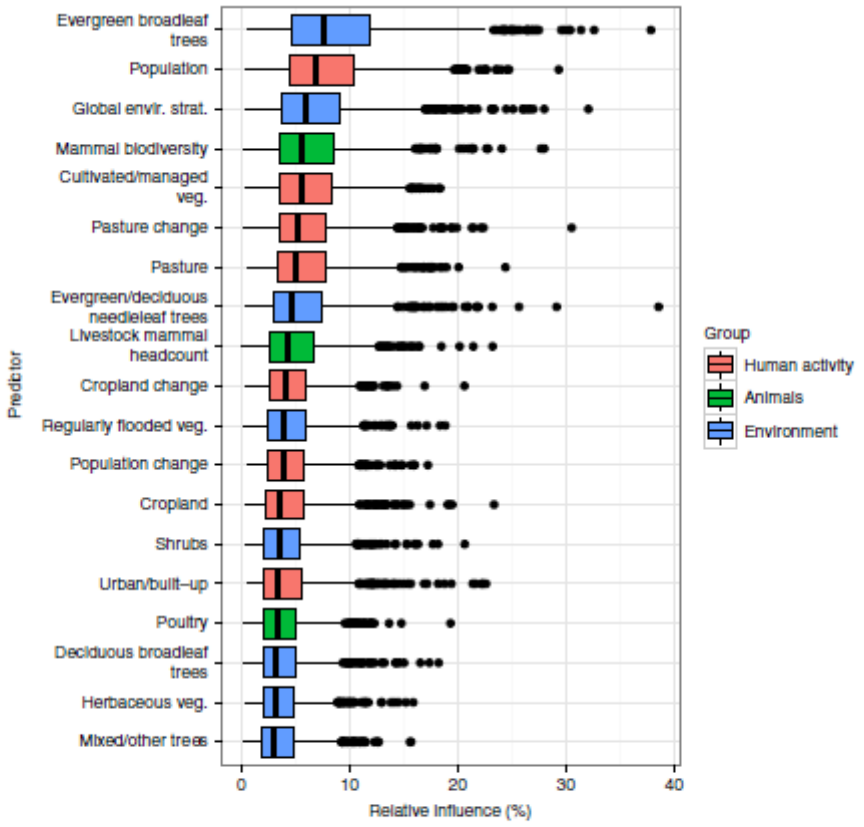


Fig. 1 The relative influence of predictors on EID event occurrence probability. The box plots show the spread of relative influence across 1000 replicate model runs to account for uncertainty in EID event location (see above). Whiskers represent the minimum or maximum datum up to 1.5 times the inter-quartile range beyond the lower or upper quartile. BRTs do not provide *p*-values or coefficients, but rank variables by their relative influence in explaining variation in the outcome[26]

[198] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5654761/

6.3. Summary of World Bank Technical Report analysis

These findings suggest that the World Bank technical report has significantly mischaracterized its key references regarding drivers of zoonotic spillover. Moreover, based on this mischaracterization, the World Bank is advocating for increased spending to address high spillover rates. While noting the apparent impact of reporting bias in raising rates in high income countries (restated in Annex I), it fails to address the obvious extension of this to a temporal bias in reporting, where the techniques used to identify and characterize many outbreaks in the last few decades did not even exist a few decades earlier. The basis of the proposed spending to reduce deforestation in support of EID reduction, and more broadly the entire urgency of addressing what the World Bank claims is a rapidly increasing threat, appears unevidenced based on their cited sources.

7. Key evidence papers

7.1. Bernstein et al. (2022): The costs and benefits of primary prevention of zoonotic pandemics

Bernstein et al. published a heavily cited review in 2022 in *Science Advances* on the costs and benefits of PPPR: "The costs and benefits of primary prevention of zoonotic pandemics."[199] This paper is broadly consistent with the findings of the G20 Bali Leaders Declaration and the World Bank examined above, concluding that savings in averted expenditure in a pandemic would greatly exceed expenditure on PPPR. In this case accrued savings are calculated to be 20 times the expenditure on PPPR.

The paper has been influential, with over 41,000 downloads, 39 citations and attention by 60 news outlets as of 11/12/2023.[200] The analysis of Bernstein et al. formed the basis of the financial claims in a significant *Nature* journal publication and blog on the justification for investing in PPPR in May 2022.[201]

Key claims

The key claims of Bernstein et al. are that investment of approximately $20 billion annually in prevention and mitigation of zoonotic spillovers will realize savings of 20 times that amount in costs of human lives saved, and 10 times that amount in economic losses avoided. This is based on an evaluation of "*every novel viral zoonosis that has appeared since 1918 (to 2020) that killed at least 10 people*". Lives lost are calculated as an average of 3.3 million every year (on a 2019 global population estimate), with a costing of these lives at between $350 billion and $21 trillion dollars (a wide range of uncertainty depending on where the lives are lost). An estimated cost of $10 billion to 'halve these losses' then adopts the upper end of this range of lives lost (without explanation), leading to a conclusion that $10 trillion will accrue in savings.

Methods and evidence

The spillover events ("all") include the 1918-19 Spanish Flu, and the first 18 months (2020 to July 2021) of recorded COVID-19 mortality. As apparent from Figure 18, the 1918-19 pre-antibiotic

[199] https://www.science.org/doi/10.1126/sciadv.abl4183?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed
[200] Ibid.
[201] https://www.nature.com/articles/d41586-022-01312-y

event dominates the overall numbers. Most deaths in this outbreak are considered to have been due to secondary bacterial infection, and so highly unlikely to occur in such numbers today.[202]

The cost of lives lost is calculated as Standardized Mortality Units (SMU); "*where one SMU is the percent of the population who die multiplied by 10^4*" (described in Bernstein et al.'s Supplementary materials). This assumes all lives lost are of equal burden, and thus does not take into account life-years lost. This is significant when dealing with COVID-19, as an example, where average age of death was commonly near 80 years, and usually in people with significant life-shortening co-morbidities.

The authors include no spillover events between 1919 and 1951. They have then calculated average annual lives lost from this data, using the 70 years (1950 to 2019) as a denominator and adjusting the global population and mortality rate for population in the year of each outbreak. However, Spanish Flu deaths are included in this truncated (70 year) period of analysis, despite occurring 30 years earlier and in the pre-antibiotic era. The authors note that failure to include the Spanish Flu would change the results by "almost an order of magnitude".

> *"To set the annual probability of any outbreak, we use the frequency of outbreaks since 1950 (the first year at which reasonable mortality data are available for most outbreaks). We observe 28 episodes in 70 years or about 40%...*
>
> *Our core analysis includes Spanish influenza; this improves our ability to calibrate the tail of the distribution composed of severe events that only occur a few times in 100 years."*

The table of spillover events and their mortality at time of the event, and adjusted mortality per million population, is shown in Figure 18.

[202] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2599911/

Figure 18. Table of "all" zoonotic spillover events from 1918 to mid-2021, from Bernstein et al. (2022). Outbreaks contributing most to the total are highlighted here for emphasis.

Table 1. Mortality from zoonotic viral emergence since 1918. Mortality rounded to the nearest 10 of novel viral zoonotic outbreaks with greater than 10 deaths since 1918.

Virus	Year	Deaths	World population	Deaths per million
Spanish influenza	1918	50,000,000	1,830,000,000	27,322
Hantaan virus	1951	46,430	2,584,034,261	18
South American hantaviruses	1956	1990	2,822,443,282	0.71
Kyasanur forest disease	1957	1,000	2,873,306,090	0.35
H2N2 influenza	1957	1,100,000	2,873,306,090	383
Junin virus	1958	5,900	2,925,686,705	2.02
Lacrosse virus	1960	300	3,034,949,748	0.10
Machupo virus	1963	290	3,211,001,009	0.09
Marburg virus	1967	370	3,478,769,962	0.11
H3N2 influenza	1968	1,000,000	3,551,599,127	282
Lassa fever	1969	250,000	3,625,680,627	69
Venezuelan equine encephalitis	1969	300	3,625,680,627	0.08
Monkeypox	1970	5,000	3,700,437,046	1.35
Ebola	1976	12,930	4,154,666,864	3.11
Rift Valley fever	1977	3,000	4,229,506,060	0.71
HIV	1980	10,700,000	4,458,003,514	2,400*
Puumala virus	1980	10	4,458,003,514	0.00
Guanrito virus	1989	140	5,237,441,558	0.03
Sin Nombre virus	1993	260	5,581,597,546	0.05
Andes	1995	130	5,744,212,979	0.02
Nipah	1998	200	5,984,793,942	0.03
West Nile	1999	2,330	6,064,239,055	0.38
SARS	2002	770	6,301,773,188	0.12
Chikungunya	2004	35,000	6,461,159,389	5.42
H1N1 influenza	2008	284,000	6,789,088,686	42
Severe fever thrombocytopenia syndrome	2009	370	6,872,767,093	0.05
MERS	2012	860	7,125,828,059	0.12
Zika	2015	50	7,379,797,139	0.01
COVID-19†	2020	4,000,000†	7,794,798,739	496

*HIV mortality spread over the following decades. †COVID-19 deaths are those to July 2021.

A few concerns immediately stand out from Bernstein et al.'s data in Figure 18, that significantly influence the paper's conclusions:

1. Although outbreak mortality is averaged from 1950 onward, pre-antibiotic Spanish Flu from 1918 is included. This event dominates mortality, and these deaths were dominated by pre-antibiotic era secondary bacterial infections.
2. The complete lack of zoonotic spillover outbreaks between 1919 and 1951 drives a perceived increase in outbreak incidence. As with later outbreak frequency, the authors

have taken no account of improved detection methods; development of, and then expanded access to, serology tests, antigen detection, and PCR.

3. All pre-2020 numbers after the Spanish Flu are dominated by the 1957 and 1968 influenza outbreaks, and HIV. HIV is unusually included here in a list of acute zoonotic spillover events. Although it is probably due to a spillover event, it is not commonly considered within the scope of the PPPR agenda as it is a several decades-long event and is now an endemic disease with well-developed mitigation programs.[203]
4. COVID-19 also dominates. There is controversy regarding the origin of this outbreak; whether it is a zoonotic spillover or a derivative of laboratory research.[204,205]
5. The mortality of events excluding influenza and HIV/AIDS pre-Covid is rarely above 1 per million population. Thus, there are only 5 events with mortality greater than that of seasonal influenza in the 103 years considered by the authors.[206]

Re-evaluation of evidence

Bernstein et al. calculated 3.3 million deaths per year by including events over the 70 years to 2021, adding Spanish Flu mortality from 2018-9, as mortality per million at time of the event. This was then adjusted to approximately 7.5 billion population for 2021 (actual value not provided).

In response, we have also recalculated Bernstein results for a population of 8 billion (consistent with the global; population at the end of 2023) (Figure 19). The figure also demonstrates what these numbers would be if calculated only from outbreaks over the 52 years from 1969 (after the last significant influenza pandemic).

[203] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3234451/
[204] https://www.bmj.com/content/382/bmj.p1556
[205] https://www.dni.gov/files/ODNI/documents/assessments/Unclassified-Summary-of-Assessment-on-COVID-19-Origins.pdf
[206] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6815659/

Figure 19. Re-calculation of Bernstein et al. 2022 data (from Table 1 of their paper). First row follows Bernstein, including Spanish Flu but averaging over 70 years. Subsequent rows reflect 52 years from 1969 to 2020, since the last significant influenza pandemic. Column second from right reflects total world population of 7.5 billion (approximating Bernstein's denominator) and right column reflects population at end of 2023.

	Mortality per million	Mortality in 7.5 billion	Mortality in 8 billion (2024)
TOTAL /million	31,027	3,324,306	3,545,927
TOTAL excl Spanish Flu	3,705	396,949	423,413
TOTAL since 1968 flu	3,018	435,358	464,382
TOTAL since 1968 excl HIV	618	89,204	95,151
TOTAL since 1968 flu excl Covid	2,522	363,819	388,074
TOTAL since 1968 flu excl HIV and Covid	**122**	**17,665**	**18,843**

* Denominator **70 yrs** when incl. Spanish flu, **52 yrs** when post 1968

As Figure 19 demonstrates, Bernstein et al.'s claims of 3.3 million per year average mortality from zoonotic spillovers, and therefore their return on investment, are almost wholly driven by the pre-antibiotic Spanish Flu event, with the remainder dominated by two influenza outbreaks over half a century ago, the HIV epidemic, and by the recent COVID-19 event. Excluding HIV/AIDS and COVID-19 from the last 50 years results in a total global mortality form spillover outbreaks of less than 19,000 annually, the equivalent of about 5 days of tuberculosis mortality.[207] There are strong programs already in place for influenza surveillance globally, and it is highly unlikely that HIV would be missed today as it was for an entire generation in central Africa in the period before PCR and modern point of care diagnostics, road infrastructure and improvements in communication.[208]

The underlying drivers of Bernstein et al.'s conclusions are illustrated in the first figure in their paper (Figure 20). This demonstrates a fairly steady mortality rate from outbreaks recorded over the past 60 years, but an increasing cost of response to outbreaks. One could claim that mortality has been kept constant by increasing expenditure, but an equally valid interpretation would be a change in the type of response with no material benefit in lives saved. The data suggests, at a minimum, that analysis of the value of recent responses is warranted before they are used as evidence of justifiable economic costs of outbreaks.

[207] https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2022
[208] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3234451/

Figure 20. Fig. 1 from Bernstein et al. (2022), demonstrating a relatively constant frequency of outbreaks, but an increasing cost (larger diameter circles) over time.

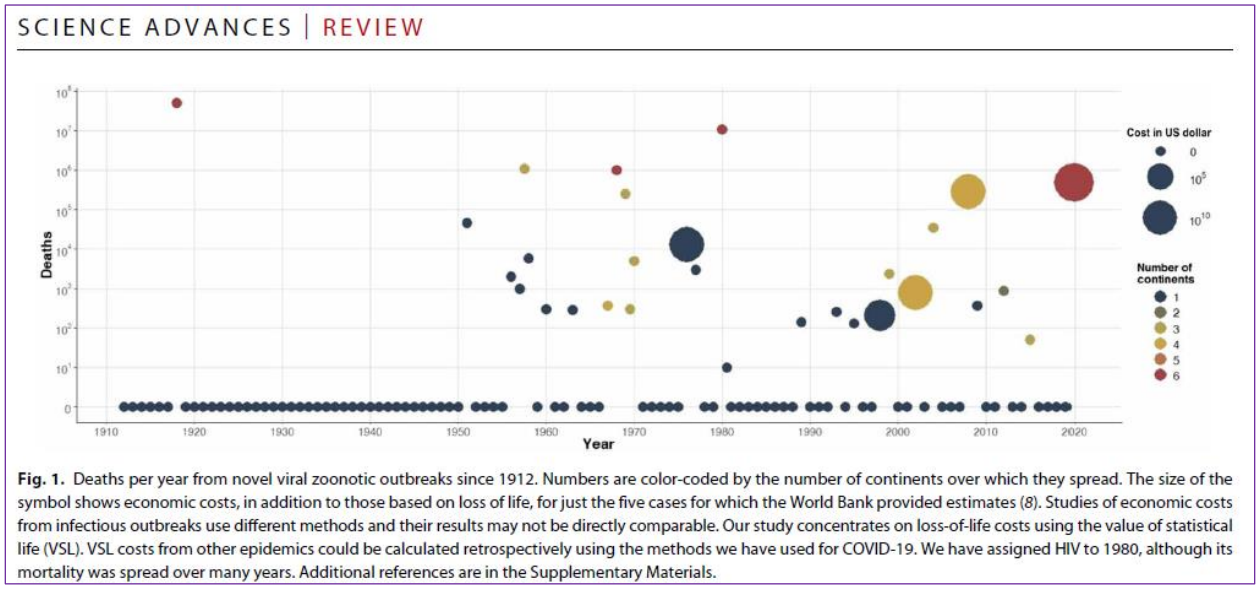


Fig. 1. Deaths per year from novel viral zoonotic outbreaks since 1912. Numbers are color-coded by the number of continents over which they spread. The size of the symbol shows economic costs, in addition to those based on loss of life, for just the five cases for which the World Bank provided estimates (*8*). Studies of economic costs from infectious outbreaks use different methods and their results may not be directly comparable. Our study concentrates on loss-of-life costs using the value of statistical life (VSL). VSL costs from other epidemics could be calculated retrospectively using the methods we have used for COVID-19. We have assigned HIV to 1980, although its mortality was spread over many years. Additional references are in the Supplementary Materials.

Summary

Bernstein et al. make claims to support a very high average annual mortality from zoonotic spillovers, 3.3 million deaths, equivalent to WHO's estimates of deaths with SARS-COV-2 during the COVID-19 outbreak. These numbers are driven almost entirely by pre-antibiotic era Spanish Flu mortality, and mortality from the 1957 and 1968 influenza outbreaks and HIV. The first 19 months of COVID-19 also contribute significantly, though natural origin is subject to debate. Remaining mortality is dominated by Ebola virus outbreaks that are confined to few countries in central and western Africa.

Claims of return on investment then assume that investment can achieve major reduction in frequency and/or mortality, and that the highest end of the range of costs, $20 trillion annually, is realistic. For instance, Bernstein et al. claim that strategies that reduce the risk of any epidemic by half would reduce mortality costs by up to $10 trillion. The authors suggest that the highest cost intervention ($19 billion) is closing down wildlife farming in China, followed by curbing deforestation ($1.53 to $9.59 billion). Given the lack of evidence for wildlife farming being the origin of the major outbreaks listed – Spanish Flu and HIV, and the controversy regarding COVID-

19 origins, the impact of this expenditure requires further clarification. Similarly, the relationship between deforestation and outbreaks is complicated,[209,210] as discussed elsewhere in this report.

Bernstein et al.'s estimates on costs and return on investment therefore rely on enormous assumptions that are not well supported by the evidence provided. Influenza and HIV, the main drivers of their numbers, already have extensive existing surveillance programs in place, while it is unclear how COVID-19 would have been averted or mitigated through their proposed investments (nor increased surveillance mechanisms if it was a result of laboratory escape). The paper does not provide strong evidence either of increasing pandemic risk, or of return on PPPR investment approaching the claim.

[209] https://www.bmj.com/content/382/bmj.p1556
[210] https://www.dni.gov/files/ODNI/documents/assessments/Unclassified-Summary-of-Assessment-on-COVID-19-Origins.pdf

7.2. Marani et al. (2021): Intensity and frequency of extreme novel epidemics

Marani et al. 2021 (Proceedings of the National Academy of Science (PNAS)) seek to determine the risk of occurrence of epidemics of various intensity. The paper has been widely referenced regarding the frequency of infectious disease outbreaks. The 2022 World Bank report "Putting Pandemics behind us" references Marani as:[211]

> *"the yearly probability of an occurrence of large outbreaks could increase up to threefold in the coming decades (Marani et al. 2021)"*

while Vora et al., 2022 (Nature)[212] cite it as a main reference for evidence of rapidly increasing outbreak frequency.

Methods and evidence

A historical record of infectious disease epidemics was assembled from 1600 to 2020, based on 476 documented epidemics derived from a literature search. To calculate epidemic intensity specifically, falling between 1600 and 1945 were selected (395 events), from which 182 with known duration and an estimated mortality above a threshold of 0.001% deaths per year were selected.

By basing the intensity calculations only on pre-1945 epidemics, the authors were able to exclude epidemics that were (possibly) ended by the introduction of vaccines or effective treatments, while outbreak frequency was based on all in the data set. Marani et al. assume the probability distribution of epidemic intensity in this pre-1945 interval to be time-invariant, meaning that an increase in the frequency of outbreaks would be expected to lead to an increase in the frequency of severe epidemics.

"Epidemic intensity" is defined by mortality per year (Figure 21). Many of the listed outbreaks are either bacterial or rickettsial infections for which antibiotics are now available and effective (e.g. typhus or bubonic plague) or in which most actual death was associated with secondary bacterial infection (Spanish Flu).[213] The main exceptions are smallpox (now eliminated through vaccination) and yellow fever (also relatively well controlled).

[211] https://documents.worldbank.org/en/publication/documents-reports/documentdetail/099530010212241754/p17840200ca7ff098091b7014001a08952e
[212] https://www.nature.com/articles/d41586-022-01312-y
[213] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2599911/

Figure 21. Fig. 1. from Marani et al. (2021). Epidemic intensity and probability of occurrence (exceedance), 1600-1944, and cause of major epidemics.

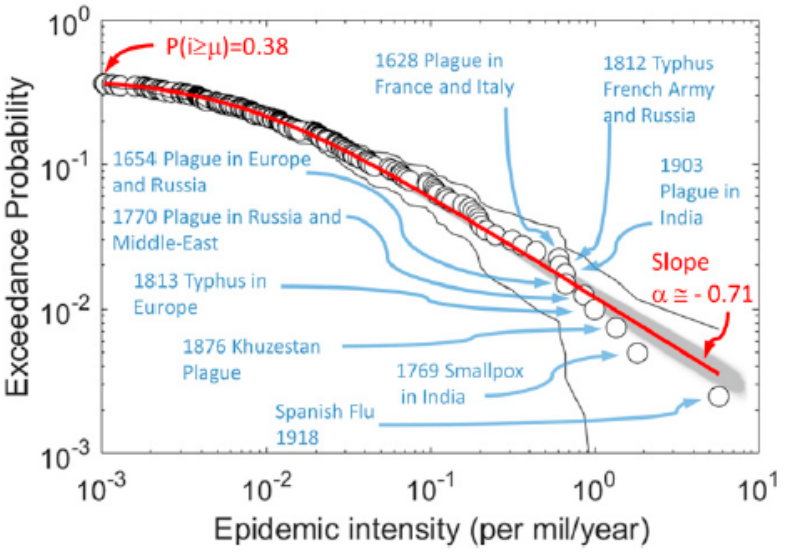


Fig. 1. Empirical exceedance frequency of epidemic intensity i (open circles). Black solid lines show the 95% CI around these empirical frequencies (29). The red line is the GPD distribution obtained from maximum likelihood fitting for $i \geq \mu = 1.000 \times 10^{-3}$ ‰/year (μ being the position parameter, scale parameter $\sigma = 0.0113$ ‰/year, and shape parameter $\xi = 1.40$). The value $P(i \leq \mu) = 0.62$ is determined from the number of observed intensities below μ (244 out of 395, including epidemics—105—for which the number of deaths is not available, but historical information suggests $i \leq \mu$). The GPD, for large values of its argument, becomes a power law with exponent $\alpha = -1/\xi \cong -0.71$. The value $|\alpha| < 1$ denotes a fat-tail behavior in which the probability of intense events decreases slowly with event intensity. The gray area results from the overlap of the 10,000 GPD distributions fitted to sample realizations obtained by applying to each observed intensity a random perturbation uniformly distributed in [−50%, +50%] to account for uncertainties in historical records.

Considering the entire dataset from 1600 to 2020, the assumption of increasing frequency of outbreaks looks less solid (Figure 21). As the authors note, we see "an increase in the yearly number of outbreaks until the end of World War II and subsequent rapid decline thereafter", even as global population markedly rises. This is at odds with other datasets in this report (e.g. the GIDEON dataset illustrated in Morand and Walther (2020) where an increase in event is recorded up to the decade of 2000 to 2010,[214] or that of Jones et al. (2008) showing a decline from 1990.[215] This earlier decline probably reflects the emphasis of Marani et al. on larger pandemics, often of a bacterial (i.e. antibiotic-susceptible) aetiology.

[214] https://www.biorxiv.org/content/10.1101/2020.04.20.049866v2
[215] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5960580/

Figure 22. From Figure S1 from supplementary material of Marani et al. 2021: Number of epidemics (without consideration of numerical epidemic intensity) occurring in each year on record.

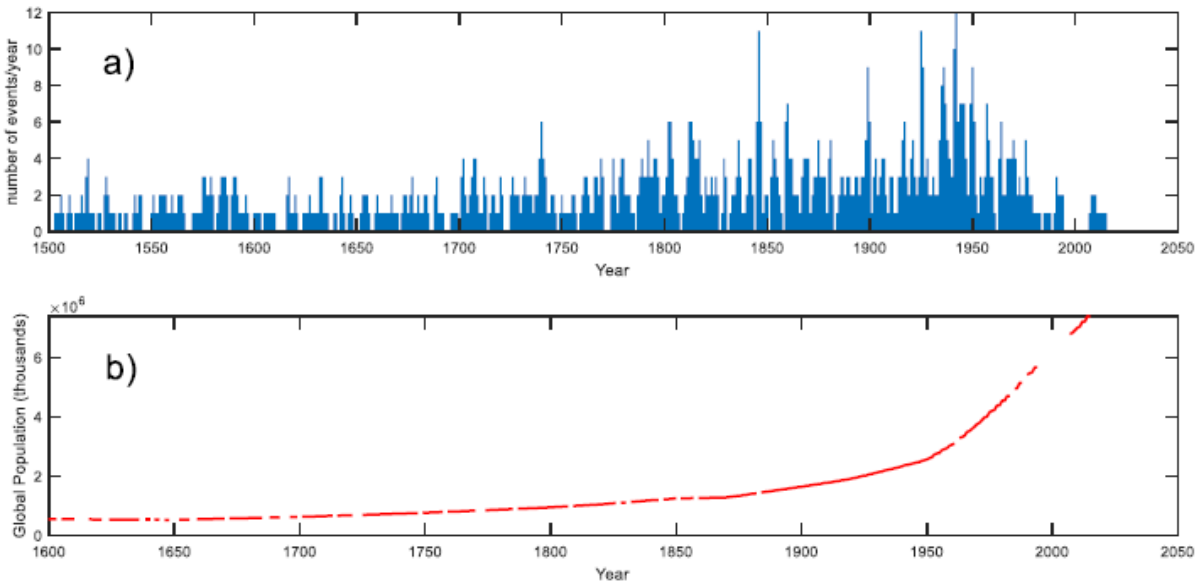


Figure S1. a) Number of epidemics (without consideration of numerical epidemic intensity) occurring in each year on record showing an increase in the yearly number of outbeaks until the end of World War II and subsequent rapid decline thereafter. b) Global population at the beginning of each outbreak $S_o(t)$ in a) used for intensity calculations.

Most importantly for this report, Marani et al.'s data in Figure 22, found in their supplementary data, contradicts both some conclusions of the paper (a threefold increase in severe pandemics is likely) and the related citation in the World Bank's Putting Pandemics Behind Us report (discussed above): "the yearly probability of an occurrence of large outbreaks could increase up to threefold in the coming decades." This is odd, and appears to be based on Marani et al.'s modelling based on pre-1945 (i.e. pre-frequency decline) data, and on two secondary sources cited in turn within Marani et al.'s paper:

1. Jones et al. 2008.[183] This (discussed elsewhere in this report) is misinterpreted as it does not show an increase to the 1980s driven significantly by HIV and associated infections, and by antibiotic resistance mutations that are considered independent outbreaks (both of which Marani exclude).

2. Daszak et al. 2001,[184] which mainly discusses epidemic infectious disease outbreaks *in* wildlife, but also infections of very limited burden in humans and provides opinion, not specific evidence for human cases.

Marani et al. therefore appear to have somewhat mis-represented Jones et al.'s findings and produced modelling that fails to reflect the changes they found post-1945, and then in turn the World Bank have inadvertently assumed a real increase pandemic risk.

The advent of modern antibiotics is probably important in the decline in outbreak frequency in Figure 22 It seems likely (intuitively) that this will reduce intensity more than frequency, as it will cure infections more than stop zoonotic spillovers or underlying virus transmission. An example is influenza, where zoonotic spillover events occur irrespective of antibiotic use, but the mortality of influenza is greatly reduced by treatment of secondary bacterial infections. By assuming a constant probability distribution of epidemic intensity derived from pre-1945 data, Marani et al.'s model implicitly assumes we still live in a world without antibiotics.

Conclusions and outcomes

An initial error in calculations in the paper of Marani et al. is corrected in a later erratum published in PNAS, May 2023. The corrected outcomes predict a Spanish Flu-like event to occur once every 877 years. Adjusting for a perceived recent increase in outbreak frequency (discussed above as poorly justified), results in a predicted frequency for a Spanish Flu-like event of once every 292 years, while COVID-19 is predicted to recur every 129 years.

These low recurrence rates for events equivalent to the Spanish Flu and COVID-19 are obtained despite failing to factor in the mitigating effects expected from improved hygiene and sanitation over recent centuries as well as the advent of antibiotics and modern medicine in the past century. This has two key implications for PPPR. First, neither type of event is expected to occur within an average life span, suggesting that the risk from such an event is much lower than current narratives portray. Second, that this lower risk allows time for proper PPPR policy reflections that can triangulate evidence on risk, need and optimal response.

This paper offers very poor justification for an increasing and existential pandemic threat. Marani et al. actually show that pandemics such as the Spanish Flu, or even COVID-19, are rare. This is contrary to claims elsewhere that their threat is high, another COVID-19 like event or worse is likely soon, and there is an urgency to get measures in place. Its use to justify World Bank predictions and proposed financing and key conclusions of Vora et al. and others must therefore suggest that such claims merit reassessment.

7.3. Smith et al. (2014): Global rise in human infectious disease outbreaks

Smith et al., (2014) is a widely cited paper as evidence of increasing frequency and risk of infectious disease outbreaks. It is cited by both Meadows et al. (2023) and Marani et al. (2021) discussed elsewhere in this report. The paper assesses the diversity and number of recorded outbreaks.

Methods and evidence

The authors analyze a dataset from 1980 to 2013. Exact bounds are unclear as text indicates a "33-year dataset (1980–2013)" which should therefore be 34 years, whilst figures indicate 1980 to 2009 (for comparison) and Table 2 indicates up to 2010. This is not important to the conclusions.

A total of 12,102 outbreaks are recorded, including 215 diseases and 44 million cases. Bacteria are the major cause (37%), viruses 33%, and then parasites, fungi and protozoans respectively. Outbreaks are defined as incidence above normal background.

Smith et al.'s analysis controlled for a number of confounders: latitude, gross domestic product (GDP), press freedom, internet usage, population size and population density. Only internet usage had a significant association. No attempt was made beyond this to directly address changes in reporting through development of increased access to and reporting of diagnostics and surveillance techniques (PCR, as example, was first developed in 1983 and not widely available until far later).

Figure 23 (Figure 2 in Smith et al.) indicates a marked increase in outbreak diversity in Africa, Asia and Eastern Europe in particular. This is consistent with an increase in diagnostic capacity and reporting in these lower- and middle-income countries, and those recently emerged from behind the Iron Curtain. This pattern at least strongly suggests that such factors are influencing total numbers, as it is counterintuitive that pre-1980 outbreak diversity would have been far higher in populations in more highly developed economies than in less developed. The association of increased internet use with greater reporting suggests some role for the development of technology use in reporting frequency.

Conclusions and outcomes

Smith et al. demonstrate an increase in a range of outbreak reporting (frequency and diversity) over the three decades from 1980, but a reduction in per capita mortality. The increase in frequency appears likely in part or predominantly due to increased reporting capacity

(development and increased access to diagnostic and reporting systems, particularly in emerging economies).

The reduction in per capita risk runs strongly counter to claims elsewhere of increasing risk from disease outbreaks and is inconsistent with citations suggesting evidence for increasing risk overall. The data would strongly support a hypothesis that the world is getting better at detecting outbreaks, and identifying and distinguishing pathogens, whilst also improving capacity to address these challenges.

Figure 23. Change in outbreak diversity with time in Smith et al. (2014), suggesting a rapid increase in pathogen detection and identification in emerging economies since 1980.[216]

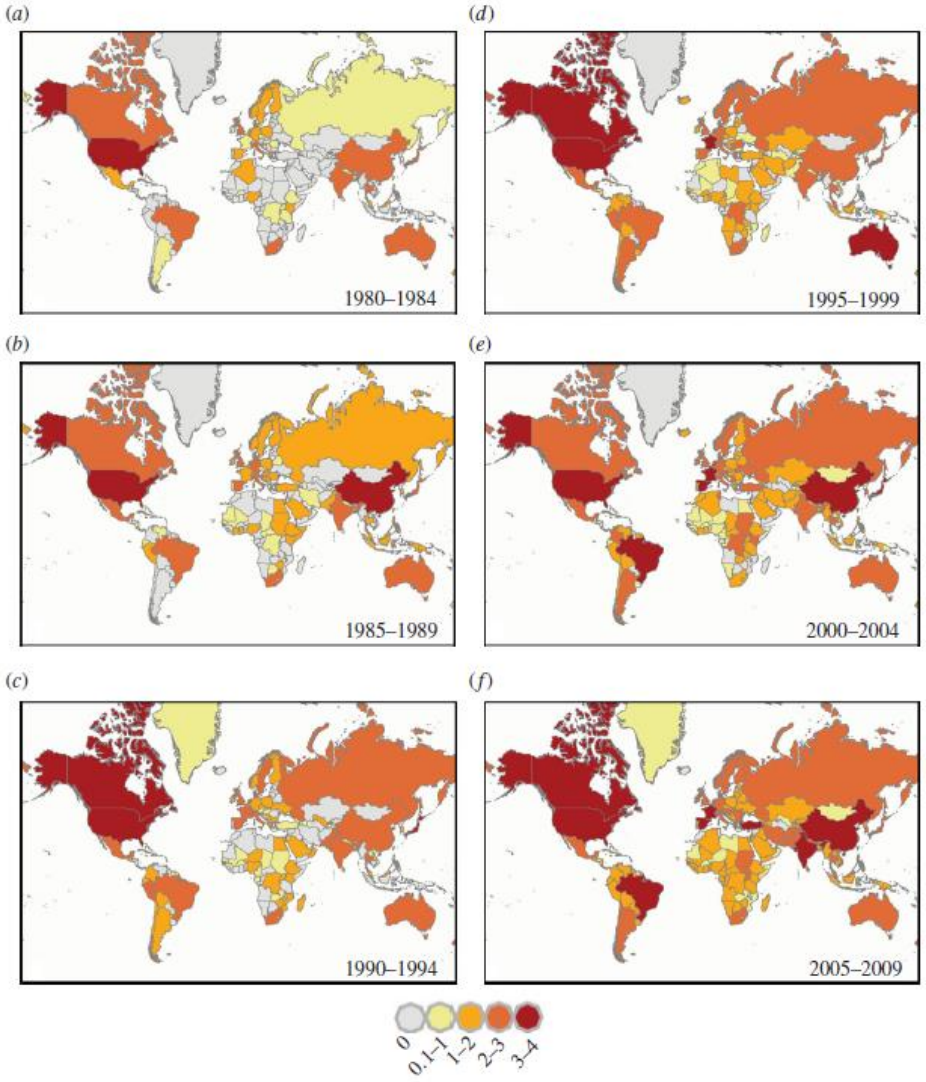


Figure 2. Global outbreak diversity for the nations of the world over time. Diversity is calculated for each nation using Shannon's diversity index (SDI) as described in the methods. Nations with the highest diversity of outbreaks are represented by larger values and darker shading. (Online version in colour.)

[216] This figure is often reproduced in policy documents. The same figure is also included in Section 5.5 (Figure 11) and repeated here for ease of engagement.

7.4. Jones et al. (2008): Global trends in emerging infectious diseases

Jones et al. 2008 (Nature) is widely cited as evidence of increasing frequency of emerging infectious disease (EID) outbreaks,[217] including by Marani et al. (2021) and Meadows et al. (2023) discussed in this report.

Methods and evidence

The authors assess the frequency of 335 EID events from 1940 to 2004. EIDs in their publication include variants of species of bacteria (e.g. *Eschericia coli* serotypes and sub-types of *Shigella* and *Vibrio spp*.) and new drug resistant mutations of known pathogens. The first emergence (i.e. identified) event is recorded.

Most (60.3%) of EIDs are zoonoses, with 54% being bacterial or rickettsia.

The authors recognize the risk of reporting bias. To address this, they compare the number of publications in the Journal of Infectious Diseases (JID) with the frequency of recorded outbreaks. The total number of JID articles from 1940-2004 (17,979) is compared against the reporting rate over time, and publications since 1973 are compared by geographic location of the study with the spatial distribution of reported EID events.

While comparing with JID publication rates may provide some insight into the likelihood that an outbreak will reach the public record, the relationship is likely to be poor, as it fails to account for:

1. Different geographies prioritizing different journals (including due to linguistic barriers).
2. PCR, point-of-care antigen testing and serology have been developed or access greatly increased since 1940, with accessibility concentrated in high income countries. Point of care testing beyond microscopy was rare in low-income countries into the 1990s.
3. Differing pressures, reasons and available resources to compile and publish data.
4. Changing funding priorities – an increased interest in outbreaks in recent decades would likely result in more outbreaks being detected and those detected more likely to be reported.

Conclusions and outcomes

The authors demonstrate a steady increase in reported EID events from 1940, peaking in the 1980s and then declining somewhat in the 1990s (Figure 24). Some categories (viruses and prions, and protozoa), EIDs of zoonotic origin, and vector-borne diseases, continue to show

[217] https://www.nature.com/articles/nature06536

increased reporting through the 1990s (Figure 24). The authors attribute the 1980s peak to host immunodeficiency secondary to the poorly controlled expansion of the HIV/AIDS epidemic through the 1980s, with improved management in the following decade:

> *"Increased susceptibility to infection caused the highest proportion of events during 1980–90 (25.5%), and we therefore suggest that the spike in EID events in the 1980s is due largely to the emergence of new diseases associated with the HIV/AIDS pandemic".*

Human population density was a significant predictor of overall EID emergence (unlike Marani et al., above), and this may reflect the inclusion of bacterial outbreaks, including those consisting of new antimicrobial phenotypes that are more likely to arise, transmit and be detected in high density settings. Wildlife host richness was also a significant factor, contrary to the suggestions of Vora at al. (2023) and others that degradation of ecosystems is likely to increase zoonotic spillover:

> *"human population density was a common significant independent predictor of EID events in all categories, …. Wildlife host species richness is a significant predictor for the emergence of zoonotic EIDs with a wildlife origin, with no role for human population growth, latitude or rainfall."*

Figure 24. Figure 1 from Jones et al. (2008), showing temporal occurrence of infectious disease (EID) events recorded from 1940 to 2000.

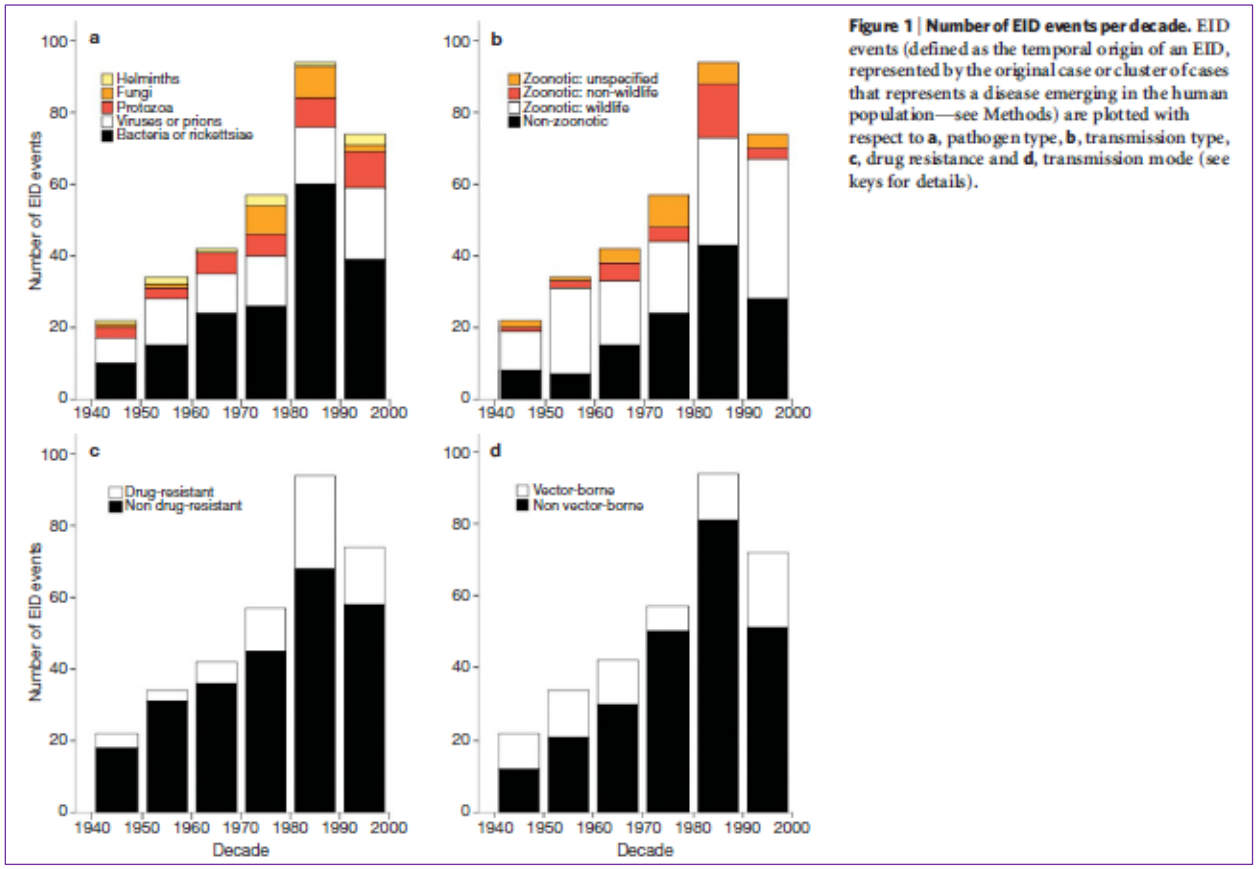


Figure 1 | Number of EID events per decade. EID events (defined as the temporal origin of an EID, represented by the original case or cluster of cases that represents a disease emerging in the human population—see Methods) are plotted with respect to **a**, pathogen type, **b**, transmission type, **c**, drug resistance and **d**, transmission mode (see keys for details).

The second figure in Jones et al. (Figure 25) shows the geographic origins of EIDs. Reporting is overwhelmingly dominated by the United States (especially the northeast), Europe, and Australia and Japan, with few reports from Africa, South America or South or Central Asia. This apparent correlation with higher income economies and laboratory capacity, rather than population and wildlife habitat, suggests that capacity to detect and differentiate EIDs is likely to be a major driver, or the major driver, of reporting.

Figure 25. Figure 2 from Jones et al. (2008), showing geographical distribution of infectious disease (EID) events recorded from 1940 to 2000.

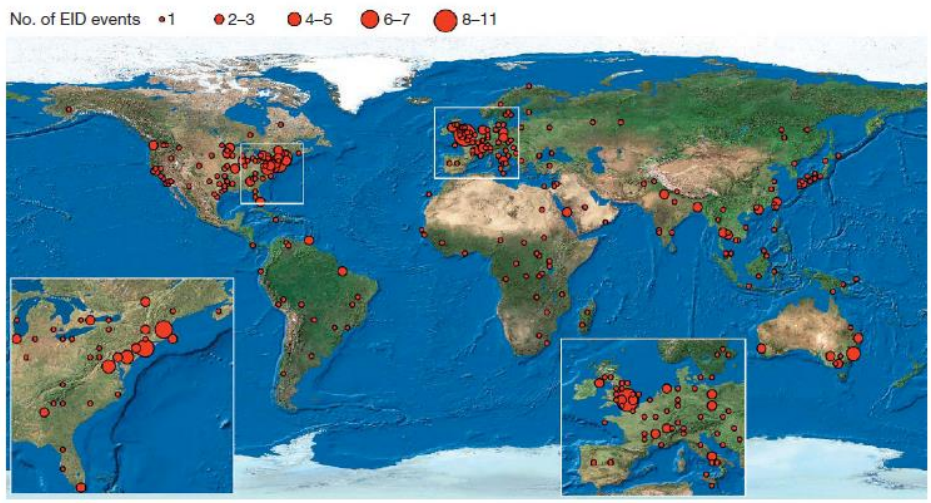


Figure 2 | Global richness map of the geographic origins of EID events from 1940 to 2004. The map is derived for EID events caused by all pathogen types. Circles represent one degree grid cells, and the area of the circle is proportional to the number of events in the cell.

Inevitably, as new techniques more suitable to broad deployment become accessible, such as point of care antigen and serology testing and the development and late deployment of PCR, an increase in reporting from lower-resourced areas will rapidly drive overall EID detection.

Rather than providing compelling evidence of a steady increase in EID events, the data provided by Jones et al. suggests that the likelihood of detection and related factors are at least a major driver of reporting. Moreover, the HIV/AIDS epidemic underlines the importance of host fitness, with an overall decline in reporting despite increasing reporting capacity as HIV/AIDS came under better control in the 1990s.

Reporting of zoonotic spillover and vector-borne events continued to increase through the study period. Outbreaks such as Chikungunyah and Nipah virus would not have been detected and identified across most geographies during the early decades of this study, as the technology required (e.g., PCR) did not exist.

7.5. Morand & Walther (2020, Updated 2023): The accelerated infectious disease risk in the Anthropocene: more outbreaks and wider global spread

Morand and Walther (2020)[218] are a major reference for the World Bank Putting Pandemics Behind Us report.

The authors rely on the GIDEON database archive of outbreaks:

> *"Using the most complete, reliable, and up-to-date database on human infectious disease outbreaks (GIDEON)"*
>
> *"…we show that the number of disease outbreaks, the number of diseases involved in these outbreaks, and the number of countries affected have increased during the entire Anthropocene. Furthermore, the spatial distribution of these outbreaks is becoming more globalized…"*

This does not consider any change or increase in reporting.

> *"However, the imposition in the 1980s of the so- called Washington Consensus imposed by the International Monetary Fund, World Bank, and United States Department of the Treasury and the resulting the structural adjustment programs dramatically decreased the public health and education capabilities of many developing countries (e.g., references 68, 69) which should also have affected reporting rates. However, we see no evidence of a slowdown of our trends (Figures 1D-F) in the 1980s and 1990s. But still, when controlling for population, annual outbreak numbers and annual disease numbers trend down over past 10-20 years.*"

The authors did test whether a reduction in funding due to imposed structural adjustments on some lower-income countries in the 1980s and 1990s caused a noticeable reduction in reporting (at the time of the main HIV epidemic). Finding no clear effect, they then ignore potential effects of an absence of modern diagnostic and reporting technologies before the 1980s that are now widely used, such as PCR, point of care antigen tests and digital communications. Whilst acknowledging the possibility of under-reporting in some 'developing countries' in the early part of the 'Anthropocene', they fail to incorporate this into their analysis.

The World Bank Technical Report of 2022 (page 6) noted a relative reduction in Africa's share of reports during the 1980s and 1990s based on the same data set,[219] lending more weight to the hypothesis that reporting rates are a significant driver of an increase in reported outbreaks. The

[218] https://www.biorxiv.org/content/10.1101/2020.04.20.049866v2
[219] https://documents1.worldbank.org/curated/en/099042023145037128/pdf/P17840202eae520aa0ab910137cb6f1a142.pdf

relatively low contribution of the African continent compared to North America and Europe in Fig. 3 from Morand and Walther (Figure 26) supports this conclusion.

Figure 26. Fig. 3. from Morand and Walther (2020, updated 2023), demonstrating the correlation with more developed surveillance capacity for outbreaks in the GIDEON database.

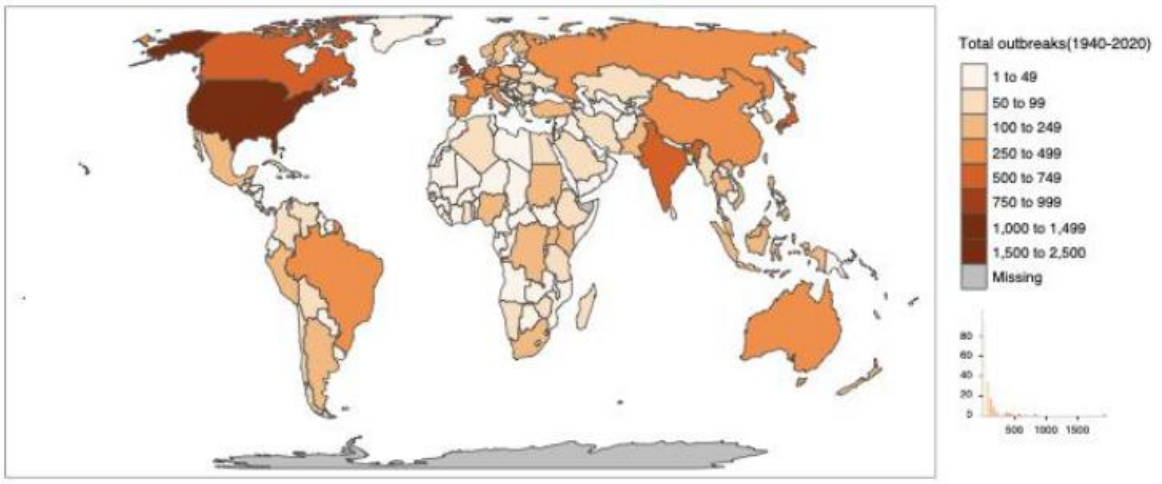


Fig. 3. | World map of total disease outbreaks from 1940 to 2020. The frequency histogram is also included.

The authors find that:

> *"From the 1940s to around 2010, the annual total outbreak number (Fig. 1D), the annual total disease number (Fig. 1E), and the annual total country number (Fig. 1F) increased exponentially (Supplementary Data S1)."*

Adjustment for population, however, still shows a downward trend (Figure 27):

> *"When we control for the number of the global human population, the growing trend for the annual total outbreak number (Fig. 2D) reverses downward around 2010, and the growing trend for annual total disease number (Fig. 2E) actually decreases shortly after 2000 and dramatically in 2020."*

In the Discussion, the authors therefore conclude:

> *"We note, however, that the per capita trend for the annual total outbreak number slowed down (Fig. 1D) and the per capita trend for the annual total disease number even reversed (Fig. 1E) after 2000. These results mirror results by Smith et al. who found that per capita cases decreased significantly over time."*

Figure 27. Fig. 2 from Morand and Walther (2020, updated 2023), showing marked recent reductions in disease number and outbreak numbers in the GIDEON database.

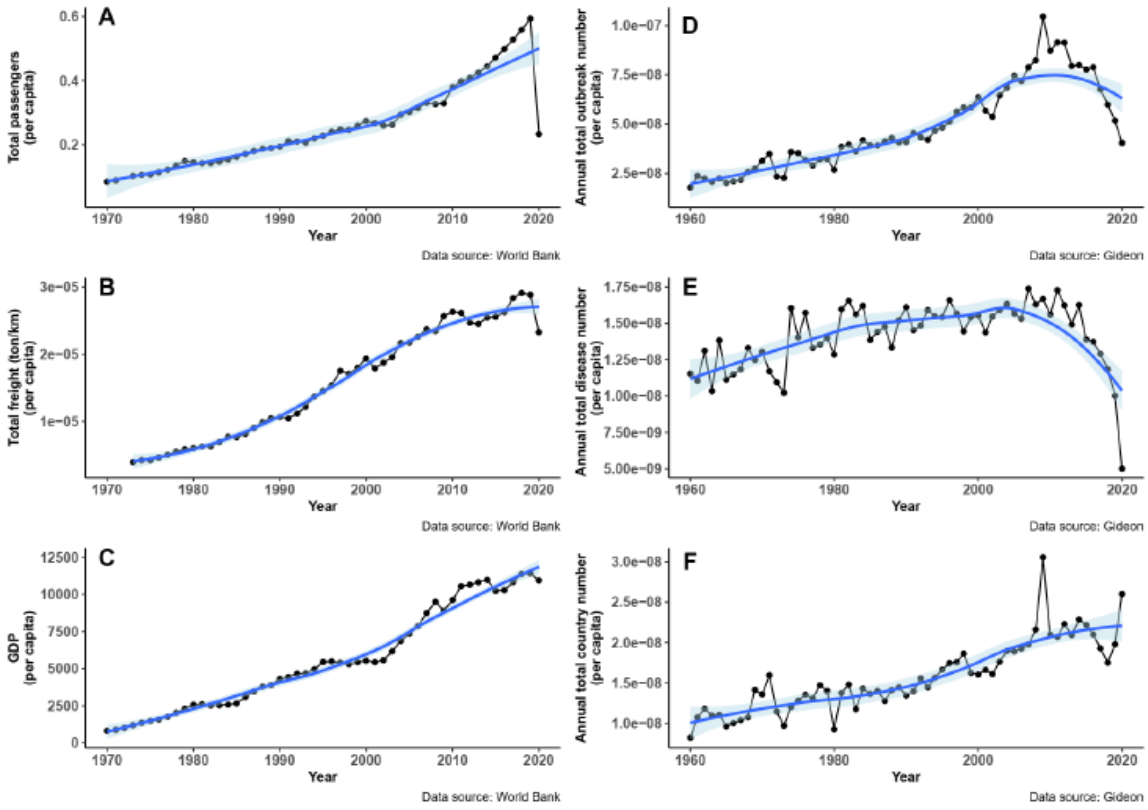


Fig. 2. | The increase of air travel, GDP, and disease outbreaks since the 1940s controlled by population. Resulting graphs from plotting the same data as in Fig. 1, but controlled for by global human population (per capita). Fitted smooth regressions (in blue) with confidence intervals (in light blue) are shown.

7.6. Other papers considered in the preparation of this report:

Badker R, Miller K, Pardee C, Oppenheim B, Stephenson N, Ash B, Philippsen T, Ngoon C, Savage P, Lam C, Madhav N. Challenges in reported COVID-19 data: best practices and recommendations for future epidemics. BMJ Glob Health. 2021 May;6(5):e005542. doi: 10.1136/bmjgh-2021-005542. PMID: 33958393; PMCID: PMC8103560.

Baker RE, Mahmud AS, Miller IF, Rajeev M, Rasambainarivo F, Rice BL, Takahashi S, Tatem AJ, Wagner CE, Wang LF, Wesolowski A, Metcalf CJE. Infectious disease in an era of global change. Nat Rev Microbiol. 2022 Apr;20(4):193-205. doi: 10.1038/s41579-021-00639-z. Epub 2021 Oct 13. PMID: 34646006; PMCID: PMC8513385.

Chadha MS, Comer JA, Lowe L, Rota PA, Rollin PE, Bellini WJ, Ksiazek TG, Mishra A. Nipah virus-associated encephalitis outbreak, Siliguri, India. Emerg Infect Dis. 2006 Feb;12(2):235-40. doi: 10.3201/eid1202.051247. PMID: 16494748; PMCID: PMC3373078.

Daszak P, Cunningham AA, Hyatt AD. Anthropogenic environmental change and the emergence of infectious diseases in wildlife. Acta Trop. 2001 Feb 23;78(2):103-16. doi: 10.1016/s0001-706x(00)00179-0. PMID: 11230820.

Dobson AP, Pimm SL, Hannah L, Kaufman L, Ahumada JA, Ando AW, Bernstein A, Busch J, Daszak P, Engelmann J, Kinnaird MF, Li BV, Loch-Temzelides T, Lovejoy T, Nowak K, Roehrdanz PR, Vale MM. Ecology and economics for pandemic prevention. Science. 2020 Jul 24;369(6502):379-381. doi: 10.1126/science.abc3189. PMID: 32703868.

Epstein JH, Field HE, Luby S, Pulliam JR, Daszak P. Nipah virus: impact, origins, and causes of emergence. Curr Infect Dis Rep. 2006 Jan;8(1):59-65. doi: 10.1007/s11908-006-0036-2. PMID: 16448602; PMCID: PMC7088631.

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8. Conclusion and Recommendations

The WHO Managing Epidemics report summarizes the basis for urgent prioritization of policy development and financial investment to prevent, identify and mitigate pandemics:

> *"Epidemics and pandemics of infectious diseases are occurring more often, and spreading faster and further than ever, in many different regions of the world."*

A thorough review of the evidence base on which WHO, the World Bank and G20 rely to promote this important public health agenda demonstrates that this statement is contrary to their own cited sources, and that over the past decade risk may actually be reducing. The implication is that the largest investment in international public health in history is based on misinterpretations of key evidence as well as a failure to thoroughly analyze existing data.

While pandemics occur, and will continue to do so, the analysis in this report strongly indicates that the urgency expressed in key global health policy documents regarding natural pandemic risk is exaggerated. Considerable public health harm may therefore accrue through inappropriate diversion of resources if time is not taken to ensure responses are appropriate and proportionate. While the risk of outbreaks due to human manipulation of potential pathogens is not addressed here, WHO, the World Bank and G20 proposals are clearly based on perceptions of natural risk, particularly from zoonotic spillover events. The recent COVID-19 pandemic, if considered of natural origin, appears as an outlier in the context of recent outbreak trajectory, rather than indicative of a trend. However, when weighed against other endemic and chronic disease burdens in standard metrics incorporating life-years lost, the mortality from COVID-19 will also overstate its relative impact.

Reported outbreaks have increased in the decades before the year 2000. However, it is inevitable that reporting of such outbreaks will be influenced by changes in both the capacity and incentive to report. These include the development of, and increasing access to, major diagnostic platforms including PCR and point-of-care antigen and serology tests, as well as the development of communication infrastructure. Fifty years ago, many pathogens now readily identifiable could simply not be detected, or the diseases they cause be distinguished from other clinically similar conditions. Increased interest from funders and research groups in outbreak detection may also be influencing the frequency of recording, while human population increase should also influence data. It is remarkable that reports backing the expenditure of tens of billions of dollars annually have only partially taken these issues into account or ignored them altogether.

The development of improved diagnostic technologies not only impacts reporting rates but has implications in understanding the term 'emerging infectious disease'. While this frequently used term suggests that new pathogens are emerging, examples such as the Nipah Virus outbreaks

discussed in the World Bank report *Putting Pandemics Behind Us* appear more likely to involve identification of pre-existing diseases that were, and remain, of small overall burden. The development of such technologies should reduce risk, and the impression of increasing risk due to their use is a trap that needs to be understood and avoided.

Most data underlying the WHO, World Bank and G20 reports demonstrate a flattening of the increase in outbreak reporting over the past two decades, with a reduction in mortality, and some in outbreak frequency, over the past 10 years. The exception in the Metabiota dataset is explained by inclusion of Ebola virus disease outbreaks, a single geographically confined disease.

Overall, actual mortality from these outbreaks is also historically very low, and very low in contrast to other current health burdens. The much-quoted analysis of Bernstein et al. (2022) achieves an annual mortality in the millions by including pre-antibiotic era Spanish Flu and the multi-decade HIV event. The first is inappropriate as a guide to mortality as most deaths were likely due to secondary bacterial infection, whilst the latter is not commonly considered in the PPPR agenda. Both influenza and HIV have extensive international mechanisms already in place (although there is room for improvement).

In this context, the analyses of WHO, the World Bank and the G20, and in certain cases the sources they cite, are disappointing in terms of scholarship and balance. They raise concern that a desire to address a perceived threat is driving analysis, rather than analysis objectively determining the extent of threat. However well intentioned, this seems unlikely to effectively address the needs of public health or the populations it serves. Disease outbreaks harm people and shorten lives and must be addressed. This is best achieved on the basis of well-compiled evidence and scholarly analysis.

The evidence, assessed objectively, paints a picture of an increasing ability to identify and report outbreaks up to the decade 2000 to 2010, followed by a reduction in burden consistent with an increasing ability to successfully address these relatively low-burden events through current public health mechanisms. Alternatively, it may reflect a general reduction in poverty, and thereby improved resilience against disease, over this period. Whatever the underlying mechanisms, the data on which the major international agencies base their claims strongly indicates that the imperative of using health resources wisely in the context of overall public health and economic need should outweigh the current urgency to put mechanisms in place for health threats that are poorly defined and almost certainly overstated.

In considering the development of PPPR policy, the following recommendations therefore arise:

1. There is a clear need to commission better evidence to accurately determine the scale and urgency of pandemic risk.

2. An appropriate determination of pandemic risk must account for recent advancements in diagnostic capacity, information sharing, and improving disease control mechanisms.
3. Understanding relative disease burden is crucial for identifying the cost-benefit of pandemic investment and how to best select interventions and promote overall public health outcomes.
4. Given the poor evidence underlying risk assessment, it is prudent not to rush into new pandemic initiatives such as the Pandemic Agreement until underlying assumptions receive proper assessment based on robust evidence, recognized need, and overall benefit.
5. Similarly, ongoing discussions after the adoption of the IHRs should be informed by proper risk assessments and cost-benefit analysis. Given that many last-minute items were included in the IHRs without proper deliberation, and given that many new key "core competencies" such as fighting "infodemics" remain poorly defined, there is a need for continued scrutiny and reassessment regarding how, and to what degree, these measures should be fully benchmarked and implemented. Failure to do so could lead to disproportionate policies that undermine overall global health.
6. WHO Member States should support proportional pandemic preparedness efforts based on substantiated evidence, careful deliberation, and rational reflection.

As WHO notes, health is a state of physical, mental and social wellbeing. Public health therefore requires the balancing of a broad range of competing priorities, including the burden caused by outbreaks of infectious disease. To achieve such balance, evidence must be rigorously sought, carefully analyzed, and presented honestly and in context. In view of their influence, international agencies working in health have a particular responsibility to ensure this happens. It is hoped that the evaluation presented in this report will contribute to such an effort.

Annex I. Assumptions and sources for analysis of mortality due to outbreaks listed in Annex D of the G20 HLIP Report.

HLIP Report Annex D lists "Major Infectious Disease Outbreaks in the Past Two Decades". Without providing location or mortality. We have attempted to assign historic outbreaks to these diseases and years, based on WHO, CDC and other published data. Data includes all recorded mortality for full duration of outbreak starting in the year listed in the table.

Mortality for Chikungunya is difficult to determine as it may occur in the frail elderly and is difficult to distinguish from other diseases. The 2014 outbreak may be intended to reflect an outbreak in the Caribbean, but we were unable to determine mortality estimates. This may therefore underestimate total outbreak mortality.

Zika figures are derived from a published analysis of the Brazil outbreak (Paixao et al., 2022). The rate of excess mortality in babies recorded as having Zika congenital syndrome was estimated from the mortality rates in Paixao et al. (2022), by deriving attributable risk (0.102). All mortality is therefore in these infants and children.

Outbreak (HLIP Annex D)	**Mortality**	**Notes**	**Source for mortality estimate**
2019 SARS-CoV-2	...	Discussed separately elsewhere in this report.	
2018 Lassa	114	Nigeria	https://www.who.int/emergencies/disease-outbreak-news/item/20-april-2018-lassa-fever-nigeria-en
2017 Zika	362	Assumed to be 2016-2017 outbreak.	https://www.nejm.org/doi/pdf/10.1056/NEJMoa2101195
2017 Ebola	3	DRC	https://www.cdc.gov/vhf/ebola/outbreaks/drc/2017-may.html
(2018 Ebola)	33	DRC (Bikoro)	https://www.cdc.gov/vhf/ebola/outbreaks/drc/2018-may.html
(2018-2020)	2287	DRC (n Kivu, Ituri, S Kivu).	https://www.who.int/emergencies/disease-outbreak-news/item/2020-DON284
2014 Chikungunya	0	Location of 2014 outbreak unclear. Mortality is low, but may occur among the elderly.	
2014 Ebola	11,325	West Africa outbreak.	https://www.who.int/emergencies/situations/ebola-outbreak-2014-2016-West-Africa
2012 MERS	858	Global	https://www.who.int/health-topics/middle-east-respiratory-syndrome-coronavirus-mers#tab=tab_1

2010 Cholera	9,792	Haiti (2010-2019)	https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON415
2009 H1N1 Influenza	164,000	Median of WHO estimate 123,000-203,000.	https://apps.who.int/iris/bitstream/handle/10665/329438/9789241516839-eng.pdf?ua=1
2004 H5N1 Influenza	32	Southeast Asia	https://www.ncbi.nlm.nih.gov/books/NBK22148/
2003 SARS-CoV-1	774	Global	https://www.who.int/publications/m/item/summary-of-probable-sars-cases-with-onset-of-illness-from-1-november-2002-to-31-july-2003
2001 Enterovirus 71	26	Taiwan	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9188855/
2001 Nipah	45	Bangladesh	https://www.who.int/emergencies/disease-outbreak-news/item/2023-DON490