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The elusive definition of pandemic influenza

Peter Doshi ^a

a. Program in History, Anthropology, Science, Technology and Society, Massachusetts Institute of Technology, 77 Massachusetts Avenue (E51-070), Cambridge, MA, 02138, United States of America.

Correspondence to Peter Doshi (e-mail: pdoshi@post.harvard.edu).

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Introduction

In 2009, governments throughout the world mounted large and costly responses to the H1N1 influenza outbreak. These efforts were largely justified on the premise that H1N1 influenza and seasonal influenza required different management, a premise reinforced by the decision on the part of the World Health Organization (WHO) to label the H1N1 influenza outbreak a “pandemic”. However, the outbreak had far less serious consequences than experts had predicted, a fact that led many to wonder if the public health responses to H1N1 had not been disproportionately aggressive.^{1–3} In addition, concern over ties between WHO advisers and industry fuelled suspicion about the independence and appropriateness of the decisions made at the national and international levels.⁴

Central to this debate has been the question of whether H1N1 influenza should have been labelled a “pandemic” at all. The Council of Europe voiced serious concerns that the declaration of a pandemic became possible only after WHO changed its definition of pandemic influenza. It also expressed misgivings over WHO’s decision to withhold publication of the names of its H1N1 advisory Emergency Committee.³ WHO, however, denied having changed any definitions and defended the scientific validity of its decisions, citing “numerous safeguards” for handling potential conflicts of interest.⁵

At stake in this debate are the public trust in health officials and our collective capacity to respond effectively to future disease threats. Understanding this controversy entails acknowledging that both parties are partially correct, and to resolve it we must re-evaluate how emerging threats should be defined in a world where the simple act of labelling a disease has enormous social, economic and political implications.

What sparked the controversy

Since 2003, the top of the WHO Pandemic Preparedness homepage has contained the following statement: “An influenza pandemic occurs when a new influenza virus appears against which the human population has no immunity, resulting in several simultaneous epidemics worldwide with enormous numbers of deaths and illness.”⁶ However, on 4 May 2009, scarcely one month before the H1N1 pandemic was declared, the web page was altered in response to a query from a *CNN* reporter.⁷ The phrase “enormous numbers of deaths and illness” had been removed and the revised web page simply read as follows: “An influenza pandemic may occur when a new influenza virus appears against which the human population has no immunity.” Months later, the Council of Europe would cite this alteration as evidence that WHO changed its definition of pandemic influenza to enable it to declare a pandemic without having to demonstrate the intensity of the disease caused by the H1N1 virus.³

A description versus a definition

Harvey Fineberg, chairman of a WHO-appointed International Health Regulations (IHR) Review Committee that evaluated WHO’s response to H1N1 influenza, identified the definition of pandemic influenza as a “critical element of our review”.⁸ In a draft report released in March, the committee faulted WHO for “inadequately dispelling confusion about the definition of a pandemic” and noted WHO’s “reluctance to acknowledge its part in allowing misunderstanding”⁹ of the web page alteration, which WHO has characterized as a change in the “description” but not in the “definition” of pandemic influenza. “It’s not a definition, but we recognize that it could be taken as such ... It was the fault of ours, confusing descriptions and definitions”,¹⁰ a WHO communications officer declared. Indeed, the Council of Europe was not alone in claiming that the “definition” had been changed.^{7, 11, 12}

WHO argues that this phrase – which could be more neutrally referred to as a *description–definition* – had little bearing on policy responses; a WHO press release states that it was “never part of the formal definition of a pandemic” and was never sent to Member States, but simply appeared in “a document on WHO’s website for some months”.¹³ In actuality, the *description–definition* was displayed at the top of the WHO Pandemic Preparedness home page for over six years and is consistent with the descriptions of pandemic influenza put forth in various WHO policy documents over the years.^{14–16} However, while the original *description–definition* unambiguously describes disease severity and certainly reflects general assumptions about pandemic influenza before novel H1N1 emerged, it is unrelated to the criteria WHO applied to declare H1N1 influenza a pandemic.

Definitions of pandemic phases, not pandemic influenza

In a press conference, WHO explained that “the formal definitions of pandemics by WHO can be seen in the guidelines”.⁵ This was a reference to WHO’s pandemic influenza preparedness guidelines, first developed in 1999 and revised in 2005 and 2009. However, none of

these documents contains what might reasonably be considered a formal definition of pandemic influenza (Table 1), a fact that may explain why WHO has refrained from offering a quotable definition despite its repeated assurances that “the definition” was never changed.^{5, 13, 20} The startling and inevitable conclusion is that despite ten years of issuing guidelines for pandemic preparedness, WHO has never formulated a formal definition of pandemic influenza.

[Table 1. World Health Organization \(WHO\) pandemic influenza guidelines, 1999–2009](#)
html, 5kb

What WHO’s pandemic preparedness guidelines¹⁹ do contain are “pandemic phase” definitions. WHO declared a pandemic on 11 June 2009, after determining that the novel reassortant H1N1 virus was causing community-level outbreaks in at least two WHO regions, in keeping with the definition of pandemic phase 6. The declaration of phase 6 reflected wider global dissemination of H1N1, not disease severity. But unlike other numerical scales, such as the Saffir–Simpson Hurricane Wind Scale based on five “categories”, WHO’s six-point pandemic phase determinations do not correlate with clinical severity but rather with the likelihood of disease occurrence.²¹ This point has received widespread attention and criticism.^{3, 7, 22, 23}

“The phased approach to pandemic alert was introduced by WHO in 1999,” explained WHO Director-General Margaret Chan to the IHR Review Committee, “to allow WHO to gradually increase the level of preparedness and alert without inciting undue public alarm. In reality, it had the opposite effect.”²⁴ Indeed, WHO’s concern that declaring phase 6 could “cause an unnecessary panic”²⁵ may explain why it momentarily considered adding a severity index to its phasing system before declaring phase 6.²² WHO subsequently decided that developing a pandemic severity index was too complex.²³ However, the IHR Review Committee has called on WHO to “develop and apply measures that can be used to assess the severity of every influenza epidemic”, while noting that “assessing severity does not require altering the definition of a pandemic to depend on anything other than the degree of spread”.⁹

WHO’s defence of its decision to declare H1N1 influenza a pandemic because it met “hard to bend”, “clearly defined virological and epidemiological criteria”²⁶ overlooks the fact that these criteria changed over time. As Gross noted, under WHO’s previous (2005) guidelines the 2009 H1N1 virus would not have been classified as a pandemic influenza virus simply because it was not a new subtype.²⁷ The 2009 plan, by contrast, only required a novel “reassortant” virus (Table 1).


Statements from WHO such as “Is this a real pandemic. Here the answer is very clear: yes”⁵ suggest that pandemics are something inherently natural and obvious, out there in the world and not the subject of human deliberation, debate and changing classificatory schemes. But what would and would not be declared a pandemic depends on a host of arbitrary factors such as who is doing the declaring and the criteria applied to make such a declaration.

Bridging the gap

Had the novel 2009 H1N1 virus caused exceptionally severe disease, the extensive preparations and planning in recent years would have surely put us in a better position to respond to such a crisis, and decision-making at WHO would not have come under intense scrutiny.²⁸ But in the case of H1N1, governments mounted extraordinary and costly responses to what turned out to be mostly ordinary disease.^{29, 30} This resulted in much scrutiny and controversy over the decision-making process. As future policy responses to emerging infectious diseases will not succeed without the trust and understanding of the public, officials must revise the way they think about and characterize emerging diseases.

A first step is to openly acknowledge past failures in risk assessment. The *description–definition* of pandemic influenza that was on WHO’s web site for so long, unchallenged and unchanged for years, is perhaps the most striking illustration that expert institutions assumed pandemics to be, in their basic nature, catastrophic events. (According to the IHR Review Committee, the *description–definition* was “understandable in the context of expectations about [avian influenza] H5N1”,⁹ but its appearance dates back to at least early 2003, when only 18 human cases of H5N1 were known.)⁶ But it is by no means the only example of false assumptions. A 2005 WHO preparedness document titled *Ten things you need to know about pandemic influenza*³¹ stated that “large numbers of deaths will occur” and “economic and social disruption will be great”. Statistical projections of future pandemic mortality varied widely, but even the self-described “best case scenarios”³² yielded numbers that were four to 30 times greater than the estimated number of deaths from seasonal influenza.³³ Also, over the last five years public health experts and policy-makers have helped consolidate the idea that a pandemic is of necessity a catastrophe through repeated mention of the severe 1918 pandemic “in order to rouse governments and the public”.³⁴ Descriptions of H5N1 as a pandemic candidate virus because it had met all the “requirements” only reinforced the message that a serious outbreak was inevitable (Fig. 1). The focus on 1918 and H5N1 came at the cost of preparing for possible future outbreaks similar to the 1957 and 1968 pandemics. These outbreaks, in contrast to the one in 1918, were similar to seasonal influenza and sometimes milder;^{37–39} indeed, historical descriptions of events in 1957 and 1968 have been mixed, a fact that highlights the lack of standardized measures of severity (Table 2). Preparations for future outbreaks must take stock of all the evidence, not just the most alarming.

Fig. 1. Requirements for an influenza pandemic, World Health Organization (WHO) and US Centers for Disease Control and Prevention (CDC)^a

World Health Organization (18 May 2009)	US Centers for Disease Control and Prevention ^a (1 March 2009)
 <h3 data-bbox="232 191 407 243">Requirements for a Pandemic</h3> <p data-bbox="207 275 428 296">Global outbreak of disease</p> <ul data-bbox="115 310 480 464" style="list-style-type: none"> • New influenza A virus emerges in humans • Minimal or no population immunity • Causes serious illness; high morbidity/mortality • Spreads easily from person to person <p data-bbox="94 485 537 516">Pandemic Influenza – Rapid Response</p>	<h3 data-bbox="613 201 922 254">Requirements for an Influenza Pandemic</h3> <ul data-bbox="573 285 946 459" style="list-style-type: none"> • A new influenza A subtype emerges that can infect humans AND • Causes serious illness AND • Spreads easily from human-to-human
	<h3 data-bbox="618 552 911 577">Influenza Pandemic Viruses</h3> <ul data-bbox="561 604 927 730" style="list-style-type: none"> ✓ A new influenza A subtype can infect humans AND ✓ Causes serious illness AND ? Spreads easily from human-to-human <p data-bbox="634 751 922 804">The first two prerequisites have been met, but not the last</p>

^a These are slides from WHO³⁵ and CDC³⁶ training materials posted to the WHO web site (<http://influenzatraining.org>). The dates indicate when the materials were last updated.

[Table 2. Descriptions of influenza outbreaks^a that have carried the “pandemic” label](#)
html, 6kb

Second, it is time to re-examine assumptions driven by virus-centric thinking. The fact that the spread of overwhelmingly mild⁴⁷ disease by a “novel” virus such as H1N1 could meet current phase 6 criteria highlights the shortcomings of virological assumptions and their central role in defining pandemic response measures. The enduring belief is that highly transmissible novel influenza viruses can be expected to cause serious disease and even death because the population lacks immunity against them.⁴⁹ However, this view is challenged by the recent experience with H1N1 and other influenza pandemics.^{37, 50–52} During the 2009 H1N1 outbreak, relatively few elderly people got sick,^{51, 53, 54} despite the widespread circulation of the so-called novel virus, and when they did, the symptoms were mild in most cases.

Virus-centric thinking is also at the bottom of the current practice of dichotomizing influenza into “pandemic” and “interpandemic” or “seasonal” influenza on the basis of genetic mutations in the virus. This approach, however, ignores the fact that the severity and impact of epidemics, whether caused by influenza viruses or other pathogens, occur along a spectrum and not in catastrophic versus non-catastrophic proportions. We need responses that are calibrated to the nature of the threat rather than driven by these rigid categories.¹¹ The IHR Review Committee has called for simplifying the pandemic phase structure and for plans that “emphasize a risk-based approach to enable a more flexible response to different scenarios”.⁹ However, implementing this

will remain difficult as long as health officials feel compelled to “err on the side of safety”⁹ and respond to any novel influenza virus as if it were potentially a worst case scenario. We therefore need evidence-based ways to address hypothetical scenarios of non-zero probability, such as the fear – based on a very partial reading of history⁵⁵ – that novel influenza pathogens acquire increased virulence during successive “waves” of infection.

Virus-centric thinking may heavily influence pandemic influenza planning because of the considerable weight of expert opinion. Bonneux and Van Damme have argued that disease experts are not necessarily competent to judge a disease’s relative importance against competing health priorities, and “final evidence-based policy advice should be drafted by independent scientists trained in evaluation and priority setting”.⁵⁶ This advice is consistent with the views of Neustadt and Fineberg, who noted over three decades ago in their review of the 1976 swine flu affair in the United States of America that “panels tend toward ‘group think’ and over-selling, tendencies nurtured by long-standing interchanges and intimacy, as in the influenza fraternity. Other competent scientists, who do not share their group identity or vested interests, should be able to appraise the scientific logic applied to available evidence.”⁵⁷ However, the IHR Review Committee’s draft report, issued in March 2011, is less demanding. It calls for an “appropriate spectrum of expertise” to advise WHO’s Director-General but fails to specify whether this should include non-influenza experts such as general epidemiologists, general practitioners and health economists.⁹

Third, we must come to broader agreement about acceptable sources of expert advice. While the IHR Review Committee “found no evidence of malfeasance”, it urged WHO to “clarify its standards and adopt more transparent procedures for the appointment of members of expert committees”.⁹ Since the 1980s, “partnerships” between industry and academia have grown increasingly close.⁵⁸ Today, for example, both government officials and academic influenza scientists belong to the Neuraminidase Inhibitor Susceptibility Network, a group funded by GlaxoSmithKline and Roche.⁵⁹ Much work is needed to ensure that decisions are not unwittingly influenced by industrial interests.

Finally, we must remember the purpose of “pandemic preparedness”, which was fundamentally predicated on the assumption that pandemic influenza requires a different policy response than does annual, seasonal influenza. The “pandemic” label must of necessity carry a notion of severity, for otherwise the rationale behind the original policy of having “pandemic plans” distinct from ongoing public health programmes would be called into question. Insofar as these plans allow us to effectively respond to the spread of severe infectious diseases, regardless of the pathogen that causes them, planning for hypothetical “worst case” scenarios has value. But such scenarios are rare and, when they do occur, few people will require convincing that urgent action is needed. Indeed, if we do face the threat of widespread disease causing severe symptoms, the definition of pandemic influenza will likely become moot.

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