## Citation

## Published Version
[doi:10.1371/journal.pmed.1001354](http://doi.org/10.1371/journal.pmed.1001354)

## Accessed
March 16, 2018 3:45:44 PM EDT

## Citable Link
[http://nrs.harvard.edu/urn-3:HUL.InstRepos:10579568](http://nrs.harvard.edu/urn-3:HUL.InstRepos:10579568)

## Terms of Use
This article was downloaded from Harvard University's DASH repository, and is made available under the terms and conditions applicable to Other Posted Material, as set forth at [http://nrs.harvard.edu/urn-3:HUL.InstRepos:dash.current.terms-of-use#LAA](http://nrs.harvard.edu/urn-3:HUL.InstRepos:dash.current.terms-of-use#LAA)

(Article begins on next page)
Outbreaks, Driving Factors, and Development

Outbreaks of emerging infectious diseases place significant burden on public health and global economies [1]. The process leading to spillover, localized emergence, and finally pandemic spread is complex, but is generally driven by underlying ecological, political, or socioeconomic changes [2,3] (Figure 1). These “drivers” [2,4] include for example, climate change, urbanization, international travel and trade, land use change, and the breakdown or complete lack of public health measures. Yet despite the growing literature on driving factors [4], the impact of these drivers lacks appropriate attention and is currently an understudied area of research [5].

Examining a dataset of outbreaks of international concern assembled as part of a recently published study by Chan et al. [6], we assess the distribution of outbreaks across driving factors. We find that the most prominent driver is the breakdown or lack of public health infrastructure and argue that there is a mismatch between the drivers of public health events and current trends in public health spending and pandemic prevention. We propose a three-pronged approach within development agencies as the most promising solution to this disconnect. The approach includes: (1) Developing policies that deal with different stages of emergence, from spillover and localized outbreaks to pandemic spread; (2) Actively engaging a systems approach to pandemic prevention that changes pathogen dynamics at the intersection of people and their environment; and (3) Shifting the funding framework in development agencies from short-term emergency funding to a longer-term strategy.

Determining Drivers of Outbreaks of International Concern

Epidemiological data on officially confirmed outbreaks of international concern collected by the Global Alert and Response (GAR) department of the World Health Organization (WHO) can facilitate understanding of threats to global health, with particular attention to the local spread of pathogens (Figure 1B) at the critical juncture following spillover into humans but preceding pandemic spread. Events of “international concern” are published in Disease Outbreak News (DON), available online, http://www.who.int/csr/don/en/ and defined according to the International Health Regulations (IHR) as either specific diseases (Table S1) or events that are “serious” or “unusual” or pose the potential risk of spreading globally or imposing restrictions on travel or trade (http://www.who.int/ ihr). The inclusion criteria for events evolved from 1969 when the IHR covered only six diseases, to amendments in 1973 and 1982 to focus specifically on cholera, yellow fever, and plague, and to revisions again in 1997 to cover almost all public health risks (biological, chemical, radiological, or nuclear), though these final revisions were only formally adopted in 2005 and did not go into effect until 15 June 2007. The IHR now require states to have or develop “minimum core public health capacities,” including the detection, assessment, and notification of events.

Using the Chan et al. [6] dataset of 397 outbreaks from DON reports between 1996 and 2009, we identified the proximate driver implicated in each outbreak through manual evaluation of WHO outbreak reports related to each event (Text S1). Driving factors were defined according to the Institute of Medicine...
Summary Points

- The way in which public health programs are designed and funded has
  changed significantly; however, the trend toward establishing vertical, disease-
  specific global health programs may be at the cost of strengthening basic
  public health infrastructure and development in the long term.
- In a review of nearly 400 public health events of international concern, we
  found that a breakdown or absence of public health infrastructure was the
  driving factor in the largest fraction of outbreaks (39.5%). No single other
  driving factor accounted for more than 10% of outbreaks.
- The relative roles of emergency response versus long-term development
  strategies to mitigate infectious disease threats are being debated within
  bilateral and intergovernmental aid agencies.
- We propose a systems approach within development agencies to address
  pandemic prevention at the intersection of people and their environment
  where the risk of disease emergence is highest. To achieve this goal,
  mainstream development funding, rather than emergency funding, is required.

Limitations to Determining Drivers of Outbreaks of International Concern

The ability to accurately assess the driving factors of outbreaks and target
aid is limited by strong disincentives that still exist for states to report outbreaks of
disease (e.g., disruption to tourism or trade) [7]. Further, a lack of standard
practices for sharing biological samples limits our ability to detect and report
disease threats rapidly. The Nagoya Protocol to the Convention on Biological
Diversity set the groundwork for sample sharing, but does not include human
samples and still requires significant deliberation prior to implementation of a fair
sharing system [7].

Despite disincentives and surveillance
issues, the significant subset of events that
do get reported thorough IHR mecha-
nisms point to a role for development in
preventing future outbreaks. Currently,
the role of international development in
global health and pandemic prevention
programs in the United States and interna-
tionally is being debated.

The Changing Role of International Development in
Pandemic Prevention

Historically, dealing with infectious
disease outbreak threats has been under
the aegis of state, national, and interna-
tional public health agencies (e.g., US
Centers for Disease Control, WHO), and
basic public health infrastructure develop-
ment has been the responsibility of
bilateral and international development aid
agencies (e.g., United States Agency
for International Development [USAID]
and World Bank, respectively), and na-
tional and international non-governmental
organizations (e.g., Bill & Melinda Gates
Foundation). There has been an increased
role for bilateral and international devel-
opment aid agencies in addressing pan-
demic prevention as a development issue,
typically funded through emergency re-
sponse avenues. This shift followed the
emergence of highly pathogenic H5N1
avian influenza, in which developing
countries such as Indonesia and Egypt
were identified as regions with repeated,
small-scale outbreaks that suggested
chronic persistence [8]. The connection
between H5N1 and backyard poultry
production in particular has led to signif-
icant interest and support in a “systems
approach” to combating avian influenza
as a development agenda driven by
agricultural, cultural, poverty, and equity
constraints, rather than a purely human
health issue (also see http://www.
apiresearch.net/main.php) [9]. These ef-
forts have led to broader programs
including inter-agency “One Health” ini-
tiatives, and global programs specifically

Figure 1. Figurative description of the multi-scale, multi-step process of pan-
demic emergence. Pandemic impact is highest when diseases are transmitted rapidly
from human to human, and spread via travel and trade networks (A). At that point, their
impact is greatest in developed countries, with economic dependence on globalized
trade and travel (e.g., SARS). However, most emerging diseases do not reach this stage,
and emerge in localized outbreaks, often
small and contained (B, red spikes), or
spillover repeatedly from animals (B, green
line). Here, control is most effective at
the countries of origins that are often developing
countries, where breakdown of public health
measures exacerabes human-to-human
spread. Prior to localized outbreaks of zoo-
noeses, perturbations in the environment lead to
spillover of pathogens from one animal
species to another or their range expansion
(C, green circles). The most effective pandem-
ic prevention at this early stage would be via
measures that target the underlying causes of
disease emergence.
doi:10.1371/journal.pmed.1001354.g001
targeting pandemic infectious disease threats through development [10, 11].

Within development agencies trends in health spending have moved from broad systems based investments to a more specialized, infectious disease model, resulting in a decline in systems capacities, potentially contributing to increased risk of disease spread. According to the Organization for Economic Co-operation and Development (OECD), infectious disease control aid commitments have increased from 8% between 1990 and 1998 to 16% between 2005 and 2008, while basic health infrastructure aid commitments have declined from 11% to 5% during this period. In response, aid has been criticized as duplicative and inefficient, aimed at high-profile diseases (e.g., HIV/AIDS) rather than public health in general, and too often tied to short-term numerical targets, such as patients treated or lives saved [12]. Further, the proliferation of donors with program-specific “earmarking” of funds for vertical spending may create a fragmented landscape of development aid and translate into additional costs on donor and recipient countries [13]. Therefore, the decline in broad health systems capacities could be due not simply to the structure of aid being too vertical or “stovepiped” along “high profile diseases,” but also to inflexible funding cycles bent on metrics with little long-term effect. While vertical programs do have their successes, often programmatic and structural details helped overcome the vertical nature of the program, e.g., the high coverage of excellent and evolving vertically oriented interventions that contributed to smallpox eradication [14].

Conclusion and Recommendations

We suggest a central role for development agencies in pandemic prevention and highlight three critical policy issues. The first is to develop policies that deal with different stages of emergence, from spill-over and localized outbreaks to pandemic spread. Stronger public health infrastructure (e.g., expanded surveillance, better diagnostic capacity, and rapid reporting and control) in developing countries will likely help prevent localized outbreaks of newly emerged pathogens becoming pandemic. For example, in China the SARS crisis exposed weaknesses in the health system and the ability to effectively communicate and control an epidemic threat [15]. China has made a series of changes to public health policy and infrastructure specifically targeting SARS-like illnesses, as well as other emerging diseases [16, 17]. It is likely that any future spillover of SARS, either from animals or via laboratory accidents, or emergence of a similar but novel disease would be less likely to result in international spread [17–19]. Similarly, extensive national and intergovernmental efforts to detect and control influenza A/ H5N1 in Indonesia and other southeast Asian countries may have played a role in the lack of sustained human-to-human transmission in the region [20]. The majority of the events that the WHO has classified as internationally significant are in fact vaccine preventable or can be contained with basic public health measures, e.g., yellow fever, polio, cholera, and meningitis, making the bulk of events in the Chan et al. [6] dataset preventable.

These generalized approaches are distinct from efforts to target specific diseases that have emerged, particularly those with rapid, silent (during the asymptomatic period) transmission, such as the proposed distribution of oseltamivir as a prophylaxis during the early stages of the 2009 H1N1 pandemic [21]. Here, the practicalities of distribution among individuals or households to achieve optimal coverage proved difficult and this model of pandemic control via prophylaxis is seen as overly optimistic [22, 23], especially in the context of a developing country.

Second, we propose that development agencies should actively engage a systems approach to pandemic prevention that changes pathogen dynamics at the intersection of people and their environment, broadening the development toolkit significantly and imaginatively. A systems approach to pandemic prevention moves beyond the “One Health” concept of linking human and veterinary medicine with an understanding of environmental drivers of health to focus also on the socio-ecological context of disease emergence [24]. There has been significant movement in One Health, however, “operationalizing” One Health seems to hit a glass ceiling because there is not a specific defined budget among the agencies, and each relevant agency competes for funds. For H5N1, reducing the risk of the emergence of a new pandemic variant includes increasing biosecurity on poultry farms and within backyard flocks [25] as well as strengthening surveillance along routes from farms to markets. To address the key drivers of most pandemics, this will mean development agencies playing a role in such diverse strategies as strengthening animal health diagnostic laboratories, training veterinarians in public health (e.g., epidemiology for disease surveillance, outbreak detection, investigation, and intervention), the promotion of biosecurity measures on farms, educating bushmeat hunters on disease risks, and working with the extractive industries in emerging
infectious disease “hotspots” to reduce the
risk of new pathogens emerging (See figure 1 in [6]). In 2009, USAID launched the
Emerging Pandemic Threats program with the specific aim of reducing opportu-
nity for the emergence of new, potentially
pandemic zoonoses at their source by
building local public health capacity to
predict, identify, respond to, and prevent
disease emergence (http://avianflu.aed.org/epitprogram/).

Third and finally, we point to the need
for a critical shift in the funding framework
from which disease-oriented development
assistance is administered. Within develop-
ment agencies, pandemic prevention pro-
grams are most commonly funded through
emergency or disaster relief mechanisms. In
this transition, development agencies
should consider adopting a long-term
funding strategy that invests in a develop-
ment approach to pandemic prevention
consistent with a systems approach. These
recommendations align with others who
have urged previously for a strengthening
of national health systems with a “diago-
nal” approach [26], where interest in
particular initiatives or diseases can be used
to drive broad-based improvements to the
overall public health system. Not only will
this better address the most significant
global health threats, but it will also provide
the broad scale first line of defense against
the next unknown contagion.

Supporting Information

Table S1 WHO Diseases of Focus
(http://www.who.int/csr/disease/en/).

Table S2 Summary of outbreak informa-
tion extracted from the WHO Disease
Outbreak News reports by
disease, country, and date, with
corresponding driver classification.

Table S3 Number of outbreaks by
driver as used in Figure 2.

Text S1 Supplemental online mate-
rial.

Acknowledgments

We thank C. Viboud, B.T. Grenfell, D. Joly,
and T. Hulstadder for helpful comments.

Author Contributions

Analyzed the data: TLB RC DS LP. Wrote
the first draft of the manuscript: TLB. Contrib-
uted to the writing of the manuscript: TLB RC
DS EC PD JSB. ICMJE criteria for authorship
read and met: TLB RC EC DS LP AC DC PD JSB.

Table S3 Number of outbreaks by
driver as used in Figure 2.

PDF

We thank C. Viboud, B.T. Grenfell, D. Joly,
and T. Hulstadder for helpful comments.

Author Contributions

Analyzed the data: TLB RC DS LP. Wrote
the first draft of the manuscript: TLB. Contrib-
uted to the writing of the manuscript: TLB RC
DS EC PD JSB. ICMJE criteria for authorship
read and met: TLB RC EC DS LP AC DC PD JSB.

References

challenge of emerging and re-emerging infectious
Microbial threats to health: emergence, detection,
and response. Washington (D.C.): The National
3. Daszak P, Zambrana-Torrelio C, Bogich TL,
Fernandez M, Epstein JH, et al. (2012) Interdisci-
plinary approaches to understanding disease
emergence: the past, present, and future drivers of
Nipah virus emergence. Proc Natl Acad Sci U S A.
5. Lloyd-Smith JO, George D, Pepin KM, Pitzer
VE, Pulliam JRC, et al. (2009) Epidemic
dynamics at the human-animal interface. Science
326: 1302–1307.
6. Chan EH, Brewer TF, Madoff LC, Pollack MP,
Sonricker AL, et al. (2010) Global capacity for
emerging infectious disease detection. Proc Natl
security: closing the gaps in responding to
to infectious disease emergencies. Glob Health Gov
IV.
R, Capua I, et al. (2010) Main achievements of
the World Organisation for Animal Health/
United Nations Food and Agriculture Organiza-
tion Network on animal influenza. Avian Dis 54:
300–303.
10. Coker R, Rushdon J, Mourier-Jack S, Karimur-
ibo E, Latumba P, et al. (2011) Towards a
conceptual framework to support one-health
research for policy on emerging zoonoses. Lancet
Infec Dis 11: 326–331.
J, et al. (2011) Predicting pandemics: using a one
health approach to identify and mitigate the
disease emergence and spread of zoonoses from
wildlife. Ecohealth 7: S137–S137.
Foreign Aff 86: 14–38.
13. World Bank International Development Associa-
of the main trends in official development assist-
org/ida/papers/IDAI5_Replenishment/
14. Feuer F, Henderson DA, Arita I, Jezek Z,
15. Liu YL. (2004) China’s public health-care system:
facilitating the challenges. Bull World Health Organ
82: 532–538.
in China’s ability to detect emerging infectious
diseases despite advances since the onset of
al. (2008) Health system reform in China 2
Emergence and control of infectious diseases in
18. Institute of Medicine (2004) Learning from
epidemics. Washington (D.C): The National
Academies Press.
19. Mondor L, Brownstein JS, Chan E, Madoff LC,
Pollack MP, et al. (2012) Timeliness of nongov-
ernmental versus governmental global outbreak
20. Eagles D, Siregar ES, Dung DH, Weaver J, Weng F,
et al. (2009) H5N1 highly pathogenic avian influenza
21. Ghani AC, Baguelin M, Gräflin J, Flasche S,
dynamics of H1N1pdm influenza in the United
currents.RRN1130
contain pandemic influenza transmission? PLoS
ONE 6: e17764. doi:10.1371/journal.pone.
0017764
treatment? Optimal use of an antiviral stockpile
during an influenza pandemic. Math Biosci
24. Zinsstag J, Schelling E, Walther-Toews D,
Tanner M (2011) From “one medicine” to “one
health” and systemic approaches to health and
25. Azhar M, Lubis AS, Siregar ES, Alders RG,
Brun E, et al. (2010) Participatory disease
surveillance and response in Indonesia: strength-
ening veterinary services and empowering commu-
nities to prevent and control highly pathogenic
strengthening national health systems as the next
doi:10.1371/journal.pmed.1000089