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Item Type	Article
Authors	Doshi, Peter
Publication Date	2008-07-01
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Keywords	Humans; Influenza A Virus, H1N1 Subtype; Influenza, Human--epidemiology; Influenza, Human--virology; Pandemics; Semantics; World Health Organization
Citation	Doshi, P. (2008). The elusive definition of pandemic influenza. Bulletin of the World Health Organization. 89(7):532-8. DOI: 10.2471/BLT.11.086173
DOI	<a href="https://doi.org/10.2471/BLT.11.086173">10.2471/BLT.11.086173</a>
Publisher	World Health Organization
Download date	20/02/2024 18:06:30
Link to Item	<a href="http://hdl.handle.net/10713/6669">http://hdl.handle.net/10713/6669</a>

## The elusive definition of pandemic influenza

Peter Doshi<sup>a</sup>

**Abstract** There has been considerable controversy over the past year, particularly in Europe, over whether the World Health Organization (WHO) changed its definition of pandemic influenza in 2009, after novel H1N1 influenza was identified. Some have argued that not only was the definition changed, but that it was done to pave the way for declaring a pandemic. Others claim that the definition was never changed and that this allegation is completely unfounded. Such polarized views have hampered our ability to draw important conclusions. This impasse, combined with concerns over potential conflicts of interest and doubts about the proportionality of the response to the H1N1 influenza outbreak, has undermined the public trust in health officials and our collective capacity to effectively respond to future disease threats.

WHO did not change its definition of pandemic influenza for the simple reason that it has never formally defined pandemic influenza. While WHO has put forth many descriptions of pandemic influenza, it has never established a formal definition and the criteria for declaring a pandemic caused by the H1N1 virus derived from "pandemic phase" definitions, not from a definition of "pandemic influenza". The fact that despite ten years of pandemic preparedness activities no formal definition of pandemic influenza has been formulated reveals important underlying assumptions about the nature of this infectious disease. In particular, the limitations of "virus-centric" approaches merit further attention and should inform ongoing efforts to "learn lessons" that will guide the response to future outbreaks of novel infectious diseases.

Abstracts in عربي, 中文, Français, Русский and Español at the end of each article.

### 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.<sup>1–3</sup> 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.<sup>4</sup>

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.<sup>3</sup> WHO, however, denied having changed any definitions and defended the scientific validity of its decisions, citing "numerous safeguards" for handling potential conflicts of interest.<sup>5</sup>

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."<sup>6</sup> 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.<sup>7</sup> 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.<sup>3</sup>

### 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."<sup>8</sup> 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"<sup>9</sup> 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",<sup>10</sup> a WHO

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(Submitted: 13 January 2011 – Revised version received: 30 March 2011 – Accepted: 31 March 2011)

Table 1. World Health Organization (WHO) pandemic influenza guidelines, 1999–2009

WHO pandemic influenza guidelines	Contains definition of pandemic influenza?	Contains clear basis for declaring a pandemic?	Content
1999 <sup>17</sup>	Unclear (nothing presented as a formal definition)	Yes	<i>Text most resembling a definition of pandemic influenza:</i> “At unpredictable intervals, however, novel influenza viruses emerge with a key surface antigen (the haemagglutinin) of a totally different sub-type from strains circulating the year before. This phenomenon is called “antigenic shift”. If such viruses have the potential to spread readily from person-to-person, then more widespread and severe epidemics may occur, usually to a similar extent in every country within a few months to a year, resulting in a pandemic” (p. 6) <i>Basis for declaring a pandemic:</i> “The pandemic will be declared when the new virus sub-type has been shown to cause several outbreaks in at least one country, and to have spread to other countries, with consistent disease patterns indicating that serious morbidity and mortality is likely in at least one segment of the population” (p. 14)
2005 <sup>18</sup>	No	Yes	A pandemic will be said to have begun when a new <sup>a</sup> influenza virus subtype is declared to have reached Phase 6. Phase 6 is defined as “Increased and sustained transmission in the general population” (p. 9)
2009 <sup>19</sup>	No	Yes	WHO writes, “Phase 6, the pandemic phase, is characterized by community level outbreaks in at least one other country in a different [second] WHO region in addition to the criteria defined in Phase 5. Designation of this phase will indicate that a global pandemic is under way” (p. 26) Phase 5: “The same identified virus has caused sustained community level outbreaks in at least two countries in one WHO region” (p. 27) Phase 4: “Human-to-human transmission of an animal or human-animal influenza reassortant virus able to sustain community-level outbreaks has been verified” (p. 27)

<sup>a</sup> WHO provides a “Definition of new: a subtype that has not circulated in humans for at least several decades and to which the great majority of the human population therefore lacks immunity” (p. 6).

communications officer declared. Indeed, the Council of Europe was not alone in claiming that the “definition” had been changed.<sup>7,11,12</sup>

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”.<sup>13</sup> 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.<sup>14–16</sup> 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”.<sup>5</sup> 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.<sup>5,13,20</sup> 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.

What WHO’s pandemic preparedness guidelines<sup>19</sup> 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.<sup>21</sup> This point has received widespread attention and criticism.<sup>3,7,22,23</sup>

“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.”<sup>24</sup> Indeed, WHO’s concern that declaring phase 6 could “cause an unnecessary panic”<sup>25</sup> may explain why it momentarily considered adding a severity index to its phasing system before declaring phase 6.<sup>22</sup> WHO subsequently decided that developing a pandemic severity index was too complex.<sup>23</sup> 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”.<sup>9</sup>

WHO’s defence of its decision to declare H1N1 influenza a pandemic because it met “hard to bend”, “clearly defined virological and epidemiological criteria”<sup>26</sup> 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.<sup>27</sup> The 2009 plan, by contrast, only required a novel “reassortant” virus (Table 1).

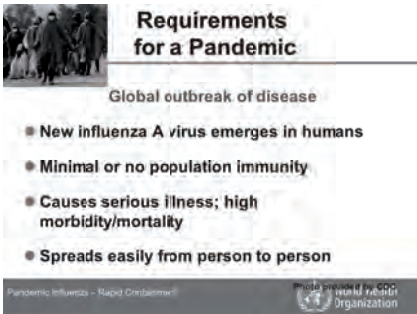
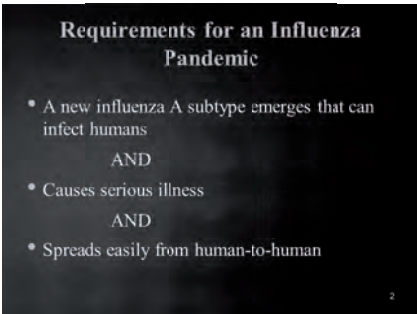
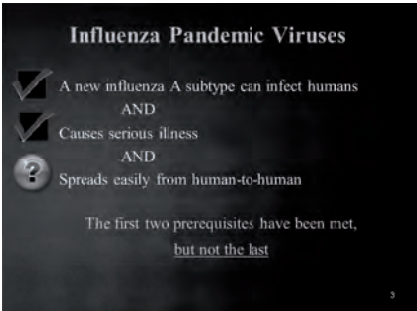
Statements from WHO such as “Is this a real pandemic. Here the answer is very clear: yes”<sup>25</sup> suggest that pandemics are something inherently natural and obvious, out there in the world and not the subject of human deliberation, debate and changing classificatory schemes. But what would and 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.<sup>28</sup> But in the case of H1N1, governments mounted extraordinary and costly responses to what turned out to be mostly ordinary disease.<sup>29,30</sup> 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”<sup>9</sup> but its appearance dates back to at least early 2003, when only 18 human cases of H5N1 were known.)<sup>6</sup> 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*<sup>31</sup> 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

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

World Health Organization (18 May 2009)	US Centers for Disease Control and Prevention <sup>a</sup> (1 March 2009)
 <p><b>Requirements for a Pandemic</b></p> <p>Global outbreak of disease</p> <ul style="list-style-type: none"> <li>• New influenza A virus emerges in humans</li> <li>• Minimal or no population immunity</li> <li>• Causes serious illness; high morbidity/mortality</li> <li>• Spreads easily from person to person</li> </ul>	 <p><b>Requirements for an Influenza Pandemic</b></p> <ul style="list-style-type: none"> <li>• A new influenza A subtype emerges that can infect humans</li> <li>AND</li> <li>• Causes serious illness</li> <li>AND</li> <li>• Spreads easily from human-to-human</li> </ul>
	 <p><b>Influenza Pandemic Viruses</b></p> <ul style="list-style-type: none"> <li>✓ A new influenza A subtype can infect humans</li> <li>AND</li> <li>✓ Causes serious illness</li> <li>AND</li> <li>? Spreads easily from human-to-human</li> </ul> <p>The first two prerequisites have been met, but not the last</p>

<sup>a</sup> These are slides from WHO<sup>35</sup> and CDC<sup>36</sup> training materials posted to the WHO web site (<http://influenza.training.org>). The dates indicate when the materials were last updated.

scenarios”<sup>32</sup> yielded numbers that were four to 30 times greater than the estimated number of deaths from seasonal influenza.<sup>33</sup> 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”.<sup>34</sup> 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;<sup>37–39</sup> 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.

Second, it is time to re-examine assumptions driven by virus-centric thinking. The fact that the spread of overwhelmingly mild<sup>47</sup> 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.<sup>49</sup> However, this view is challenged by the recent experience with H1N1 and other influenza pandemics.<sup>37,50–52</sup> During the 2009 H1N1 outbreak, relatively few elderly people got sick,<sup>51,53,54</sup> 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.<sup>11</sup> 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”.<sup>9</sup> However, implementing this will remain difficult as long as health officials feel compelled to “err on the side of safety”<sup>9</sup> 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 history<sup>55</sup> – 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”.<sup>56</sup> 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.”<sup>57</sup> 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.<sup>9</sup>

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

Table 2. Descriptions of influenza outbreaks<sup>a</sup> that have carried the “pandemic” label

Year	Virus	Nickname	Descriptions
1918	H1N1	Spanish flu	“devastating pandemic” (US CDC) <sup>40</sup> “severe” (US CDC) <sup>41</sup> “exceptional” (WHO) <sup>42</sup>
1957	H2N2	Asian flu	“comparatively mild” (WHO) <sup>42</sup> “substantial pandemic” (WHO) <sup>17</sup> “severe” (US CDC) <sup>41</sup> “moderate” (US HHS) <sup>43</sup>
1968	H3N2	Hong Kong flu	“moderate” (US CDC) <sup>41</sup> “huge economic and social disruption” (UK DoH) <sup>44</sup> “mild” (WHO) <sup>45</sup> “substantial pandemic” (WHO) <sup>17</sup> “Few people who lived through it even knew it occurred.” (John Barry) <sup>46</sup>
1977	H1N1	Russian flu	“mild” (US CDC) <sup>41</sup> “benign pandemic” (WHO) <sup>17</sup>
2009	H1N1	Swine flu	“moderate” (WHO) <sup>5,47</sup> “largely reassuring clinical picture” (WHO) <sup>48</sup>

US CDC, United States Centers for Disease Control and Prevention; UK DoH, United Kingdom Department of Health; US HHS, United States Department of Health and Human Services; WHO, World Health Organization.

<sup>a</sup> Whether it is called an outbreak, epidemic, or pandemic, influenza has a cyclic propensity to capture the world’s attention and to generate large public health responses. However, with the exception of the 1918 pandemic, which all agree was catastrophically severe, the impact of more recent outbreaks carrying the “pandemic” label is difficult to gauge, as their divergent descriptions suggest.

procedures for the appointment of members of expert committees”.<sup>9</sup> Since the 1980s, “partnerships” between industry and academia have grown increasingly close.<sup>58</sup> Today, for example, both government officials and academic influenza scientists belong to the Neuraminidase Inhibitor Susceptibility Network, a group funded by GlaxoSmithKline and Roche.<sup>59</sup> 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. ■

### Acknowledgements

I am grateful to Yuko Hara, Peter Graumann and Tom Jefferson for their perceptive observations and comments. I also wish to thank the Hugh Hampton Young Memorial Fellowship committee at MIT for their generous support of my research.

**Competing interests:** None declared. I would, however, like to acknowledge financial support from the UK National Institute for Health Research Health Technology Assessment programme for work on a Cochrane review of neuraminidase inhibitors (<http://www.hta.ac.uk/2352>).

## التعريف المراءوغ لجائحة الأنفلونزا

ظل جدل واسع النطاق يدور طوال العام المنصرم، ولاسيما في أوروبا، حول ما إذا كانت منظمة الصحة العالمية قد غيّرت أم لم تتغير من تعريفها لجائحة الأنفلونزا في عام 2009، بعد اكتشاف فيروس H1N1 الجديد. البعض رأى أن التغيير لم يقتصر على التعريف وحسب، بل أنه هدف إلى تمهيد الطريق للإعلان عن الجائحة. ويدّعي البعض الآخر أن التعريف لم يتغير على الإطلاق وأن هذا الزعم ليس له أي أساس من الصحة. وقد أعاق هذا الاستقطاب في الآراء قدرتنا على الوصول إلى استنتاجات هامة. هذا التأزم، بجانب مشاعر القلق المحيطة باحتمال وجود تضارب في المصالح والشكوك حول عدم التوازن النسبي في الاستجابة لفاشية أنفلونزا H1N1، قد أدى إلى إضعاف ثقة الناس في المسؤولين الصحيين وإضعاف قدرتنا الجماعية على الاستجابة الفعّالة لتهديدات الأمراض في المستقبل.

## 流感大流行难以捉摸的定义

世界卫生组织对大流行性流感提出了很多描述,但是其从未确立其正式定义,而因甲型H1N1流感病毒引起的大规模流行病的宣布标准是源自“流行病阶段”的定义,而不是“大流行性流感”的定义。尽管为大规模流行性疾病已经做了十年的准备工作,但是尚未制定大流行性流感的正式定义,这一事实揭示了关于这种传染病性质的重要基本假设。特别是“以病毒为中心”的方法的局限性值得进一步关注,并且现行研究工作应“吸取教训”,这将引导应对未来新型传染性疾病的暴发。

## L'insaisissable définition de la grippe pandémique

L'OMS n'a pas modifié sa définition de la grippe pandémique pour la simple raison qu'elle ne l'a jamais définie de manière officielle. Alors que l'OMS a proposé de nombreuses descriptions de la grippe pandémique, elle n'a jamais élaboré une définition formelle. De plus, les critères de déclaration d'une pandémie causée par le virus H1N1 ont leur origine dans les définitions de la «phase pandémique», et non dans une définition de la «grippe pandémique». Le fait que, malgré dix années d'activités de préparation à une pandémie, aucune définition officielle de la grippe pandémique n'ait été formulée révèle des hypothèses sous-jacentes importantes sur la nature de cette maladie infectieuse. Les limitations des approches «axées sur les virus» méritent en particulier une plus grande attention et doivent contribuer aux efforts incessants pour «tirer des leçons» qui guideront la réponse aux apparitions futures de nouvelles maladies infectieuses.

## Неуловимое определение пандемического гриппа

Другие заявляли, что определение никогда не менялось и что это утверждение абсолютно беспочвенно. Подобная поляризация мнений мешает нам прийти к важным выводам. Этот тупик, сочетающийся с озбоченностью по поводу потенциального конфликта интересов и сомнениями в пропорциональности реакции на вспышку гриппа H1N1, подрывает доверие общественности к высокопоставленным

deятелям системы здравоохранения и ослабляет нашу коллективную способность эффективно реагировать на угрозы заболеваний в будущем.

ВОЗ никогда не меняла определение пандемического гриппа по той простой причине, что она никогда не давала такого определения. Хотя ВОЗ предлагала множество описаний пандемического гриппа, она так и не выработала его формального определения, а критерии объявления пандемии, вызванной вирусом H1N1, вытекали из определений «пандемической фазы», а не из определения «пандемического гриппа». Хотя мероприятия по

обеспечению готовности к пандемическому гриппу длились десять лет, какого-либо формального определения пандемического гриппа не было сформулировано, что свидетельствует о важных исходных предположениях относительно характера этого инфекционного заболевания. В частности, ограниченность «вирусоцентрических» подходов заслуживает дальнейшего внимания и должна определять продолжающиеся усилия по «извлечению уроков», которые будут формировать реакцию на вспышки новых инфекционных болезней в будущем.

## Resumen

### La evasiva definición de la gripe pandémica

Durante el pasado año, fundamentalmente en Europa, se generó una considerable polémica sobre si la Organización Mundial de la Salud (OMS) habría cambiado su definición de gripe pandémica en el año 2009, tras la identificación de la nueva gripe H1N1. Algunos argumentan que no solo se cambió la definición, sino que se hizo para despejar el camino hacia la declaración de una pandemia. Otros aseguran que la definición nunca se cambió y que esta alegación está completamente infundada. Estos puntos de vista tan opuestos han dificultado nuestra capacidad para extraer conclusiones relevantes. Este callejón sin salida, unido a las preocupaciones sobre los posibles conflictos de intereses y las dudas sobre la proporcionalidad de la respuesta al brote de la gripe H1N1, ha menoscabado la confianza de la población en los responsables de la salud y en nuestra capacidad colectiva para responder con eficacia a futuras amenazas de este tipo.

La OMS no cambió su definición de gripe pandémica por el simple motivo de que nunca antes había definido formalmente el concepto de gripe pandémica. Si bien la OMS ha propuesto numerosas descripciones de gripe pandémica, nunca estableció una definición formal y los criterios para la declaración de una pandemia provocada por el virus H1N1 procedían de las definiciones de «fase de alerta pandémica», no de una definición de «gripe pandémica». El hecho de no contar con una definición formal de gripe pandémica, a pesar del bagaje de los diez años de actividades de preparación contra las pandemias, revela importantes suposiciones subyacentes sobre la naturaleza de esta enfermedad infecciosa. En particular, las limitaciones de los enfoques «centrados en el virus» reclaman una mayor atención y se debe informar sobre los esfuerzos que se realicen para «aprender las lecciones» que dirijan nuestra respuesta ante los futuros brotes de nuevas enfermedades infecciosas.

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## Round table discussion

### Pandemic influenza and its definitional implications

Daniel J Barnett<sup>a</sup>

In his thoughtful analysis, Doshi aptly describes the need for establishing greater definitional precision of “pandemic influenza” as the basis for future public health preparedness and response efforts.<sup>1</sup> Importantly, his assessment highlights a critical ongoing divide between competing perceptions of the very concept of a “pandemic”: namely, between “pandemic” as predominantly a function of geography and virology, versus disease severity.

This is not a minor semantic distinction, but rather one with enormous bearing on planning priorities. For instance, while the United States of America applies an all-hazards approach in its federal, state and local public health emergency readiness efforts, a major piece of 2006 national preparedness legislation was notably called the Pandemic and All-Hazards Preparedness Act.<sup>2</sup> Such explicit separation between “pandemic” and “all-hazards” in the title reflects a unique concern about a pandemic’s potential impact and severity, with implications for resource-intensive planning efforts among a myriad of stakeholders. Additionally, milder-than-feared global infectious disease events can subsequently engender a dangerous sense of complacency among frontline responders and the general public, erode trust in public health authorities and potentially reduce compliance with essential protective guidance in the face of future threats.

In keeping with these important considerations, Doshi proposes a more severity-driven approach to the declaration of an influenza pandemic. This strategy has certain merits: research suggests that people are more likely to engage in desired protective behaviours in the face of uncertain risk if they perceive the threat to be legitimately severe and relevant to them (and thus motivating), and if they view the recommended intervention as efficacious.<sup>3–5</sup> This would argue for severity as the main definitional predicate for pandemic declaration, rather than geography and virology.

However, a primarily severity-based trigger for pandemic declaration would involve certain operational challenges that must be acknowledged. In the light of wide global variations in public health response infrastructure, population-specific vulnerabilities and the potentially unpredictable course of “pandemic influenza” itself (however defined), “severity” can be experienced very differently in different places and for different community segments at a given point in time.

At the international level, this variability introduces difficulties in yielding standardized severity-governed definitional criteria as the basis for pandemic influenza declaration. Geographic and virologic criteria thus remain more feasible and realistic definitional drivers, despite their admittedly inherent shortcomings from a risk perception standpoint. At the same

time, however, severity indices do have considerable utility at national and subnational levels, where the above variations can and should factor directly into tailored, severity-based preparedness and response efforts for pandemic influenza.

In a broader sense, Doshi’s assessment speaks powerfully to risk communication as among the greatest challenges in the international response to threats of global public health significance. In the context of pandemic influenza, explicitly establishing a consistent definition is a necessary first step that must be followed by aggressive pre-event education of the global community regarding that definition and its rationale. If we wait to ensure such clarity when the next influenza pandemic strikes, it will simply be too late. ■

**Funding:** Preparedness & Emergency Response Research Center (PERRC) [CDC/Grant 1P01P00288-01; Grant# 104264]. The funders had no role in content, decision to publish, or preparation of this invited commentary.

**Competing interests:** None declared.

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### Health is more than influenza

Luc Bonneux<sup>b</sup> & Wim Van Damme<sup>c</sup>

The repeated pandemic health scares caused by an avian H5N1 and a new A(H1N1) human influenza virus are part of the culture of fear.<sup>1–3</sup> Worst-case thinking replaced balanced risk assessment. Worst-case thinking is motivated by the belief that the danger we face is so overwhelmingly catastrophic that we must act immediately. Rather than wait for information, we need a pre-emptive strike. But if resources buy lives, wasting resources wastes lives. The precautionary stocking of largely useless antivirals and the irrational vaccination policies against an unusually benign H1N1 virus wasted many billions of euros and eroded the trust of the public in health officials.<sup>4–6</sup> The pandemic policy was never informed by evidence, but by fear of worst-case scenarios.

In both pandemics of fear, the exaggerated claims of a severe public health threat stemmed primarily from disease advocacy by influenza experts. In the highly competitive market of health governance, the struggle for attention, bud-

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gets and grants is fierce. The pharmaceutical industry and the media only reacted to this welcome boon. We therefore need fewer, not more “pandemic preparedness” plans or definitions. Vertical influenza planning in the face of speculative catastrophes is a recipe for repeated waste of resources and health scares, induced by influenza experts with vested interests in exaggeration. There is no reason for expecting any upcoming pandemic to be worse than the mild ones of 1957 or 1968,<sup>7</sup> no reason for striking pre-emptively, no reason for believing that a proportional and balanced response would risk lives.

The opposite of pre-emptive strikes against worst-case scenarios are adaptive strategies that respond to emerging diseases of any nature based on the evidence of observed virulence and the effectiveness of control measures. This requires more generic capacity for disease surveillance, problem identification, risk assessment, risk communication and health-care response.<sup>1</sup> Such strengthened general capacity can respond to all health emergencies, not just influenza. Resources are scarce and need to be allocated to many competing priorities. Scientific advice on resource allocation is best handled by generalists with a comprehensive view on health. Disease experts wish to capture public attention and sway resource allocation decisions in favour of the disease of their interest. We referred previously to the principles of guidance on health by the British National Institute for Health and Clinical Excellence (NICE),<sup>2</sup> cited as “We make independent decisions in an open, transparent way, based on the best available evidence and including input from experts and interested parties.”<sup>8</sup> Support from disease experts is crucial in delivering opinion, scholarly advice and evidence to a team of independent general scientists. But this team should independently propose decisions to policy-makers and be held accountable for them.

The key to responsible policy-making is not bureaucracy but accountability and independence from interest groups. Decisions must be based on adaptive responses to emerging problems, not on definitions. WHO should learn to be NICE: accountable for reasonableness in a process of openness, transparency and dialogue with all the stakeholders, and particularly the public.<sup>9</sup> ■

**Competing interests:** None declared.

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## The classical definition of a pandemic is not elusive

Heath Kelly<sup>a</sup>

Doshi argues cogently that the definition of pandemic influenza in 2009 was elusive but does not refer to the classical epidemiological definition of a pandemic.<sup>1</sup> A pandemic is defined as “an epidemic occurring worldwide, or over a very wide area, crossing international boundaries and usually affecting a large number of people”.<sup>2</sup> The classical definition includes nothing about population immunity, virology or disease severity. By this definition, pandemics can be said to occur annually in each of the temperate southern and northern hemispheres, given that seasonal epidemics cross international boundaries and affect a large number of people. However, seasonal epidemics are not considered pandemics.

A true influenza pandemic occurs when almost simultaneous transmission takes place worldwide. In the case of pandemic influenza A(H1N1), widespread transmission was documented in both hemispheres between April and September 2009. Transmission occurred early in the influenza season in the temperate southern hemisphere but out of season in the northern hemisphere. This out-of-season transmission is what characterizes an influenza pandemic, as distinct from a pandemic due to another type of virus.

Simultaneous worldwide transmission of influenza is sufficient to *define* an influenza pandemic and is consistent with the classical definition of “an epidemic occurring worldwide”. There is then ample opportunity to further *describe* the potential range of influenza pandemics in terms of transmissibility and disease severity. The emerging evidence for A(H1N1) is that transmissibility, as estimated by the effective reproduction number (*R*, or average number of people infected by a single infectious person) ranged from 1.2 to 1.3 for the general population but was around 1.5 in children (Kathryn Glass, Australian National University, personal communication). Some early estimates of *R* for pandemic influenza H1N1 2009 may have been overestimated.<sup>3</sup>

Severity, as estimated by the case fatality ratio, probably ranged from 0.01 to 0.03%.<sup>4–6</sup> These values are very similar to those normally seen in the case of seasonal influenza.<sup>7,8</sup> However, the number of deaths was higher in younger people, a recognized feature of previous influenza pandemics.<sup>9</sup>

It is tempting to surmise that the complicated pandemic definitions used by the World Health Organization (WHO) and the Centers for Disease Control and Prevention of the United States of America involved severity<sup>1,10</sup> in a deliberate attempt to garner political attention and financial support for pandemic preparedness. As noted by Doshi, the perceived

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need for this support can be understood given concerns about influenza A(H5N1) and the severe acute respiratory syndrome (SARS). However, conflating spread and severity allowed the suggestion that 2009 A(H1N1) was not a pandemic. It was, in fact, a classical pandemic, only much less severe than many had anticipated or were prepared to acknowledge, even as the evidence accumulated.

In 2009 WHO declared a pandemic several weeks after the criteria for the definition of a classical pandemic had been met. Part of the delay was no doubt related to the nexus between the formal declaration of a pandemic and the manufacture of a pandemic-specific vaccine. If a classical pandemic definition had been used, linking the declaration to vaccine production would have been unnecessary. This could have been done with a severity index and, depending on the availability and quality of the emerging evidence on severity, a pandemic specific vaccine may have been deemed unnecessary. Alternatively authorities may have decided to order vaccine in much smaller quantities.

The response to A(H1N1) has been justified as being precautionary, but a precautionary response should be rational and proportionate and should have reasonable chances of success. We have argued that the population-based public health responses in Australia and, by implication, elsewhere, were not likely to succeed.<sup>11</sup> Similarly, the authors of the draft report on the response to the International Health Regulations during the 2009 pandemic note that what happened during the pandemic reflected the activity of the virus and, by implication, not the interventions.<sup>10</sup>

Risk is assessed by anticipation of severity and precaution should be calibrated to risk. As Doshi has argued, we need to *redefine* pandemic influenza. We can then *describe* the potential severity range of future pandemics. Finally, we need to use evidence to assess severity early to anticipate risk. ■

**Competing interests:** None declared.

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## Living forwards, understanding backwards

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It has been said that pandemics are lived forwards and understood backwards. The 2009 influenza pandemic is no exception. The identification of the new influenza virus strain in the United States of America coincided with many media reports describing a very severe pneumonia affecting young Mexican adults – echoes of 1918! Hard data were sparse and quoted case fatality rates ranged from 0.3% to 2.5% of confirmed cases as late as September 2009. With the benefit of hindsight it is easy to say that the disease caused by the virus was in fact mild for most people and that this action or that action should have been taken. However, in real time with little reliable data on the effects of the virus on individuals and communities and faced with the need to make time-critical decisions, sovereign nations across the world responded differently. It is important to remember that the World Health Organization (WHO) remit is to help governments determine the level of interventions required as part of their response to threats to international health.

Unfortunately, the fact that WHO issued revised pandemic guidance just as the pandemic was starting generated confusion. Under the new guidance,<sup>1</sup> pandemic phases 4 to 6 differed significantly from the 2005 guideline document,<sup>2</sup> and this made communication difficult.

Individuals have made great play of the change to the wording of one sentence that was part of a 60-page document before phase 6 (the so-called start of the pandemic) was declared. In fact, in several places the WHO 2009 guidance document describes phases 5 to 6 as the pandemic period and clearly states that “during phases 5–6 (pandemic) actions shift from preparedness to response at a global level.” From this it can be argued that the pandemic was actually declared on 29 April 2009, five days before the quoted change in definition.

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In the United Kingdom of Great Britain and Northern Ireland, a new national influenza pandemic strategy was published for consultation on 22 March 2011.<sup>3</sup> This has taken on board many of the lessons learned during the 2009 pandemic. However, the strategy still recognizes the need for an initially precautionary approach, given the speed with which the virus can spread and the paucity of data that will be available at the start of a pandemic, although it states that proportionality and flexibility should guide the response as information about the virus and its effects become available. The strategy is now better adapted to the needs of the United Kingdom and is proposing a new phased response that is not linked to the WHO phases. This reflects the fact that in the United Kingdom the first cases were detected in late April 2009 and that using the WHO phases, which are global indicators of spread, proved to be unhelpful.

Peter Doshi highlights the lack of a definition of a pandemic.<sup>4</sup> There is also no definition of a pandemic wave or severity, both key issues when it comes to describing the progress and impact of a pandemic. I don't believe this reflects a lack of willingness to formulate such definitions, but rather, a lack of international consensus stemming from the absence of key data and the recognition that severity, impact and other descriptors can only be applied with certainty historically. ■

**Competing interests:** None declared.

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## Planning for uncertainty: a European approach to informing responses to the severity of influenza epidemics and pandemics

Angus Nicoll<sup>a</sup>

The internationally accepted definition of a pandemic is straightforward and well known: “an epidemic occurring worldwide, or over a very wide area, crossing international boundaries and usually affecting a large number of people”.<sup>1</sup> However, as Doshi reminds us, for any modern influenza pandemic, with many available powerful countermeasures, it is the detailed description that is crucial in determining proportionate responses, not the definition.<sup>2</sup>

Because of the inherent unpredictability of influenza viruses, preparing for and responding to epidemics and pandemics will always be an uncertain business.<sup>3</sup> Annual epidemics and irregular pandemics have several important characteristics that summary terms such as *mild*, *moderate* and *severe* gloss over.<sup>2</sup> For example, even the “moderate” or “mild” pandemic of 2009 was severe in its impact on many intensive care units and in its initial pressures on primary care services.<sup>4,5</sup>

Data and analyses that inform on the relevant features in the early course of pandemics and epidemics become available continuously. Initial analyses can be misleading and the pattern of infection and disease can also change over time. In the 2009 pandemic, the European Centre for Disease Prevention and Control (ECDC) used updatable published risk assessments to organize this information, comment on its implications for the response and identify the most important areas of uncertainty.<sup>6</sup> This approach was based on a list of “known unknowns” of pandemics, part of a pre-planned “surveillance in a pandemic” strategy.<sup>7</sup>

As recommended by the report adopted by the 64th World Health Assembly,<sup>3</sup> ECDC has further developed this approach applying it as a matrix (Table 1) to annual seasonal epidemics, starting with the 2010–2011 season. With powerful countermeasures increasingly available – public health interventions, antivirals, vaccines and higher-level intensive care – the matrix relates more to response than to conventional measures, such as transmission and infection fatality rates. Important as these are, they are rarely available in an accurate form early on, whereas the initial impressions of impact on services often appear rapidly. In the 2009 pandemic, the experience and reports of predominantly mild illness (but with some very severe cases) received from New York City and Melbourne, once verified, were highly informative in determining the proportionate European response.<sup>8</sup> The risk assessments are undertaken by ECDC staff drawing on both European experience (from the European Influenza Surveillance Network) and whatever verifiable epidemic intelligence is available.<sup>9</sup> For seasonal epidemics the information will be presented visually using internationally recognizable red, amber and green colours (Table 1 and Table 2). Red signals situations in which the evidence suggests action is justifiable, and amber signals those in which precautionary approaches may be needed. Europe has a particular advantage in that seasonal epidemics tend to progress from west to east, so that early experience and virology can be especially helpful in preparing countries for what they will experience later.<sup>10</sup> Variants on this approach have been used since the 2007–08 season, beginning with the appearance of oseltamivir-resistant viruses in Norway (Table 3). Though concerned with responses, the severity matrix cannot prescribe actions. The ECDC's mandate is to offer scientific information, guidance and options, not to make recommendations. Decisions on risk management are made by its individual Member States and collectively by European Union bodies, such as the Health Security Committee. Capacity, preparation and disease intensity vary across countries; so what can be coped

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Table 1. **Seriousness matrix for pandemic influenza in Europe, 2009**

Category	Seriousness	Potential actions and notes
Personal measures	Amber	Alert public to strengthen personal hygiene and early self isolation
Primary care pressures	Amber	Consider enacting back-up plans
Immunization	Red	Strong arguments for immunizing risk groups when available
Antiviral resistance	Green	No change in policy justifiable
Public health measures	Green	Proactive school closures not justifiable at present
Secondary care pressures	Red	Strong case for enacting surge capacity for intensive care and paediatric capacity
Special groups	Red	Pregnant women, handicapped children risk groups in addition to those with chronic illness
Social care pressures	Green	No case for enacting support plans
Critical cross-sector services	Green	No case for enacting support plans
Special features	Red	Rapid deaths in some young healthy adults and children – acute respiratory distress syndrome

Table 2. **Seriousness matrix for seasonal influenza in Europe, December 2010**

Category	Seriousness	Potential actions and notes
Personal response	Amber	Alert public to strengthen personal hygiene and early self isolation
Primary care pressures	Amber	Consider enacting back-up plans
Immunization	Red	Recommend making clinical groups, including pregnant women, the top priority but continue immunizing older people
Antiviral resistance	Green	No change in policy justifiable but monitor resistance
Public health measures	Green	Not justified by the evidence
Secondary care pressures	Red	Some stresses on intensive care units consider back-up plans
Special groups	Red	Clinical risk groups
Social care pressures	Green	No case for enacting back-up to enact plans
Critical cross-sector services	Green	No threat – no case for enacting back-up plans
Special features	Amber	Need to respond to unexpected deaths in young healthy adults and children. Role of invasive bacterial infections?

Table 3. **Instances in which early experience with influenza in European countries has informed the response elsewhere**

Country and year or season	Characteristic	Public European alert issued <sup>a</sup>
Norway, 2007–08 season	Emergence of oseltamivir-resistant A(H1N1) 2009	Rapid communication in <i>Eurosurveillance</i>
Ireland and Portugal, 2008–09 season	Pressure on primary and secondary care services from A(H3N2) epidemics	ECDC, January 2009
United Kingdom, <sup>b</sup> 2009 pandemic	Lack of major impact on transmission and high human resource cost of attempts to contain pandemic influenza and mild disease spectrum	European Informal Health Council, July 2009
United Kingdom, <sup>b</sup> 2010–11 season	High pressure on some intensive care units	ECDC Director, December 2010

ECDC, European Centre for Disease Prevention and Control.

<sup>a</sup> In addition there were earlier rapid communications with Member States by European Union Early Warning and Response Systems and/or through alerting systems falling under the International Health Regulations.

<sup>b</sup> United Kingdom of Great Britain and Northern Ireland.

with in one setting may be stressful in another. Hence, the severity matrix will alert Member States as to what *may* give them problems and will suggest options for action. One of the general lessons learned from the pandemic, as indicated by evaluations undertaken in Europe (listed on the ECDC web site), is that interventions that were not

exercised beforehand did not work well. This explains why the ECDC uses interpandemic influenza as a practice ground for pandemic preparation, although it also merits public health action in its own right.<sup>3,11</sup> ■

**Competing interests:** None declared.

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